NICE National Institute for Health and Care Excellence

Single Technology Appraisal

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Committee Papers

NICE National Institute for Health and Care Excellence

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SINGLE TECHNOLOGY APPRAISAL

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Contents:

The following documents are made available to consultees and commentators:

Any information supplied to NICE which has been marked as confidential, has been redacted. All personal information has also been redacted.

Sacituzumab govitecan for treating unresectable triple-negative advanced breast cancer after 2 or more therapies

Single Technology Appraisal

Response to consultee, commentator and public comments on the Appraisal Consultation Document (ACD)

Type of stakeholder:

Consultees – Organisations that accept an invitation to participate in the appraisal including the companies, national professional organisations, national patient organisations, the Department of Health and Social Care and the Welsh Government and relevant NHS organisations in England. Consultees can make a submission and participate in the consultation on the appraisal consultation document (ACD; if produced). All non-company consultees can nominate clinical experts and/or patient experts to verbally present their personal views to the Appraisal Committee. Company consultees can also nominate clinical experts. Representatives from NHS England and clinical commissioning groups invited to participate in the appraisal may also attend the Appraisal Committee as NHS commissioning experts. All consultees have the opportunity to consider an appeal against the final recommendations, or report any factual errors, within the final appraisal document (FAD).

Clinical and patient experts and NHS commissioning experts – The Chair of the Appraisal Committee and the NICE project team select clinical experts and patient experts from nominations by consultees and commentators. They attend the Appraisal Committee meeting as individuals to answer questions to help clarify issues about the submitted evidence and to provide their views and experiences of the technology and/or condition. Before they attend the meeting, all experts must either submit a written statement (using a template) or indicate they agree with the submission made by their nominating organisation..

Commentators – Commentators can participate in the consultation on the ACD (if produced), but NICE does not ask them to make any submission for the appraisal. Non-company commentator organisations can nominate clinical experts and patient experts to verbally present their personal views to the Appraisal Committee. Commentator organisations representing relevant comparator technology companies can also nominate clinical experts. These organisations receive the FAD and have opportunity to report any factual errors. These organisations include comparator technology companies, Healthcare Improvement Scotland any relevant National Collaborating Centre (a group commissioned by NICE to develop clinical guidelines), other related research groups where appropriate (for example, the Medical Research Council and National Cancer Research Institute); other groups such as the NHS Confederation, the NHS Commercial Medicines Unit, the Scottish Medicines Consortium, the Medicines and Healthcare Products Regulatory Agency, the Department of Health and Social Care, Social Services and Public Safety for Northern Ireland).

Public – Members of the public have the opportunity to comment on the ACD when it is posted on the Institute's web site 5 days after it is sent to consultees and commentators. These comments are usually presented to the appraisal committee in full, but NICE reserves the right to summarise and edit comments received during consultations, or not to publish them at all, where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would be otherwise inappropriate.

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
1	Consultee	Gilead Sciences Ltd	**Long-term overall survival with SG (ACD paragraph 3.14)** **Position: Long term overall survival is best represented by the joint log-logistic extrapolations** We are pleased that the Committee agreed that the joint survival modelling approach is appropriate. We also acknowledge that there is uncertainty regarding long-term survival in the minority of patients with the best outcomes. However, with the additional one-year follow-up data presented at the technical engagement stage, as the Committee pointed out, the data is mature, more mature than for many other oncology submissions to NICE. The ACD states that the Committee "agreed that the true survival extrapolation could be anywhere between the optimistic log-logistic and the more pessimistic generalised gamma models." However, given the data maturity and the undoubtedly large OS benefit of SG in a condition where most patient die in less than 1 year on conventional treatment, we believe that there is much stronger evidence for the joint log-logistic extrapolation than the generalised gamma distribution and that it is not accurate or reasonable to describe the true values as being "anywhere" between the two distributions. Two facts point to the greater plausibility of the joint log-logistic extrapolation compared with the generalised gamma distribution: 1. In the additional mature follow-up data from the ASCENT trial presented at Technical Engagement there was a highly statistically significant HR for median OS (0.51, p<0.0001). Observed survival rates at 30 months were 17.8% in the SG arm and 4.4% in the TPC arms, according to the Kaplan-Meier curves. These figures were higher than the predictions of both extrapolation types for both SG and TPC and clearly demonstrate the prolonged impact of SG on long-term survival. The trial data fit the predicted 30-month survival by the joint log-logistic extrapolation more closely than the generalised gamma distribution: a. Joint log-logistic extrapolation: 14.2% with SG and 5.5% with TPC b. Joint generalised gamma distribution: 12.2% with SG and 2.5% with TPC Based on these figures, the joint log-logistic extrapolation represents a slight underestimation of the treatment effect of SG and a slight overestimation of the	Comment noted. At its second meeting, the committee concluded that joint log-logistic model was uncertain but acceptable (Final Appraisal Document section 3.15).

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			effect of TPC. Therefore, it represents a relatively conservative approach. Indeed, the generalised gamma distribution represents a considerable underestimation for both treatment arms compared to survival observed in the ASCENT trial, but particularly that of patients treated with SG. 2. The clinician at the meeting suggested that the 60-month overall survival on TPC is about 1.4%. While this is slightly lower than the 1.7% estimated with the joint log-logistic curve, it is a lot closer than the 0.1% predicted survival by the joint generalised gamma distribution. In addition, clinical expert opinion elicited by Gilead universally dismissed joint generalised gamma as a plausible scenario, being too pessimistic in predicting overall survival at 5 years. In addition, slide 26 presented in the committee meeting slides (illustrated below) shows that the chosen base case of joint log-logistic is not the most favourable extrapolation from the perspective of SG. The independent log-logistic produces the most favourable predicted survival difference between SG and TPC (1.4% survival at 60 months for TPC and 5.2% for SG). This is a clinically plausible scenario that aligns with clinical expectation for TPC provided in the committee meeting. The results at 30 months also align better with observed data in the ASCENT trial than other extrapolations but still underestimate the observed survival for SG (15.1% [model] vs 17.8% [ASCENT] in the SG arm and 4.9% [model] vs 4.4% [ASCENT] in the TPC arm). Applying the independent log-logistic extrapolation in the model results in an ICER of £45,484, £3,275 lower than our revised base case. Therefore, our choice of joint log-logistic extrapolation in the base case is a conservative approach.	

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<tr><th>Comment number</th><th>Type of stakeholder</th><th>Organisation name</th><th>Stakeholder comment
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Please respond to each comment</th></tr>
<tr><td></td><td></td><td></td><td>
Table- projected survival rates up to 60 months (5 years) with different OS extrapolations
<table>
<tr><th></th><th colspan="2">Estimated survival rates</th><th>30 months</th><th>48 months</th><th>60 months</th></tr>
<tr><td rowspan="2">1</td><td rowspan="2">Joint log-logistic</td><td>SG</td><td>14.2%</td><td>6.8%</td><td>4.6%</td></tr>
<tr><td>TPC</td><td>5.5%</td><td>2.5%</td><td>1.7%</td></tr>
<tr><td rowspan="2">2</td><td rowspan="2">Joint generalised gamma</td><td>SG</td><td>12.2%</td><td>3.6%</td><td>1.6%</td></tr>
<tr><td>TPC</td><td>2.6%</td><td>0.4%</td><td>0.1%</td></tr>
<tr><td rowspan="2">3</td><td rowspan="2">Independent log-logistic</td><td>SG</td><td>15.1%</td><td>7.5%</td><td>5.2%</td></tr>
<tr><td>TPC</td><td>4.9%</td><td>2.2%</td><td>1.4%</td></tr>
<tr><td rowspan="2">4</td><td rowspan="2">Independent generalised gamma</td><td>SG</td><td>11.5%</td><td>2.9%</td><td>1.1%</td></tr>
<tr><td>TPC</td><td>3.0%</td><td>0.6%</td><td>0.2%</td></tr>
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</td><td></td></tr>
<tr><td>2</td><td>Consultee</td><td>Gilead Sciences Ltd</td><td>
Utility values post-progression (ACD paragraph 3.12 and 3.13)
Position: Some carry-over benefit from pre-progression utilities is expected.

A factually incorrect statement (corrected at the factual inaccuracy step upon review of the ERG report) was still presented in the Committee Slides (slide 21 “clinical study report concluded that EORTC QLQ C30 scores were similar for SG and TPC”) and paragraph 3.12 in the ACD (“It also noted the clinical study report concluded that EORTC QLQ-C30 scores were similar for sacituzumab govitecan and treatment of physician’s choice”). While the clinical study report did include this statement, the report had been superseded by subsequent post-hoc analysis described within the submission and provided to the ERG (linear mixed-effect regression model for repeated measures). The analysis showed clinically important and statistically significant improvements in several dimensions of quality of life (pain, fatigue), as measured on the EORTC QLQ-C30, that mapped into higher pre-progression utilities for SG.

In light of the considerably higher pre-progression utilities, higher post-progression utilities 4 weeks after progression are clinically explained: these patients progressing from a much-improved tumour status. Progression, measured as growth of the target lesion that previously shrunk to a large extent, will be much less burdensome for the patients, compared to someone who did not have a treatment response.

This was confirmed by the discussion that took place at the appraisal committee meeting [only briefly reflected in the ACD, in paragraph 3.13] – that the clinical lead of the CDF and the
</td><td>
Comment noted. At its second meeting, the committee considered four approaches to modelling post-progression utilities, including one which applied a carryover effect. The committee concluded that this was the least flawed approach but recognised the uncertainty surrounding the rebound utility in the comparator arm (Final Appraisal Document sections 3.13 and 3.14).

In relation to the factual accuracy, the amendment has been applied (section 3.12 in the Final Appraisal Document).
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			clinician still present at the meeting suggested that a carry-over effect of the utility benefit after progression is clinically plausible. Gilead has received additional input from three clinical experts following the ACD meeting who agreed that carry-over utility benefit due to SG is a reasonable assumption. Thereafter utilities would converge for patients receiving SG and those receiving TPC in the same way that overall survival projections eventually converge, with both utility and survival benefits of SG beyond progression being driven by reduced tumour burden at the point of progression. In our revised based case model we have taken a more conservative approach than previously and assumed complete convergence over 6 months. This additional clinical input confirms that that the ERG / Committee preferred approach of identical utilities immediately after progression is unreasonable and is not a valid interpretation of the evidence submitted or clinical opinion. The carry-over utility effect has been implemented for the revised model base case, by a partition of the progressive disease health state, into two tunnel states: one tracking patients with disease progression and alive for exactly 6 months; and one to track time beyond 6 months until death. Utility values were applied accordingly based on patients' time post-progression (i.e., 6-month cut-off).	
3	Consultee	Gilead Sciences Ltd	**Uncertainty in QoL data (impact of drop-out on QoL; ACD paragraph 3.7)** The ERG raised the issue of missing QoL data for 11.7% of the treatment arm and 30.2% of the comparator arm and the ACD notes the opinion of clinical experts that participants in the TPC arm likely had earlier disease progression and deteriorated more quickly and that attrition upon progression is inevitable (ACD paragraph 3.7). Additional post-hoc analysis of patients who had baseline measurement but no follow-up due to withdrawal or progression confirms the opinion of the clinical experts. Analysis of 62 of the 79 (78%) QoL unevaluable patients in the TPC arm with baseline measures found that these patients had a larger number of prior therapies and had higher tumour burden (including a greater proportion with brain metastases) compared with patients in the TPC arm who completed at least 1 post-baseline assessment. 62 patients providing baseline EORTC measurements also indicate a clinically meaningful lower quality of life (Global health status of 50.0 vs 58.1) compared with those who completed at least 1 post-baseline assessment. Post-hoc analysis also shows that the non-evaluable population progressed more rapidly on treatment, with median PFS of 43 days for non-evaluable patients in the TPC arm versus 79 days in those who completed at least 1 post-baseline assessment. Overall survival of the QoL evaluable and non-evaluable patients on TPC also suggests a worse overall prognosis for patients not contributing to QoL data (Figure 1). **Figure 1. Overall survival in ASCENT in the TPC arm (QoL evaluable vs non-evaluable)**	Comment noted. At its second meeting, the committee discussed the impact of dropout in the comparator arm, on quality-of-life data. It maintained that the dropout resulted in uncertainty in the data (Final Appraisal Document section 3.7).

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4	Consultee	NCRI	Although there is only one post-progression quality of life assessment available for the technology, I do not agree that it should be discounted. As clearly documented in the committee papers, patients who respond to treatment have a reduced burden of disease and improved quality of life. Although this can reasonably be expected to deteriorate post-progression with both the technology and the standard of care chemotherapy, because the burden of disease is lower for patients who received the technology, their QoL will, on average, remain superior to that of patients who did not receive the technology over time. The clear overall survival benefit demonstrates that patients will deteriorate and die sooner if they do not receive the technology, therefore accordingly their QoL will also deteriorate sooner.	Comment noted. The committee considered post-progression quality-of-life data submitted by the company and concluded that including a carryover benefit with sacituzumab govitecan was the least flawed option (Final Appraisal Document sections 3.13 and 3.14).
5	Consultee	NCRI	The committee have recognised that this is an important drug for TNBC which represents a genuine step-change for this very poor prognosis cancer, where there is a significant unmet need. As such, approval of this agent is critical for women living with advanced TNBC.	Comment noted. The committee concluded that sacituzumab govitecan met the end-of-life criteria and recognised the high unmet need in triple-negative breast cancer (Final Appraisal Document sections 3.1 and 3.16).
6	Consultee	Breast	Breast Cancer Now welcomes the opportunity to respond to the Appraisal Consultation	Comments noted. The

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		Cancer Now	Document (ACD) for sacituzumab govitecan (Trodelvy) for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies. We are incredibly disappointed that NICE has been provisionally unable to recommend Trodelvy for routine use on the NHS. This draft decision has left patients with profound anxiety and uncertainty about their future treatment options. Patients living with this life-limiting disease already face the devastating reality of short prognoses and limited treatment options, however, this new drug could offer certain patients the hope of precious extra months spend with family and friends, doing what matters most to them. Our views on this are reflected in our original patient organisation submission. We urge Gilead and NICE to find a solution to ensure this treatment can become routinely available, including Gilead ensuring the drug is priced fairly for the NHS. As of 28th April 2022, over 93,000 people have signed an open letter calling on Gilead, NICE and NHS England to urgently find a solution.	committee considered all the evidence submitted by the company and concluded that that sacituzumab govitecan is within what NICE considers cost-effective use of NHS resources. It recognised the high unmet need with triple-negative breast cancer and considered this in its decision-making (Final Appraisal Document sections 3.1and 3.17).
7	Consultee	Breast Cancer Now	Given the significance of this treatment for this group of patients, we believe it essential that the patient and clinical experts are invited back to the second committee meeting. We are also extremely disappointed that NICE has had to delay the second committee meeting by a month due to the number of the topics on the agenda for the original date scheduled of 10th May. This is unacceptable given the high unmet need that NICE has recognised in the ACD document for this group of patients, who do not have time to wait. We are concerned that these capacity issues are undermining the ambitions in the UK Life Sciences Vision and the purpose of the MHRA joining Project Orbis which promised to deliver quicker access to treatments. We believe this is something that needs to be considered as part of the 10-year Cancer Plan to ensure innovation can truly be harnessed and reach patients quickly, at a price that is fair for the NHS. We would also welcome clarity on the prioritisation process that has taken place which has resulted in Trodelvy being delayed. We would urge NICE to do everything they can to ensure the process following the committee meeting, which we desperately hope will be a positive recommendation, runs as smoothly as possible and without delay, especially if further conversations are required between NICE and the drug company.	Comment noted. Patient experts were invited to the second committee meeting. The views of clinical experts and patients representatives were considered by the Appraisal Committee when formulating its recommendations.
8	Consultee	Breast Cancer Now	Are the provisional recommendations sound and a suitable basis for guidance to the NHS? We do not currently accept that a decision to not recommend would be a sound and suitable basis for guidance to the NHS. As NICE has recognised there is a high unmet need for	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-

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			effective treatments for triple negative locally advanced or secondary breast cancer who have a poor prognosis and this treatment is considered a highly effective for this group of patients and offers considerable benefit compared with standard care Although we appreciate that NICE and the SMC are independent and have different approaches, with this treatment recommended for use on the NHS in Scotland in March 2022, unless a positive decision is reached, patients could be left behind as they face the prospect of a new clinically-effective treatment that could delay progression and extend their lives compared to chemotherapy left just out of reach. This treatment is also now available elsewhere, including Canada and Australia and this provisional rejection comes at a time when the Government is looking to radically transform cancer outcomes as part of the new 10-year Cancer Plan. We would reiterate comments from our initial submission that incurable secondary triple negative breast cancer is an aggressive disease with often a poor prognosis. It can have a substantial impact both physically and psychologically on patients and their families. This group of patients have limited treatment options and there is a significant unmet need for effective treatment options that can delay progression of the disease and extend life, for which the side effects can be generally tolerable. Trodelvy has been shown to prolong both progression free and overall survival compared to standard chemotherapies	negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. All the submitted evidence were considered before making a recommendation. NICE expects its advisory bodies to use their scientific and clinical judgement in deciding whether the available evidence is sufficient to provide a basis for recommending or rejecting particular clinical or public health measures (Social Value Judgements; 'Principles for the development of NICE guidance', principle 1).
9	Consultee	Breast Cancer Now	Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? We welcome the Committee's recognition that: - There is a high disease burden for people with triple negative breast cancer - There is a high unmet need for effective treatments for triple negative locally advanced or secondary breast cancer who have a poor prognosis - Sacituzumab govitecan is considered a highly effective treatment for this group of patients and offers considerable benefit compared with standard care There is clear evidence of the significant benefit this treatment can bring as highlighted in our original patient organisation submission and throughout the appraisal process. It would be deeply concerning given the evidence if NICE and the company could not collectively resolve the issues and ensure Trodelvy can be recommended for routine use on the NHS. Breast Cancer Now believes generally the summaries of clinical and cost-effectiveness are reasonable interpretations of the evidence, however, there is one particular area that we would like to raise. Whilst we are pleased that the committee has recognised that it is plausible that quality of life is better while taking Trodelvy compared with standard chemotherapy, it is noted in the ACD that this is not necessarily the case after progression	Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The unmet need was recognised by the committee in its decision making (Final Appraisal Document sections 3.2 and 3.17).

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			despite clinical experts highlighting that it is plausible that this could carry over upon disease progression. Secondary triple negative breast cancer is an incurable disease and patients can experience symptoms and decreased quality of life, such as fatigue, bone pain, breathlessness. It is possible that by patients receiving Trodelvy which can help to reduce tumour size and support bringing the disease under control, that patient symptom burden can be meaningfully decreased and have a positive impact on quality of life for a certain period of time after they have progressed on Trodelvy. Whilst we are unable to put a timeframe on this and it could differ from patient to patient, it is possible that immediately post-progression and up to a certain point that patients may have a better experience in the post-progression state if they have received a more effective treatment, like Trodelvy compared to standard chemotherapy. The longer a patient's disease and symptoms are controlled means a longer time a patient may experience an improved quality of life which could allow patients to continue doing what matters to them, such as social activities and spending time with their loved one. The value of this for the patient and their family should not be underestimated and the quotes below demonstrate this, including the benefits for younger women who may have young children. Furthermore, patients are aware of the clinical benefits that can be associated with Trodelvy. Accessing this medicine, could provide reassurance to both them and their family and they are receiving the optimum treatment available at this time. The psychological benefit of this could also carry over to the post-progression state. As a result of this we would urge a proportionate and flexible approach to be taken and hope that the committee can come to a decision which is between the company's and the ERG's estimate and reflective of the clinical experts statements. We hope that this is being discussed and that the company can submit an updated scenario to reflect this.	
10	Consultee	Breast Cancer Now	Please tell us if the preliminary recommendations could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology As we noted in our original submission, triple negative breast cancer is more common in black women, women under 40 and those who have inherited an altered BRCA gene. Therefore, a final negative recommendation would disproportionately impact certain groups. It should also be noted that patients with secondary triple negative breast cancer are acutely aware of treatment advances, including targeted treatments, for other types of breast cancer and can feel disadvantaged as there has been limited progress in the treatment of triple negative breast cancer.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The committee considered the high unmet need in its decision-making (Final Appraisal Document section 3.17).

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11	Consultee	Breast Cancer Now	Has all of the relevant evidence been taken into account? Following the provisional decision, Breast Cancer Now launched an open letter calling on NICE, Gilead and NHS England to urgently work together to find a solution. We would like the Committee to take account of this open letter which as of 28th April, over 93,000 people have signed. We will officially update you of the final number prior to the second committee meeting. This illustrates the strength of feeling regarding the importance of this treatment for this group of patients This open letter follows a petition launched in September 2021, asking Gilead to agree an interim access arrangement for Trodelvy with NHS England, like other drug companies had done for oncology drugs licensed through Project Orbis. Nearly 230,000 people signed this petition, again showing the overwhelming strength of feeling about the importance of this drug reaching eligible patients. Breast Cancer Now has received a number of statements from women and their families who are 1) currently being treated with Trodelvy and want others to have the same opportunity to benefit from this treatment 2) have incurable secondary triple negative breast cancer and need this drug to be available so they can access it when they need it or 3) people who have had primary triple negative breast cancer and fear recurrence and spread to secondary and want to know clinically-effective treatments are available for them on the NHS if they need them. These statements from patients (documented below) highlight the value that patients attach to the delay in progression of their disease, and the hope of more months to live. We would like the Committee to take account of these statements in making its final decision as we feel that these people's personal experiences of the drug and the implications of not having access for whom this will be a future treatment option form a significant base of important qualitative evidence for this appraisal.	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The committee acknowledged the unmet need with triple-negative breast cancer and considered this in its decision-making (Final Appraisal Document sections 3.2 and 3.16).
12	Consultee	Breast Cancer Now	Patients who are currently receiving Trodelvy: - *"I recently started Trodelvy. I've had 2 infusions. For me, even after 1 cycle/2 infusions I can already "feel" things are better. For someone who has had immunotherapy and a chemotherapy prior to this, with the immunotherapy causing hyper progression and the second also showing progression but smaller, Trodelvy is going to be an absolute lifeline for me. I'm lucky I managed to get started on Trodelvy otherwise my changes of having any targeted treatment was down to zero. [redacted], it means I haven't yet got to tell my sons I'm dying……It'll hopefully mean and show them I'm living and will live for as long as possible. I really really hope Trodelvy is approved otherwise we're left with nothing".*	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. At its second meeting, the committee considered patient perspectives

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			- *"I am currently benefitting from the Gilead pre-reimbursement scheme. This is my 5th line drug following my secondary breast cancer diagnosis in [redacted]. Only one of the 'standard' chemotherapy drugs previously worked for me. Triple negative breast cancer is such an aggressive cancer and this is the first time we have seen a targeted drug. There is considerable excitement amongst the UK cancer community, especially when we talk to other patients in the USA who are having amazing results. I am awaiting scans but I can feel the difference in my lymph nodes after 2.5 cycles. I am very concerned that other patients will not be able to benefit from this new drug. This feels like a massive backwards step for the cancer community and will drive private funding which will bring financial divisions. It makes a mockery of all the fundraising and research trials if we find a drug that works but cannot make it accessible. I hope you can come to some agreement with Gilead to give EVERY patient with triple negative breast cancer the treatment and hope they deserve. The side effects of this treatment have been manageable for me".* - *"My husband and I campaigned with our hospital to get Trodelvy as our research led us to believe this was the best chance of saving my life. I'm due my third session of Trodelvy next week but the impact it's had on my overall-wellbeing and massively reduced my pain has been astonishing. My scan won't be for a good while yet, but I'm expecting to see a positive change in the cancer behaviour and size when it done. [redacted] our children are now adults. This my time to enjoy life."*	alongside the evidence on clinical and cost effectiveness.
13	Consultee	Breast Cancer Now	Patients with secondary triple negative breast cancer who may need Trodelvy in the future explain: - *"I am [redacted] and live with my fiancé and beautiful [redacted] baby. I was diagnosed with triple negative breast cancer [redacted] when I was 6 months pregnant. I had a CT scan [redacted] and unfortunately this scan showed spread to multiple bones which looked like they had been there all along as they'd been 'treated' by the chemotherapy. I had another CT scan [redacted] which then showed progression to my liver. I am waiting to see what treatment I should start on. I'm still in absolute shock that I am living with secondary breast cancer All I know right now is that I need to do absolutely everything I possibly can to fight to be here for as long as possible for my little baby boy. I am certain that at some point I am going to need access to Trodelvy to give me extra time with my baby which is why it's so important NICE approves this treatment for use on the NHS".* - *"I was diagnosed with Stage 4 TNBC [redacted] I am still on my first-line treatment, capecitabine, but the evidence suggests it's coming to the end of its usefulness. Since my primary treatment of EC and paclitaxel was so recent, the proposed plan was to move on to Trodelvy. NHS Scotland has already made the*	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. At its second meeting. the committee considered patients perspectives in its decision making.

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			decision to use Trodelvy as a third-line treatment. I don't know what they have based their decision on but, if Scotland can do it, so, surely, can England and Wales. Otherwise there is a huge imbalance and injustice across the UK. NICE acknowledges that there is clear evidence that Trodelvy fills a massive gap in the treatment of Triple Negative breast cancer. It acknowledges that it not only extends life expectation (which it knows is limited) but it improves quality of life. That is what every human being, regardless of their value to society, deserves. It should be our right. I believed it was until I read this document. By the end, I recognised that, to save money, I and my fellow secondary triple negative breast cancer sufferers are expendable. A few lines just wipe away what may be the only opportunity remaining for a few more years with our loved ones. Many women are in their 20s to 40s. They have young families they will never see grow to adulthood. Trodelvy might at least give them more time together. Myself, I'm 70, I've lived a lot of my life, a useful and productive life dedicated to education - but I've not lived all of it. When I first heard about Trodelvy, it gave me a quiet hope. I didn't dwell on it because I knew it had been added to my treatment plan. I have implicit trust in my oncologist and he believes this is the drug for me when the time comes. But he is practical - he knows how few treatment options there are so he is eking out capecitabine for as long as possible so we don't run out of options too quickly. I hope that, between them, NICE, Gilead and NHS England/Wales will consider the human impact of whatever deal they manage or fail to manage to arrive at. I feel hopeless and expendable now." - *"I've just found out my TNBC has spread to my liver, with [redacted] this couldn't be worse news. My breast care nurse told me about this drug today, but then I've seen the news that it's unlikely to be approved and it's dashed my hopes once again."* - *"I have been living with secondary breast cancer for [redacted]. I have had 8 different treatments so far with only 2 of them being successful. I am now out of options. I have been asking my hospital to try access trodelvy for the last 6 months but keep being told it isn't an option at this time. I don't have time to wait around. I deserve the chance to live longer, to be there for my children longer, to make memories and see them grow up. I NEED trodelvy to help me manage that and it needs to be available to EVERY woman that needs it."* - *"My Mother has stage 4 triple negative breast cancer. Her options are running out – currently it looks like capecitabine tablets have stopped working. We are devastated by the news that NICE have not recommended to approve Trodelvy for routine use on the NHS. It has produced fantastic results and would prolong my Mother's life. I am desperate to have the extra time that Trodelvy would give her and make memories with her before she is gone forever. I love her so much, she's my best friend and has helped me so much throughout my life to become the man I am*	

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			today". - *"I've had every NICE approved chemo since my secondary TNBC [redacted], all palliative. This 6th line of chemo has taken me from a Hepatectomy in June 2018 wondering if my then [redacted], would be alone in the world, to having the hope of seeing her reach [redacted]. I'm currently on cycle 10 of Eribulin which is according to my consultant the last effective option she has confidence in. Once it stops she can't show the cancer anything new so it's my last chance of any effective defence on NHS. The importance to me of Trodelvy being approved for use on the NHS is simply about hope. Hope to enjoy another Summer with my [redacted] children, possibly seeing a couple of more Springs to walk my dog in the bluebells. There has been very little progress with TNBC. It feels like an extra burden on top of the cancer being terminal that it has less treatment options."* - *"I am [redacted] currently living with metastatic triple negative breast cancer that has spread to my lungs, liver and bones. Trodelvy would be one of the few treatment options available to me. I'm 2 years into diagnosis and am already on my third line of treatment. There are much more limited treatments for people with metastatic triple negative breast cancer and every treatment line can provide me with months or even years with loved ones. To not have this drug approved would suggest that the extra time it could give someone like me is not worth it and that for those us living with an extremely aggressive type of breast cancer, we should accept our current limited options and poor prognosis as our fate. [redacted], I don't feel that this is something I should have to do. Should it not be available on the NHS, I would have the option to try and pay for it myself, however due to the side effects from previous lines of treatment I am currently working reduced hours, already placing a strain on our financial situation. Friends and family have also already invested a lot of money is helping with my care and creating memories for us. The difference that this decision could make is life or death. At a time when we run out of the current lines of treatment, which are few with TNBC, Trodelvy could offer us longer to live as opposed to beginning end of life care."* - *"I was relying on starting Trodelvy following my current treatment. Without it, I have a year to live, if I'm lucky. I was diagnosed with TNBC stage [redacted]. I had 6 months of chemo treatment consisting of 4 different drugs. I then had a mastectomy and lymph node clearance. Histology showed that there was 70% cancer cells remaining in the nodes and my tumour had only shrunk from 6.4cm to 5.1cm when removed. Breast margins were also still positive. Had 15 sessions of radiotherapy which completed the treatment in January. I had a repeat scan [redacted] which showed that I had liver metastases. I have been started on another chemo drug this week that my oncologist feels may not work but at least I had a chance to start Trodelvy if this was unsuccessful. Trodelvy would have given me a little longer with my family than I have already been given. A chance to see children, now in their*	

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			twenties, get married and settle down. I know I am luckier than most who have small children and will never get the chance to see them grow up. Trodelvy would just give so much hope to so many people in my position." - *"I have triple negative metastatic breast cancer in my lymph nodes. I was hoping that Trodelvy would be available as a treatment when every day is precious. What is the point of producing a drug that can't be given to people who have very few other treatment options? So disappointed and hurt by this."* - *"I have triple negative breast cancer and fighting breast cancer for the 2nd time at the [redacted] I have a [redacted] daughter this drug could help me see my daughter reach [redacted] I don't think there should be a price on this, as to me its priceless to me and my family and many other families fighting this horrible disease!!! It is hard enough without being denied treatment that has the potential to extend our lives!!"* - "*There's so little research done and available options for people with this type of breast cancer it's shocking that Trodelvy isn't being made available. So the alternative is to just sit back and wait to die."* - *"This drug may be needed to help [redacted] She has breast cancer which spread to her lungs and now to her brain and it is just a question of time. She is so brave, she has not given up and is at present holidaying in Yorkshire, visiting places on her bucket list."* - *"[redacted]. After my first diagnosis in [redacted] I found out my TNBC is back [redacted].I have signed the open letter to address access and cost of Trodelvy for TNBC on NHS in the U.K. as we are a group of patients that have few very treatment options available and we often face a particularly bleak outlook - that this drug is so important. I am part of online communities where ladies with TNBC around the world are saying it is working for them and I am devastated that in the U.K. on the NHS our ladies may not have the same chance as elsewhere. TNBC patients are often younger age with young families and we are desperate to try everything we can to stay with our families."*	
14	Consultee	Breast Cancer Now	We have also heard from a number of women who have experience of primary triple negative breast cancer and who fear that if their cancer was to return and spread to become secondary triple negative breast cancer, that there would be limited treatment options available: - *"I have had triple negative breast cancer in both breasts and am very worried that should I need Trodelvy in the future it won't be available on the NHS. So please, please make it available on the NHS."*	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for

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			- *"I was diagnosed December 2020 with triple negative breast cancer. I have just completed my treatment but am aware that I have a higher chance of reoccurrence due to having TNBC. I would like to know that in the future if I did get a reoccurrence or spread that I would be able to get any drugs that could help me spend more time with my precious* [redacted] *Families shouldn't be robbed of precious time just due to funding especially when there are limited treatments for aggressive cancers."* - *"I have recently finished treatment for primary Triple Negative Breast Cancer and had a complete response to the chemotherapy. Obviously, I hope that my cancer stays away and doesn't come back as secondaries, but the thought of there being fewer options available to extend my life should it happen is truly terrifying. This is especially scary / worrying as it is based on cost and not science!!!!"* - *"I suffered from triple negative breast cancer, both my mum and grandmother died from it I had mastectomy and chemotherapy...at present in remission but fully aware it could reoccur and the drug could mean the difference between life and death.....".* - *"I have had breast cancer twice 9 years apart, with the second occurrence resulting in a double mastectomy. I am now 9 years post the second occurrence, and having been told I have a very high chance of it returning am incredibly disappointed that this drug may not be available should I or others need it in the future as part of their treatment.* *Living with the ever increasing fear of cancer returning and learning that a new drug may not be readily available is, quite frankly, horrendous and frustrating in my mind."* - *"As someone who has had the all clear after surgery, chemotherapy and radiotherapy for TNBC, I am very concerned to hear that should my cancer return I would be limited in my treatment options because of cost. I fully support the work to find a solution that will ensure that those who have, or who could still develop, triple negative secondary cancer have Trodelvy available to them as a treatment option."* - *"I was diagnosed* [redacted] *with triple negative breast cancer in* [redacted]*, underwent removal and sentinel node. I wasn't able to have chemotherapy due to other co-morbidities, so just had radiotherapy. There are no other drugs for me at this present time to prevent recurrence. I am obviously worried it may return and believe that Trodelvy would be my only hope, should it do so. So I wholeheartedly support the work to make it available on the NHS."* - *"I am begging you all to reverse this devastating provisional rejection of sacituzumab govitecan (Trodelvy). What is the value of a life? My daughters life was priceless. It is truly breath-taking to know that there is a drug that could provide hope and time for other patients. The wonderful drug Sacituzumab Govitecan may in years to come be spoken about in the same way as Edward Jenner's Smallpox vaccine. It could	advanced disease. The committee noted the unmet need with triple-negative breast cancer and considered all the company's evidence. It concluded that sacituzumab govitecan is a cost-effective use of NHS resources (Final Appraisal Document sections 3.2 and 3.17).

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			change the course of Breast Cancer history. Please think of the patients like my daughter who have so few treatment lines to help them. Please think of the joy your amazing drug could give. It is too late for my daughter but I beg you to think of not only the patients but their families and reconsider your provisional decision. A drug is only beneficial if it is being used for the good of its patients."	
25	Public	METUPUK	Has all of the relevant evidence been taken into account? The NHS is a devolved service, but the British public does not expect this to translate to inequalities in accessing essential treatment. Trodelvy is available to patients who need it in Scotland. We fail to understand how NICE has reached a different conclusion to the SMC by not approving Trodelvy for routine NHS treatment. When Breast Cancer Now launched the Time for Trodelvy campaign in 2021 to ensure all eligible patients could access the drug through the Gilead pre-reimbursement scheme, over 220,000 people signed their petition. Over 90,000 people have signed latest the Breast Cancer Now petition about the provisional rejection of Trodelvy for use on the NHS. These petitions reflect the strength of public opinion. Trodelvy was one of the first drugs to be fast tracked through Project Orbis, a programme which aims to deliver faster patient access to innovative cancer drugs. For patients in England, Project Orbis has failed to deliver Trodelvy. The evidence that patients and the public will infer from Trodelvy not being approved is that postcode lotteries remain within the NHS. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? It is difficult to comment meaningfully with the confidential discounts and redactions. It is clear that the company and the committee will need to work together to agree a price structure for Trodelvy. This is a step change treatment for a breast cancer subtype which up until now has only had conventional chemotherapy as a treatment. Are the recommendations sound and a suitable basis for guidance to the NHS? No, the recommendations are not sound and suitable guidance. We understand that the NHS has to balance the cost of new technologies with the needs of the entire healthcare system. However, Trodelvy is the only targeted treatment available for mTNBC, addressing an unmet need for an aggressive subtype. Patients have contacted us, and are very distressed by the prospect of Trodelvy being unavailable to them. [redacted] who was diagnosed with mTNBC [redacted] She is currently failing her 3rd line treatment and her only chance of surviving more than 6 months is being prescribed Trodelvy. She writes: "I am absolutely devastated, Trodelvy is my only hope of surviving till the end of the year, I want to spend precious time with my partner and	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.

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			[redacted]. NICE's decision not to fund Trodelvy has a massive impact on patients like me who have run out of options. We are supposed to have patient centred care, this is totally the opposite." [redacted] less than seven months after her secondary diagnosis. She writes: "Please think of the patients [redacted] who have so few treatment lines to help them. It is too late for my [redacted] but I beg you to think of not only the patients but their families and reconsider your provisional decision. A drug is only beneficial if it is being used for the good of its patients." We believe that the committee and the company are in agreement about the benefits Trodelvy can offer patients with mTNBC and hope they can work together to ensure all eligible patients have access to this innovative treatment. Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity? Although the incidence and prevalence of diseases are beyond the scope of NICE technology appraisals, it is important for us as a patient group to acknowledge that triple negative breast cancer does discriminate. Triple negative breast cancer disproportionately affects younger people, almost always women, and also people of colour. In addition, younger people, particularly those in their 20s and 30s are most likely to have a delayed, missed or late stage diagnosis, and are most likely to be pregnant or post pregnancy. These groups are also most likely to have the poorest outcomes and shortest disease free survival.	
15	Public	Patient 1	I am currently benefiting from the Gilead/NHS reimbursement scheme. This is my 5th line drug following my secondary breast cancer [redacted]. Only one of the 'standard' chemo drugs previously worked for me. TNBC is such an aggressive cancer and this is the first time we have seen a targeted drug. There is considerable excitement amongst the UK cancer community, especially when we talk to others patients in the USA who are having amazing results. I am awaiting scans but I can feel the difference in my lymph nodes after 2.5 cycles. I am very concerned that other patients will not be able to benefit from this new drug. This feels like a massive backwards step for the cancer community and will drive private funding which will bring financial divisions. It makes a mockery of all the cancer fundraising and research trials if we find a drug that works but cannot make it accessible. I hope you can come to some agreement with Gilead to give EVERY patient with TNBC the treatment and hope they deserve.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The committee considered all the evidence submitted by the company before its final recommendation.
16	Public	Patient 2	As someone who recently had TNBC and at high risk of it returning I appeal to you to	

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			reconsider. This drug helps extend the lives of those with terminal TNBC, many of whom are young women with young children. The disease more commonly affects younger women and provides them with vital time with their families, friends and to support their affairs out. I appreciate the NHS has limited funds but you are putting a price on life. How would you feel if it was your, your wife or sister. Thank you	
17	Public	Patient 3	Sacituzumab is the last hope for people with secondary triple negative breast cancer. It can give them and their families many valuable months together. The cost of this is priceless and cannot be measured as just a monetary amount. For this reason I feel it should be allowed and available to anyone whose other treatment options have been exhausted.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.).
18	Public	Patient 4	Has all of the relevant evidence been taken into account? No. Where is the evidence of how much anxiety and fear there is in patients unable to access this chemotherapy? It is recommended. It is working for those already receiving it. What if one of your family members needed it? Can you put a price on someone's life? As stated, triple negative cancer causes anxiety in patients, friends and family members. Not having access to life saving/life extending treatment cause more anxiety than is necessary.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
19	Public	Patient 5	This evidence seemed to be accepted yet, offering this treatment in England for women who have a poor prognosis is being denied based on cost. This evidence in Scotland is accepted and this treatment is being offered. It does not make sense that England and Scotland have looked at the same evidence and come to such a different conclusion. How can one nation in the United Kingdom offer something to women based on clinical need and another nation in the UK deny it based on cost. Are women in England inherently worth less in terms of their length and quality of life than women in Scotland? Some women in England will be able to advocate or have advocates who will somehow manage to get the medication. Or they will move to Scotland. A woman who has less social capital (based on her race, or disability such as a learning disability) is far less likely to find a way to get this medication that a white, well connected non-disabled woman could.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
20	Public	Patient 6	You cannot put a price on someone's life, people with TNBC need the option of using this drug, I myself will need this product and you are denying me that right, you have no right to decide who lives and dies	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-

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				negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
21	Public	Patient 7	I am a [redacted] and have just completed my 8th cycle on this drug and it has given me great stability and pain relief. My quality of life at present it far better than when I was on conventional chemotherapies. I work full time for the NHS and have done so with few sick days on this treatment. The NHS budgets are stretched for sure but when you factor in the demographic profile of young women effected, their families, children and careers there is a contribution to society which is unquantifiable. We have so much yet to give the world and those we love. I wish you can renegotiate so everyone who finds themselves in this tragic set of circumstances like me to have the opportunity to this treatment. The past few years living with covid have been brutal and for those living with cancer even more of a challenge. Please allow TNBC some desperately needed access to what I believe to be a kinder treatment.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
22	Public	Patient 8	Has all of the relevant evidence been taken into account? Yes Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? Yes Are the recommendations sound and a suitable basis for guidance to the NHS? Yes Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity? No [redacted]. I have recently been diagnosed with Metastatic Triple Negative Breast Cancer so have personal insight into the terrifying process women are facing regarding treatment options for this horrendous disease. Trodelvy brings hope, simply. Hope to watch children grow and witness milestones taken for granted by those in the world of the well. It is my view that this treatment should be available on the NHS to help facilitate this.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
23	Public	Patient 9	I am a stage 4 triple negative breast cancer patient. [redacted] and have been living with	Comment noted.

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			this diagnosis for now [redacted]. I have [redacted] I sincerely hope that an agreement can be reached for funding for this drug. The thought of a potential life line for me breaks my heart. This drug is my glimmer of hope, hope of more time with my family. More time to see those special milestones, more time to create precious memories. I'm not ready to leave my children yet, please let them spend more time with their mummy. They don't deserve this.	Sacituzumab govitecanhas now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.
24	Public	Patient 10	<u>Has all of the relevant evidence been taken into account?</u> Have NICE considered evidence (outside of trials) from the US where the drug is being used to treat primary triple negative breast cancers? It's plausible that quality of life is better while taking sacituzumab govitecan compared with standard chemotherapy, but not necessarily after progression I am an administrator [redacted] for ladies with stage 4 triple negative breast cancer. Many of the group members have been granted sacituzumab govitecan on compassionate grounds by Gilead. The majority of those taking the drug have had remarkable results - unsurpassed by any previous chemotherapy/immunotherapy treatments. In several cases, ladies have achieved no evidence of disease meaning treatment has been stopped and maintenance provided to monitor ongoing health. It is not known whether the NED will be permanent or whether the patients may suffer a relapse but during this pause in treatment, the NHS is not funding any other drugs and therefore this should be taken into consideration. Certainly quality of life for many has been greatly improved. 3 years is far too long to wait to review the guidance. This drug is having excellent results with some stage 4 patients in the UK. Discussions with Gilead, especially as the only barrier to providing the drug to patients in England is cost, should recommence.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease
25	Public	Patient 11	<u>Has all of the relevant evidence been taken into account?</u> Sadly I do not believe that all evidence has been taken into account. Based on my personal circumstances, I do not believe that you can put a price on delaying the onset of metastatic TNBC I am not in the consultations typical demographic, I'm a [redacted] white British women, who has 2 children [redacted]. I'm about to tell them that they will lose their mum sooner than needed as the NHS is not willing to pay for the best treatment for me How ludicrous does that sound! <u>Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?</u>	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.

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			Given the costs are withheld from the document it makes it impossible for me to comment fairly on this. However, I would say that there shouldn't be a price associated with prolonging life, particularly in an area that has such poor outlooks - new medicine available should be received with open arms, and as wider studies prove their effectiveness, then negotiations on a larger scale can take place. Given TNBC is a small subset of total breast cancers, the cost per patient being treated can afford to be a little higher. Remember the NHS has budgeted to look after me into my 80's, just spend a little of that money sooner please. <u>Are the recommendations sound and a suitable basis for guidance to the NHS?</u> Given I was advised my TNBC had metastasised on [redacted] and told by an NHS breast care nurse on [redacted] that this new drug Trodelvy would be available for my future treatment from June, and that it had really positive outcomes I do not feel that it's a sound and suitable basis for NHS guidance. It shows the importance that the teams dealing with patients place on this drug as an improved option for those suffering. This drug could literally prolong the quality of my life and my life overall. The fact that she was unaware that the recommendation is to not provide to the NHS shows they thought it would absolutely be approved. The time it gives patients, and me, may be enough for me to see my children grow up and support [redacted] how can saying something is too expensive be a justification for guidance to the NHS. Work together and find a solution, I beg you <u>Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?</u> I do believe that because TNBC generally targets black women not as much effort has been put into reaching a positive conclusion. I am a white English [redacted] woman so am not in the demographics you place reliance on within the recommendations. Perhaps you need to fully consider the views and stop being discriminatory. Every sort of person deserves to be able to fight their cancer with the best possible drugs available, don't limit availability because of cost. When you're dying you realise that money doesn't make the world go round, it's love and compassion. Please sort out a deal so we can use the life saving treatment sooner rather than later, so it's not too late for me. I would say it's actually discriminatory against those fighting TNBC, other types of breast cancer have long term drugs available for them, why are you not prepared to spend the same	

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			amount of money on this one, even if it's over a shorter period of time. Has all of the relevant evidence been taken into account? It's a fairly hard read for someone that was only [redacted] I don't believe the statistical sample includes enough on different races and would propose that by putting this drug as available to the NHS over the next 5 years would ensure you get statistical relevance and save or prolong the quality of lives for hundreds of patients Has the long-term costs of hormone therapies been taken into account when considering the costs? Whilst the life may be shorter, the richness of the quality of that life cannot be overlooked. Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? The costs were withheld from the documents, but not cost should be too much to save a person's life. What nobody knows the answer to is what leaps in medicine this drug could provide. If you don't try, you don't get etc. please reach a compromise to ensure treatment can be given. My life depends on it You also need to consider the scale of the use of the drug. Because TNBC is a smaller subset of breast cancers, this means that the higher costs are in fact limited to that smaller subset. [redacted] I understand the tendering process and the need to keep tight cost control, however, when looking at the overall size of the target audience I think it's much smaller in the case of TNBC and therefore overall costs aren't as significant. Percentages and figures only tell part of the story, look beyond them to see the overall impact of approving this drug, vs the negative impact of not.	
26	Public	Patient 12	Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity? This decision setting up a disparity in access to the drug via the NHS in the UK. It raises the spectre of unequal access across the UK, as the Scottish Medicines Consortium (SMC) has already accepted its use north of the border. That is discriminatory. My Mother has stage 4 triple negative breast cancer with spread to bone and skin. Her options are running out – currently it looks like capecitabine tablets have stopped working. We are devastated by the news that NICE have not recommended to approve Trodelvy for routine use on the NHS. It has produced fantastic results and would prolong my mother's life. It seems even more cruel that Trodelvy has been approved in Scotland and not England thus setting up a disparity in access to the drug via the NHS in the UK. This approval shows that the cost cannot be too high as stated by NICE. I am desperate to have the extra time that	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease.

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			Trodelvy would give her and make memories with her before she is gone forever. I love her so much, she's my best friend and has helped me so much throughout my life to become the man I am today. There is a lack of targeted treatment compared with other types of Breast Cancer. NICE says it already recommends use of Roche's PD-L1 inhibitor Tecentriq (atezolizumab) as an alternative for Metastatic Triple Negative Breast Cancer-sadly this would not help my mother as she is PD-L1 negative on primary tumour. Trodelvy would offer a realistic increase in overall survival with a tolerable side effect profile and the impact psychologically of being diagnosed with a poor prognosis cancer with lack of treatment options. I urge you to change this terrible decision which will destroy all hope and tear apart families lives. If price is the issue as is alluded to- surely a deal can be negotiated at a price point which is acceptable to all parties to avoid a premature loss of life to many Metastatic Breast Cancer patients. The impact of this decision cannot be underestimated on myself and other families. I cannot sleep, eat or drink worrying about what the future holds. If this drug had been available to my mother as a first- or second-line treatment, I may not have had to give up my full time job to become a carer this soon. I have gone from earning 2k a month to £68 a week carers allowance. My mother is fit and ready and waiting to receive this treatment. She can't wait.	
27	Public	Patient 13	The committee considered sacituzumab govitecan to be "a highly effective treatment for people with triple-negative locally advanced or metastatic breast cancer who have a poor prognosis. " The clinical efficacy is proven yet offering this treatment in England for women who have a poor prognosis is being denied based on cost. The evidence in Scotland has been accepted and this treatment is being offered. Therefore, there is a discrepant outcome between England and Scotland based on the same evidence. Women in England feel they are being denied life saving treatment because their lives are not considered worth the cost. There is a risk of further inequity of access in England as some women will be financially able to move to Scotland for treatment while others will not. Those women already disadvantaged by poverty and discrimination will be further disadvantaged by treatment being dependent on financial means.	Comment noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The committee considered the high unmet need in people with triple-negative breast cancer in its decision-making (Final Appraisal Document sections 3.2 and 3.17).
28	Public	Patient 14	My cousin in her 30's has been having this treatment & it seems to have benefited her hugely. She recovers from treatment so rapidly which allows her to manage everyday life & so much more. She has been travelling & getting outdoors the whole way through. This would not be the case if it was very tough rounds of chemotherapy. She is so young & this is another reason she needs to bounce back so fast for herself & her family who are spending as much time with her when she is able between treatments.	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
				one of which was for advanced disease. The unmet need in triple-negative breast cancer was recognised by committee and taken into account in its decision-making (Final Appraisal Document sections 3.2 and 3.17).
29	Public	Patient 15	Hi there, a cousin of mine has just finished my 8th cycle of this drug and is finding it very beneficial. The NHS funding of this is vital to ensure that she receives the treatment she vitally needs. I hope the decision makers here take such cases into account.	Comment noted. At its second meeting, the committee considered patient perspectives alongside the evidence on clinical and cost effectiveness.
30	Public	Patient 16	My sister has been on this treatment for several months now and has remained stable. Trodelvy has given her a much better quality of life than previous chemotherapies. Please don't restrict access to the people who need this life line.	Comment noted. At its second meeting, the committee considered the patient perspectives alongside the evidence on clinical and cost effectiveness.
31	Public	NHS professional	I read the NICE appraisal document on the "Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer" with great interest. As a health professional looking after patients with metastatic triple negative breast cancer and their poor survival outcome, I was very hopeful that the drug would become available for patients in the NHS as this is an important area of unmet need. It was disappointing that the drug has been declined by NICE especially based on the cost-effective estimates. I would like to draw attention to two points as a clinician on the appraisal: a. "It's plausible that quality of life is better while taking sacituzumab govitecan compared with standard chemotherapy, but not necessarily after progression": As a treating clinician, I would expect that the QOL is dependent on the tumour burden and based on RR, the quality of life is expected to be better not only during the treatment phase but up to 3-6 months post progression. b. The long-term overall survival benefit for sacituzumab govitecan is uncertain: Based on the presented data, the joint generalised gamma curve is too pessimistic and not reflective of real time data for TPC arm. The clinical expert in the appraisal agreed that the 5-year OS for TPC is much closer to the joint log-logistic survival rates and I would agree this to be the case. Would the drug be cost effective using the joint log-logistic curve? If so, with some degree of	Comments noted. Sacituzumab govitecan has now been recommended for treating unresectable triple-negative locally advanced or metastatic breast cancer in adults after 2 or more systemic therapies, at least one of which was for advanced disease. The committee considered a carryover utility post-progression and joint-log logistic extrapolation in its decision making (Final Appraisal Document sections 3.13, 3.14 and 3.15)

Comment number	Type of stakeholder	Organisation name	Stakeholder comment Please insert each new comment in a new row	NICE Response Please respond to each comment
			uncertainty, will it not be beneficial for the drug to be made available for the needing patients. I sincerely hope that NICE committee will look more favourable to the innovation with Sacituzumab govitecan and the drug would become available for NHS patients in the near future.	

Document processed	Organisation name – Stakeholder or respondent	Disclosure on tobacco funding / links	Number of comments extracted	Comments
ID3942 sacituzumab ACD stakeholder comments form Gilead Sciences Ltd 29042022RB [noACIC].docx	Gilead Sciences Ltd	Gilead has no links to the Tobacco industry	3	
ID3942 sacituzumab govitecan for triple negative ACD stakeholder comments NCRI 28042022RR [noACIC].doc	NCRI	No links to the tobacco industry I have a number of disclosures (speakers fees, advisory boards and research funding) relating to my work with pharmaceutical companies including Gilead, as previously stated	2	
ID3942 sacituzumab ACD stakeholder comments Breast Cancer Now 29042022RB [noACIC].doc	Breast Cancer Now	N/A	8	
ID3942 sacituzumab ACD Compiled Web Comments 03052022 RB [DPD; noACIC]	Patients and METUPUK	N/A	16	
NHS East Sussex and North Essex CCG (Public Comment)	NHS Professional	N/A	1	

NICE National Institute for Health and Care Excellence

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Consultation on the appraisal consultation document – deadline for comments 5pm on **Friday 29 April 2022**. Please submit via NICE Docs.

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. The Appraisal Committee is interested in receiving comments on the following: • **has all of the relevant evidence been taken into account?** • **are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** • **are the provisional recommendations sound and a suitable basis for guidance to the NHS?** NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations: • could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced**.**
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Gilead Sciences Ltd
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	Gilead has no links to the Tobacco industry
Name of commentator person completing form:	Eleonora Lovato

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Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

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Comment number	Comments Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
	Introduction We have carefully considered the Committee's assessment of the evidence submitted for the single technology appraisal for SG for treating triple-negative, advanced breast cancer [ID3942]. We thank the National Institute for Health and Care Excellence (NICE) for the opportunity to comment on the Appraisal Consultation Document (ACD). We are disappointed by the conclusions reached by the Committee and the resulting preliminary guidance not to recommend SG. We present a revised case with ICER of £48,760 per QALY for the Committee's consideration. This includes settings agreed at the ACD committee, apart from two critical points discussed below, and a revised PAS offer. Note that as agreed with NICE on 28 March, RDI was applied to the calculation of drug costs with wastage (in case vial sharing is not allowed). In summary: • We believe that there is strong evidence that the approach used by Gilead to estimate long-term survival of patients, the joint log-logistic extrapolation, is robust and represents the most reasonable interpretation of the available evidence: o Mature survival data observed at 30 months indicated higher survival in the ASCENT trial for both SG and TPC than applied in the model through the joint log-logistic extrapolation and much higher than the generalised gamma estimates o Clinical input during the committee meeting fits the joint log-logistic extrapolation more closely o Generalised gamma has been widely dismissed among clinical experts as too pessimistic o In fact, clinical input during the committee meeting aligned with the separately fitted log-logistic extrapolation for TPC. Assuming that is true for SG as well, it would result in a considerably lower ICER (£45,484). Therefore, our choice of joint log-logistic extrapolation in the base case can be considered conservative • NICE has not allowed for persistent improvement in utilities for patients receiving SG vs current treatment after progression. In doing so they have failed to take account of all available evidence presented and supported by the opinion of clinical experts in the committee meeting. Specifically: o Higher post-progression utilities for SG vs TPC, due to a much lower tumour burden at the time of progression, are highly plausible and widely supported by expert clinical opinion. Clinical opinion also suggests that this difference is expected to last several months in the progressed state. o This effect is likely to last for an extended period post-progression. The revised base case utilises a difference in post-progression utilities for up to 6 months. Gilead deems this to be a plausible duration, as patients whose tumours shrunk in the pre-progression state are more likely to have a subsequent therapy and longer overall survival relative to their SG PFS. SG is a ground-breaking innovation, receiving an MHRA Innovative Licensing and Access Pathway designation. As the Committee stated, it "considered sacituzumab govitecan to be a

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

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	highly effective treatment for people with triple-negative locally advanced or metastatic breast cancer who have a poor prognosis." Negative guidance will impact severely on the small group of women with mTNBC but will have a disproportionate impact on young black women who are more often diagnosed with this condition. We believe that current guidance fails to take account of evidence concerning post-progression utility and does not interpret the evidence around utilities or survival extrapolation properly resulting in provisional guidance that does not represent sound guidance to the NHS. In what follows we give a detailed response on these two key points raised within the ACD and clarify a point that was only briefly mentioned in the ACD document. We hope that this response, together with the revised offer, will be sufficient to provide a positive recommendation to SG.
1	**Issues Raised in the ACD: Long-term overall survival with SG (ACD paragraph 3.14)** **Position: Long term overall survival is best represented by the joint log-logistic extrapolations** We are pleased that the Committee agreed that the joint survival modelling approach is appropriate. We also acknowledge that there is uncertainty regarding long-term survival in the minority of patients with the best outcomes. However, with the additional one-year follow-up data presented at the technical engagement stage, as the Committee pointed out, the data is mature, more mature than for many other oncology submissions to NICE. The ACD states that the Committee "agreed that the true survival extrapolation could be anywhere between the optimistic log-logistic and the more pessimistic generalised gamma models." However, given the data maturity and the undoubtedly large OS benefit of SG in a condition where most patient die in less than 1 year on conventional treatment, we believe that there is much stronger evidence for the joint log-logistic extrapolation than the generalised gamma distribution and that it is not accurate or reasonable to describe the true values as being "anywhere" between the two distributions. Two facts point to the greater plausibility of the joint log-logistic extrapolation compared with the generalised gamma distribution: 1. In the additional mature follow-up data from the ASCENT trial presented at Technical Engagement there was a highly statistically significant HR for median OS (0.51, p<0.0001). Observed survival rates at 30 months were 17.8% in the SG arm and 4.4% in the TPC arms, according to the Kaplan-Meier curves. These figures were higher than the predictions of both extrapolation types for both SG and TPC and clearly demonstrate the prolonged impact of SG on long-term survival. The trial data fit the predicted 30-month survival by the joint log-logistic extrapolation more closely than the generalised gamma distribution: a. Joint log-logistic extrapolation: 14.2% with SG and 5.5% with TPC b. Joint generalised gamma distribution: 12.2% with SG and 2.5% with TPC Based on these figures, the joint log-logistic extrapolation represents a slight underestimation of the treatment effect of SG and a slight overestimation of the effect of TPC. Therefore, it represents a relatively conservative approach. Indeed, the generalised gamma distribution represents a considerable underestimation for both treatment arms compared to survival observed in the ASCENT trial, but particularly that of patients treated with SG. 2. The clinician at the meeting suggested that the 60-month overall survival on TPC is about 1.4%. While this is slightly lower than the 1.7% estimated with the joint log-logistic curve,

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it is a lot closer than the 0.1% predicted survival by the joint generalised gamma distribution. In addition, clinical expert opinion elicited by Gilead universally dismissed joint generalised gamma as a plausible scenario, being too pessimistic in predicting overall survival at 5 years.

In addition, slide 26 presented in the committee meeting slides (illustrated below) shows that the chosen base case of joint log-logistic is not the most favourable extrapolation from the perspective of SG. The independent log-logistic produces the most favourable predicted survival difference between SG and TPC (1.4% survival at 60 months for TPC and 5.2% for SG). This is a clinically plausible scenario that aligns with clinical expectation for TPC provided in the committee meeting. The results at 30 months also align better with observed data in the ASCENT trial than other extrapolations but still underestimate the observed survival for SG (15.1% [model] vs 17.8% [ASCENT] in the SG arm and 4.9% [model] vs 4.4% [ASCENT] in the TPC arm). Applying the independent log-logistic extrapolation in the model results in an ICER of £45,484, £3,275 lower than our revised base case. Therefore, our choice of joint log-logistic extrapolation in the base case is a conservative approach.

Table- projected survival rates up to 60 months (5 years) with different OS extrapolations

	Estimated survival rates		30 months	48 months	60 months
1	Joint log-logistic	SG	14.2%	6.8%	4.6%
		TPC	5.5%	2.5%	1.7%
2	Joint generalised gamma	SG	12.2%	3.6%	1.6%
		TPC	2.6%	0.4%	0.1%
3	Independent log-logistic	SG	15.1%	7.5%	5.2%
		TPC	4.9%	2.2%	1.4%
4	Independent generalised gamma	SG	11.5%	2.9%	1.1%
		TPC	3.0%	0.6%	0.2%

2

Issues Raised in the ACD: 2. utility values post-progression (ACD paragraph 3.12 and 3.13)
Position: Some carry-over benefit from pre-progression utilities is expected.

A factually incorrect statement (corrected at the factual inaccuracy step upon review of the ERG report) was still presented in the Committee Slides (slide 21 “clinical study report concluded that EORTC QLQ C30 scores were similar for SG and TPC”) and paragraph 3.12 in the ACD (“It also noted the clinical study report concluded that EORTC QLQ-C30 scores were similar for sacituzumab govitecan and treatment of physician’s choice”). While the clinical study report did include this statement, the report had been superseded by subsequent post-hoc analysis described within the submission and provided to the ERG (linear mixed-effect regression model for repeated measures). The analysis showed clinically important and statistically significant improvements in several dimensions of quality of life (pain, fatigue), as measured on the EORTC QLQ-C30, that mapped into higher pre-progression utilities for SG.

In light of the considerably higher pre-progression utilities, higher post-progression utilities 4 weeks after progression are clinically explained: these patients progressing from a much-improved tumour status. Progression, measured as growth of the target lesion that previously shrunk to a large extent, will be much less burdensome for the patients, compared to someone who did not have a treatment response.

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

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	This was confirmed by the discussion that took place at the appraisal committee meeting [only briefly reflected in the ACD, in paragraph 3.13] – that the clinical lead of the CDF and the clinician still present at the meeting suggested that a carry-over effect of the utility benefit after progression is clinically plausible. Gilead has received additional input from three clinical experts following the ACD meeting who agreed that carry-over utility benefit due to SG is a reasonable assumption. Thereafter utilities would converge for patients receiving SG and those receiving TPC in the same way that overall survival projections eventually converge, with both utility and survival benefits of SG beyond progression being driven by reduced tumour burden at the point of progression. In our revised based case model we have taken a more conservative approach than previously and assumed complete convergence over 6 months. This additional clinical input confirms that that the ERG / Committee preferred approach of identical utilities immediately after progression is unreasonable and is not a valid interpretation of the evidence submitted or clinical opinion. The carry-over utility effect has been implemented for the revised model base case, by a partition of the progressive disease health state, into two tunnel states: one tracking patients with disease progression and alive for exactly 6 months; and one to track time beyond 6 months until death. Utility values were applied accordingly based on patients' time post-progression (i.e., 6-month cut-off).
3	**Issues Raised in the ACD: 3. Uncertainty in QoL data (impact of drop-out on QoL; ACD paragraph 3.7)** The ERG raised the issue of missing QoL data for 11.7% of the treatment arm and 30.2% of the comparator arm and the ACD notes the opinion of clinical experts that participants in the TPC arm likely had earlier disease progression and deteriorated more quickly and that attrition upon progression is inevitable (ACD paragraph 3.7). Additional post-hoc analysis of patients who had baseline measurement but no follow-up due to withdrawal or progression confirms the opinion of the clinical experts. Analysis of 62 of the 79 (78%) QoL unevaluable patients in the TPC arm with baseline measures found that these patients had a larger number of prior therapies and had higher tumour burden (including a greater proportion with brain metastases) compared with patients in the TPC arm who completed at least 1 post-baseline assessment. 62 patients providing baseline EORTC measurements also indicate a clinically meaningful lower quality of life (Global health status of 50.0 vs 58.1) compared with those who completed at least 1 post-baseline assessment. Post-hoc analysis also shows that the non-evaluable population progressed more rapidly on treatment, with median PFS of 43 days for non-evaluable patients in the TPC arm versus 79 days in those who completed at least 1 post-baseline assessment. Overall survival of the QoL evaluable and non-evaluable patients on TPC also suggests a worse overall prognosis for patients not contributing to QoL data (Figure 1). **Figure 1. Overall survival in ASCENT in the TPC arm (QoL evaluable vs non-evaluable)**

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Insert extra rows as needed

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- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise and all information submitted under 'academic in confidence' in yellow. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the appraisal consultation document, please submit these separately.

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Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory committees.

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Breast Cancer Now
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	N/A
Name of commentator person completing form:	[redacted]
Comment number	**Comments**

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	Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
1	Breast Cancer Now welcomes the opportunity to respond to the Appraisal Consultation Document (ACD) for sacituzumab govitecan (Trodelvy) for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies. We are incredibly disappointed that NICE has been provisionally unable to recommend Trodelvy for routine use on the NHS. This draft decision has left patients with profound anxiety and uncertainty about their future treatment options. Patients living with this life-limiting disease already face the devastating reality of short prognoses and limited treatment options, however, this new drug could offer certain patients the hope of precious extra months spend with family and friends, doing what matters most to them. Our views on this are reflected in our original patient organisation submission. We urge Gilead and NICE to find a solution to ensure this treatment can become routinely available, including Gilead ensuring the drug is priced fairly for the NHS. As of 28th April 2022, over 93,000 people have signed an open letter calling on Gilead, NICE and NHS England to urgently find a solution.
2	Given the significance of this treatment for this group of patients, we believe it essential that the patient and clinical experts are invited back to the second committee meeting. We are also extremely disappointed that NICE has had to delay the second committee meeting by a month due to the number of the topics on the agenda for the original date scheduled of 10th May. This is unacceptable given the high unmet need that NICE has recognised in the ACD document for this group of patients, who do not have time to wait. We are concerned that these capacity issues are undermining the ambitions in the UK Life Sciences Vision and the purpose of the MHRA joining Project Orbis which promised to deliver quicker access to treatments. We believe this is something that needs to be considered as part of the 10-year Cancer Plan to ensure innovation can truly be harnessed and reach patients quickly, at a price that is fair for the NHS. We would also welcome clarity on the prioritisation process that has taken place which has resulted in Trodelvy being delayed. We would urge NICE to do everything they can to ensure the process following the committee meeting, which we desperately hope will be a positive recommendation, runs as smoothly as possible and without delay, especially if further conversations are required between NICE and the drug company.
3	Are the provisional recommendations sound and a suitable basis for guidance to the NHS? We do not currently accept that a decision to not recommend would be a sound and suitable basis for guidance to the NHS. As NICE has recognised there is a high unmet need for effective treatments for triple negative locally advanced or secondary breast cancer who have a poor prognosis and this treatment is considered a highly effective for this group of patients and offers considerable benefit

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	compared with standard care Although we appreciate that NICE and the SMC are independent and have different approaches, with this treatment recommended for use on the NHS in Scotland in March 2022, unless a positive decision is reached, patients could be left behind as they face the prospect of a new clinically-effective treatment that could delay progression and extend their lives compared to chemotherapy left just out of reach. This treatment is also now available elsewhere, including Canada and Australia and this provisional rejection comes at a time when the Government is looking to radically transform cancer outcomes as part of the new 10-year Cancer Plan. We would reiterate comments from our initial submission that incurable secondary triple negative breast cancer is an aggressive disease with often a poor prognosis. It can have a substantial impact both physically and psychologically on patients and their families. This group of patients have limited treatment options and there is a significant unmet need for effective treatment options that can delay progression of the disease and extend life, for which the side effects can be generally tolerable. Trodelvy has been shown to prolong both progression free and overall survival compared to standard chemotherapies
5	<u>Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?</u> We welcome the Committee's recognition that: - There is a high disease burden for people with triple negative breast cancer - There is a high unmet need for effective treatments for triple negative locally advanced or secondary breast cancer who have a poor prognosis - Sacituzumab govitecan is considered a highly effective treatment for this group of patients and offers considerable benefit compared with standard care There is clear evidence of the significant benefit this treatment can bring as highlighted in our original patient organisation submission and throughout the appraisal process. It would be deeply concerning given the evidence if NICE and the company could not collectively resolve the issues and ensure Trodelvy can be recommended for routine use on the NHS. Breast Cancer Now believes generally the summaries of clinical and cost-effectiveness are reasonable interpretations of the evidence, however, there is one particular area that we would like to raise. Whilst we are pleased that the committee has recognised that it is plausible that quality of life is better while taking Trodelvy compared with standard chemotherapy, it is noted in the ACD that this is not necessarily the case after progression despite clinical experts highlighting that it is plausible that this could carry over upon disease progression. Secondary triple negative breast cancer is an incurable disease and patients can experience symptoms and decreased quality of life, such as fatigue, bone pain, breathlessness. It is possible that by patients receiving Trodelvy which can help to reduce tumour size and support bringing the disease under control, that patient symptom burden can be meaningfully decreased and have a positive impact on quality of life for a certain period of time after they have progressed on Trodelvy. Whilst we are unable to put a timeframe on this and it could differ from patient to patient, it is possible that immediately post-progression and up to a certain point that patients may have a better experience in the post-progression state if they have received a more effective treatment, like Trodelvy compared to standard chemotherapy. The longer a patient's disease and symptoms are controlled means a longer time a patient may experience an improved quality of life which could allow patients to continue doing what matters to them, such as social activities and spending time with their loved one. The value of this for the patient and their family should not be underestimated and the quotes below demonstrate this, including the benefits for younger women who may have young children.

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

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	Furthermore, patients are aware of the clinical benefits that can be associated with Trodelvy. Accessing this medicine, could provide reassurance to both them and their family and they are receiving the optimum treatment available at this time. The psychological benefit of this could also carry over to the post-progression state. As a result of this we would urge a proportionate and flexible approach to be taken and hope that the committee can come to a decision which is between the company's and the ERG's estimate and reflective of the clinical experts statements. We hope that this is being discussed and that the company can submit an updated scenario to reflect this.
6	please tell us if the preliminary recommendations could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology As we noted in our original submission, triple negative breast cancer is more common in black women, women under 40 and those who have inherited an altered BRCA gene. Therefore, a final negative recommendation would disproportionately impact certain groups. It should also be noted that patients with secondary triple negative breast cancer are acutely aware of treatment advances, including targeted treatments, for other types of breast cancer and can feel disadvantaged as there has been limited progress in the treatment of triple negative breast cancer.
7	Has all of the relevant evidence been taken into account? Following the provisional decision, Breast Cancer Now launched an open letter calling on NICE, Gilead and NHS England to urgently work together to find a solution. We would like the Committee to take account of this open letter which as of 28th April, over 93,000 people have signed. We will officially update you of the final number prior to the second committee meeting. This illustrates the strength of feeling regarding the importance of this treatment for this group of patients This open letter follows a petition launched in September 2021, asking Gilead to agree an interim access arrangement for Trodelvy with NHS England, like other drug companies had done for oncology drugs licensed through Project Orbis. Nearly 230,000 people signed this petition, again showing the overwhelming strength of feeling about the importance of this drug reaching eligible patients. Breast Cancer Now has received a number of statements from women and their families who are 1) currently being treated with Trodelvy and want others to have the same opportunity to benefit from this treatment 2) have incurable secondary triple negative breast cancer and need this drug to be available so they can access it when they need it or 3) people who have had primary triple negative breast cancer and fear recurrence and spread to secondary and want to know clinically-effective treatments are available for them on the NHS if they need them. These statements from patients (documented below) highlight the value that patients attach to the delay in progression of their disease, and the hope of more months to live. We would like the Committee to take account of these statements in making its final decision as we feel that these people's personal experiences of the drug and the implications of not having access for whom this will be a future treatment option form a significant base of important qualitative evidence for this appraisal.
8	Patients who are currently receiving Trodelvy: - *"I recently started Trodelvy. I've had 2 infusions. For me, even after 1 cycle/2 infusions I can already "feel" things are better. For someone who has had immunotherapy and a*

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	chemotherapy prior to this, with the immunotherapy causing hyper progression and the second also showing progression but smaller, Trodelvy is going to be an absolute lifeline for me. I'm lucky I managed to get started on Trodelvy otherwise my changes of having any targeted treatment was down to zero. For a [redacted] it means I haven't yet got to tell my sons I'm dying……It'll hopefully mean and show them I'm living and will live for as long as possible. I really really hope Trodelvy is approved otherwise we're left with nothing". - *"I am currently benefitting from the Gilead pre-reimbursement scheme. This is my 5th line drug following my secondary breast cancer diagnosis in [redacted]. Only one of the 'standard' chemotherapy drugs previously worked for me. Triple negative breast cancer is such an aggressive cancer and this is the first time we have seen a targeted drug. There is considerable excitement amongst the UK cancer community, especially when we talk to other patients in the USA who are having amazing results. I am awaiting scans but I can feel the difference in my lymph nodes after 2.5 cycles. I am very concerned that other patients will not be able to benefit from this new drug. This feels like a massive backwards step for the cancer community and will drive private funding which will bring financial divisions. It makes a mockery of all the fundraising and research trials if we find a drug that works but cannot make it accessible. I hope you can come to some agreement with Gilead to give EVERY patient with triple negative breast cancer the treatment and hope they deserve. The side effects of this treatment have been manageable for me".* - *"My husband and I campaigned with our hospital to get Trodelvy as our research led us to believe this was the best chance of saving my life. I'm due my third session of Trodelvy next week but the impact it's had on my overall-wellbeing and massively reduced my pain has been astonishing. My scan won't be for a good while yet, but I'm expecting to see a positive change in the cancer behaviour and size when it done. I'm 48 and our children are now adults. This my time to enjoy life."*
9	Patients with secondary triple negative breast cancer who may need Trodelvy in the future explain: - *"I am [redacted] and live with my fiancé and beautiful [redacted]. I was diagnosed with triple negative breast cancer in [redacted] when I was 6 months pregnant. I had a CT scan in late [redacted] and unfortunately this scan showed spread to multiple bones which looked like they had been there all along as they'd been 'treated' by the chemotherapy. I had another CT scan at the [redacted] which then showed progression to my liver. I am waiting to see what treatment I should start on. I'm still in absolute shock that I am living with secondary breast cancer All I know right now is that I need to do absolutely everything I possibly can to fight to be here for as long as possible for my little baby boy. I am certain that at some point I am going to need access to Trodelvy to give me extra time with my baby which is why it's so important NICE approves this treatment for use on the NHS".* - *"I was diagnosed with Stage 4 TNBC [redacted] I am still on my first-line treatment, capecitabine, but the evidence suggests it's coming to the end of its usefulness. Since my primary treatment of EC and paclitaxel was so recent, the proposed plan was to move on to Trodelvy. NHS Scotland has already made the decision to use Trodelvy as a third-line treatment. I don't know what they have based their decision on but, if Scotland can do it, so, surely, can England and Wales. Otherwise there is a huge imbalance and injustice across the UK. NICE acknowledges that there is clear evidence that Trodelvy fills a massive gap in the treatment of Triple Negative breast cancer. It acknowledges that it not only extends life expectation (which it knows is limited) but it improves quality of life. That is what every*

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	human being, regardless of their value to society, deserves. It should be our right. I believed it was until I read this document. By the end, I recognised that, to save money, I and my fellow secondary triple negative breast cancer sufferers are expendable. A few lines just wipe away what may be the only opportunity remaining for a few more years with our loved ones. Many women are in their 20s to 40s. They have young families they will never see grow to adulthood. Trodelvy might at least give them more time together. Myself, I'm 70, I've lived a lot of my life, a useful and productive life dedicated to education - but I've not lived all of it. When I first heard about Trodelvy, it gave me a quiet hope. I didn't dwell on it because I knew it had been added to my treatment plan. I have implicit trust in my oncologist and he believes this is the drug for me when the time comes. But he is practical - he knows how few treatment options there are so he is eking out capecitabine for as long as possible so we don't run out of options too quickly. I hope that, between them, NICE, Gilead and NHS England/Wales will consider the human impact of whatever deal they manage or fail to manage to arrive at. I feel hopeless and expendable now." - *"I've just found out my TNBC has spread to my liver, with [redacted] this couldn't be worse news. My breast care nurse told me about this drug today, but then I've seen the news that it's unlikely to be approved and it's dashed my hopes once again."* - *"I have been living with secondary breast cancer for [redacted] of and have [redacted] I have had 8 different treatments so far with only 2 of them being successful. I am now out of options. I have been asking my hospital to try access trodelvy for the last 6 months but keep being told it isn't an option at this time. I don't have time to wait around. I deserve the chance to live longer, to be there for my children longer, to make memories and see them grow up. I NEED trodelvy to help me manage that and it needs to be available to EVERY woman that needs it."* - *"My Mother has stage 4 triple negative breast cancer. Her options are running out – currently it looks like capecitabine tablets have stopped working. We are devastated by the news that NICE have not recommended to approve Trodelvy for routine use on the NHS. It has produced fantastic results and would prolong my Mother's life. I am desperate to have the extra time that Trodelvy would give her and make memories with her before she is gone forever. I love her so much, she's my best friend and has helped me so much throughout my life to become the man I am today".* - *"I've had every NICE approved chemo since my secondary TNBC [redacted] all palliative. This 6th line of chemo has taken me from a Hepatectomy in June 2018 wondering if my then [redacted], would be alone in the world, to having the hope of seeing her reach her 21st. I'm currently on cycle 10 of Eribulin which is according to my consultant the last effective option she has confidence in. Once it stops she can't show the cancer anything new so it's my last chance of any effective defence on NHS. The importance to me of Trodelvy being approved for use on the NHS is simply about hope. Hope to enjoy another Summer with my [redacted] children, possibly seeing a couple of more Springs to walk my dog in the bluebells. There has been very little progress with TNBC. It feels like an extra burden on top of the cancer being terminal that it has less treatment options."* - *"I am [redacted] currently living with metastatic triple negative breast cancer that has spread to my lungs, liver and bones. Trodelvy would be one of the few treatment options available to me. I'm 2 years into diagnosis and am already on my third line of treatment. There are much more limited treatments for people with metastatic triple negative breast cancer and every treatment line can provide me with months or even years with loved ones. To not have this drug approved would suggest that the extra time it could give someone like me is not worth it and that for those us living with an extremely aggressive type of breast cancer, we should*

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	accept our current limited options and poor prognosis as our fate. [redacted], I don't feel that this is something I should have to do. Should it not be available on the NHS, I would have the option to try and pay for it myself, however due to the side effects from previous lines of treatment I am currently working reduced hours, already placing a strain on our financial situation. Friends and family have also already invested a lot of money is helping with my care and creating memories for us. The difference that this decision could make is life or death. At a time when we run out of the current lines of treatment, which are few with TNBC, Trodelvy could offer us longer to live as opposed to beginning end of life care." - *"I was relying on starting Trodelvy following my current treatment. Without it, I have a year to live, if I'm lucky. I was diagnosed with TNBC stage [redacted]. I had 6 months of chemo treatment consisting of 4 different drugs. I then had a mastectomy and lymph node clearance. Histology showed that there was 70% cancer cells remaining in the nodes and my tumour had only shrunk from 6.4cm to 5.1cm when removed. Breast margins were also still positive. Had 15 sessions of radiotherapy which completed the treatment in January. I had a repeat scan in February which showed that I had liver metastases. I have been started on another chemo drug this week that my oncologist feels may not work but at least I had a chance to start Trodelvy if this was unsuccessful. Trodelvy would have given me a little longer with my family than I have already been given. A chance to see children, now in their twenties, get married and settle down. I know I am luckier than most who have small children and will never get the chance to see them grow up. Trodelvy would just give so much hope to so many people in my position."* - *"I have triple negative metastatic breast cancer in my lymph nodes. I was hoping that Trodelvy would be available as a treatment when every day is precious. What is the point of producing a drug that can't be given to people who have very few other treatment options? So disappointed and hurt by this."* - *"I have triple negative breast cancer and fighting breast cancer for the 2nd time at the age of [redacted]. I have a [redacted] daughter this drug could help me see my daughter reach [redacted] I don't think there should be a price on this, as to me its priceless to me and my family and many other families fighting this horrible disease!!! It is hard enough without being denied treatment that has the potential to extend our lives!!"* - "*There's so little research done and available options for people with this type of breast cancer it's shocking that Trodelvy isn't being made available. So the alternative is to just sit back and wait to die."* - *"This drug may be needed to help my [redacted]. She has breast cancer which spread to her lungs and now to her brain and it is just a question of time. She is so brave, she has not given up and is at present holidaying in Yorkshire, visiting places on her bucket list."* - *"I am a [redacted] After my first diagnosis in [redacted] I found out my TNBC is back in [redacted] I have signed the open letter to address access and cost of Trodelvy for TNBC on NHS in the U.K. as we are a group of patients that have few very treatment options available and we often face a particularly bleak outlook - that this drug is so important. I am part of online communities where ladies with TNBC around the world are saying it is working for them and I am devastated that in the U.K. on the NHS our ladies may not have the same chance as elsewhere. TNBC patients are often younger age with young families and we are desperate to try everything we can to stay with our families."*
10	We have also heard from a number of women who have experience of primary triple negative breast

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	cancer and who fear that if their cancer was to return and spread to become secondary triple negative breast cancer, that there would be limited treatment options available: - *"I have had triple negative breast cancer in both breasts and am very worried that should I need Trodelvy in the future it won't be available on the NHS. So please, please make it available on the NHS."* - *"I was diagnosed December 2020 with triple negative breast cancer. I have just completed my treatment but am aware that I have a higher chance of reoccurrence due to having TNBC. I would like to know that in the future if I did get a reoccurrence or spread that I would be able to get any drugs that could help me spend more time with my precious [redacted] Families shouldn't be robbed of precious time just due to funding especially when there are limited treatments for aggressive cancers."* - *"I have recently finished treatment for primary Triple Negative Breast Cancer and had a complete response to the chemotherapy. Obviously, I hope that my cancer stays away and doesn't come back as secondaries, but the thought of there being fewer options available to extend my life should it happen is truly terrifying. This is especially scary / worrying as it is based on cost and not science!!!!"* - *"I suffered from triple negative breast cancer, both my mum and grandmother died from it I had mastectomy and chemotherapy...at present in remission but fully aware it could reoccur and the drug could mean the difference between life and death.....".* - *"I have had breast cancer twice 9 years apart, with the second occurrence resulting in a double mastectomy. I am now 9 years post the second occurrence, and having been told I have a very high chance of it returning am incredibly disappointed that this drug may not be available should I or others need it in the future as part of their treatment.* *Living with the ever increasing fear of cancer returning and learning that a new drug may not be readily available is, quite frankly, horrendous and frustrating in my mind."* - *"As someone who has had the all clear after surgery, chemotherapy and radiotherapy for TNBC, I am very concerned to hear that should my cancer return I would be limited in my treatment options because of cost. I fully support the work to find a solution that will ensure that those who have, or who could still develop, triple negative secondary cancer have Trodelvy available to them as a treatment option."* - *"I was diagnosed [redacted] with triple negative breast cancer in [redacted] underwent removal and sentinel node. I wasn't able to have chemotherapy due to other co-morbidities, so just had radiotherapy. There are no other drugs for me at this present time to prevent recurrence.I am obviously worried it may return and believe that Trodelvy would be my only hope, should it do so. So I wholeheartedly support the work to make it available on the NHS."*
	- *"I am begging you all to reverse this devastating provisional rejection of sacituzumab govitecan (Trodelvy). What is the value of a life? My daughters life was priceless. It is truly breathtaking to know that there is a drug that could provide hope and time for other patients. The wonderful drug Sacituzumab Govitecan may in years to come be spoken about in the same way as Edward Jenner's Smallpox vaccine. It could change the course of Breast Cancer history. Please think of the patients like my daughter who have so few treatment lines to help them. Please think of the joy your amazing drug could give. It is too late for my*

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	daughter but I beg you to think of not only the patients but their families and reconsider your provisional decision. A drug is only beneficial if it is being used for the good of its patients."

Insert extra rows as needed

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- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise and all information submitted under 'academic in confidence' in yellow. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more information.
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- Do not use abbreviations
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	METUPUK
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	[**Insert disclosure here**]
Name of commentator person completing form:	[redacted]
Comment number	**Comments**

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	Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.
Example 1	We are concerned that this recommendation may imply that ……..
1	• Has all of the relevant evidence been taken into account? The NHS is a devolved service, but the British public does not expect this to translate to inequalities in accessing essential treatment. Trodelvy is available to patients who need it in Scotland. We fail to understand how NICE has reached a different conclusion to the SMC by not approving Trodelvy for routine NHS treatment. When Breast Cancer Now launched the Time for Trodelvy campaign in 2021 to ensure all eligible patients could access the drug through the Gilead pre-reimbursement scheme, over 220,000 people signed their petition. Over 90,000 people have signed latest the Breast Cancer Now petition about the provisional rejection of Trodelvy for use on the NHS. These petitions reflect the strength of public opinion. Trodelvy was one of the first drugs to be fast tracked through Project Orbis, a programme which aims to deliver faster patient access to innovative cancer drugs. For patients in England, Project Orbis has failed to deliver Trodelvy. The evidence that patients and the public will infer from Trodelvy not being approved is that postcode lotteries remain within the NHS.
2	• Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? It is difficult to comment meaningfully with the confidential discounts and redactions. It is clear that the company and the committee will need to work together to agree a price structure for Trodelvy. This is a step change treatment for a breast cancer subtype which up until now has only had conventional chemotherapy as a treatment.
3	• Are the recommendations sound and a suitable basis for guidance to the NHS? No, the recommendations are not sound and suitable guidance. We understand that the NHS has to balance the cost of new technologies with the needs of the entire healthcare system. However, Trodelvy is the only targeted treatment available for mTNBC, addressing an unmet need for an aggressive subtype. Patients have contacted us, and are very distressed by the prospect of Trodelvy being unavailable to them. [redacted] is [redacted] medically retired doctor who was diagnosed with mTNBC in December 2020. [redacted] is currently failing her 3rd line treatment and her only chance of surviving more than 6 months is being prescribed Trodelvy. [redacted] writes: “I am absolutely devastated, Trodelvy is my only hope of surviving till the end of the year, I want to spend precious time with my [redacted] and [redacted] NICE’s decision not to fund Trodelvy has a massive impact on patients like me who have run out of options. We are supposed to have patient centred care, this is totally the opposite.” [redacted] died [redacted], less than seven months after her secondary diagnosis. She writes: “Please think of the patients like [redacted] who have so few treatment lines to help them. It is

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	too late for my [redacted], but I beg you to think of not only the patients but their families and reconsider your provisional decision. A drug is only beneficial if it is being used for the good of its patients." We believe that the committee and the company are in agreement about the benefits Trodelvy can offer patients with mTNBC and hope they can work together to ensure all eligible patients have access to this innovative treatment.
4	• Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity? Although the incidence and prevalence of diseases are beyond the scope of NICE technology appraisals, it is important for us as a patient group to acknowledge that triple negative breast cancer does discriminate. Triple negative breast cancer disproportionately affects younger people, almost always women, and also people of colour. In addition, younger people, particularly those in their 20s and 30s are most likely to have a delayed, missed or late stage diagnosis, and are most likely to be pregnant or post pregnancy. These groups are also most likely to have the poorest outcomes and shortest disease free survival.
5	
6	

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Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	NCRI
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	No links to the tobacco industry I have a number of disclosures (speakers fees, advisory boards and research funding) relating to my work with pharmaceutical companies including Gilead, as previously stated
Name of commentator person completing form:	Dr Alicia Okines

Comment number	**Comments**

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Example 1	We are concerned that this recommendation may imply that ……..
1	Although there is only one post-progression quality of life assessment available for the technology, I do not agree that it should be discounted. As clearly documented in the committee papers, patients who respond to treatment have a reduced burden of disease and improved quality of life. Although this can reasonably be expected to deteriorate post-progression with both the technology and the standard of care chemotherapy, because the burden of disease is lower for patients who received the technology, their QoL will, on average, remain superior to that of patients who did not receive the technology over time. The clear overall survival benefit demonstrates that patients will deteriorate and die sooner if they do not receive the technology, therefore accordingly their QoL will also deteriorate sooner.
2	The committee have recognised that this is an important drug for TNBC which represents a genuine step-change for this very poor prognosis cancer, where there is a significant unmet need. As such, approval of this agent is critical for women living with advanced TNBC.
3	
4	
5	
6	

Insert extra rows as needed

Checklist for submitting comments

- Use this comment form and submit it as a Word document (not a PDF).
- Complete the disclosure about links with, or funding from, the tobacco industry.
- Combine all comments from your organisation into 1 response. We cannot accept more than 1 set of comments from each organisation.
- Do not paste other tables into this table – type directly into the table.
- Please underline all confidential information, and separately highlight information that is submitted under 'commercial in confidence' in turquoise and all information submitted under 'academic in confidence' in yellow. If confidential information is submitted, please also send a 2nd version of your comment with that information replaced with the following text: 'academic / commercial in confidence information removed'. See the Guide to the processes of technology appraisal (section 3.1.23 to 3.1.29) for more information.
- Do not include medical information about yourself or another person from which you or the person could be identified.
- Do not use abbreviations
- Do not include attachments such as research articles, letters or leaflets. For copyright reasons, we will have to return comments forms that have attachments without reading them. You can resubmit your comments form without attachments, it must send it by the deadline.
- If you have received agreement from NICE to submit additional evidence with your comments on the appraisal consultation document, please submit these separately.

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NICE National Institute for Health and Care Excellence

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Consultation on the appraisal consultation document – deadline for comments 5pm on **Friday 29 April 2022**. Please submit via NICE Docs.

Note: We reserve the right to summarise and edit comments received during consultations, or not to publish them at all, if we consider the comments are too long, or publication would be unlawful or otherwise inappropriate.

Comments received during our consultations are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the comments we received, and are not endorsed by NICE, its officers or advisory committees.

Please return to: **NICE DOCS**

Comments on the ACD received from the public through the NICE Website

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

I am currently benefiting from the Gilead/NHS reimbursement scheme. This is my 5th line drug following my secondary breast cancer in [redacted]. Only one of the 'standard' chemo drugs previously worked for me.
TNBC is such an aggressive cancer and this is the first time we have seen a targeted drug. There is considerable excitement amongst the UK cancer community, especially when we talk to others patients in the USA who are having amazing results.
I am awaiting scans but I can feel the difference in my lymph nodes after 2.5 cycles.
I am very concerned that other patients will not be able to benefit from this new drug. This feels like a massive backwards step for the cancer community and will drive private funding which will bring financial divisions. It makes a mockery of all the cancer fundraising and research trials if we find a drug that works but cannot make it accessible.
I hope you can come to some agreement with Gilead to give EVERY patient with TNBC the treatment and hope they deserve.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

As someone who recently had TNBC and at high risk of it returning I appeal to you to reconsider. This drug helps extend the lives of those with terminal TNBC, many of whom are young women with young children.the disease more commonly affects younger women and provides them with vital time with their families, friends and to support their affairs out.

I appreciate the NHS has limited funds but you are putting a price on life. How would you feel if it was your, your wife or sister. Thank you

Name	[redacted]
Role	
Other role	

Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Recommendations

Sacituzumab is the last hope for people with secondary triple negative breast cancer. It can give them and their families many valuable months together. The cost of this is priceless and cannot be measured as just a monetary amount. For this reason I feel it should be allowed and available to anyone whose other treatment options have been exhausted.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Has all of the relevant evidence been taken into account?

No. Where is the evidence of how much anxiety and fear there is in patients unable to access this chemotherapy?

It is reccomended. It is working for those already recieving it. What if one of your family members needed it? Can you put a price on someones life??

As stated, triple negative cancer causes anxiety in patients, friends and family members. Not having access to life saving/life extending treatment cause more anxiety than is nessecary.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Recommendations

This evidence seemed to be accepted yet, offering this treatment in England for women who have a poor prognosis is being denied based on cost. This evidence in Scotland is accepted and this treatment is being offered. It does not make sense that England and Scotland have looked at the same evidence and come to such a different conclusion.

How can one nation in the United Kingdom offer something to women based on clinical need and another nation in the UK deny it based on cost. Are women in England inherently worth less in terms of their length and quality of life than women in Scotland?

Some women in England will be able to advocate or have advocates who will somehow manage to get the medication. Or the will move to Scotland. A woman who has less social capital (based on her race, or disability such as a learning disability) is far less likely to find a way to get this medication that a white, well connected non-disabled woman could.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

You can not put a price on someone's life, people with tnbc need the ootion of using this drug, I myself will need this product and you are denying me that right, you have no right to decide who lives and dies

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

Dear all,

I am a [redacted] female and have just completed my 8th cycle on this drug and it has given me great stability and pain relief. My quality of life at present it far better than when I was on conventional chemotherapies. I work full time for the nhs and have done so with few sick days on this treatment. The nhs budgets are stretched for sure but when you factor in the demographic profile of young women effected, their families, children and careers there is a contribution to society which is unquantifiable. We have so much yet to give the world and those we love. I wish you can renegotiated so everyone who finds themselves in this tragic set of circumstances like me to have the opportunity to this treatment. The past few years living with covid have been brutal and for those living with cancer even more of a challenge. Please allow TNBC some desperately needed access to what I believe to be a kinder treatment.

Kind regards
[redacted]

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Has all of the relevant evidence been taken into account? Yes
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence? Yes
- Are the recommendations sound and a suitable basis for guidance to the NHS? Yes
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity? No

[redacted] old Emergency Department Sister, I have recently been diagnosed with Metastatic Triple Negative Breast Cancer so have personal insight into the terrifying process women are facing regarding treatment options for this horrendous disease. Trodelvy brings hope, simply. Hope to watch children grow and witness milestones taken for granted by those in the world of the well. It is my view that this treatment should be available on the NHS to help facilitate this. Thank you. [redacted]

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

I am a stage 4 triple negative breast cancer patient. [redacted] and have been living with this diagnosis for now [redacted]. I have [redacted]

I sincerely hope that an agreement can be reached for funding for this drug. The thought of a potential life line for me breaks my heart. This drug is my glimmer of hope, hope of more time with my family. More time to see those special milestones, more time to create precious memories. I'm not ready to leave my children yet, please let them spend more time with their mummy. They don't deserve this.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Has all of the relevant evidence been taken into account?

The committee considered sacituzumab govitecan to be a highly effective treatment for people with triple-negative locally advanced or metastatic breast cancer who have a poor prognosis. " This evidence seemed to be accepted yet, offering this treatment in England for women who have a poor prognosis is being denied based on cost. This evidence in Scotland is accepted and this treatment is being offered. It does not make sense that England and Scotland have looked at the same evidence and come to such a different conclusion.

- Are the recommendations sound and a suitable basis for guidance to the NHS?

No. How can one nation in the United Kingdom offer something to women based on clinical need and another nation in the UK deny it based on cost. Are women in England inherently worth less in terms of their length and quality of life than women in Scotland?

- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Yes, some women in England will be able to advocate or have advocates who will somehow manage to get the medication. Or the will move to Scotland. A woman who has less social capital (based on her race, or disability such as a learning disability) is far less likely to find a way to get this medication that a white, well connected non-disabled woman could.

It is unacceptable that NICE in England is denying women in England an effective treatment, particularly one that is being offered in Scotland.

Name	[redacted]
Role	
Other role	
Organisation	[redacted]
Location	
Conflict	
Notes	

Comments on the ACD:

- Has all of the relevant evidence been taken into account?

The NHS is a devolved service, but the British public does not expect this to translate to inequalities in accessing essential treatment. Trodelvy is available to patients who need it in Scotland. We fail to understand how NICE has reached a different conclusion to the SMC by not approving Trodelvy for routine NHS treatment. When Breast Cancer Now launched the Time for Trodelvy campaign in 2021 to ensure all eligible patients could access the drug through the Gilead pre-reimbursement scheme, over 220,000 people signed their petition. Over 90,000 people have signed latest the Breast Cancer Now petition about the provisional rejection of Trodelvy for use on the NHS. These petitions reflect the strength of public opinion.
Trodelvy was one of the first drugs to be fast tracked through Project Orbis, a programme which aims to deliver faster patient access to innovative cancer drugs. For patients in England, Project Orbis has failed to deliver Trodelvy. The evidence that patients and the public will infer from Trodelvy not being approved is that postcode lotteries remain within the NHS.

- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

It is difficult to comment meaningfully with the confidential discounts and redactions. It is clear that the company and the committee will need to work together to agree a price structure for Trodelvy. This is a step change treatment for a breast cancer subtype which up until now has only had conventional chemotherapy as a treatment.

- Are the recommendations sound and a suitable basis for guidance to the NHS?

No, the recommendations are not sound and suitable guidance. We understand that the NHS has to balance the cost of new technologies with the needs of the entire healthcare system. However, Trodelvy is the only targeted treatment available for mTNBC, addressing an unmet need for an aggressive subtype. Patients have contacted us, and are very distressed by the prospect of Trodelvy being unavailable to them.
[redacted] is [redacted] who was diagnosed with mTNBC in December 2020. She is currently failing her 3rd line treatment and her only chance of surviving more than 6 months is being prescribed Trodelvy. She writes: "I am absolutely devastated, Trodelvy is my only hope of surviving till the end of the year, I want to spend precious time with my partner and two children aged 12 and 14. NICE's decision not to fund Trodelvy has a massive impact on patients like me who have run out of options. We are supposed to have patient centred care, this is totally the opposite."

[redacted] daughter [redacted] died aged 37, less than seven months after her secondary diagnosis. She writes: "Please think of the patients like Amy who have so few treatment lines to help them. It is too late for my Amy, but I beg you to think of not only the patients but their families and reconsider your provisional decision. A drug is only beneficial if it is being used for the good of its patients."

We believe that the committee and the company are in agreement about the benefits Trodelvy can offer patients with mTNBC and hope they can work together to ensure all eligible patients have access to this innovative treatment.

- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any

group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

Although the incidence and prevalence of diseases are beyond the scope of NICE technology appraisals, it is important for us as a patient group to acknowledge that triple negative breast cancer does discriminate. Triple negative breast cancer disproportionately affects younger people, almost always women, and also people of colour. In addition, younger people, particularly those in their 20s and 30s are most likely to have a delayed, missed or late stage diagnosis, and are most likely to be pregnant or post pregnancy. These groups are also most likely to have the poorest outcomes and shortest disease free survival.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Has all of the relevant evidence been taken into account?

Have NICE considered evidence (outside of trials) from the US where the drug is being used to treat primary triple negative breast cancers?

- Recommendations (committee-discussion)

It's plausible that quality of life is better while taking sacituzumab govitecan compared with standard chemotherapy, but not necessarily after progression

I am an administrator [redacted] for ladies with stage 4 triple negative breast cancer. Many of the group members have been granted sacituzumab govitecan on compassionate grounds by Gilead. The majority of those taking the drug have had remarkable results - unsurpassed by any previous chemotherapy/immunotherapy treatments. In several cases, ladies have achieved no evidence of disease meaning treatment has been stopped and maintenance provided to monitor ongoing health. It is not known whether the NED will be permanent or whether the patients may suffer a relapse but during this pause in treatment, the NHS is not funding any other drugs and therefore this should be taken into consideration. Certainly quality of life for many has been greatly improved.

- Proposed date for review of guidance

3 years is far too long to wait to review the guidance. This drug is having excellent results with some stage 4 patients in the UK. Discussions with Gilead, especially as the only barrier to providing the drug to patients in England is cost, should recommence.

Name	[redacted]

Role	
Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Has all of the relevant evidence been taken into account?

Sadly I do not believe that all evidence has been taken into account. Based on my personal circumstances, I do not believe that you can put a price on delaying the onset of metastatic TNBC
I am not in the consultations typical demographic, I'm a [redacted] white British women, who has 2 children [redacted]. I'm about to tell them that they will lose their mum sooner than needed as the NHS is not willing to pay for the best treatment for me How ludicrous does that sound!

- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

Given the costs are withheld from the document it makes it impossible for me to comment fairly on this. However, I would say that there shouldn't be a price associated with prolonging life, particularly in an area that has such poor outlooks - new medicine available should be received with open arms, and as wider studies prove their effectiveness, then negotiatons on a larger scale can take place.
Given TNBC is a small subset of total breast cancers, the cost per patient being treated can afford to be a little higher. Remember the NHS has budgeted to look after me into my 80's, just spend a little of that money sooner please.

- Are the recommendations sound and a suitable basis for guidance to the NHS?

Given I was advised my TNBC had metastasised on [redacted], and told by an NHS breast care nurse on [redacted] this new drug Trodelvy would be available for my future treatment from June, and that it had really positive outcomes I do not feel that it's a sound and suitable basis for NHS guidance.
It shows the importance that the teams dealing with patients place on this drug as an improved option for those suffering. This drug could literally prolong the quality of my life and my life overall. The fact that she was unaware that the recommendation is to not provide to the NHS shows they thought it would absolutely be approved.
The time it gives patients, and me, may be enough for me to see my children grow up and support my [redacted] how can saying something is too expensive be a justification for guidance to the NHS. Work together and find a solution, I beg you

- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

I do believe that because TNBC generally targets black women not as much effort has been put into reaching a positive conclusion. I am a white English

[redacted] woman so am not in the demographics you place reliance on within the recommendations. Perhaps you need to fully consider the views and stop being discriminatory. Every sort of person deserves to be able to fight their cancer with the best possible drugs available, don't limit availability because of cost. When you're dying you realise that money doesn't make the world go round, it's love and compassion. Please sort out a deal so we can use the life saving treatment sooner rather than later, so it's not too late for me.
I would say it's actually discriminatory against those fighting TNBC, other types of breast cancer have long term drugs available for them, why are you not prepared to spend the same amount of money on this one, even if it's over a shorter period of time.

- Has all of the relevant evidence been taken into account?

It's a fairly hard read for someone that was only [redacted]. I don't believe the statistical sample includes enough on different races and would propose that by putting this drug as available to the NHS over the next 5 years would ensure you get statistical relevance and save or prolong the quality of lives for hundreds of patients
Has the long term costs of hormone therapies been taken into account when considering the costs? Whilst the life may be shorter, the richness of the quality of that life cannot be overlooked.

- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

The costs were withheld from the documents, but not cost should be too much to save a persons life. What nobody knows the answer to is what leaps in medicine this drug could provide. If you don't try, you don't get etc. please reach a compromise to ensure treatment can be given. My life depends on it
You also need to consider the scale of the use of the drug. Because TNBC is a smaller subset of breast cancers, this means that the higher costs are in fact limited to that smaller subset. As a [redacted] I understand the tendering process and the need to keep tight cost control, however, when looking at the overall size of the target audience I think it's much smaller in the case of TNBC and therefore overall costs aren't as significant. Percentages and figures only tell part of the story, look beyond them to see the overall impact of approving this drug, vs the negative impact of not.

Name	[redacted]
Role	

Other role	
Organisation	
Location	
Conflict	
Notes	

Comments on the ACD:

- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

This decision setting up a disparity in access to the drug via the NHS in the UK. It raises the spectre of unequal access across the UK, as the Scottish Medicines Consortium (SMC) has already accepted its use north of the border. That is discriminatory.

- Recommendations

My Mother has stage 4 triple negative breast cancer with spread to bone and skin. Her options are running out – currently it looks like capecitabine tablets have stopped working. We are devastated by the news that NICE have not recommended to approve Trodelvy for routine use on the NHS. It has produced fantastic results and would prolong my Mother's life. It seems even more cruel that Trodelvy has been approved in Scotland and not England thus setting up a disparity in access to the drug via the NHS in the UK. This approval shows that the cost cannot be too high as stated by NICE. I am desperate to have the extra time that Trodelvy would give her and make memories with her before she is gone forever. I love her so much, she's my best friend and has helped me so much throughout my life to become the man I am today. There is a lack of targeted treatment compared with other types of Breast Cancer. NICE says it already recommends use of Roche's PD-L1 inhibitor Tecentriq (atezolizumab) as an alternative for Metastatic Triple Negative Breast Cancer-sadly this would not help my mother as she is PD-L1 negative on primary tumour. Trodelvy would offer a realistic increase in overall survival with a tolerable side effect profile and the impact psychologically of being diagnosed with a poor prognosis cancer with lack of treatment options. I urge you to change this terrible decision which will destroy all hope and tear apart families lives. If price is the issue as is alluded to- surely a deal can be negotiated at a price point which is acceptable to all parties to avoid a premature loss of life to many Metastatic Breast Cancer patients. The impact of this decision cannot be underestimated on myself and other families. I cannot sleep, eat or drink worrying about what the future holds. If this drug had been available to my mother as a first or second line treatment, I may not have had to give up my full time job to become a carer this soon. I have gone from earning 2k a month to £68 a week carers allowance. My mother is fit and ready and waiting to receive this treatment. She can't wait.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

The committee considered sacituzumab govitecan to be "a highly effective treatment for people with triple-negative locally advanced or metastatic breast cancer who have a poor prognosis. " The clinical efficacy is proven yet offering this treatment in England for women who have a poor prognosis is being denied based on cost. The evidence in Scotland has been accepted and this treatment is being offered. Therefore there is a discrepant outcome between England and Scotland based on the same evidence.

Women in England feel they are being denied life saving treatment because their lives are not considered worth the cost.

There is a risk of further inequity of access in England as some women will be financially able to move to Scotland for treatment while others will not . Those women already disadvantaged by poverty and discrimination will be further disadvantaged by treatment being dependent on financial means..

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

My cousin in her 30’s has been having this treatment & it seems to have benefited her hugely. She recovers from treatment so rapidly which allows her to manage everyday life & so much more. She has been travelling & getting outdoors the whole way through. This would not be the case if it was very tough rounds of chemotherapy. She is so young & this is another reason she needs to bounce back so fast for herself & her family who are spending as much time with her when she is able between treatments.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

Hi there a cousin of my is just finished my 8th cycle of this drug and is finding it very beneficial. The nhs funding of this is vital to ensure that she receives the treatment she vitally needs. I hope the decision makers here take such cases into account.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

My sister has been on this treatment for several months now and has remained stable. Trodelvy has given her a much better quality of life than previous chemotherapies. Please don't restrict access to the people who need this life line.

Name	[redacted]
Role	
Other role	
Organisation	
Location	
Conflict	
Notes	
Comments on the ACD:	

- Recommendations

My sister has been on this treatment for several months now and has remained stable. Trodelvy has given her a much better quality of life than previous chemotherapies. Please don't restrict access to the people who need this life line.

Name	[redacted]
Role	[redacted]
Other role	
Organisation	[redacted]
Location	
Conflict	
Notes	
Comments on the ACD:	

I read the NICE appraisal document on the "Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer" with great interest. As a health professional looking after patients with metastatic triple negative breast cancer and their poor survival outcome, I was very hopeful that the drug would become available for patients in the NHS as this is an important area of unmet need. It was disappointing that the drug has been declined by NICE especially based on the cost-effective estimates.

I would like to draw attention to two points as a clinician on the appraisal:

a. "It's plausible that quality of life is better while taking sacituzumab govitecan compared with standard chemotherapy, but not necessarily after progression": As a treating clinician, I would expect that the QOLis dependent on the tumour burden and based on RR, the quality of life is expected to be better not only during the treatment phase but up to 3-6 months post progression.

b. The long-term overall survival benefit for sacituzumab govitecan is uncertain: Based on the presented data, the joint generalised gamma curve is too pessimistic and not reflective of real time data for TPC arm. The clinical expert in the appraisal agreed that the 5-year OS for TPC is much closer to the joint log-logistic survival rates and I would agree this to be the case. Would the drug be cost efefctive using the joint log-logistic curve? If so, with some degree of uncertainty, will it not be beneficial for the drug to be made available for the needing patients.

I sincerely hope that NICE committee will look more favourable to the innovation with Sacituzumab govitecan and the drug would become available for NHS patients in the near future.

NICE National Institute for Health and Care Excellence

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Consultation on the appraisal consultation document – deadline for comments 5pm on **Friday 29 April 2022**. Please submit via NICE Docs.

	Please read the checklist for submitting comments at the end of this form. We cannot accept forms that are not filled in correctly. The Appraisal Committee is interested in receiving comments on the following: • **has all of the relevant evidence been taken into account?** • **are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?** • **are the provisional recommendations sound and a suitable basis for guidance to the NHS?** NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the preliminary recommendations may need changing in order to meet these aims. In particular, please tell us if the preliminary recommendations: • could have a different impact on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. Please provide any relevant information or data you have regarding such impacts and how they could be avoided or reduced**.**
Organisation name – Stakeholder or respondent (if you are responding as an individual rather than a registered stakeholder please leave blank):	Gilead Sciences Ltd
Disclosure Please disclose any past or current, direct or indirect links to, or funding from, the tobacco industry.	Gilead has no links to the Tobacco industry
Name of commentator person completing form:	Eleonora Lovato

Comment number	**Comments** Insert each comment in a new row. Do not paste other tables into this table, because your comments could get lost – type directly into this table.

Please return to: **NICE DOCS**

NICE National Institute for Health and Care Excellence

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

Consultation on the appraisal consultation document – deadline for comments 5pm on **Friday 29 April 2022**. Please submit via NICE Docs.

Introduction

We have carefully considered the Committee's assessment of the evidence submitted for the single technology appraisal for SG for treating triple-negative, advanced breast cancer [ID3942]. We thank the National Institute for Health and Care Excellence (NICE) for the opportunity to comment on the Appraisal Consultation Document (ACD).

We are disappointed by the conclusions reached by the Committee and the resulting preliminary guidance not to recommend SG.

We present a revised case with ICER of £48,760 per QALY for the Committee's consideration. This includes settings agreed at the ACD committee, apart from two critical points discussed below, and a revised PAS offer. Note that as agreed with NICE on 28 March, RDI was applied to the calculation of drug costs with wastage (in case vial sharing is not allowed).

In summary:

- We believe that there is strong evidence that the approach used by Gilead to estimate long-term survival of patients, the joint log-logistic extrapolation, is robust and represents the most reasonable interpretation of the available evidence:
    - Mature survival data observed at 30 months indicated higher survival in the ASCENT trial for both SG and TPC than applied in the model through the joint log-logistic extrapolation and much higher than the generalised gamma estimates
    - Clinical input during the committee meeting fits the joint log-logistic extrapolation more closely
    - Generalised gamma has been widely dismissed among clinical experts as too pessimistic
    - In fact, clinical input during the committee meeting aligned with the separately fitted log-logistic extrapolation for TPC. Assuming that is true for SG as well, it would result in a considerably lower ICER (£45,484). Therefore, our choice of joint log-logistic extrapolation in the base case can be considered conservative
- NICE has not allowed for persistent improvement in utilities for patients receiving SG vs current treatment after progression. In doing so they have failed to take account of all available evidence presented and supported by the opinion of clinical experts in the committee meeting. Specifically:
    - Higher post-progression utilities for SG vs TPC, due to a much lower tumour burden at the time of progression, are highly plausible and widely supported by expert clinical opinion. Clinical opinion also suggests that this difference is expected to last several months in the progressed state.
    - This effect is likely to last for an extended period post-progression. The revised base case utilises a difference in post-progression utilities for up to 6 months. Gilead deems this to be a plausible duration, as patients whose tumours shrunk in the pre-progression state are more likely to have a subsequent therapy and longer overall survival relative to their SG PFS.

SG is a ground-breaking innovation, receiving an MHRA Innovative Licensing and Access Pathway designation. As the Committee stated, it "considered sacituzumab govitecan to be a highly effective treatment for people with triple-negative locally advanced or metastatic breast cancer who have a poor prognosis." Negative guidance will impact severely on the small group of women with mTNBC but will have a disproportionate impact on young black women who are more often diagnosed with this condition.

We believe that current guidance fails to take account of evidence concerning post-progression utility and does not interpret the evidence around utilities or survival extrapolation properly resulting in

Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies [ID3942]

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	provisional guidance that does not represent sound guidance to the NHS. In what follows we give a detailed response on these two key points raised within the ACD and clarify a point that was only briefly mentioned in the ACD document. We hope that this response, together with the revised offer, will be sufficient to provide a positive recommendation to SG.
1	**Issues Raised in the ACD: Long-term overall survival with SG (ACD paragraph 3.14)** **Position: Long term overall survival is best represented by the joint log-logistic extrapolations** We are pleased that the Committee agreed that the joint survival modelling approach is appropriate. We also acknowledge that there is uncertainty regarding long-term survival in the minority of patients with the best outcomes. However, with the additional one-year follow-up data presented at the technical engagement stage, as the Committee pointed out, the data is mature, more mature than for many other oncology submissions to NICE. The ACD states that the Committee "agreed that the true survival extrapolation could be anywhere between the optimistic log-logistic and the more pessimistic generalised gamma models." However, given the data maturity and the undoubtedly large OS benefit of SG in a condition where most patient die in less than 1 year on conventional treatment, we believe that there is much stronger evidence for the joint log-logistic extrapolation than the generalised gamma distribution and that it is not accurate or reasonable to describe the true values as being "anywhere" between the two distributions. Two facts point to the greater plausibility of the joint log-logistic extrapolation compared with the generalised gamma distribution: 1. In the additional mature follow-up data from the ASCENT trial presented at Technical Engagement there was a highly statistically significant HR for median OS (0.51, p<0.0001). Observed survival rates at 30 months were 17.8% in the SG arm and 4.4% in the TPC arms, according to the Kaplan-Meier curves. These figures were higher than the predictions of both extrapolation types for both SG and TPC and clearly demonstrate the prolonged impact of SG on long-term survival. The trial data fit the predicted 30-month survival by the joint log-logistic extrapolation more closely than the generalised gamma distribution: a. Joint log-logistic extrapolation: 14.2% with SG and 5.5% with TPC b. Joint generalised gamma distribution: 12.2% with SG and 2.5% with TPC Based on these figures, the joint log-logistic extrapolation represents a slight underestimation of the treatment effect of SG and a slight overestimation of the effect of TPC. Therefore, it represents a relatively conservative approach. Indeed, the generalised gamma distribution represents a considerable underestimation for both treatment arms compared to survival observed in the ASCENT trial, but particularly that of patients treated with SG. 2. The clinician at the meeting suggested that the 60-month overall survival on TPC is about 1.4%. While this is slightly lower than the 1.7% estimated with the joint log-logistic curve, it is a lot closer than the 0.1% predicted survival by the joint generalised gamma distribution. In addition, clinical expert opinion elicited by Gilead universally dismissed joint generalised gamma as a plausible scenario, being too pessimistic in predicting overall survival at 5 years. In addition, slide 26 presented in the committee meeting slides (illustrated below) shows that the chosen base case of joint log-logistic is not the most favourable extrapolation from the perspective of SG. The independent log-logistic produces the most favourable predicted survival difference between SG and TPC (1.4% survival at 60 months for TPC and 5.2% for SG). This is a clinically plausible scenario that aligns with clinical expectation for TPC provided in the committee meeting. The results at 30 months also align better with observed data in the ASCENT trial than other extrapolations but still underestimate the observed survival for SG (15.1% [model] vs 17.8% [ASCENT] in the SG arm and 4.9% [model] vs 4.4% [ASCENT] in the TPC arm). Applying the independent log-logistic extrapolation in the model results in an

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ICER of £45,484, £3,275 lower than our revised base case. Therefore, our choice of joint log-logistic extrapolation in the base case is a conservative approach.

Table- projected survival rates up to 60 months (5 years) with different OS extrapolations

	Estimated survival rates		30 months	48 months	60 months
1	Joint log-logistic	SG	14.2%	6.8%	4.6%
		TPC	5.5%	2.5%	1.7%
2	Joint generalised gamma	SG	12.2%	3.6%	1.6%
		TPC	2.6%	0.4%	0.1%
3	Independent log-logistic	SG	15.1%	7.5%	5.2%
		TPC	4.9%	2.2%	1.4%
4	Independent generalised gamma	SG	11.5%	2.9%	1.1%
		TPC	3.0%	0.6%	0.2%

ERG Response

The new estimated company base case ICER is £48,760. This value already incorporates clinical arguments that
1. Tumor burden is reduced because the tumor shrinks in response to treatment, and that
2. The benefit of response lasts several months.

As these are not related with the choice of distribution and will be discussed in Point 3 of this response, the starting ICER for the ERG is the ICER that incorporates all agreed assumptions during AGM1.

With regards to the choice of extrapolation distribution, given that there is agreement around this being a true uncertainty in the appraisal, it is useful to maintain a sense of cumulative logic.

1. The two data cuts presented during the appraisal show minimal difference, as would be expected when the majority of deaths in a clinical trial have already been observed in the less mature data cut. Despite considerable maturity, trial data were never, at any point in the appraisal, used to compare the statistical performance of joint vs independent fitting. The statistical models were limited to testing which distribution should be preferred given a choice of joint vs independent fit.

   In this case, the joint model is chosen as a default, in the absence of statistical analyses to test whether the independent model provides a better statistical fit. Once this approach is accepted, any combination of independently fitted curves becomes irrelevant to the decision problem. Therefore, it is implausible to argue that a combination of independently fitted model (log-log) should be still used to assess which model is more optimistic.

   At this stage of the process, the choice of OS distribution is reduced to the joint - log-logistic or joint generalized gamma. The ICERs corresponding to the two distributions are £50,786 (log-logistic) and £54,384 (generalized gamma). The £50,786 ICER is the

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	base case at the new price offered by the manufacturer and is the most optimistic ICER in the plausible range.

2	**Issues Raised in the ACD: 2. utility values post-progression (ACD paragraph 3.12 and 3.13)** **Position: Some carry-over benefit from pre-progression utilities is expected.** A factually incorrect statement (corrected at the factual inaccuracy step upon review of the ERG report) was still presented in the Committee Slides (slide 21 "clinical study report concluded that EORTC QLQ C30 scores were similar for SG and TPC") and paragraph 3.12 in the ACD ("It also noted the clinical study report concluded that EORTC QLQ-C30 scores were similar for sacituzumab govitecan and treatment of physician's choice"). While the clinical study report did include this statement, the report had been superseded by subsequent post-hoc analysis described within the submission and provided to the ERG (linear mixed-effect regression model for repeated measures). The analysis showed clinically important and statistically significant improvements in several dimensions of quality of life (pain, fatigue), as measured on the EORTC QLQ-C30, that mapped into higher pre-progression utilities for SG. In light of the considerably higher pre-progression utilities, higher post-progression utilities 4 weeks after progression are clinically explained: these patients progressing from a much-improved tumour status. Progression, measured as growth of the target lesion that previously shrunk to a large extent, will be much less burdensome for the patients, compared to someone who did not have a treatment response. This was confirmed by the discussion that took place at the appraisal committee meeting [only briefly reflected in the ACD, in paragraph 3.13] – that the clinical lead of the CDF and the clinician still present at the meeting suggested that a carry-over effect of the utility benefit after progression is clinically plausible. Gilead has received additional input from three clinical experts following the ACD meeting who agreed that carry-over utility benefit due to SG is a reasonable assumption. Thereafter utilities would converge for patients receiving SG and those receiving TPC in the same way that overall survival projections eventually converge, with both utility and survival benefits of SG beyond progression being driven by reduced tumour burden at the point of progression. In our revised based case model we have taken a more conservative approach than previously and assumed complete convergence over 6 months. This additional clinical input confirms that that the ERG / Committee preferred approach of identical utilities immediately after progression is unreasonable and is not a valid interpretation of the evidence submitted or clinical opinion. The carry-over utility effect has been implemented for the revised model base case, by a partition of the progressive disease health state, into two tunnel states: one tracking patients with disease progression and alive for exactly 6 months; and one to track time beyond 6 months until death. Utility values were applied accordingly based on patients' time post-progression (i.e., 6-month cut-off).
ERG Response	**Utility improvement due to lower tumor burden after progression: Method applied by the company** The new model version submitted by the company includes an allowance for higher post-progression utility applied to SG, compared with TPC. The calculations added to the model are as follows: 1. At any cycle in the model, the proportion of people progressed at or within the prior 6 months is extracted from the (incident) progression curve in the model 2. The total state occupancy in post-progression is split between within 6 months after progression and after 6 months after progression

3. Utility weights are then applied to the first 6 months post-progression and to the remaining period in post progression.

Because the incident progression rate is net of deaths, the method applied seems correct. The table below provides the (discounted) estimated time spent in the first six months, and 6 months to end of alive period post -progression.

State	SG	TPC
LYs in PD (within 6 months)	[redacted]	[redacted]
LYs in PD (beyond 6 months)	[redacted]	[redacted]
SUM	[redacted]	[redacted]

The company applied utility weights listed in the table below:

Utility, PD-SG	[redacted]
Utility, PD-TPC	[redacted]
PD-overall	[redacted]

The value 0.653 is derived from TA639; it is the utility applied by the ERG to the post-progression period, for both treatments. The value for PD – TPC, [redacted], is derived from [redacted], applying the company estimated utility difference of [redacted] for SG. The company did not provide an explanation for the derivation of the value [redacted].
The company then recalculates the QALYs in the model as follows:

	Life years		Utility weights		QALYs	
State	**SG**	**TPC**	**SG**	**TPC**	**SG**	**TPC**
PD (within 6 months)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
PD (beyond 6 months)	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
SUM	[redacted]	[redacted]			[redacted]	[redacted]
Pre-progression					[redacted]	[redacted]
Total QALYs					[redacted]	[redacted]
Incremental QALYs					[redacted]	

The corresponding new estimated ICER is £48,760, the company's new base case.
This value is based on clinical arguments that
1. Tumor burden is reduced because the tumor shrinks in response to treatment, and that
2. The benefit of response lasts several months.

Critique

Data from the ASCENT CSR for response rates and duration for SG and TPC are reported in the Tables below. SG is undoubtedly associated with higher response rates, 35% vs less than 5% in

TPC. This difference finds a correspondence with clinical advice received by the company. The advice received also stated that longer response is likely, this is also reflected in the ASCENT data.

Response rates (ORR) / CR and PR	**SG**	**TPC**
ITT population	267	262
Measurable disease at baseline, n=	230	230
Objective Response Rate (CR or PR)	82 (34.9%)	11 (4.7%)
ITT objective response rate*	31%	4.2%
Best overall response		
Complete response (CR)	10 (4.3%)	2 (0.9%)
Partial response (PR)	72 (30.6%)	9 (3.9%)
Note: Independent Review Committee adjudicated data; Source: Table 27, ORR by IRC and Investigator Assessment (BM-ve Population), ASCENT IMMU-132 05 CSR, page 85. *ITT Data: Table Table 14.2.3.2, Analysis of Objective Response Rate (ORR) and Clinical Benefit Rate (CBR) - Independent Review, ITT Population. Page 195.		

Duration of response	**SG**	**TPC**
Evaluable patients, n=	82	11
Duration of response (months)	**6.64**	**3.5**
Duration of response (min-max)	1.3-19.5	1.4 – 8.8
Time to response	2.67	1.86
Source: Table 14.2.5.6 , Summary of Time to Objective Response and Duration of Response for Objective Responders- Independent Review ITT Population, ASCENT IMMU-132 05 CSR, Post-Text Tables, page 837		

However, the method used to apply the data from the ASCENT CSR is not coherent with the quantification of clinical benefit supported by the data and leads to the overestimation of the benefit.

1. **<u>Duration of response is measured from *time to response*, not from *time to progression*</u>**

   Women who respond to SG in ASCENT maintain response for an average 6.5 months. This period is measures starting from the time of ***response***, ***not after***

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	progression. This is reflected in the study definition of DOR very clearly and, we believe, in clinical advice.[1] The company applied higher utility for 6 months ***post-progression***, not ***post-response***. Time to response from the ASCENT CSR is 2.7 months into treatment, well before mean time spent in pre-progression in the model, 8.1 months. Of 6.65 mean months in response (ASCENT), 5.5 months are spent in the pre-progression state, where higher utility is already accounted for. Only approximately 1.2 months on average can be spent in response post-progression. This is the upper bound of the duration for ***post-progression*** improvement in utility that could be applied in the model, not 6 months. From another angle, the company's application of post-progression utility gain results in modelling utility as if DOR lasted 11.4 months *on average* (14.1 months post-model start – time to response, 2.7 months) for the alive cohort, almost double that reported in ASCENT. Whilst there are some patients that maintain duration of response for longer, these are a minority (the tail of the distribution), and most likely, patients that spend the longest time in pre-progression. We think it is implausible to assign an ***average*** duration of response of 11.4 months with SG. **2. <u>Proportion of people modelled to retain a higher utility as carry over from treatment.</u>** The company assumes that 100% of the cohort alive post-progression receives a benefit due to tumor shrinkage, and assigns higher post-progression utility to all. Data from ASCENT show response rates of 35%2. This is the conditional rate (conditional on being alive) that should be applied to the alive cohort in the model when incorporating improved utility based on the argument of tumor shrinkage carry-over. The rate of utility carry-over in the post-progression state cannot be higher than the response rate in pre-progression. The CSR also reports the proportion of women that achieve "clinical benefit", defined as CR, PR or stable disease for longer than 6 months; this rate is 48.9% (ASCENT CSR, Table 14.2.3.14, page 826). Assuming that stable disease is also associated with improved utility post-progression, 50% is the maximum possible proportion of the alive cohort that benefits from treatment, based on evidence. The 100% post-progression carry over applied by the company is not compatible with the data. 50% is the most optimistic assumption, with 35% being plausible and because this proportion includes approximately 30% partial responders and slightly less than 5% complete responders, the likely proportion of women that retain higher utility post-progression is likely to be somewhat lower.

[1] ASCENT investigators used RECIST criteria to determine progression, based on at least 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, as in Eisenhauer EA, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47.New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1)

[2] As a clarification, response rates can only be measured as long as people are alive, therefore the higher rates of response cannot be attributed to a larger number of people that survive.

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3. **<u>The company implies that for patients on TPC, utilities *improve* after 6 months in post-progression have passed</u>**

   This is an effect that often goes under the term 'rebound'. The application of utilities in the model for people in TPC –

   - [redacted] (pre-progression),
   - [redacted] (post-progression, first 6 months)
   - [redacted] (post progression, period from 6 months after to death)

   is implausible. Whilst this rebound ultimately has little effect on the TPC arm, because there are very few patients in the model at or after 12 months, it has the effect of retaining in the SG cohort some of the [redacted] utility gain assumed whilst on treatment with SG – in other words, utility with SG does not decrease by [redacted] post progression but only by [redacted].

Scenario analyses

The ERG recalculated the ICER using a range of assumptions for post-progression utility, proportion of the cohort that benefits and utility values.

ERG-calculated ICERs assume combinations of the following assumptions:

1. Duration of response 1.2 months past progression (base case) and an optimistic scenario, 3 months (corresponding to 8.5 months average DOR);
2. Proportion of responders to whom higher utility is applied: 50% or 35%
3. No utility rebound for TPC, implemented using the following utilities for the two comparators:
   a. Lower utility in post-progression for both SG and TPG, but higher for responders with SG
      i. utility for pre-progression and response with SG equal to utility in TA690, 0.653 (as per company assumptions)
      ii. utility in post-progression with TPC equal to utility with SG [redacted]) (as per company assumptions)
      iii. utility in post-progression, past duration of response: equal for SG and TPC, [redacted], with SG having lost the benefit accrued during treatment. This value differs from the [redacted] used by the company.

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Summary of results

- ERG ICER: Base case £50,876
- Adding response benefit post-progression for 1.2 months (base case)

		Proportion of responders, post-progression	
Utility post-progression		35%	50%
Utility with SG, whilst still in response	0.653	£52,557	£52,467
Utility with SG, post-response, post-progression	[redacted]		
Utility with TPC, post-progression	[redacted]		

Proportion of responders, post-progression			
35%	Cost	QALY	ICER
SG	[redacted]	[redacted]	£52,557
TPC	[redacted]	[redacted]	
50%	Cost	QALY	ICER
SG	[redacted]	[redacted]	£52,467
TPC	[redacted]	[redacted]	

- Adding response benefit post-progression for 3 months (average duration of response 9.6 months)

	Proportion of responders, post-progression	
Utility post-progression	35%	50%

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Utility with SG, whilst still in response	0.653	52,227	51,998
Utility with SG, post-response, post-progression	[redacted]		
Utility with TPC, post-progression	[redacted]		

Proportion of responders, post-progression			
35%	Cost	QALY	ICER
SG	[redacted]	[redacted]	£52,227
TPC	[redacted]	[redacted]	
50%	Cost	QALY	ICER
SG	[redacted]	[redacted]	£51,998
TPC	[redacted]	[redacted]	

In summary:

1. The proportion of responders that carry over utility gain from treatment despite 50% not reporting at best no response or clinical benefit, or progress without response, has a small impact on the ICER;
2. The ICER is rather sensitive to the assumption that patients on SG retain a fraction of the utility accrued with SG despite having progressed, not being in response and being on different treatments than SG (i.e. using the post-progression post response utility of [redacted]) (regardless of proportion of women in response)
3. The duration of response post progression, for values in excess of 11 months post-progression, has some effect on the ICER. The threshold value of duration of response **post-progression** (assuming 50% response during treatment) is approximately 16 months equivalent to a duration of response of 23.5 months.

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3	**Issues Raised in the ACD: 3. Uncertainty in QoL data (impact of drop-out on QoL; ACD paragraph 3.7)** The ERG raised the issue of missing QoL data for 11.7% of the treatment arm and 30.2% of the comparator arm and the ACD notes the opinion of clinical experts that participants in the TPC arm likely had earlier disease progression and deteriorated more quickly and that attrition upon progression is inevitable (ACD paragraph 3.7). Additional post-hoc analysis of patients who had baseline measurement but no follow-up due to withdrawal or progression confirms the opinion of the clinical experts. Analysis of 62 of the 79 (78%) QoL unevaluable patients in the TPC arm with baseline measures found that these patients had a larger number of prior therapies and had higher tumour burden (including a greater proportion with brain metastases) compared with patients in the TPC arm who completed at least 1 post-baseline assessment. 62 patients providing baseline EORTC measurements also indicate a clinically meaningful lower quality of life (Global health status of [redacted]) compared with those who completed at least 1 post-baseline assessment. Post-hoc analysis also shows that the non-evaluable population progressed more rapidly on treatment, with [redacted]. Overall survival of the QoL evaluable and non-evaluable patients on TPC also suggests a worse overall prognosis for patients not contributing to QoL data (Figure 1). **Figure 1. Overall survival in ASCENT in the TPC arm (QoL evaluable vs non-evaluable)** [redacted]

Insert extra rows as needed

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- Complete the disclosure about links with, or funding from, the tobacco industry.
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Time For Trodelvy

Dear Dr Véronique Walsh (General Manager & VP - UK & Ireland, Gilead), Amanda Pritchard (Chief Executive, NHS England) and Dr Samantha Roberts (Chief Executive, NICE),

We, the **114,366** signatories of this open letter, are writing urging you all to do everything you can and work together to find a solution to reverse this devastating provisional rejection of sacituzumab govitecan (Trodelvy) so this important new treatment can be made available for routine use on the NHS for eligible patients with incurable secondary triple negative breast cancer.

This group of patients already face devastatingly poor prognoses and limited treatment options which is why we need you to all put this group of patients first so that they are not left with the prospect of being denied the chance of more time to live as the drug isn't cost-effective at its current price.

Patients have already faced a rollercoaster of emotions regarding access to Trodelvy. Initially there was hope when this drug was making its way through the MHRA regulatory process. This was almost immediately replaced by uncertainty, due to the failure of Gilead to agree an interim access scheme with NHS England and concerns about whether Gilead could guarantee their pre-reimbursement access scheme was sufficient and ensure access for all eligible patients.

It is now absolutely crushing that we are left in a situation where there is a risk that patients could miss out on the hope of more time with their loved ones unless this provisional decision is reversed.

We can and must now find a way through this and we urge Gilead, NICE and NHS England to urgently work together to ensure Trodelvy can be recommended for routine use on the NHS. This includes Gilead doing everything possible to ensure the drug is priced at a level that ensures its routine availability on the NHS.

Finally, whilst we find ourselves in this uncertain situation, we urgently call on Gilead to guarantee that their pre-reimbursement access scheme will remain open and continue to accept all new eligible patients until a final positive decision is made by NICE.