National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

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

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Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	Breast Cancer Now	Yes it is appropriate to refer this topic to NICE for appraisal.	Comment noted.
	Gilead Sciences	This topic should be referred to NICE as matter of urgency due to the high unmet needs and extremely poor outcomes in this population who with existing therapy may only have as little 6 months of life left (ASCENT trial data).	Thank you for your comment. NICE has scheduled this topic into its work programme
Wording	Breast Cancer Now	Yes the remit reflects the issue correctly.	Comment noted.
	Gilead Sciences	Gilead anticipate that the marketing authorisation will be for "XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX", and therefore propose a change to the wording to reflect this.	Thank you for the licensing update. No changes needed to the remit as it is intended to be a broad outline of the appraisal question.
Timing Issues	Breast Cancer Now	It is crucial that this appraisal progresses as quickly as possible.	Thank you for your comment. NICE has

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		Firstly, triple negative breast cancer continues to lack new and effective treatment options and remains one of the greatest areas of unmet need in breast cancer. Triple negative tends to be more aggressive and patients have a poorer prognosis than other types of breast cancer. This new treatment provides hope for this patient group of a new treatment option with promising progression free survival and overall survival results. We now want to see this treatment assessed for use on the NHS to ultimately drive forward access to this innovative treatment for patients. Secondly, NICE aims to publish guidance within 90 days of marketing authorisation. We understand that this treatment could receive a marketing authorisation in the coming months through Project Orbis. It is therefore crucial that this appraisal is scheduled promptly in line with NICE's strategy to provide rapid, robust and responsive technology evaluation.	scheduled this topic into its work programme.
	Gilead Sciences	Adult patients with mTNBC have extremely poor outcomes and survival. Real-world data shows that mTNBC has the worst outcomes across all breast cancer subtypes by a significant margin (14.8 months median overall survival vs 58 months for HER2-positive and 44.8 months for HR-positive breast cancer, Delaloge et al, ESMO 2020), and has remained largely unchanged for many years. The latest CRUK figures suggest that as many as 1,700 patients may die from mTNBC in the next 12 months, and clinical expert and patient feedback is that there is an extremely high and urgent clinical need for sacituzumab govitecan, which is a novel therapy with proven efficacy in a phase III trial.	Comments noted.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Breast Cancer Now	The background information highlights that triple negative breast cancer is more frequently diagnosed in younger women and that it is more frequent amongst women with BRCA1 mutations. It should also be noted that black women are more likely to be diagnosed with triple negative breast cancer.	Thank you for your comment. The background information has been updated.
	Roche	We note the absence of reference to atezolizumab (Tecentriq®) in combination with nab-paclitaxel being available as the standard of care for the first-line treatment of patients with PD-L1+ (programmed death-ligand 1 positive) triple-negative breast cancer.	Thank you for your comment. This has not been included in the scope because it is used earlier in the pathway than the technology being appraised.
The technology/ intervention	Breast Cancer Now	Yes to the best of our knowledge.	Comment noted.
	Gilead Sciences	NICE clinical guideline 81 (2009, updated 2017) is discussed within the draft scope; however, this guideline does not specifically detail treatments for advanced TNBC. The NICE treatment pathway for advanced triple negative disease is found within the NICE pathway 'Managing advanced breast cancer' (updated 2020). Treatments discussed within guideline 81 and the NICE pathway are broadly similar for advanced breast cancer and advanced TNBC; atezolizumab with nab-paclitaxel is included within the pathway only, for patients whose tumours express PD-L1 at a level of 1% or more and who have not had previous chemotherapy for metastatic disease. For completeness and to highlight impact on end of life criteria, the typical life expectancy of patients with metastatic TNBC should be included: the survival outcome of patients with metastatic TNBC is approximately 14 months from diagnosis.	Thank you for your comments. No changes needed as atezolizumab is used earlier in the pathway than the technology being appraised.

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Population	Breast Cancer Now	The population appears to be defined appropriately.	Comment noted.
	Gilead Sciences	Gilead anticipate that the marketing authorisation will be for "XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX", and therefore propose a change to the wording to reflect this.	Thank you for your comment.
Comparators	Breast Cancer Now	We agree that capecitabine, vinorelbine and eribulin are the main options given on the NHS for the patient group being considered for this appraisal.	Comments noted.
	Gilead Sciences	Defining specific comparators at certain stages of the metastatic TNBC treatment pathway is challenging, as the choice of an individual patient's treatment is dependent on a number of factors, such as prior therapies received, which can vary depending on stage at diagnosis, the patient's fitness level with regard to what they can tolerate, and an individual patient's preferences. In particular, for patients diagnosed at and treated for early stage disease, the most effective therapies (anthracyclines, taxanes, alkylating agents, and platinum compounds) are used in the neoadjuvant setting, meaning they are not available for metastatic disease. However, after consultation with clinical experts, Gilead's view is that the three comparators identified in the scope are appropriate for the population outlined in the decision problem, and are well represented in the treatment of physician's choice arm of the ASCENT trial. Of the three comparators, clinical expert feedback suggests that eribulin may be described as "best alternative care".	Thank you for your comments.
Outcomes	Breast Cancer Now	Yes.	Comment noted.

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	Gilead Sciences	Please note that while treatment response rate will be considered as outcomes of interest in the clinical sections of the submission we do not anticipate it will play a prominent role in the CE model. The CE model will primarily be informed by the key clinical efficacy measures of overall survival and progression-free survival.	Comments noted.
Equality and Diversity	Breast Cancer Now	Please see comment above about the groups of women more likely to be diagnosed with triple negative breast cancer.	Comment noted.
	Gilead Sciences	We do not envisage any equality issues arising from the proposed remit and scope. However, it should be noted that the prevalence of TNBC is higher among people of African ancestry than among white people. Consequently, guidance that restricts the use of SG may disproportionately impact black people with TNBC.	Comments noted, this has been added to the background section of the scope.
Innovation	Breast Cancer Now	Yes we consider this to be an innovative antibody-drug conjugate which would be a step-change in the management of locally advanced and secondary (metastatic) triple negative breast cancer. There remain limited options in this setting and patients progress and urgently need new treatments with higher response rates, progression free survival and overall survival. It should be noted that this treatment is going through Project Orbis – which recognises the importance of delivering faster patient access to *innovative* cancer treatments with potentially significant benefits.	Thank you for your comments. The appraisal committee will consider the innovative nature of sacituzumab govitecan during the appraisal.
	Gilead Sciences	Sacituzumab govitecan is an innovative first-in-class antibody-drug conjugate that provides a targeted agent for the treatment of patients with mTNBC. Patients with mTNBC have very limited treatment options since the most effective agents have usually been used in early stage disease. Recent approvals of targeted, biomarker-driven therapies have provided treatment options for a subset of patients with mTNBC; however, not all patients with	Thank you for your comments. The appraisal committee will consider the innovative nature of sacituzumab

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		mTNBC express these biomarkers, and those who do still progress despite receiving targeted therapy. Therefore, many mTNBC patients have few treatment options other than chemotherapy at second and later lines and survival is poor. The substantially improved efficacy observed in the pivotal trial, including improvement in overall survival of approximately 5 months and a reduction in the risk of death of 52%, represents a step change from current disease management with cytotoxic chemotherapies and a significant amount of extra time for patients.	govitecan during the appraisal.
Questions for consultation	Gilead Sciences	*Have all relevant comparators for sacituzumab govitecan been included in the scope? Is a comparison with best supportive care relevant for this population?* Please see comments on comparators above. Best supportive care is not a relevant comparator for this population, since patients eligible to be treated with SG will also be eligible for current standard of care. *Are there any subgroups of people in whom sacituzumab govitecan is expected to be more clinically effective and cost effective or other groups that should be examined separately?* No. All pre-defined subgroups in the ASCENT trial showed numerical clinical benefit in favour of SG vs treatment of physician's choice (TPC). *Where do you consider sacituzumab govitecan will fit into the existing NICE pathway, Managing advanced breast cancer - NICE Pathways?* Clinical expert feedback states that SG should be used as early in the treatment pathway as possible, particularly in patients with no targets such as PD-L1 or BRCA mutations, due to high unmet need and significant patient drop-off between lines of therapy. According to the anticipated licence, XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	Comments noted.

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		XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX XXXXXXXXXXXXXXXXXXXXXXXX. *Do you consider that the use of sacituzumab govitecan can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?* People with TNBC are typically younger than those with other forms of breast cancer, and consequently are more likely to have paid employment and young children. The significant prolongation of life conferred by a drug such as SG is therefore likely to have benefits to society in terms of recipients continued economic activity and the reduced need for society to care for their children. *Would it be appropriate to use the cost comparison methodology for this topic?* Cost-effectiveness analysis will be included in this submission. Sacituzumab govitecan is expected to provide improved clinical outcomes at likely greater cost than current treatment, making cost-comparison an inappropriate choice. *Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?* Sacituzumab govitecan has demonstrated significantly improved efficacy over physician's choice of chemotherapy as shown in the ASCENT trial. The trial demonstrated improvements in median PFS (4.8 versus 1.7 months; HR: 0.433; p<0.0001) and OS (11.8 vs 6.9 months; HR: 0.51; p<0.0001) in the ITT population for sacituzumab govitecan versus physician's choice of chemotherapy.	

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		Total resource use associated with sacituzumab govitecan has not been determined at this stage but may be expected to be higher than comparators due to the generally low acquisition cost of chemotherapy. *Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?* The primary and secondary endpoints from the ASCENT trial are PFS and OS, which are clinically relevant endpoints in oncology clinical trials. *Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?* Not to the best of Gilead's knowledge.	