Pembrolizumab with chemotherapy for neoadjuvant and adjuvant treatment of early and locally advanced non-metastatic triple negative breast cancer

For public – all confidential information redacted

Technology appraisal committee A - 13 September 2022

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Company: MSD

Process: STA 2018

NICE

Key clinical issues

Clinical effectiveness and generalisability

- Marketing authorisation includes adults with locally advanced disease or early stage disease at high risk of recurrence, for neoadjuvant treatment and *continued* as adjuvant treatment
  - is population in KEYNOTE-522 (key clinical trial) generalisable to the marketing authorisation and to people treated in the NHS?
  - is it expected that full neoadjuvant and adjuvant treatment course will always be given?
- KEYNOTE-522 includes various chemotherapy treatments as neoadjuvant treatment
  - is the chemotherapy regimen for neoadjuvant treatment in the intervention and placebo arm reflective of NHS practice?
- KEYNOTE-522 compares pembrolizumab monotherapy as adjuvant treatment with placebo (watch and wait)
  - is the watch and wait approach in adjuvant stage reflective of NHS practice; is capecitabine used?
- Pre-specified subgroup analysis of KEYNOTE-522 does not show benefit with pembrolizumab for people with ECOG score 1 or people in Europe
  - does KEYNOTE-522 provide sufficient evidence of effectiveness with pembrolizumab for people with a) any ECOG status and b) people treated in the NHS?
  - is there a biological reason for any differences in effect by geographical location?

Adverse events

- Adverse events (serious adverse events and death) with pembrolizumab are higher than with comparator
  - are the adverse events seen with pembrolizumab in KEYNOTE-522 acceptable?

Abbreviations

Table 1 Abbreviations

TNBC	Triple-negative breast cancer
OS	Overall survival
DFS	Disease-free survival
QALY	Quality-adjusted life year
ICER	Incremental cost-effectiveness ratio
pCR	Pathological complete response

Background on triple negative breast cancer (TNBC)

TNBC associated with poor prognosis, high risk of relapse and short survival rates

Causes

- Some, but not all, TNBC associated with BRCA1 mutation and may run in families

Epidemiology

- Around 8,000 new TNBC cases every year, accounting for 15% of breast cancer diagnoses
- “More common in women aged under 40 and black women” (Breast Cancer Now)

Diagnosis and classification

- Characterised by lack of oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER-2) expression
- In early stage disease the cancer is small and only in the breast tissue or lymph nodes close to the breast
- Locally advanced disease has spread from the breast to lymph nodes close to the breast, to the skin of the breast or the chest wall, but not spread further

Prognosis

- TNBC has worse prognosis than hormone receptor-positive breast cancers

Patient expert perspectives

Limited treatment options available for a particularly high risk breast cancer with relatively poor prognosis

Submission from Breast Cancer Now

- Breast cancer diagnosis can cause considerable anxiety and impact emotional wellbeing, especially due to fear of recurrence
- Side effects and hospital visits for treatment impact wellbeing, everyday activities, ability to work and relationships
- Risk of triple negative breast cancer returning and spreading in the first few years after treatment is higher than for other breast cancers but there have been fewer treatment advances in recent years
- There may be side effects and additional hospital visits associated with adding pembrolizumab to current treatment, but patients often conclude that benefits of treatment outweigh side effects and additional burden

"When I thought my diagnosis couldn't get any worse, I was given the news that I had triple negative breast cancer"

"Higher risk of [cancer] returning…but there are fewer treatment options available to reduce that risk"

Professional organisation perspectives

Evidence of higher pathological complete response rates with pembrolizumab which is an important outcome for patients

Submission from NCRI-ACP-RCP-RCR

- Principle aim of neoadjuvant treatment is to induce pathological complete response (pCR) which is highly correlated with disease-free survival and highly prognostic
- pCR also associated with breast conservation surgery (rather than mastectomy or breast reconstruction)
- Potential increase in adverse events with adding pembrolizumab to treatment
- There is considerable heterogeneity in choice of neoadjuvant chemotherapy for TNBC
- For TNBC that does not achieve pCR with neoadjuvant chemotherapy, the treatment options for adjuvant treatment are non-standardised

Abbreviations: TNBC, triple-negative breast cancer; NCRI – National Cancer Research Institute; Association of Cancer Physicians; Royal College of Physicians; Royal College of Radiologists

Pembrolizumab (Keytruda, MSD)

Table 2 Technology details

Marketing authorisation – granted May 22	Indicated for treatment of adults with locally advanced, or early-stage triple-negative breast cancer at high risk of recurrence in combination with chemotherapy as neoadjuvant treatment and then continued as monotherapy as adjuvant treatment after surgery
Mechanism of action	Anti-programmed cell death 1 (PD-1) antibody which blocks immune suppression and reactivates T-cell anti-tumour activity
Administration	Neoadjuvant: • Pembrolizumab 200mg IV every 3 weeks for 8 cycles, plus chemotherapy Adjuvant: • Pembrolizumab 200mg IV every 3 weeks for 9 cycles
Price	• List price: £2,630 per 100mg • Confidential discount applicable

Abbreviations: MHRA, Medicines and Healthcare products Regulatory Agency; IV, intravenous

Treatment pathway

This appraisal considers addition of pembrolizumab to neoadjuvant chemotherapy + adjuvant treatment as monotherapy

Early stage (at high risk of recurrence) or locally advanced triple negative breast cancer

Neoadjuvant treatment

Chemotherapy: anthracycline taxane combination + platinum*

+ pembrolizumab?

*There is variability in treatment and different chemotherapy regimens may be used

Surgery

Adjuvant treatment

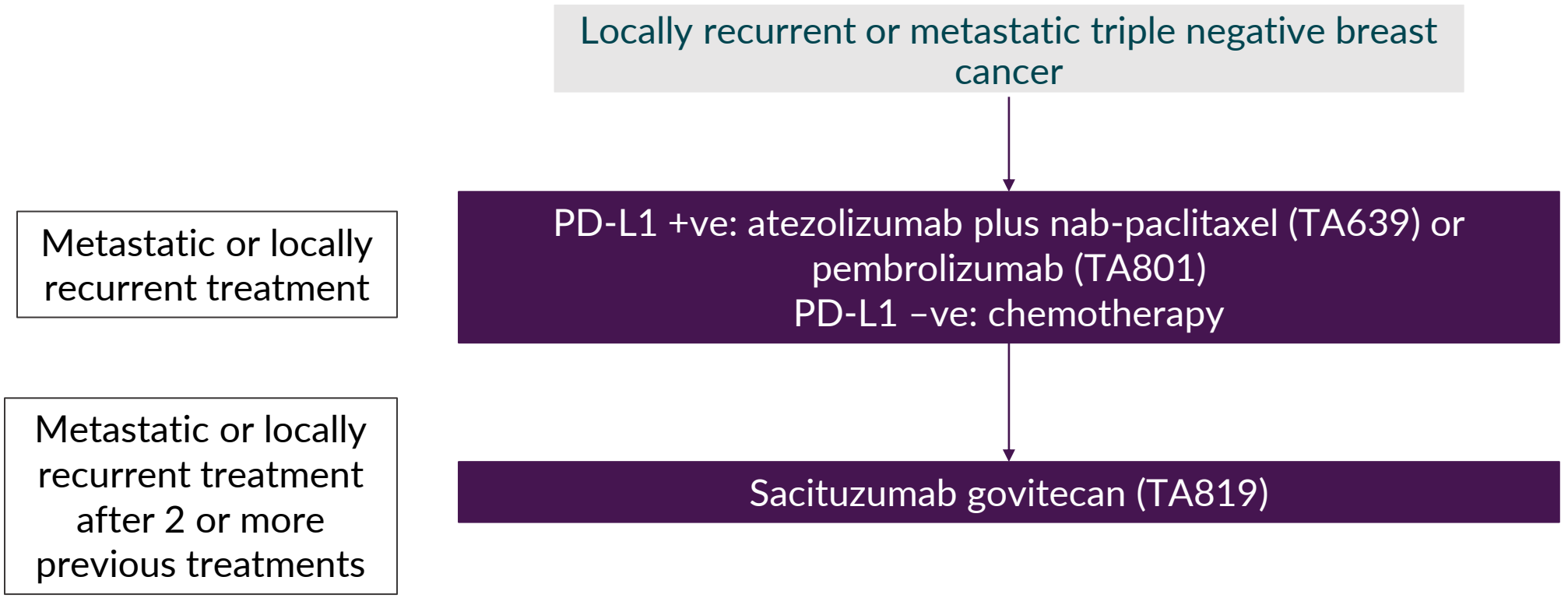
Monitoring only†

+ pembrolizumab monotherapy?

†Some people who do not obtain pathological complete response to neoadjuvant treatment may be considered for capecitabine

- How would population for treatment be defined (including high risk of recurrence)?
- Would response to neoadjuvant treatment and surgery influence choice to use adjuvant treatment?
- Would everyone receive the full neoadjuvant and adjuvant treatment course?

Metastatic or locally recurrent disease treatment pathway



If pembrolizumab was used for early stage or locally advanced disease, what would be the impact on treatment for metastatic or locally recurrent disease?

Key clinical trial: KEYNOTE-522

Table 3 Clinical trial designs and outcomes

	KEYNOTE-522
Design	Phase 3 randomised double blinded placebo controlled trial
Population	People with untreated newly diagnosed, locally advanced (and early?) centrally confirmed TNBC and have ECOG status 0 or 1
Intervention	Neoadjuvant: pembrolizumab + chemotherapy Adjuvant: pembrolizumab monotherapy
Comparators	Neoadjuvant: placebo + chemotherapy Adjuvant: placebo monotherapy
Primary outcome	Pathological complete response Event-free survival (aka disease-free survival)
Key secondary outcomes	Overall survival; adverse events; HRQoL; time on treatment
Locations	177 sites in 21 countries worldwide: 54 in Europe; 6 in UK (n=40)
Used in model?	Yes

Staging of ITT population:
- Stage 2 (75%); T1/T2 (74%)
- Stage 3 (25%); T3/T4 (26%)

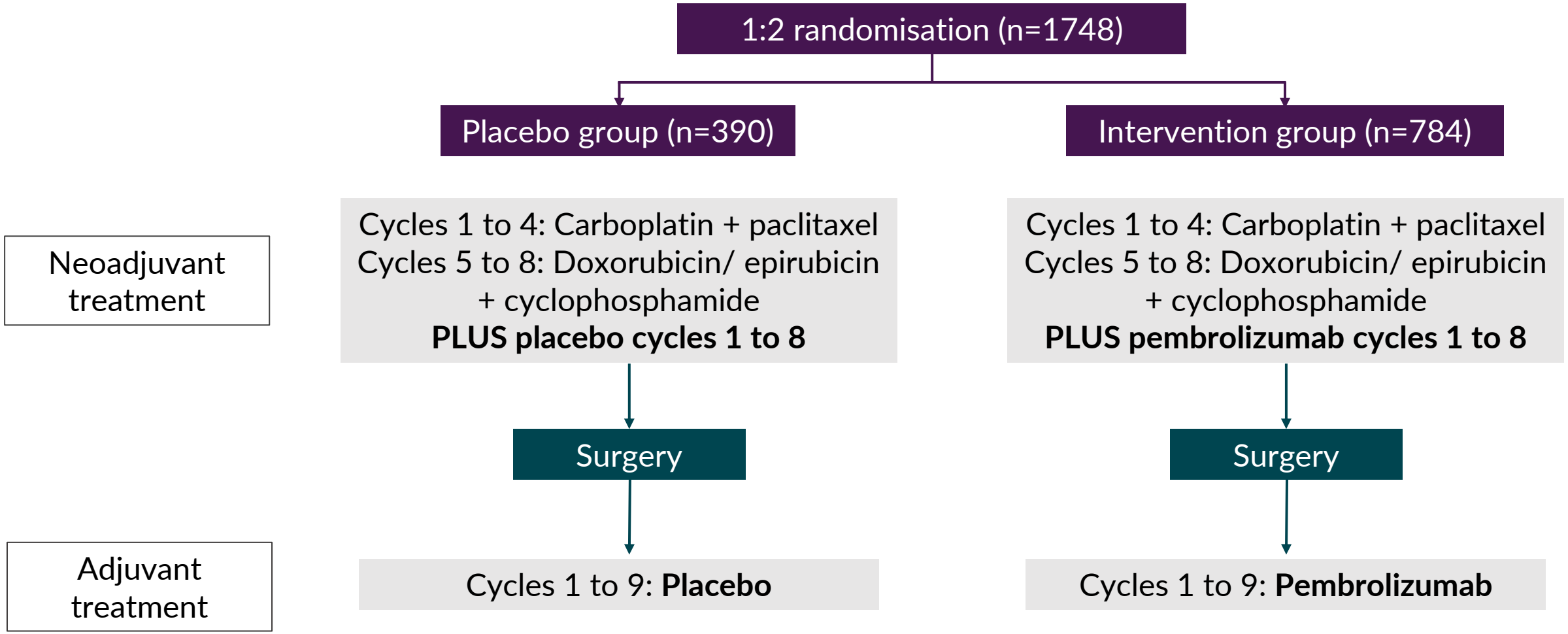
Professional organisation:
- KEYNOTE-522 is broadly reflective of NHS practice

Is the ITT population reflective of the marketing authorisation for early stage (at high risk of recurrence) and locally advanced TNBC?

Further evidence comes from KEYNOTE-355 (in metastatic TNBC; see slide 25)

Abbreviations: TNBC, triple negative breast cancer; ECOG, European Cooperative Oncology Group, ITT, intention to treat; HRQoL, health-related quality of life

KEYNOTE-522 trial design



- Is the chemotherapy given as neoadjuvant treatment generalisable to NHS practice?
- Is placebo as adjuvant treatment generalisable to NHS practice?

Decision problem

Population in company's decision problem includes early stage disease that is at high risk of recurrence only, in line with marketing authorisation

Table 4 Population and intervention from the scope

	Final scope (amended)*	Company	ERG comments	Clinical expert
Population	Adults with previously untreated early or locally advanced, non-metastatic triple-negative breast cancer	Adults with locally advanced or early triple-negative breast cancer which is **at high risk of recurrence** ***Reflects marketing authorisation***	High risk of recurrence not defined	High risk of recurrence difficult to define, but likely to include most stage 2 or 3 TNBC
Intervention	Pembrolizumab in combination with standard neoadjuvant chemotherapy followed by adjuvant pembrolizumab	As in scope	Intervention in line with scope	-

*population in scope amended at technical engagement to reflect marketing authorisation

Is the population in the company's decision problem – including people with early-stage disease at high risk of recurrence – identifiable and reflected in KEYNOTE-522?

Abbreviations: TNBC – triple negative breast cancer

Decision problem

Comparator in company's decision problem may not reflect NHS practice

Table 5 Comparators and outcomes from the scope

	Final scope	Company decision problem	ERG comments /company response at technical engagement	Clinical expert comments
Comparators	Standard neoadjuvant / adjuvant therapy without pembro	**Neoadjuvant:** Carboplatin + paclitaxel followed by doxorubicin/ epirubicin + cyclophosamide **Adjuvant:** Placebo	**ERG:** • Adjuvant phase only includes placebo monotherapy and may not reflect best available treatment - is capecitabine used? • Better efficacy with doxorubicin than epirubicin – is proportion of doxorubicin use in trial ([redacted]) reflective of use in NHS? **Company:** • Evidence for adjuvant capecitabine not comparable to KEYNOTE-522 trial design or population • Capecitabine cost low and used rarely for TNBC	Capecitabine might be considered as adjuvant treatment for TNBC that has not had pCR to neoadjuvant treatment
Outcomes	OS, pCR, DFS, AEs, HRQoL	As in scope	Outcomes in line with scope	-

- Should capecitabine adjuvant treatment be included as a comparator for TNBC that does not achieve pCR?
- Is doxorubicin use in KEYNOTE-522 generalisable to use in NHS practice?

Abbreviations: OS, overall survival; pCR, pathological complete response, DFS, disease-free survival; AE, adverse events; HRQoL, health-related quality of life

Clinical effectiveness

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KEYNOTE-522 results

KEYNORE-522 shows pembrolizumab is more effective than placebo in the ITT population for pathological complete response and disease-free survival

Median duration follow-up: 37.8 months (range 2.7 to 48.0)
Median disease-free survival and overall survival not reached in either arm

Table 6 KEYNOTE-522 results

Outcome	Pembrolizumab (n=784)	Placebo (n=390)	Hazard ratio
Pathological complete response rate (95% CI) , %	63.0 (59.5 to 66.4)	55.6 (50.6 to 60.6)	-
Disease-free survival rate at 42 months (95% CI, months) , %	83.5 (80.5 to 86.0)	74.9 (69.8 to 79.2)	0.63 (0.48 to 0.82)
Overall survival rate at 42 months (95% CI) , %	89.2 (86.7 to 91.3)	84.1 (79.5 to 87.7)	0.72 (0.51 to 1.02)

Professional organisation
Pathological complete response (pCR) is a recognised surrogate outcome and increasing the percentage of people achieving this is highly desirable

What could explain the less favourable result for overall survival compared with disease-free survival?

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Abbreviations: ITT, intention to treat, CI, confidence interval

KEYNOTE-522 results: Kaplan Meier curves for disease-free survival and overall survival

Figure 1 DFS Kaplan Meier curve from KEYNOTE 522

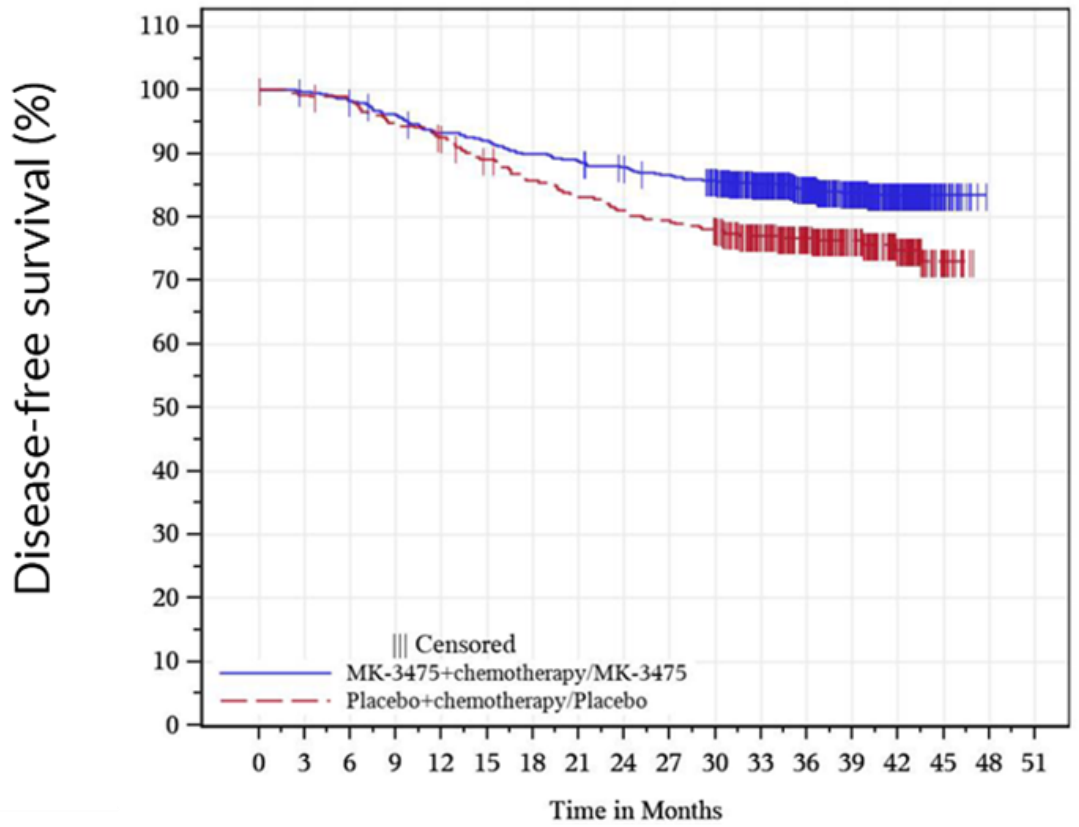
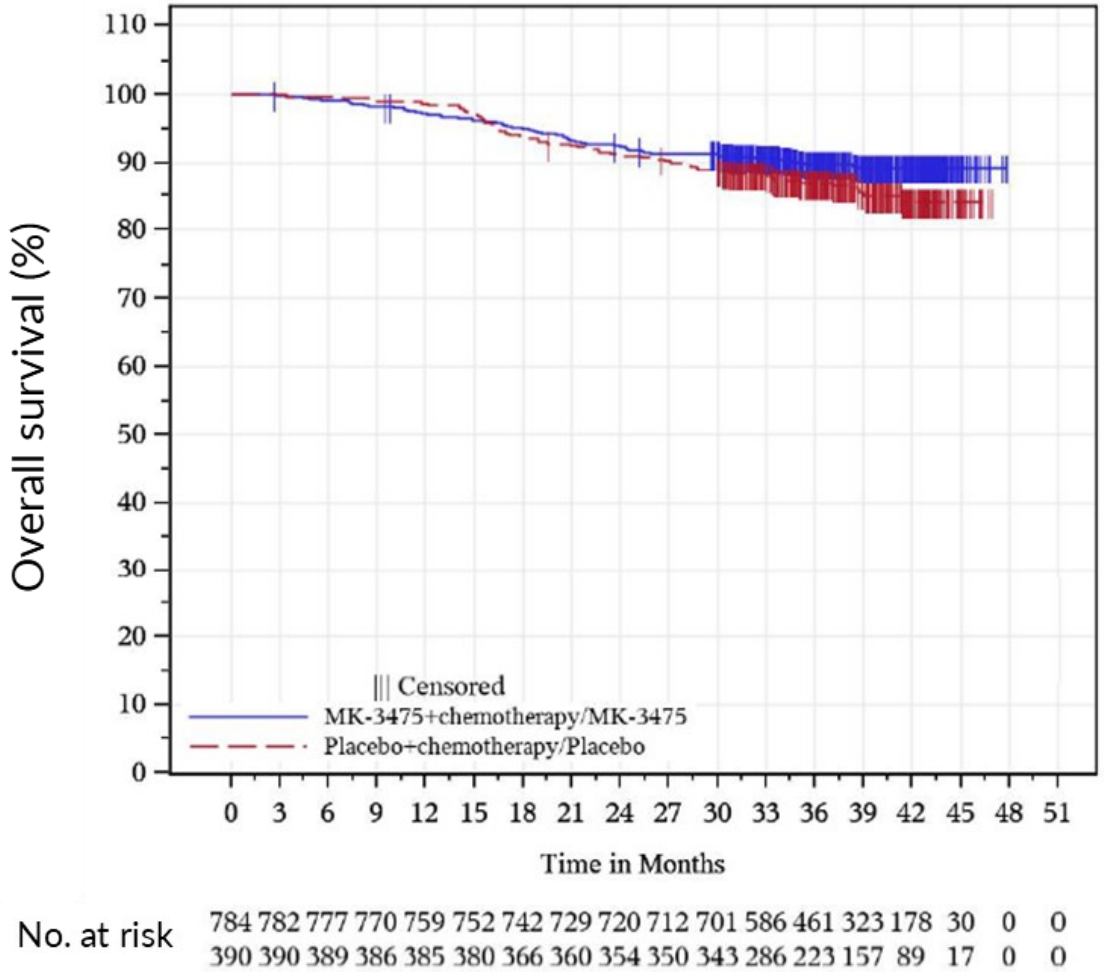


Figure 2 OS Kaplan Meier curve from KEYNOTE 522



Pembrolizumab + chemotherapy
Placebo + chemotherapy

KEYNOTE-522 subgroup results

Pembrolizumab benefit not shown for people with ECOG 1 and for people in Europe

ERG

Differences in effectiveness seen in some subgroups pre-specified in KEYNOTE-522 protocol (ECOG and region)

Table 7 KEYNOTE-522 disease free-survival (DFS) subgroup results by ECOG status or geographic region

		DFS HR (95% CI)
Overall		0.63 (0.48 to 0.82)
ECOG status score	ECOG 0 (n=1019)	0.60 (0.45 to 0.80)
	ECOG 1 (n=155)	0.81 (0.41 to 1.62)
Geographic region	Europe (n= [redacted])	[redacted]
	Rest of world (n= [redacted])	[redacted]

Company

- In ECOG 1 subgroup, participants in pembrolizumab arm were older (53.4 vs 47.0 years), included more post-menopausal people, people with PD-L1 CPS ≥10 and primary T3/T4 tumour than comparator arm
- Study not powered to show differences in these subgroups

Clinical experts

- No biological reason effects wouldn't be seen in UK population
- Unlikely ECOG score influences chance of pCR

- What is most likely explanation for difference in effectiveness across ECOG score and region?
- Should these differences be accounted for in the cost effectiveness estimate?

Abbreviations: ITT, intention to treat, HR, hazard ratio, CI, confidence interval, pCR, pathological complete response

Adverse events

Risk of death and serious adverse events within current follow up appears greater with pembrolizumab compared with placebo

Table 8 Summary of adverse events in KEYNOTE-522 (combined across neoadjuvant and adjuvant treatment)

Adverse events*, n	Pembrolizumab arm (n= 789)	Placebo arm (n= 389)
Any adverse event	777 (99.2%)	389 (100%)
Any grade 3 to 5 adverse event	645 (82.4%)	306 (78.7%)
Serious adverse event	341 (43.6%)	111 (28.5%)
Death due to drug-related adverse event	4 (0.5%)	1 (0.3%)

*measured up to 30 days (non-serious adverse events) or 90 days (serious adverse events) after last treatment

ERG

- Risk of death greater in pembrolizumab than placebo arm and difference in serious adverse events is large

Company

- No trends to indicate safety concern - no single adverse event resulting in death reported in more than 1 participant

Clinical experts

- Increase in risk of death needs to be assessed as data matures
- Insufficient evidence to attribute increased death to pembrolizumab

Is the adverse event profile acceptable for people with triple-negative breast cancer?

Cost effectiveness

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Key cost-effectiveness issues

Key:
ICER impacted mostly by: costs or QALYs

Biggest to lowest impact on ICER

Disease-free survival extrapolation

- Choice of extrapolation for disease-free survival (DFS) has large impact on ICER and is highly uncertain
  - which choice of extrapolation curves for DFS is most appropriate?

  ICER impacted by change in costs and QALYs

Pembrolizumab efficacy in model

- ERG use pembrolizumab efficacy adjusted using the Europe vs Rest of the world hazard ratio; company use KEYNOTE-522 whole population data
  - which analysis of pembrolizumab efficacy is appropriate for use in the model?

  ICER impacted mostly by change in QALYs

Data source for overall survival in distant metastasis

- OS data is immature. Company uses data from trial in metastatic triple negative breast cancer (KEYNOTE-355) to estimate overall survival (OS). ERG prefer to use KEYNOTE-522 data
  - which source of OS data is most appropriate?

  ICER impacted mostly by change in costs

Utilities

- Pooled utility values used in distant metastasis state, which are lower than values reported in other studies
  - are the utility values used for distant metastasis appropriate?

  Minimal impact on ICER

Abbreviations: DFS, disease-free survival, QALY, quality-adjusted life year, ICER, incremental cost effectiveness ratio, OS, overall survival

Company's model structure

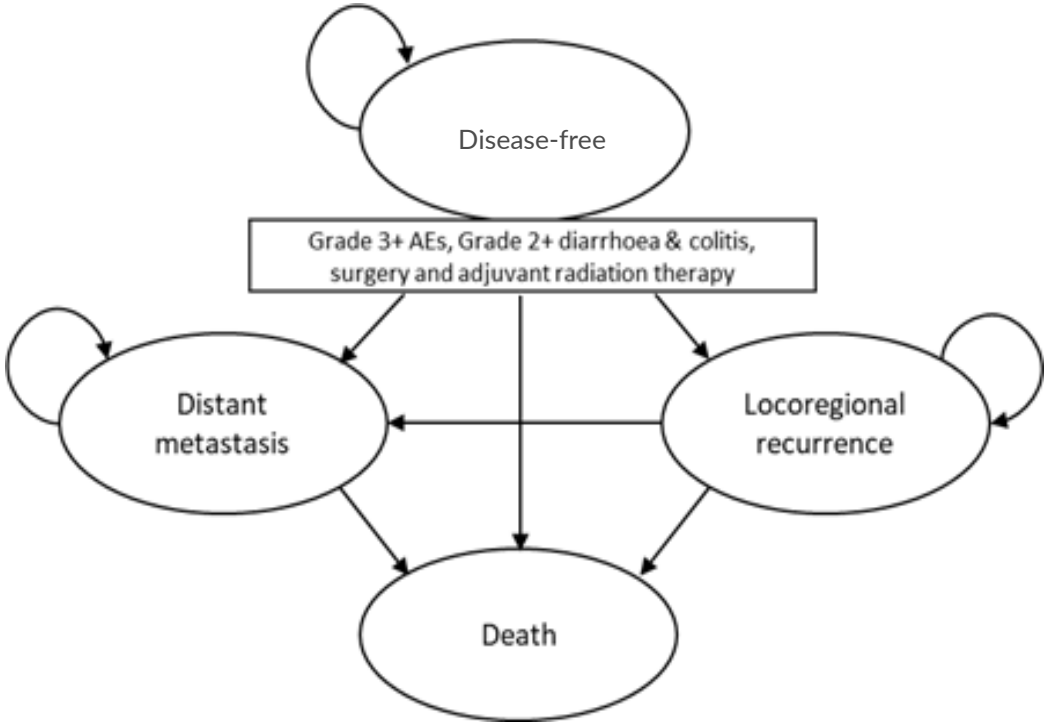

Table 9 Overview of company model inputs

Model type	• 4-state Markov cohort model • Simplified version of model in TA424*
Health states	• Disease-free • Locoregional recurrence • Distant metastasis • Death
Data sources	• KEYNOTE-522 for modelling disease-free survival • KEYNOTE-355 for modelling death from distant metastasis (see slide 25) • SEER Medicaid database for modelling death from DM for people not receiving metastatic treatment
Utilities	• EQ-5D-5L mapped to 3L from KEYNOTE-522
Treatment waning	• Not included
Time horizon	• 51 years (equates to lifetime)

*pertuzumab for locally advanced or early-stage HER2-positive breast cancer at high risk of recurrence

ERG

- Model does not differentiate between 'pre-progressed' and 'post-progressed' in DM state due to trial design
- Metastasis costed as a lump sum using multiple sources and make up third of costs in chemotherapy arm, with higher costs in chemotherapy arm

Company

- Limited data does not allow more complex modelling without making additional assumptions

SEER – Surveillance, Epidemiology and End Results; DM, distant metastasis

- Is it appropriate to not include treatment waning in model?
  - Is the model structure suitable for decision making?

Summary of company and ERG base case assumptions

ERG and company use different assumptions for DFS extrapolation, pembrolizumab efficacy and OS data source for people in distant metastasis

Table 10 Assumptions in company and ERG base case

Assumption	Company base case	ERG base case
DFS extrapolation pembrolizumab arm	Generalised gamma	Log-normal
Pembrolizumab efficacy	KEYNOTE-522 whole population data	Adjusted accounting for Europe vs Rest of world data
OS data for distant metastasis state	KEYNOTE-355	KEYNOTE-522

Biggest to smallest impact on ICER

Which assumptions does the committee prefer?

Abbreviations: OS, overall survival; DFS, disease-free survival; ToT, time on treatment

Survival models (1)

ERG and company prefer different extrapolation curves for disease-free survival (DFS) which has large impact on ICER

Company used:

- DFS: **generalised gamma** (pembrolizumab) and **log-normal** curve (placebo) - KEYNOTE-522 data
- Distant metastasis or death from locoregional recurrence: **exponential** curve (both arms) – KEYNOTE 522 data
- OS in distant metastasis state: **exponential** curve (both arms) - fitted to weighted average of people who did/did not receive treatment for metastatic disease – KEYNOTE-355 data

ERG

- Prefers **log-normal** DFS extrapolation for **both arms**
- DFS gain mostly observed in extrapolated period and post-extrapolation rate of survival gain is higher than pre-extrapolation – suggests lack of realism
- Transition probability from locoregional recurrence and distant metastases states assumed constant over entire time horizon
- Other cut points for DFS extrapolation may be appropriate

Company

- Pembrolizumab and chemotherapy have different mechanisms of action - alternative extrapolations appropriate for DFS in each arm
- Appropriate simplifying assumption to use a constant hazard to estimate transitions

Is it acceptable to use different extrapolation curves for the pembrolizumab and chemotherapy arms?

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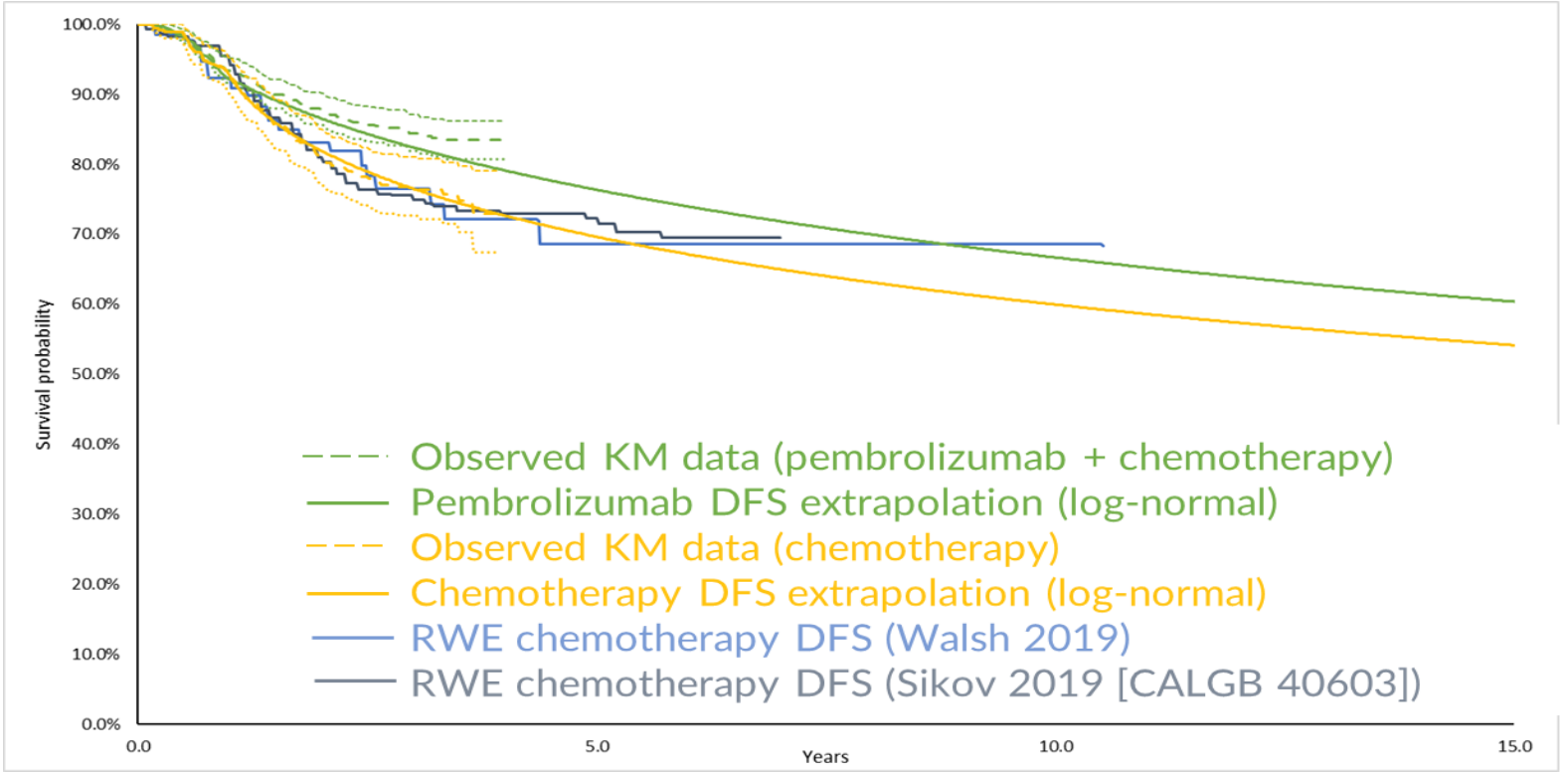
Abbreviations: DFS, disease-free survival, ICER, incremental-cost effectiveness ratio

Survival models (2)

Figure 3 Long-term DFS extrapolations, pembrolizumab arm

[redacted]

Figure 4 DFS log-normal extrapolations (both arms) compared with RWE



Company

- No plateau with pembrolizumab arm log-normal curve so too conservative – plateau seen with RWE of TNBC after chemotherapy
- Log-normal for pembrolizumab estimates 10% of events occur between 5 to 10 years – unlikely according to clinical experts

- Is a plateau in the number of events from DFS expected for early or locally advanced TNBC treated with pembrolizumab?
- Which curves best reflect what would be expected in the NHS?

Abbreviations: DFS, disease-free survival, RWE, real world evidence

Company use KEYNOTE-355 data to model overall survival in distant metastasis state

Table 11 KEYNOTE-355 trial design

	KEYNOTE-355
Design	Phase 3 randomised double blinded placebo controlled trial
Population	Recurrent inoperable or metastatic TNBC
Intervention	Pembrolizumab plus chemotherapy
Comparator	Chemotherapy alone
Primary outcome	Adverse events, PFS and OS

Company

- Used KEYNOTE-355 data as KEYNOTE-522 OS data immature

ERG

- Prefer to use KEYNOTE-522 OS data due to differences in observed survival between studies
- Note this doesn't resolve all uncertainties with OS modelling from DM state

Clinical experts

- Extrapolating evidence from KEYNOTE-355 to estimate survival in KEYNOTE-522 may not be appropriate as trials are not comparable

Is KEYNOTE-355 or KEYNOTE-522 data more appropriate to estimate OS in distant metastasis state?

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Abbreviations: PFS, progression-free survival; OS, overall survival; DM, distant metastasis

Utility values

Distant metastasis utilities relatively low but impact of changing values minimal

Background

- Model uses pooled utilities from pembrolizumab and placebo arms
- Based on KEYNOTE-522 EQ-5D-5L data, mapped to 3L

Table 12 KEYNOTE-522 pooled utility values used in model

Health state	Utility value (95% CI)
Event-free, on treatment	[redacted]
Event-free, off treatment	[redacted]
Local recurrence	[redacted]
Distant metastasis	[redacted]

ERG

- Utility for distant metastasis health state from KEYNOTE-522 relatively low compared to other studies (KEYNOTE-355 mTNBC pre-progression utility [redacted])
  - may be due to small number of EQ-5D questionnaires in distant metastasis state (n=[redacted])
  - KEYNOTE-522 does not record progression status for people with distant metastasis, therefore proportion who are progression-free vs progressed (which may influence utility value) is unknown
- Scenarios using values from metastatic breast cancer trials has limited impact on ICER

Company

- Caution against cross study comparisons of utility data due to different study populations
- Conducted 2 scenarios showing that higher utility values in distant metastasis state has limited impact on ICER

Abbreviations: mTNBC, metastatic triple negative breast cancer, ICER, incremental cost-effectiveness ratio

Cost-effectiveness results

As confidential discounts are available for subsequent treatments in the pathway, ICERs are not reported in Part 1.

ICERs including confidential discounts will be presented in Part 2.

Summary

- Company's base case is **lower** than what would usually be considered cost-effective use of NHS resources
- ERG's base case including adjusting pembrolizumab efficacy for Europe versus Rest of the World hazard ratio, is **higher** than what would usually be considered cost-effective use of NHS resources

Impact of ERG preferred assumptions on company base case ICER

Table 13 Impact of individual ERG preferred assumptions compared with company base case

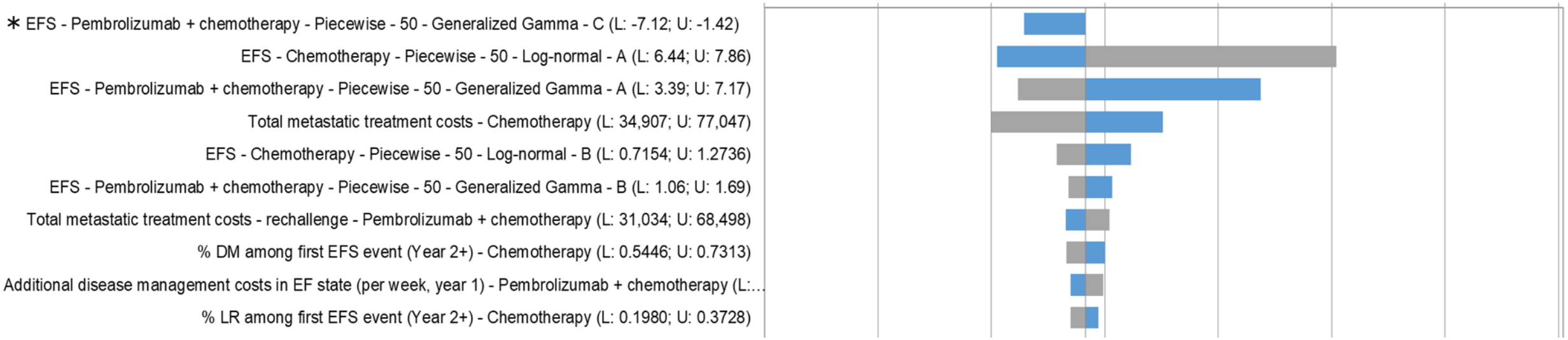
	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)
Log-normal for disease-free survival in both arms *Impacts both costs and QALY – biggest impact on ICER*			
KEYNOTE-522 data for distant metastasis survival + adjust treatment costs accordingly *Impacts costs more than QALYs*			
Correction for pembro efficacy adjusting for Europe vs Rest of the world hazard ratio *Impacts QALYs more than costs*			
ERG base case *Large increase in costs and large decrease in QALYs compared with company base case = higher ICER*			

Arrow indicates direction and scale of change in costs, QALYs or ICER **compared to company base case**

Abbreviations: ICER, incremental-cost effectiveness ratio, QALY, quality-adjusted life year

One-way sensitivity analysis on company base case

Figure 5 One-way sensitivity analysis showing biggest impacts on ICER



*Upper limit parameter pembrolizumab arm is dominated; therefore an ICER statistic cannot be presented

Abbreviations: EFS, event-free survival; ICER, incremental-cost effectiveness ratio

Impact of ERG deterministic scenario analyses on ERG base case

Table 14 Impact of ERG scenario analyses compared with ERG base case

Scenario (applied to ERG base case)	Incremental costs (£)	Incremental QALYs	ICER (£)
DFS extrapolation: log-normal (pembrolizumab), generalised gamma (placebo)*	↑	↓	↑
Using alternative distant metastasis utilities	=	=	=
DFS extrapolation: piecewise cut-off at 68 weeks	↓	↑	↓
DFS extrapolation: both arms generalised gamma	↓	↑	↓

ERG base case

Descending ICER

Arrow indicates direction and scale of change in costs, QALYs or ICER **compared to ERG base case**
= indicates no or negligible change to ERG base case

*Company state second best options as chosen by clinical experts; ERG used to explore uncertainty

Abbreviations: DFS, disease-free survival, ICER, incremental-cost effectiveness ratio, QALY, quality-adjusted life year

Other considerations

Future data

- [redacted]
- Disease-free survival null hypothesis has been rejected and therefore will not be further tested formally

Equality considerations

- None identified

Innovation

- Company: innovative treatment as first immunotherapy to be appraised by NICE for use in early stage or locally advanced triple negative breast cancer

Abbreviations: OS, overall survival

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Recent NICE appraisals for triple negative breast cancer (TNBC)

Pembrolizumab is recommended for treating advanced TNBC in some people

Pembrolizumab recently recommended for more advanced TNBC in a subgroup

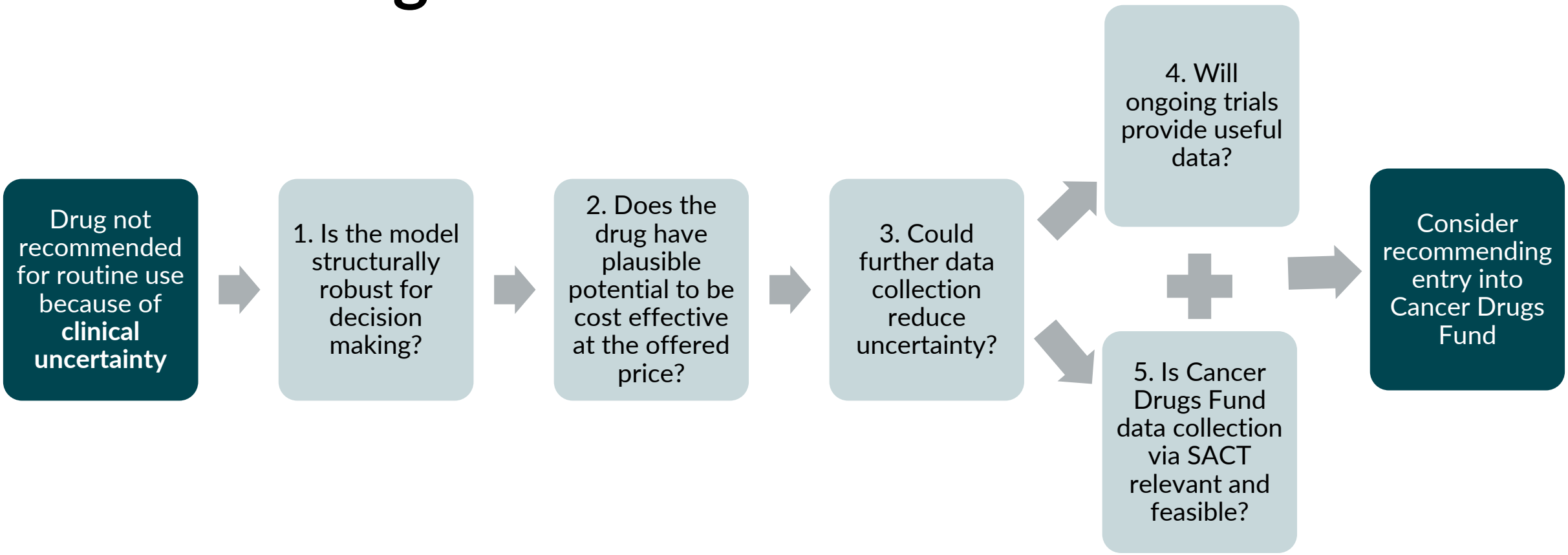
Table 15 Recent NICE appraisals

Technology appraisal	Drug	Recommendation
NICE TA801 June 2022	Pembrolizumab	Recommended with chemotherapy for triple negative, **locally recurrent unresectable or metastatic** breast cancer who have not had chemotherapy for metastatic disease (only if PD-L1 CPS ≥10 and immune cell staining <1%)

- KEYNOTE-522 results: no impact on treatment difference seen according to PD-L1 status
- No economic subgroup analysis based on PD-L1 status presented
- Professional organisation: pembrolizumab benefits not restricted to PD-L1 positive TNBC

Abbreviations: PD-L1 – programmed death-ligand 1; CPS – combined positive score; ITT – intention to treat

Cancer Drugs Fund



Define the nature and level of clinical uncertainty. Indicate the research question, analyses needed, and number of patients in the NHS in England needed to collect data.