Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after trastuzumab and a taxane

Slides for public – fully redacted

Technology appraisal committee A [11th October 2022]

Chair: Jane Adam

Lead team: Fiona MacPherson Smith, Mohit Sharma

Evidence assessment group: Newcastle NIHR

Technical team: Nigel Gumbleton, Elizabeth Bell, Henry Edwards

Company: Daiichi Sankyo

NICE National Institute for Health and Care Excellence

Key issues

Table 1 Key uncertainties and issues for discussion

Issue	ICER impact
Severity – should a severity weighting be applied	Large
Uncertain OS predictions for T-D arm after 2 years	Large
Post-progression utility values	Small
Vial wastage	Small
Generalisability of trial	Unknown

Abbreviations: AEs, adverse events; ICER, incremental cost-effectiveness ratio; OS, overall survival; PFS, progression free survival; T-D, trastuzumab deruxtecan

Context of Cancer Drugs Fund

Estimates of cost effectiveness

Company base case
> £30k/QALY

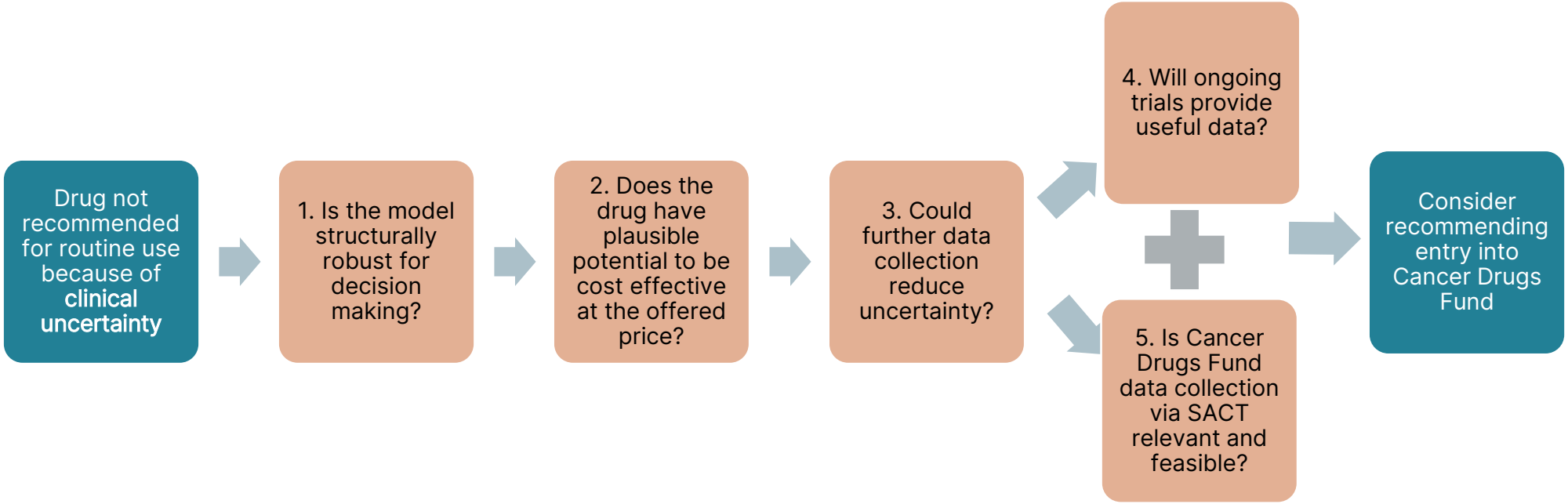
EAG base case
> £30/QALY

Company proposal for managed access

- Would like to be considered for routine use
- Company acknowledge evidential uncertainties
- Submitted a proposal for further data collection

NICE managed access feasibility assessment

- Consider it suitable for CDF
- Further data can be collected in managed access
  - Further effectiveness data in the trial
  - RWE from SACT to address generalisability



NICE

HER2-positive unresectable or metastatic breast cancer

Epidemiology

- 48,387 new BC cases in England in 2019, unresectable and metastatic are advanced forms of BC
- HER2 overexpression in 13 - 20% of BC tumours- aggressive disease that responds poorly to conventional chemotherapy and is treated with targeted treatments
- Company estimate 346 people would start treatment with T-D each year in England

Symptoms

- Metastatic disease has additional symptom burden including lethargy, reduced appetite, and weight loss, alongside symptoms specific to location of metastases

Prognosis

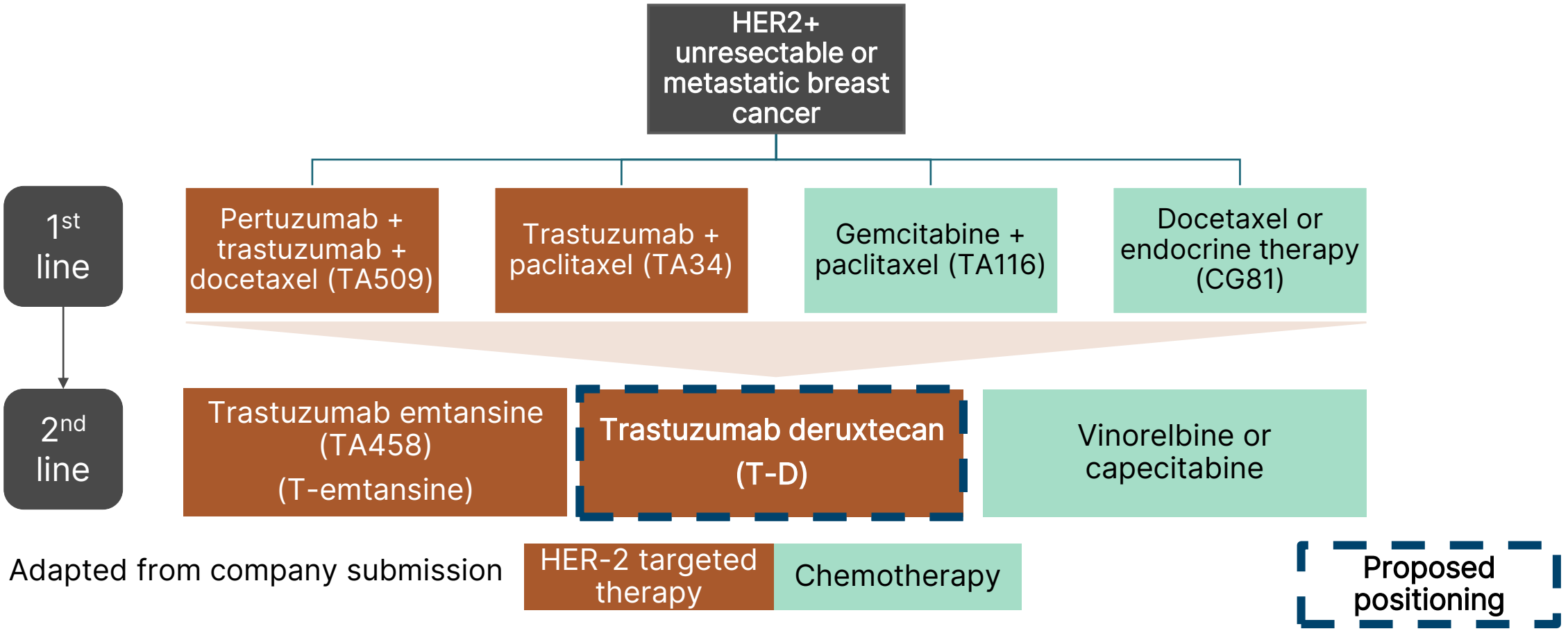
- No curative therapy for unresectable/metastatic BC. Stage IV 1- and 5-year survival of 66% and 27% respectively
    - No data identified specific to the subset of people with Stage III unresectable disease

NICE

Abbreviations: BC, breast cancer; HER2, Human Epidermal Growth Factor Receptor 2

Treatment pathway: HER2-positive unresectable or metastatic breast cancer

Figure 1 Treatment pathway in HER2-positive unresectable or metastatic breast cancer



Is this pathway consistent with UK clinical practice?

NICE

Abbreviations: BC, breast cancer; CG, Clinical Guidelines; HER2, Human Epidermal Growth Factor

Patient and carer perspectives

Submissions from: Breast Cancer Now, MET UP UK

- HER2-positive mBC is incurable and life-limiting disease → unmet need for therapies that control disease progression, extend life and have acceptable tolerability
- Value extra time progression-free
- Maintaining good quality of life for as long as possible is currently the best outcome
- Disadvantage of T-D is side effects. Experiences with side effects will vary, as will people's willingness to risk the side effects associated with treatment
- Do not want to lose T-emtansine, because there are limited lines of anti-HER2 therapies available on NHS → Not everyone will respond to T-D, and will value having T-emtansine as an option

"Keen to find treatments that will halt progression and extend life for as long as possible"

"Side effects have been manageable and in comparison to before [T-D]. I will take these side effects as what I have gained in quality of life is exceptional and I really didn't think after so long I would feel this well again"

"Important that any drug I take doesn't have horrific side effects… Drugs coming down the line for secondary breast cancer need to ensure quality of life. By the time of a secondary breast cancer diagnosis, we've been through so much"

Abbreviations: HER2, Human Epidermal Growth Factor; ILD, interstitial lung disease; mBC, metastatic breast cancer; T, trastuzumab; T-D, trastuzumab deruxtecan

Clinical perspectives

Submissions from: NCRI-ACP-RCP-RCR

- Metastatic HER2-positive breast cancer is incurable and progressive with poor prognosis and limited effective treatment options
- T-D is a HER2-targeted treatment that fills an unmet need in the 2nd line treatment. It is believed to be a therapeutic advancement due to its improved PFS rates and duration of response compared with current standard of care, T-emtansine
- D-B03 data show that T-D could lead to a prolonged period when disease is controlled with people remaining well and able to participate in family, work, and social activities
- Based on clinical experience, improvement of PFS and tumour responses relate to symptom control and subsequently better quality of life
- Special attention needs to be given to the risk of ILD (interstitial lung disease). Education is key. There should be an agreement in place regarding lung imaging in each institute

Unmet need for therapies that control disease progression for longer periods (by increasing progression free survival), extend life (by increasing overall survival) and have an acceptable tolerability and safety

T-D produces unprecedented response rates and may offer survival improvements

T-D is believed to be a therapeutic advancement due to its improved PFS rates compared with T-emtansine

Abbreviations: D-B03, DESTINY-Breast03; HER2, Human Epidermal Growth Factor; ILD, interstitial lung disease; PFS, progression free survival; T, trastuzumab; T-D, trastuzumab deruxtecan

Trastuzumab deruxtecan

Table 2 information about trastuzumab deruxtecan

Marketing authorisation	• Monotherapy for unresectable or metastatic HER2-positive breast cancer after one or more prior anti-HER2-based regimens • No stopping rule in marketing authorisation
Mechanism of action	• T-D - monoclonal antibody (trastuzumab) linked to a potent membrane-permeable topoisomerase I inhibitor (deruxtecan) • Trastuzumab selectively binds to HER2. Once bound, it is taken into the cell, carrying deruxtecan with it, which damages tumour cell DNA, resulting in cell death
Dosage and administration	• IV infusion 3 weekly (21-day cycle) until disease progression or unacceptable toxicity. The recommended dosage is 5.4 mg/kg
Price	• List price per 100mg vial = £1,455 • List price for 12 months of treatment =~£85,000 • A simple discount patient access scheme has been approved which is confidential

Decision problem: The population, intervention, comparators and outcomes in the company submission in line with the NICE scope

NICE

Abbreviations: HER2, Human Epidermal Growth Factor; IV, intravenous; T-D, trastuzumab deruxtecan

Clinical effectiveness

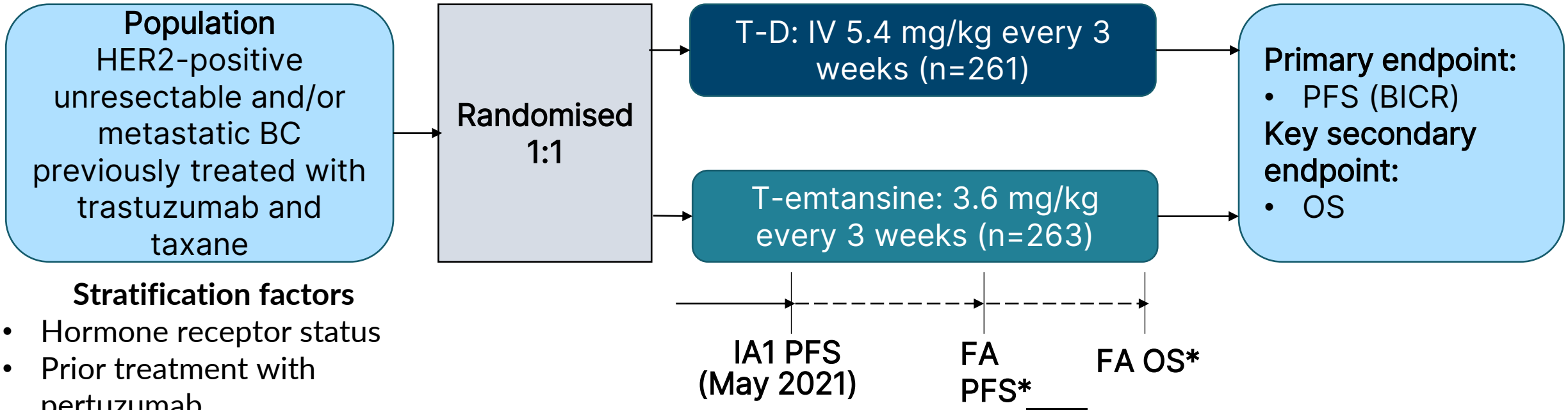
NICE National Institute for Health and Care Excellence

Key clinical trial - DESTINY-Breast03

Data for this submission from interim analysis May 2021

- Compared T-D with T-emtansine
- Phase III, multicentre, open-label, randomised, active-controlled, trial. 1:1 assignment was in parallel
- 169 centres in 15 countries; (North America, Europe (including UK), Asia, Australia, Brazil

Figure 2 DESTINY-Breast03 study design



Stratification factors

- Hormone receptor status
- Prior treatment with pertuzumab
- History of visceral disease

*planned analyses: FA of PFS by BICR at [redacted] PFS events (expected [redacted]); and FA OS at [redacted] OS events (approx. [redacted] months)

Abbreviations: BC, breast cancer; BICR, blinded independent central review; DOR, duration of response; FA, final analysis; HER2, human epidermal growth factor receptor 2; IA1, interim analysis; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; T, trastuzumab; T-D, trastuzumab deruxtecan

Generalisability of trial

Baseline characteristics may not reflect characteristics of those in England

Background

- D-B03 was an international study with [redacted] patients enrolled in UK

Differences from UK	Company response → subgroup analysis
> proportion of Asian family background	[redacted] for HR between people with Asian and non-Asian family background → [redacted] of Asian family background. TEAEs also suggest [redacted]
< proportion of smokers	Subgroup analysis of never smoked and current or former smokers showed [redacted] of T-D vs T-emtansine in both groups
> likelihood of Prior lines of therapy	Pre-specified & post-hoc analyses = no difference PFS based on lines of prior therapy
Assumed = European population	PFS by BICR showed [redacted] for T-D vs T-emtansine

EAG comments

- Small number in European subgroup is insufficient to rule out differences in outcome between regions → some uncertainties regarding generalisability to the NHS remain
- Subgroup analyses unable to assess impact of covariates or confounding

Are the results from DESTINY-Breast03 generalisable to NHS practice?

Abbreviations: D-B03, DESTINY-Breast03; CI, confidence interval; HR, hazard ratio; T, trastuzumab; T-D, trastuzumab deruxtecan; TEAE, treatment emergent adverse events

Clinical evidence - DESTINY-Breast03 results

PFS by BICR, and OS

Figure 3 Kaplan-Meier of PFS by BICR

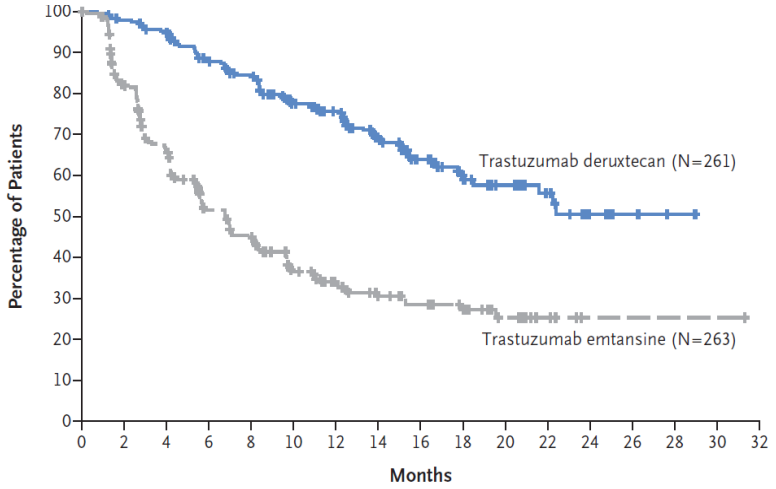


Figure 4 Kaplan-Meier of OS

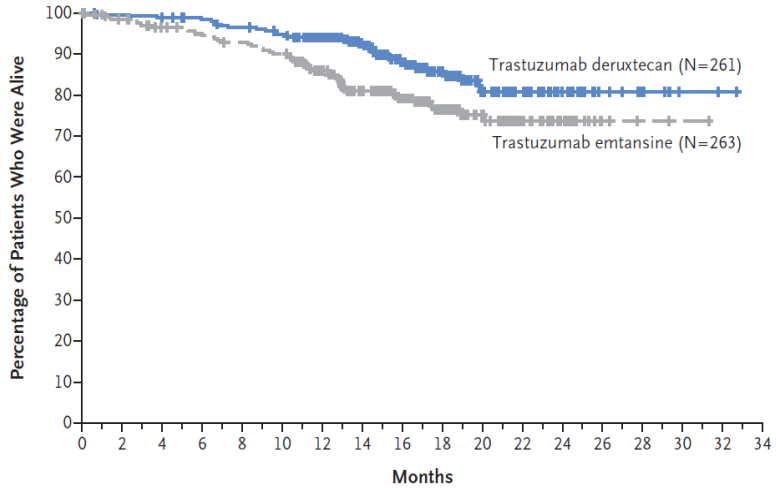


Table 3 Analysis of PFS by BICR

PFS	T-D (n=261)	T-emtansine (n=263)
Disease progression or death (%)	87 (33.3%)	158 (60.1%)
Median PFS, months (95% CI)	NR (18.5-NE)	6.8 (5.6-8.2)
12-month PFS, % (95% CI)	75.8% (69.8-80.7)	34.1 (27.7-40.5)
PFS HR (95% CI)	0.28 (0.22-0.37), p<0.001	

Table 4 Analysis of OS

	T-D (n=261)	T-emtansine (n=263)
No. alive (%)	[redacted]	[redacted]
Median OS (95% CI); months	NE (NE, NE)	NE (NE, NE)
12-month OS (95% CI); %	94.1 (90.3-96.4)	85.9 (80.9-89.7)
OS HR (95% CI)	0.55 (0.36-0.86), p=0.007	

NICE

Abbreviations: BICR, blinded independent central review; CI, confidence interval; HR, hazard ratio; NE, not estimable; OS, overall survival; PFS, progression free survival; T, trastuzumab; T-D, trastuzumab deruxtecan [12]

Immature OS data

EAG

- Complete evidence for PFS but limitations in length of follow-up of OS to determine survival gain
  - 46.76% of PS events
  - [redacted]% of OS events → data immature

Company

- PFS is a meaningful outcome and improvements in PFS are value, statistically significant 72% lower risk of progression or death compared with T-emtansine
- Efficacy of T-D confirmed through other meaningful endpoints, including response rates
- 17.9 month increase in median PFS in D-B03 (IA*)for T-D vs. T-emtansine, is expected to translate into a statistically significant OS advantage
- Literature supports PFS as surrogate for OS and correlation between HRs of PFS/OS in HER2+ mBC
- OS benefit evidenced by early separation of KM curves to end of follow-up
- OS estimates from D-B03 have been compared with EMILIA and other studies, and validated by clinical and health economics and outcomes research experts, are appropriate

*Median PFS by BICR is not available for T-D at the first interim analysis

Is the interim data for OS sufficient to estimate relative effectiveness for decision making?

NICE

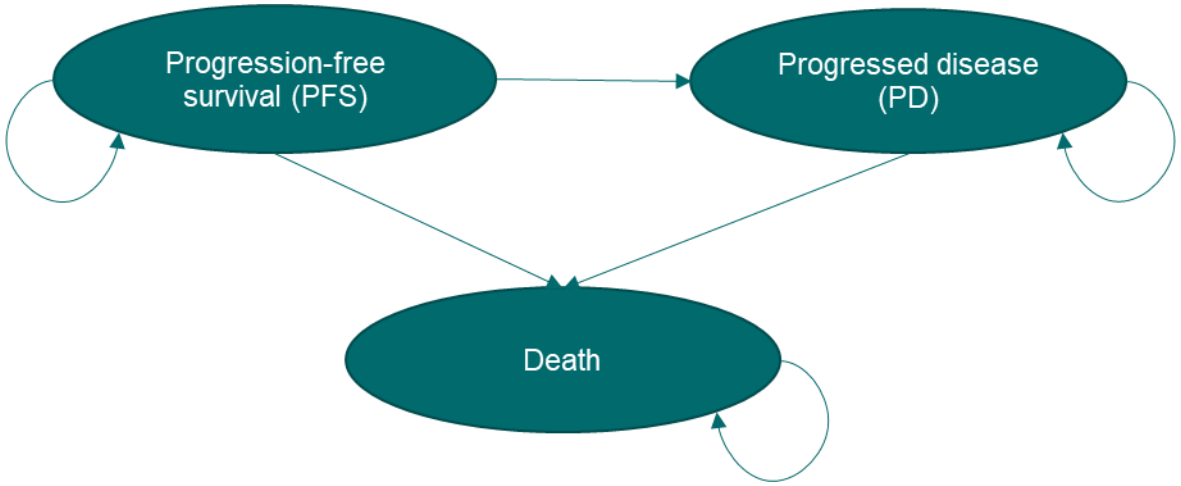
Abbreviations: BICR, blinded independent central review; D-B03, DESTINY-Breast03; HER2, Human Epidermal Growth Factor Receptor 2; HR, hazard ratio; IA, investigator-assessed; KM, Kaplan-Meier; mBC, metastatic breast cancer; OS, overall survival; PFS, progression free survival; T, trastuzumab; T-D, trastuzumab deruxtecan

Cost effectiveness

NICE National Institute for Health and Care Excellence

Company model overview

Figure 5 Model structure



Technology affects costs by:

- Extended drug treatment with T-D, raises drug costs
- Different incidences of adverse events
- Different time periods in the PF and PD health states

Technology affects QALYs by:

- Longer OS with T-D (main driver)
- Utility benefit with T-D due to longer time spent in PFS

Assumptions with greatest ICER effect:

- Whether an OS benefit is sustained across the 30-year time horizon of the model
- Utility values for the progression-free survival and the disease progression health states
- Vial wastage

Abbreviations: ICER, Incremental cost-effectiveness ratio; OS, Overall survival; PD, progressed disease; PF, progression free; PFS, progression free survival; QALY, quality adjusted life year; T-D, trastuzumab deruxtecan

How company incorporated evidence into model

Table 6 Input and evidence sources

Input	Assumption in company base case and evidence source
Baseline characteristics	From D-B03: Mean age = [redacted] years
Intervention and comparator efficacy	OS: Generalised gamma parametric curve fitted to D-B03 data (with a treatment covariate for T-D) PFS and TTD: Weibull parametric curve fitted to D-B03 data
Utilities	Pre progression - Treatment specific utilities derived from D-B03 used directly by mapping EQ-5D-5L to EQ-5D-3L using Van Hout algorithm Post progression - Treatment specific utilities derived from Lloyd et al, 2006

Abbreviations: AEs, adverse events; D-B03, DESTINY-Breast03; OS, overall survival; PD, progressed disease; PF, progression free; PFS, progression free survival; PSSRU, Personal Social Services Research Unit; T-D, trastuzumab deruxtecan; TTD, time to treatment discontinuation

Summary of company and EAG base case assumptions

Table 7 Assumptions in company and EAG base case

Assumption	Company base case	EAG base case	Inc. costs	Inc. QALY	ICER impact
PFS extrapolation	Weibull		-		
OS extrapolation of T-E	Direct extrapolation of DB03		-		
OS extrapolation of T-D (treatment effect after progression)	Treatment specific effect extrapolated beyond follow up period	Extrapolation until year 2 then no treatment effect after progression*	↓	↓	↑
Utilities	PFS = DB-03 (treatment specific) PD = Lloyd et al (treatment specific)	PFS = DB03 (treatment specific) PD = Lloyd et al (combined)	=	↓	↑
Vial wastage	Assume no vial wastage occurs in 50% of cases for T-D	Assume no vial wastage occurs in 10% of cases for T-D	↑	=	↑

- *[redacted] in T-D arm of the trial were still alive at interim data cut → OS extrapolation uncertain

Abbreviations: D-B03, DESTINY-Breast03; OS, overall survival; PD, progressed disease PFS, progression free survival; T-E, trastuzumab emtansine; T-D, trastuzumab deruxtecan

Uncertain OS predictions for T-D

Treatment effect beyond progression is uncertain

Company provided 2 methods to extrapolate OS beyond interim data-cut point:

1) Company base case = fitted dependent survival models to D-B03 data: generalised gamma
2) Patient level data replicated from T-emtansine arm of EMILIA study, parametric survival models fitted to replicated data to predict T-emtansine OS, with HR from D-B03 applied to this curve to predict T-D OS

EAG

- Company assumed trend in overall survivor curve as the proportion of people alive progression free within trial follow-up, and will continue beyond follow-up period
- EAG: strong assumption given immature data, the effect of changing disease profile over time, and the change in treatments received.
- Without survival data post progression, not clear if there is a treatment effect after progression when treatment stops
- Considered 2 alternative assumptions extrapolating OS beyond 2 years:
  A. conservative scenario with no treatment effect beyond disease progression;
  B. less conservative assumption where treatment effect wanes over time, determined by proportion of people still alive who are in PD state
- ***Assumption A in EAG base case***: assumes risk of death equal for all people in post progression

Abbreviations: D-B03, DESTINY-Breast03; HR, hazard ratio; KM, Kaplan-Meier; OS, overall survival; PD, progressed disease; PF, progression free; T, trastuzumab; T-D, trastuzumab deruxtecan

Uncertain OS predictions for T-D

Treatment effect beyond progression is uncertain

NICE

Abbreviations: HR, hazard ratio; OS, overall survival; PD, progressed disease; T, trastuzumab; T-D, trastuzumab deruxtecan

Uncertain OS predictions for T-D

Treatment effect beyond progression is uncertain

Company TE response

- Acknowledge OS data for D-B03 immature. Consider uncertainty has been explored through clinical validation, and testing of structural and parameter uncertainty within economic model:
- Treatment waning:
  - No evidence of treatment waning with T-D or after 2 years hazards start merging
  - Prior HER2+ BC appraisals did not assume OS treatment waning
  - In previous metastatic HER2+ BC trials, no evidence of treatment waning for HER2+ targeted treatments when comparing interim outcomes with final analysis sets with longer-term follow-up

EAG comments

- 'Treatment waning' is different: assumes mortality HR post-progression in T-D arm is lower than T-emtansine arm to start with, but this gradually reduces to zero (around year 8).
- May be biological/statistical reasons for mortality hazard rates lower in T-D than T-emtansine arm post-progression. Evidence for sustained lower mortality hazard rates post-progression not produced

Is an assumption of a benefit post progression acceptable?

Abbreviations: BC, breast cancer; D-B03, DESTINY-Breast03; HER2, Human Epidermal Growth Factor Receptor 2; HR, hazard ratio; OS, overall survival; PD, progressed disease; PSA, probabilistic sensitivity analysis; T, trastuzumab; T-D trastuzumab deruxtecan;

Post-progression utility values

PD utilities: Treatment specific or treatment independent?

Background

- Treatment specific utility values for PF health state are derived from D-B03 and treatment specific utility values for PD health state derived from Lloyd et.al (2006) in company base case

EAG comments

- No evidence in Lloyd et al. (which was used as the source for PD utility estimates in the company's base case model) or in the CS for a difference in PD utility values across treatment groups
- Uncertain the difference in utility values, accounting for uncertainty in the estimates, would be generalisable to the English setting.
- Compared to other health state utilities in previous TAs, the values for PFS and PD differ
- Question how valid treatment-specific progressed disease utilities are. Once people are off-treatment, utility values would be the same for both arms within a very short timeframe

Clinical and patient expert comments

- Difficult to estimate difference in post-progression utilities. Higher for people who progress on T-D for a period of time compared to T-emtansine. Disease under control for longer period and longer response rates
- People starting new treatment with less tumour burden, symptoms and potentially improved QoL

Abbreviations: CS, company submission; D-B03, DESTINY-Breast03; PD, progressed disease; PF, progression free; PFS, progression free survival; TA, Technology Appraisals; T, trastuzumab; T-D, trastuzumab deruxtecan

Post-progression utility values

PD utilities: Treatment specific or treatment independent?

Company

- Number of post-progression observations from D-B03 limited (670 out of 4,644 total) and values implausibly high. No long-term data for HRQoL for PD was collected
- Precedent of different utility values being used in prior breast cancer appraisals (TA786 and TA819)
- At TE, explored utility benefit for T-D last for period after progression then same utility for T-D and T-emtansine. 2 time points : 1) 6 months (from TA819), 2) 4 months, last collected EQ-5D from D-B03
- Assuming a utility benefit for a shorter timeframe increases the ICER slightly from the base case

EAG comments

- T-D associated with higher responses rates (79.7% vs 34.2%) but lack of evidence that HRQoL is greater in T-D post-progression than in T-emtansine post-progression

Other considerations (previous appraisals)

- TA819: 4 approaches, all associated with uncertainties and none satisfactory. Concluded company revised base case with carry-over utility benefit for 6 months was least flawed approach
- TA786: Concluded differences in post-progression health state utilities are plausible, but uncertain

Abbreviations: 2L, second line; 3L, third line; D-B03, DESTINY-Breast03; HRQoL, health related quality of life; T, trastuzumab; T-D, trastuzumab deruxtecan

Post-progression utility values

PD utilities: Treatment specific or treatment independent?

Table 9 Utility values from this appraisal and previous appraisals

	Treatment	Source	PD
ID3909	T-D	Coefficients from Lloyd et.al (2006) used to calculate treatment specific utilities by responder and non-responder weighted by response rates from DESTINY-Breast03 study	0.6183
	T-emtansine		0.5738
	Combined from Lloyd et.al (2006)	Average of treatment specific utilities	0.5960
TA598 – 1L	Pertuzumab + trastuzumab + docetaxel		0.769
TA458 – 2L	T-emtansine		0.53
TA704 – 3L	T-D		0.588
TA786 – 3L	Tucatinib + trastuzumab + capecitabine		0.698
	Eribulin		0.588
TA819 – 3L	Sacituzumab vs physician's choice	Utility difference between treatments = 0.084	

- EAG accepted Lloyd as a background source for utility data. But did not accept differential post-progression utilities for T-D and T-emtansine

Are the treatment specific or treatment independent utility values reasonable?

NICE Abbreviations: 1L, first line; 2L, second line; 3L, third line; PD, progressed disease; PF, progression free; T. trastuzumab; T-D, trastuzumab deruxtecan

Vial wastage

EAG comments

- Company has over-estimated ability for vial sharing
- Consulted clinical experts advised that vial sharing does not happen or if it does, dependent on circumstances of each clinic → vial sharing not be considered, or considered at lower rate than 50%
- When vial sharing is carried out it is also unlikely that perfect allocation of each dose occurs
- Adopted alternative waste value of vial sharing in 10% of cases (i.e. 90% of cases resulting in waste)

Company

- Vial sharing available in some UK centres, model includes an option to assume a proportion of people vial share. Base case = 50% vial sharing
- Previous appraisals have considered 50% an appropriate assumption (TA819, TA704)
- Consider 50% more appropriate than 10% and consistent with previously accepted assumptions

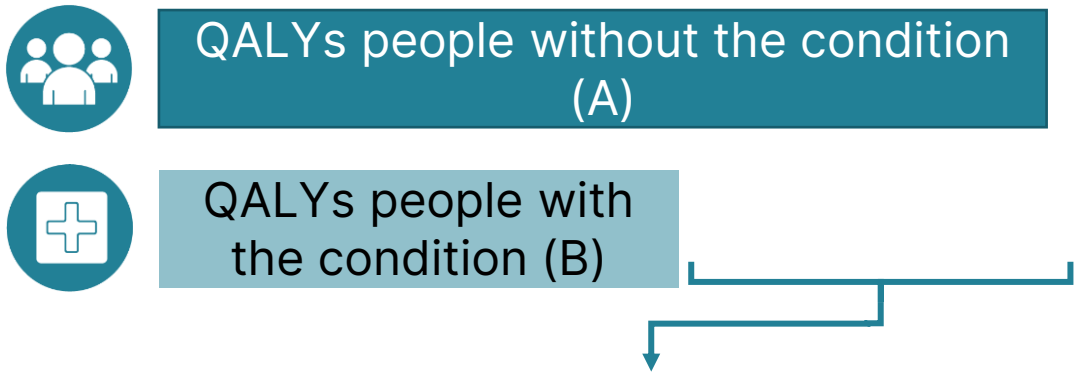
Other considerations (previous appraisals)

- TA819: committee accepted 50% is a reasonable assumption for vial sharing
- TA458: committee concluded that some wastage needs to be included in the calculation of trastuzumab emtansine treatment costs, because assuming no wastage is not plausible (company base case 50%)

Is an assumption of no vial wastage occurring in 10% or 50% of cases for trastuzumab deruxtecan appropriate for decision making?

QALY weightings for severity (1)

New severity modifier calculations and components:



Health lost by people with the condition:

- Absolute shortfall: total = A – B
- Proportional shortfall: fraction = (A – B) / A
- *Note: The QALY weightings for severity are applied based on **whichever of absolute or proportional shortfall implies the greater severity**. If either the proportional or absolute QALY shortfall calculated falls on the cut-off between severity levels, the higher severity level will apply

Table 10 QALY weightings for severity of the disease

QALY weight	Absolute shortfall (AS)	Proportional shortfall (PS)
1	Less than 12	Less than 0.85
X 1.2	12 to 18	0.85 to 0.95
X 1.7	At least 18	At least 0.95

QALY weightings for severity (2)

Components	Company	EAG	Notes
1. QALYs of people without condition (based on trial population characteristics which both EAG and company agreed on)	14.63	14.33	Difference comes from the dataset used: • Company: EQ-5D-3L data from HSE 2012 and 2014 data and MVH value set • EAG: HSE 2017/18 EQ-5D-5L plus Hernández et al algorithm.
2. QALYs with the condition on current treatment	[redacted]	[redacted]	• Company: MVH value set • EAG: Hernandez value set
3. Results			**EAG comments:** • Hernández preferred in NICE methods 2022 for mapping EQ-5D-5L to EQ-5D-3L, therefore the same algorithm should be used in estimating QALYs with and without the condition
Absolute QALY shortfall (has to be >12)	Deterministic = [redacted] Probabilistic = [redacted]	Deterministic = [redacted] Probabilistic = [redacted]	
Proportional QALY shortfall (has to be >0.85)	Deterministic = [redacted] Probabilistic = [redacted]	Deterministic = [redacted] Probabilistic = [redacted]	

Severity threshold met for 1.2x QALY weighting

Does the condition qualify for a QALY weighting based on severity of disease as defined by associated absolute or proportional QALY shortfall?

HSE, Health Survey for England; MVH, Measuring and Valuing Health; QALY, Quality-adjusted life year

Other considerations

Equality considerations

- No equality issues have been raised

Innovation

- T-D is an innovative treatment based on its potential to make a significant and substantial impact on health-related benefits, representing a step-change in management vs. T-emtansine.
- T-D is an antibody-drug conjugate, and the first to combine an anti-HER2 antibody (trastuzumab) with a topoisomerase inhibitor licensed in the UK
- The Innovative Licensing and Access Pathway (ILAP) Steering Group (MHRA, NICE, All Wales Therapeutics and Toxicology Centre (AWTTC), Scottish Medicines Consortium (SMC), and representatives from the ILAP Patient and Public Reference Group), informed Daiichi Sankyo that the innovative medicine designation, the Innovation Passport, has been awarded for T-D on the basis of the DESTINY-Breast03 trial.
- Therapeutic advancement due to its improved PFS rates and duration of response compared with current standard of care which is T-emtansine

NICE Abbreviations: ILAP, Innovative Licensing and Access Pathway; T, trastuzumab; T-D, trastuzumab deruxtecan

Managed access

Criteria for a managed access recommendation

The committee can make a recommendation with managed access if:

- the technology cannot be recommended for use because the evidence is too uncertain
- the technology has the **plausible potential** to be cost effective at the **currently agreed price**
- new evidence that could **sufficiently support the case for recommendation** is expected from ongoing or planned clinical trials, or could be collected from people having the technology in clinical practice
- data could feasibly be collected within a reasonable timeframe (up to a **maximum of 5 years**) without **undue burden**.

28

Cost-effectiveness results

As confidential discounts are available for comparators and 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 > £30k/QALY gained
- EAG's base case > £30k/QALY gained
  - Includes no treatment effect beyond progression,
  - a single combined PD utility and
  - 90% vial wastage,

Scenario analysis

The following scenarios will be presented alongside the company and EAG base case

- Varied proportion receiving subsequent treatments
- Varied distributions of subsequent treatments
- Different PFS extrapolations
- Different OS extrapolations
- Alternative OS approach using EMILIA data
- 6 and 4 month utility benefit for T-D in PD

Abbreviations: ICER, incremental-cost effectiveness ratio, OS, overall survival; PD, progressed disease; PFS, progression free survival; T-D, trastuzumab deruxtecan

NICE National Institute for Health and Care Excellence

Thank you.

30