NICE National Institute for Health and Care Excellence

Closed session – redacted (confidential material removed)

Pertuzumab for adjuvant treatment of early HER2-positive breast cancer

Chair's presentation

4th appraisal committee meeting

Committee A

Lead team: John McMurray, Pamela Rees, Stephen Sharp

ERG: Warwick Evidence

NICE technical team: Eleanor Donegan, Juliet Kenny

Company: Roche

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Key issues for consideration

- The company's analysis is based on the ERG's more conservative extrapolation of treatment effects
- Is the new commercial offer sufficient to mitigate the committee's concerns about the following issues?
  - uncertainty associated with extrapolating a small benefit over a long time-horizon
  - financial risk of altering the treatment regimen (with concomitant impact on oncology services) in the context of uncertain benefit

[redacted]

Pertuzumab (Perjeta)

Marketing authorisation	In combination with trastuzumab and docetaxel as adjuvant treatment of patients with HER2-positive early breast cancer at **high risk of disease recurrence**
Mechanism of action	The antibody binds to HER2 receptor proteins on breast cancer cells, prevents the receptors from binding to growth factor proteins which can cause the cancer cells to divide and grow
Administration	Intravenous (IV) in combination with trastuzumab and docetaxel for a total of one year (maximum of 18 cycles) regardless of the timing of surgery.
Dose	840 mg loading dose, then 420 mg every three weeks
Patient access scheme	Commercial access agreement approved by Department of Health which provides a simple discount to list price

[redacted]

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History of the appraisal (1)

- 1st committee meeting 17 April 2018
  - **Pertuzumab not recommended: ACD issued**
  - Uncertainty in the clinical effectiveness of pertuzumab as adjuvant treatment (small benefit) and little evidence that pertuzumab is more effective for high risk subgroups.
  - Implausible company's ICERs (marginal difference in invasive disease-free survival translates into a QALY gain of 0.6 for the node-positive population)
  - ERG's preferred assumptions resulted in considerably higher ICERs
  - CDF not appropriate (low event rates; implausible QALY-gain thought unlikely to be confirmed by further data)
- 2nd committee meeting 19 June 2018
  - **Pertuzumab not recommended: ACD issued**
  - Improved commercial access agreement (CAA) and revised model but QALY-gain remained implausible (0.56)
  - When the weighted average biosimilar discount and market share estimates were taken into account, the company's and the ERG's base-case ICERs were £24,985 and £39,939 per QALY gained respectively
  - Second ACD was issued to allow consultation on how the impact of biosimilar trastuzumab on cost effectiveness had been taken into account

[redacted]

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History of the appraisal (2)

- 3rd Committee meeting
  - **Pertuzumab not recommended: FAD developed but not issued**
  - Further improved CAA
  - When the weighted-average biosimilar discount and market share estimates are taken into account the ICERs were approximately £13,000 (company) and £24,000 (ERG)
  - No change to the committee's conclusions
  - Consultees and commentators notified of recommendation within 7 working days
- Following the 3rd Committee meeting
  - Further improved CAA
  - Updated ICERs based on ERG's preferred assumptions

[redacted]

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The committee's conclusions to date

- In the intention-to-treat population (ITT), the absolute difference in invasive disease-free survival event rates between the 2 treatment arms is very small
- In the 'node-positive' group, the committee accepted that the baseline risk of disease recurrence is greater than for the ITT population, but was not convinced that the relative treatment effect of pertuzumab was greater
- It is uncertain that the small IDFS benefit translates into the substantial QALY gains seen in the economic model
- The ERG's analyses gave a more conservative estimate of QALY gain, but did not resolve the uncertainty associated with extrapolating a small benefit over a long time-horizon
- Analyses including weighted-average biosimilar prices are most appropriate
- The introduction of adjuvant pertuzumab would alter the treatment pathway
  - It is not known how this might impact on the effectiveness of pertuzumab given in the metastatic setting in patients whose disease progresses.
  - It commits patients to a year of intravenous therapy with concomitant pressure on oncology services
- The ICER would need to be considerably lower than the ERG's estimate of £24,000 per QALY gained to mitigate this clinical uncertainty

[redacted]

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Consideration for the cancer drugs fund

- Further invasive disease-free survival data or mature overall-survival data from APHINITY may resolve some of the uncertainty, but the final overall-survival analysis is not due until 2023.
- Cancer Drugs Fund data collection would not provide robust evidence on overall-survival because of the timelines involved and the relatively low event-rate in this population
- It is unlikely that Cancer Drugs Fund data would corroborate the cost-effectiveness estimates presented by the company and the ERG.
- Because of the high numbers of patients who would potentially be eligible for adjuvant treatment, the committee concluded that more clinical certainty is needed for it to decide whether adjuvant treatment with pertuzumab actually improves patient outcomes in terms of survival benefit.
- The committee concluded that there is insufficient evidence of clinical benefit for adjuvant pertuzumab to be considered plausibly cost effective or to be recommended for inclusion in the Cancer Drugs Fund

[redacted]

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Updated model assumptions – lymph node-positive disease

- The company has used the same model as in ACD4 meeting (October 2018) and:
  - Increased discount to the price in the CAA
  - implemented the ERG's preferred assumptions for duration of treatment effect (treatment effect begins to wane at year 4 and ceases at year 7)
  - assumed biosimilar trastuzumab is available with 66% discount to the price

[redacted]

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Company revised base case ICERs (lymph node positive disease)

Technologies	Total cost	Total QALYs	Incremental costs	Incremental QALYs	ICER
Trastuzumab + chemo	XXXXX	XXXX	XXXXX	XXXX	XXXXX
Pertuzumab + trastuzumab + chemo	XXXXX	XXXX			

Biosimilar discount scenario analysis

Pertuzumab discount	Average discount on trastuzumab biosimilar in UK							
	55.00%	58.00%	60.00%	62.00%	64.00%	66.00%	68.00%	70.00%
XXXXXX	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX	XXXXX

[redacted]

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[redacted]

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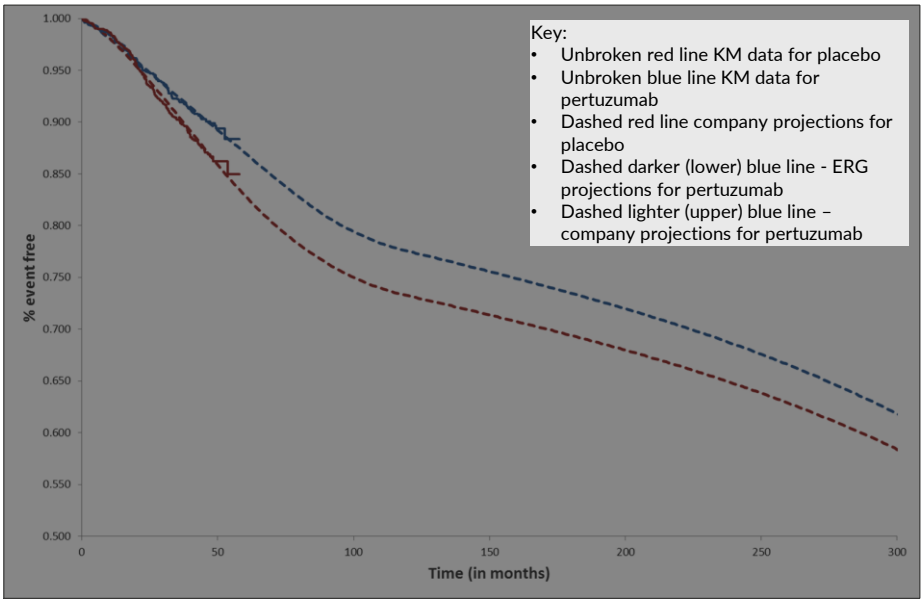
Back-up slides

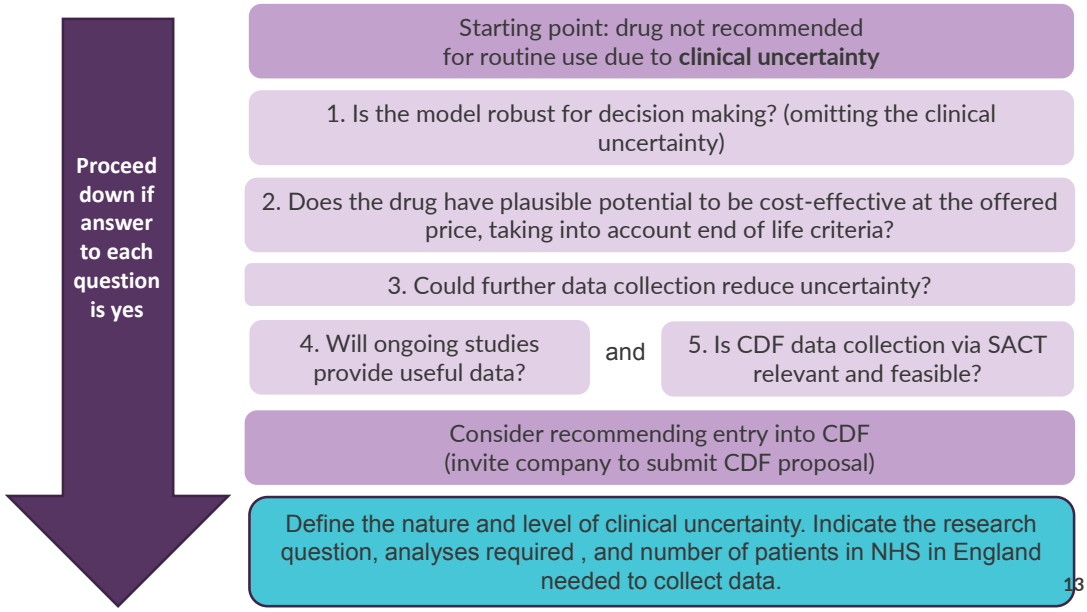
[redacted]

Change to IDFS with ERG preferred duration of treatment effect



[redacted]

CDF recommendation criteria



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