Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer

For public – contains redacted information

2nd appraisal committee meeting

Technology appraisal committee D [15 January 2025]

Chair: Amanda Adler

External assessment group: University of Bristol Technology Assessment Group

Technical team: Heather Stegenga, Rachel Williams, Ian Watson

Lead team: Paul Caulfield (lay), Sofia Dias (cost), Craig Cook (clinical)

Company: AstraZeneca

Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer

- ✓ **Background and recap 1st committee meeting**
- ❑ Response to consultation from EGFR Positive UK
- ❑ Company response to consultation + company updated base case + external assessment group (EAG) critique
- ❑ Company vs EAG base case
- ❑ Other considerations
- ❑ Summary

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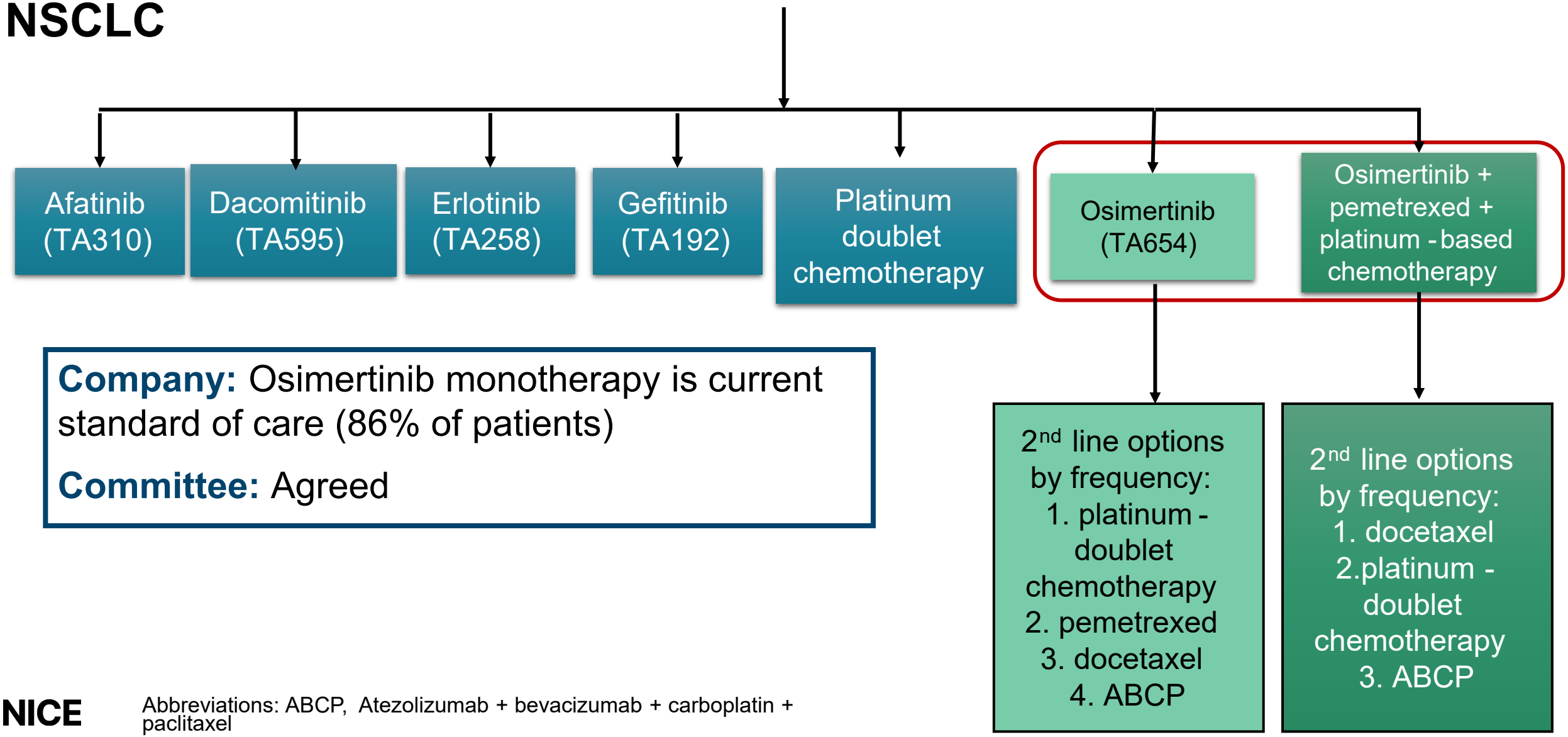
Treatment pathway for previously untreated locally advanced or metastatic epidermal growth factor receptor+ NSCLC



Company: Osimertinib monotherapy is current standard of care (86% of patients)

Committee: Agreed

Abbreviations: ABCP, Atezolizumab + bevacizumab + carboplatin + paclitaxel

Osimertinib (Tagrisso®, AstraZeneca)

Marketing authorisation	• Sept 2024 • In combination with pemetrexed and platinum-based chemotherapy 'for the first-line treatment of adult patients with advanced non-small-cell lung cancer whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations' • Osimertinib: 'until disease progression or unacceptable toxicity'

Mechanism	• Inhibits:
	  • activating sensitising EGFR mutation (EGFRm+)
	  • activating resistance mutation T790M

Administration	• 80mg oral dose once daily
Testing	• NHS offers testing for EGFRm in people with previously untreated, locally advanced/metastatic NSCLC
Price	• List price: £5,770 per 30 tablets (40 mg or 80 mg) • Average cost of a course of treatment at list price: £104,706 • Osimertinib is available to the NHS with a discount

Abbreviations: EGFR, epidermal growth factor receptor; EGFRm, epidermal growth factor receptor mutation; MHRA: Medicines and Healthcare products Regulatory Agency; PAS: patient access scheme

FLAURA-2: randomised open-label trial

Osimertinib more effective with chemotherapy than without chemotherapy

Population	*EGFR*-mutated (exon 19 deletion or L858R mutation) advanced NSCLC - previously untreated - 1st line treatment
Intervention	Osimertinib + chemotherapy (pemetrexed + **either** cisplatin or carboplatin)
Duration of treatment	Osimertinib oral to disease progression Pemetrexed IV to disease progression Platinum-based chemotherapy given for a fixed number of treatment cycles
Comparison	Osimertinib monotherapy
Primary outcome	Investigator-assessed progression-free survival 3 April 2023
Results	PFS: April 2023 HR 0.62; 95% CI 0.49-0.79; p<0.0001 OS: 2nd interim analysis Jan 2024 41% died; HR 0.75, 95% CI 0.57-0.97

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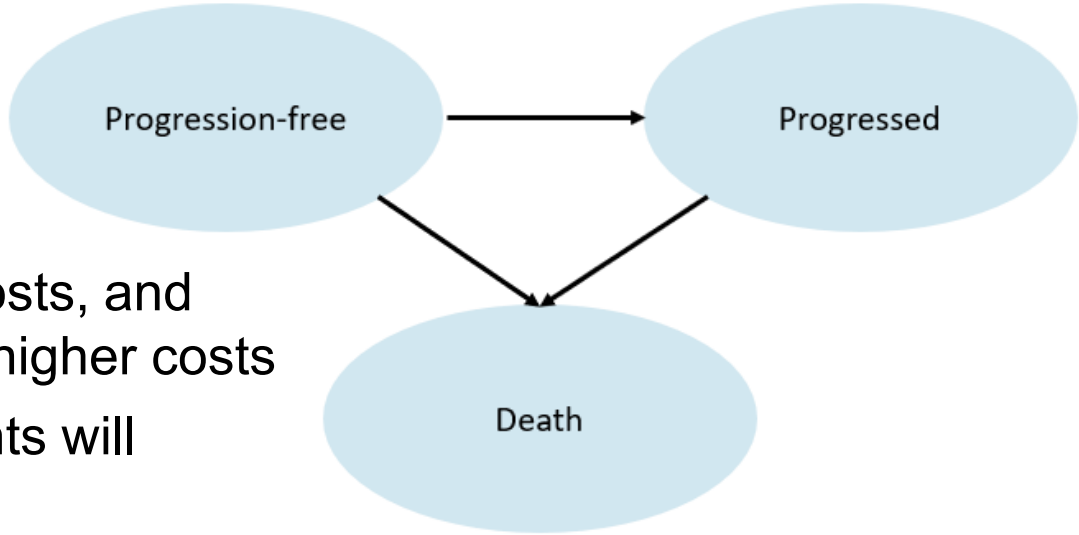
Abbreviations: CI, confidence interval; EGFR, epidermal growth factor receptor; HR, hazard ratio; IV, intravenous; NSCLC, non–small-cell lung cancer; OS, overall survival; PFS, progression free survival; For more info see appendix

Cost effectiveness model - recap

- Company assumed treatment increases QALYs by:
  - ↑ length of life – extrapolated beyond trial
  - ↑ quality of life (↑ time in progression-free state)
- 'Progression-free' has best quality of life and lowest costs, and 'progressed' health state has worst quality of life and higher costs
- The more effective the treatment, the more time patients will spend in 'progression-free' health state
- Treat to disease progression then stop unless 'receiving clinical benefit' (modelled separately for each trial arm and individual treatment)
- Costs include treatment, treatment administration, healthcare professionals and hospitals, treating adverse effects, and any subsequent treatments
- FLAURA-2 trial informs how long patients remained in each health state + quality of life
- Adverse effects – frequency from trial, utility from literature



Abbreviations: QALY, quality adjusted life-year

Committee conclusions at 1st appraisal committee Oct 2024

Committee wanted more analyses on overall survival, time to stopping treatment, utility values

Committee recommendation

- Osimertinib + pemetrexed and platinum-based chemotherapy not recommended – unable to establish cost effectiveness
- Committee concerned with several analyses

Committee preferred assumptions

- Starting age 65.6 years
- Utility
  - progression-free state 0.794 (previous value higher than UK general population)
  - progressed-disease state 0.678
- Resource use
  - Company's estimate of outpatient visits
  - Expert Advisory Group (EAG) estimate for other resources
  - NHS reference costs
- No ABCP use for follow-up treatment (requested scenario with 7% use)
- Platinum-based chemotherapy is all carboplatin
- Relative dose intensity - % of planned dose patient receives - 96.4% for carboplatin

Abbreviations: ABCP, atezolizumab, bevacizumab, carboplatin and paclitaxel combination therapy

Key issues for 2nd appraisal committee meeting – to discuss today

Consultation responses from company and EGFR Positive UK

Key issue	Company's approach	Relative ICER impact
Extrapolation overall survival time	• Maintains original choice • Further justifies choice	Large
Extrapolation time to treatment discontinuation	• Maintains original choice • Further justifies choice • Additional scenario	Large
Utility progression-free	• Analysis supporting company value	Moderate
Disutility chemotherapy	• Additional scenario	Moderate
Assumption 2nd-line treatments	• Revises, but not to committee preference	Small

Abbreviations: ICER, incremental cost - effectiveness ratio

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Patient perspectives – EGFR Positive UK

Some people want option of adding chemotherapy

Living with lung cancer

- Significant psychological distress, anxiety and depression, fear of progression
- Isolation impacts people socially and their family life

Treatment options

- Need more treatment lines and options
- Some people may prefer not to have chemotherapy because of adverse side effects and inconvenience of attending hospital, but important to have choice
- Some people concerned using combination therapy may reduce later treatment options

- *Life is.. 'hugely discombobulating where even the most joyous experiences will lead to a wave of sadness as I consider the reality of "will I be here next year"?*

"I know my treatment is keeping the cancer cells sleeping, but I can't help but wonder when they are going to wake up"

"I was diagnosed at 40, and I have two young children. There is nothing I wouldn't do to have more time with them."

Abbreviations: EGFR+, epidermal growth factor receptor positive;

Patient perspectives at 1st committee: see appendix

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Company's changes to its base case modelling

Assumption	Company revised base case
Population	• Starting age 65.6 years - committee preference
Comparator	• 100% carboplatin for platinum-based chemotherapy (vs. 50%) - committee preference • Relative dose intensity of 96.4% for carboplatin (vs. 100%) - committee preference
Overall survival	• No change and justifies
Time to treatment discontinuation	• No change and justifies; analyses with scenarios
Utility progression-free state	• Additional analyses
Utility progressed-disease state	• 0.678 (vs. 0.640 base case) - committee preference
2nd line treatments	• % receiving atezolizumab + bevacizumab + carboplatin + paclitaxel (8.2%) and other treatments % • Did not supply scenario with 7% requested by committee
Resource use	• Company's outpatient visits and EAG's estimates for other resources - committee preference
Resource costs	• NHS reference - Committee preference

Key issues

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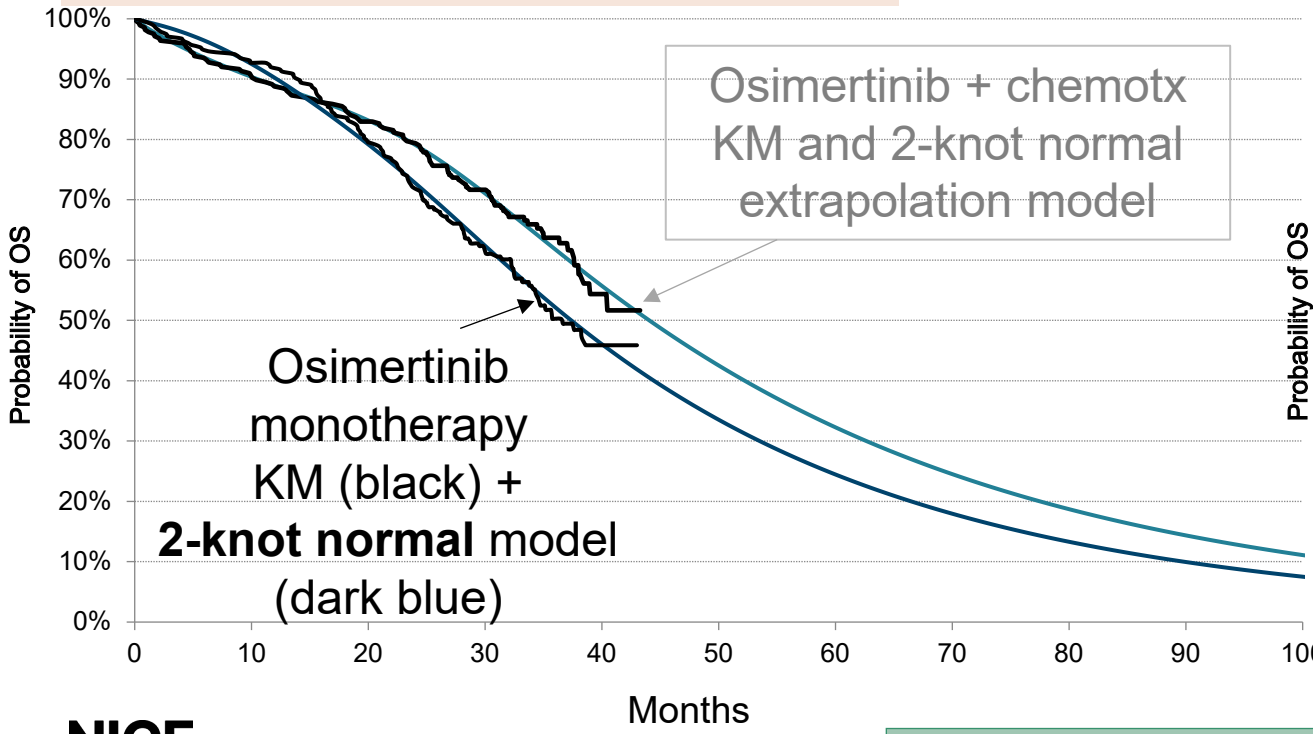
Key issue: Extrapolating overall survival control arm (1/3)

Committee requested both company and EAG justify their models

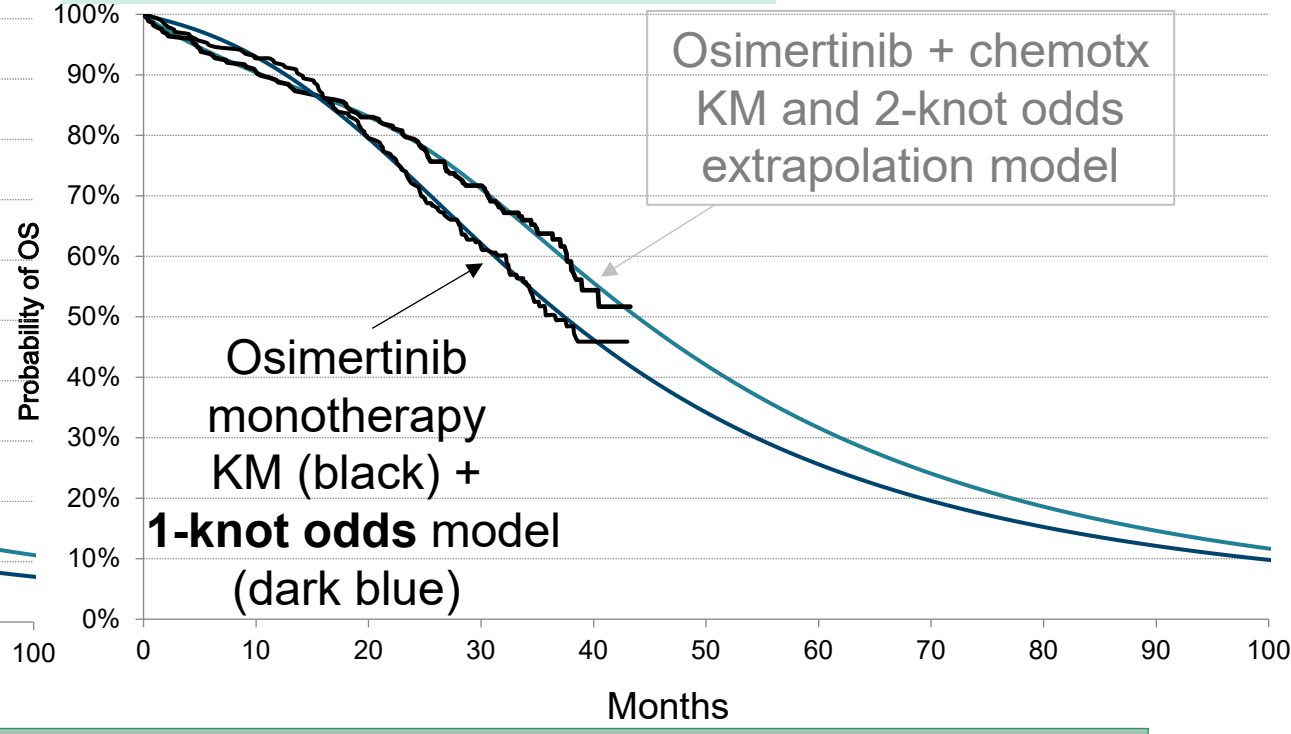
Committee at ACM1

- Proportional hazards assumption did not hold; separate extrapolation model appropriate for each treatment
- Company and EAG chose same number of knots for intervention; different models for osimertinib monotherapy
- Best approach unclear for osimertinib monotherapy - company or EAG - different numbers of knots

Company-preferred survival curves



EAG-preferred survival curves



Abbreviations: KM, Kaplan Meier

Overall survival data from 2nd interim analysis (January 2024)

Key issue: Extrapolating overall survival (2/3)

Company: best to use same knots for both arms; EAG: spline models same family, 1-knot better fit

Company

- 2-knot normal model for osimertinib monotherapy aligns with clinician's long-term estimates
- EAG's 1-knot model extrapolations not plausible
- Best practice to use same number of knots for each arm; improves comparability and consistency

EAG

- Spline models considered same family of models; shape (and so number of knots) may differ when adding chemotherapy and changing 2nd line treatment
- 1-knot model has better statistical fit for osimertinib monotherapy with OS around 35% at 4 years, 25% at 5 years, and 5% at 10 years (see appendix), which aligns with:
  - FLAURA (osimertinib mono vs standard EGFR-TKI): ~38% OS at 4 years
  - Registry data for other EGFR TKIs: 12% (with del19 or L858R mutation) and 20% (with del19 mutation) at 5 years
  - Range from company clinical experts

Abbreviations: EGFR, epidermal growth factor receptor ; OS, overall survival; TKI, tyrosine kinase inhibitor

Key issue: Extrapolating overall survival (3/3)

Company: observed hazard function falls outside predicted hazard function confidence interval

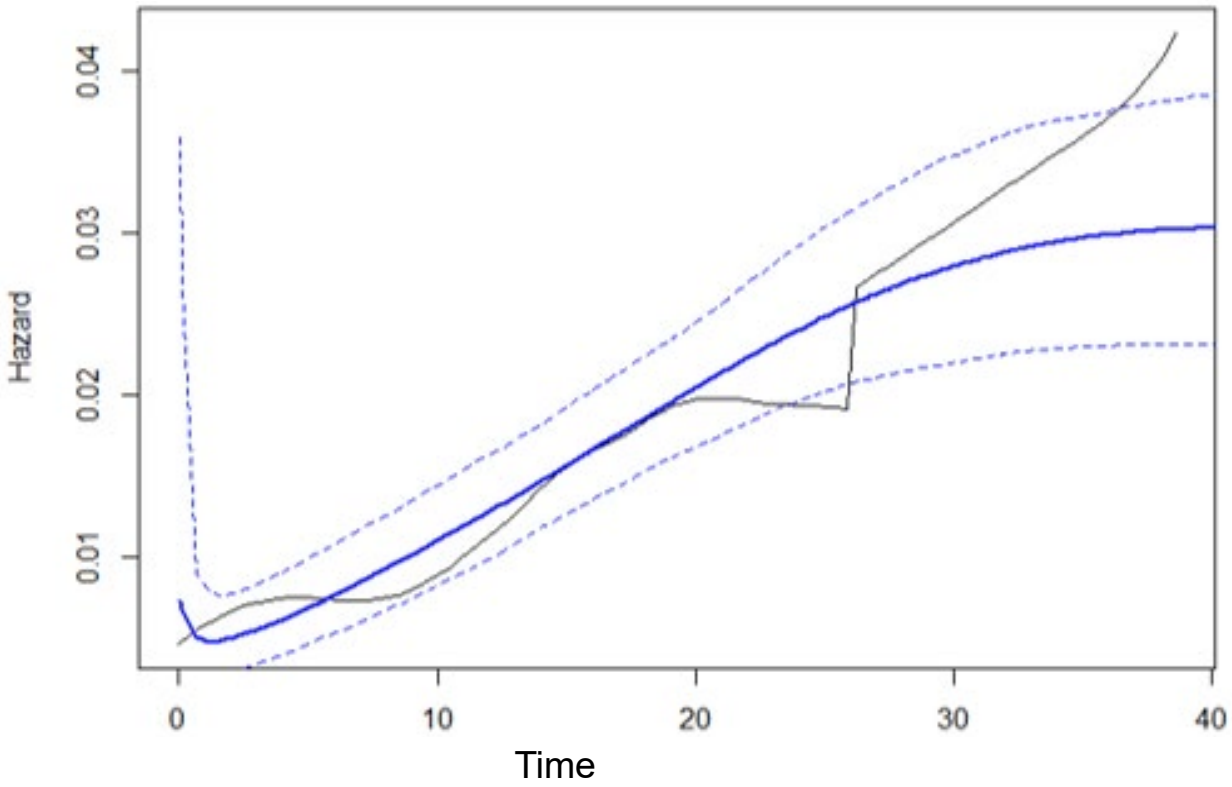
Company:

- Observed hazard function (grey line) beyond 95% confidence interval of predicted model (blue lines) for EAG 1-knot odds spline model: not good fit
- Prefer 2-knot normal model

EAG:

- Observed hazards based on small numbers at end of curve
- If confidence limits of observed hazard function displayed, would overlap with 1- and 2-knot models

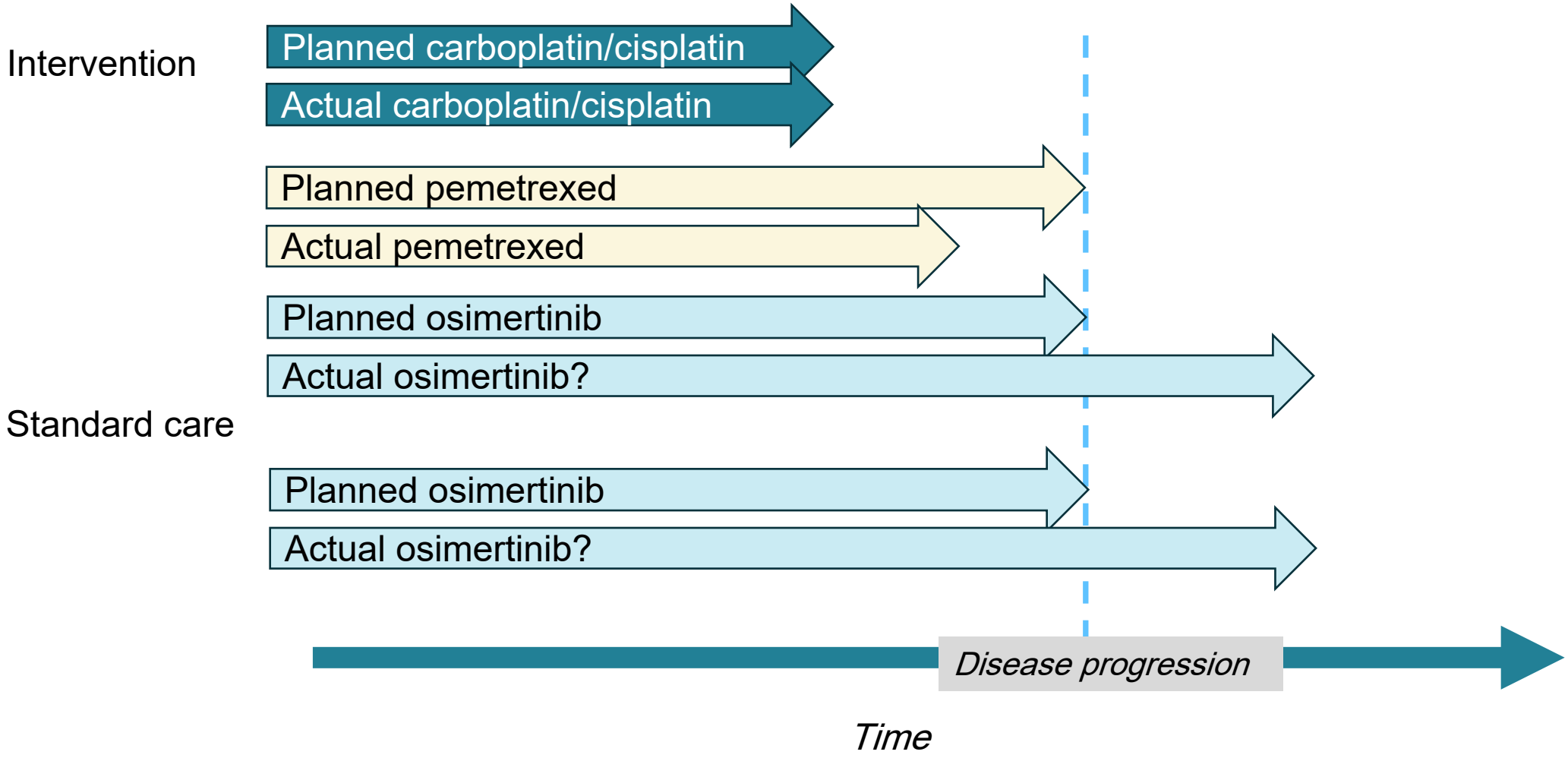
Hazard function for osimertinib mono:
1-knot spline (odds scale; EAG-preferred)



Which extrapolation model is preferred for osimertinib monotherapy? 2-knot normal spline model (company) or 1-knot odds model (EAG)

Background time to treatment discontinuation (TTD)

Platinum-based chemotx limited cycles, other drugs to disease progression



Illustrative image of planned and actual treatment duration in the FLAURA2 trial

Key issue: Extrapolating time to treatment discontinuation (1/3)

Marketing authorisation: treat to progression, but osimertinib continues in practice

Committee at ACM1

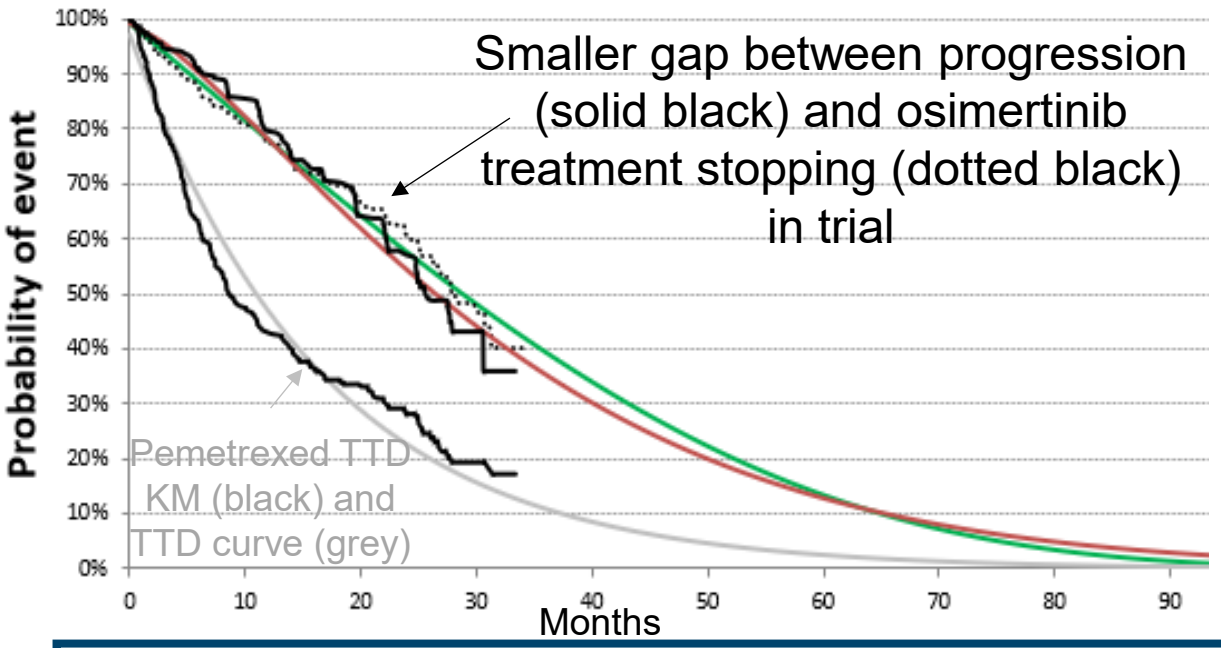
- Key driver but not enough evidence to support either company or EAG base case model
- Platinum-based chemotx fixed number cycles, so TTD relevant for osimertinib + pemetrexed
- Osimertinib treatment duration beyond progression likely similar between arms, so
  - Unexplained why treatment beyond progression greater in osimertinib monotherapy arm than osimertinib + chemotherapy arm in FLAURA2
- Requested scenarios:
  1. Same treatment duration beyond progression in both arms
  2. Treatment duration beyond progression that better reflects the arms of trial and clinical practice
- Requested cross-validation of extrapolations of treatment duration with other data on osimertinib monotherapy TTD (FLAURA trial)

Abbreviations: PFS, progression-free survival; TTD, time to treatment discontinuation

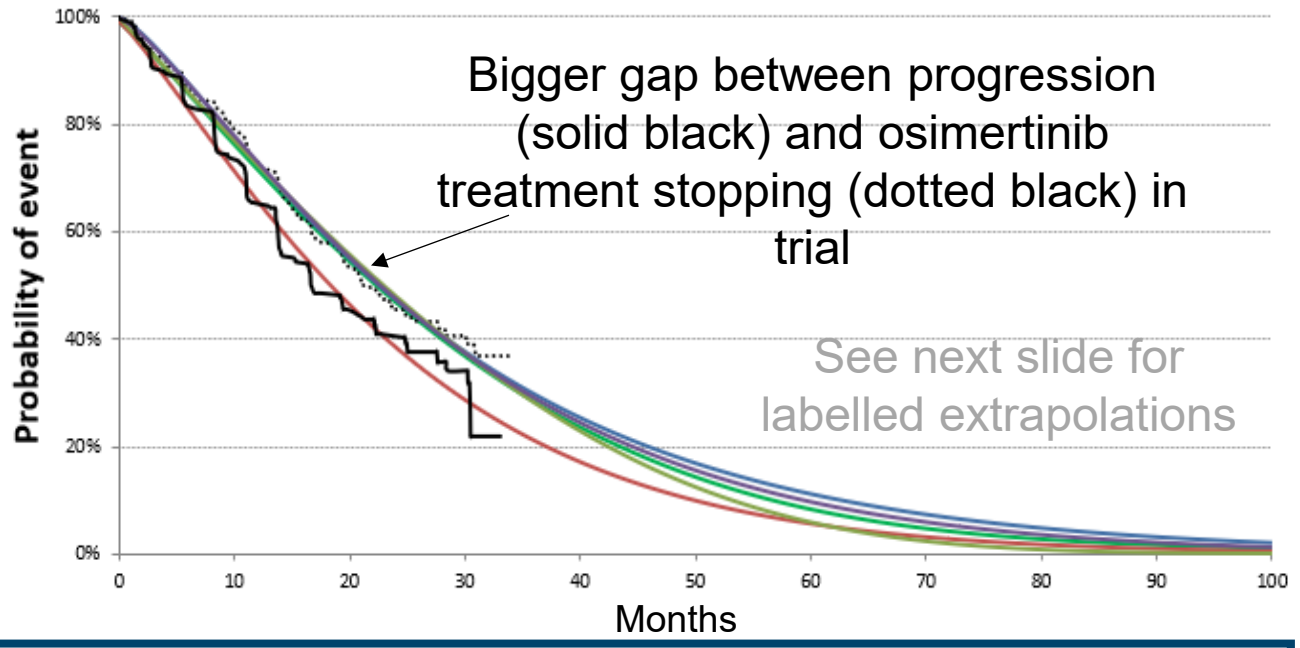
Key Issue: Extrapolating time to treatment discontinuation (2/3)

Company: adverse effects of chemotherapy may reduce osimertinib treatment beyond progression

PFS and TTD for osimertinib + chemo arm



PFS and TTD for osimertinib monotherapy arm



Company

- Smaller osimertinib treatment beyond progression in osimertinib + chemo arm may be from pre-progression adverse events. Proportion who progressed and median duration of exposure beyond progression similar between arms
- Implausible results from scenario modelling same treatment beyond progression in both arms (see appendix)

Abbreviations: PFS, progression -free survival; TTD, time to treatment discontinuation

Key Issue: Extrapolating time to treatment discontinuation (3/3)

Company maintain gamma for osimertinib monotherapy; EAG prefer average of Gompertz+gamma

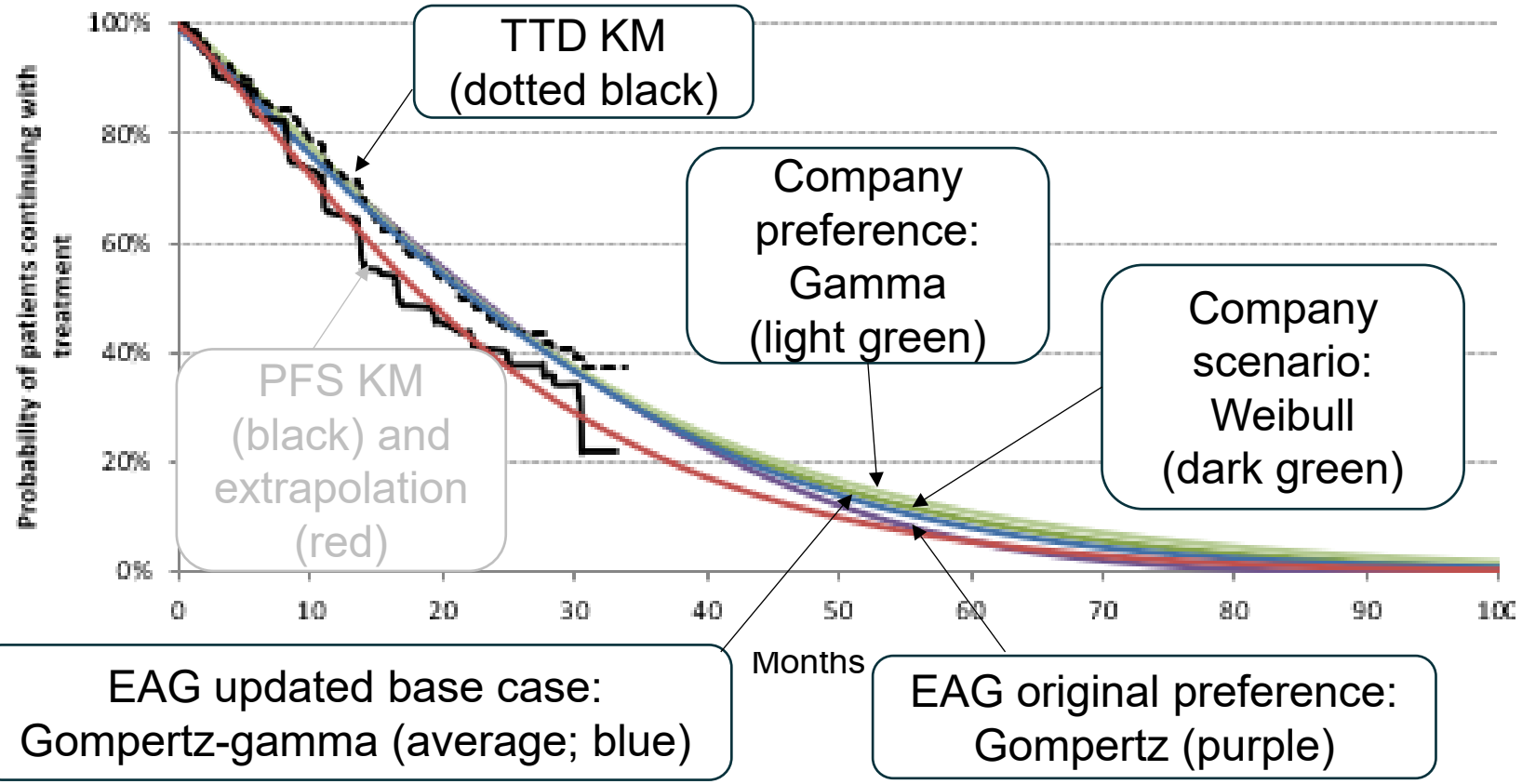
Company

- Maintain gamma in base case (Weibull in scenario)

EAG comments

- Weibull closer to gamma curve than Gompertz
- Updated base case: use average of both Gompertz and gamma in updated base case

TTD extrapolations for osimertinib monotherapy



What is the most plausible extrapolation for osimertinib monotherapy TTD?

Abbreviations: KM, Kaplan-Meier; PFS, progression-free survival; TTD, time to treatment discontinuation

Key Issue: Utility in progression-free (1/2) - health state

Committee requested more analyses, but updated value still lacks face validity

Committee at ACM1

- Company's value ([redacted]) higher than general population (0.799)
- Preferred EAG's (0.794; TA654), but still large uncertainty
- Requested:
  - Modelling to account for missing data
  - Utility data from 1st 16 weeks of FLAURA2 to inform appropriate decrement for chemotherapy
  - Using treatment arm as covariate for treatment-specific values

Company

- Compliance rate for EQ-5D-5L high and consistent between arms
- To impute missing EQ-5D-5L data, used predictive mean matching; result similar ([redacted])

EAG comments

- Chemotherapy adverse effects could explain why missing data differs between arms in first 16 weeks
- Alternative imputation better, but adjusts only for baseline covariables; should have also included other follow-up outcomes
- Much larger imputation sets needed
- Recommended alternative mapping using disease specific scores

Has committee heard anything to change its preference of EAG's 0.794 utility for progression-free health state?

Key Issue: Utility in progression-free (2/2) – adverse events

Company decrement for adverse events much smaller and shorter than EAG's

Company

- Disutility for chemotherapy applied for each AE separately (TA654)
- EAG approach not appropriate; people do not have chemotherapy for whole progression free period
- Scenario with treatment-specific disutility for duration of chemotherapy (see appendix)

EAG comments

- EAG's disutility estimated from mean utilities for whole progression-free period, so applies to entire duration. May underestimate decrement because of missing data
- Company approach does not capture compounding AEs
- Company scenario likely underestimates decrement; would have preferred multiple imputation method adjusting for baseline + outcome data, and imbalance in baseline utility (see appendix)

	Company base case	EAG base case
Decrement chemotherapy	[redacted]	[redacted]
Duration decrement estimated over	Duration of adverse events (scenario: duration of chemotherapy – 16 weeks)	Entire PFS health state

How should the model capture effect of chemotherapy on quality of life?

Abbreviations: AEs, adverse events; MMRM, mixed models for repeated measures; PF, progression free; QoL, quality of life

Key Issue: Assumptions on treatments at 2nd line

Company and EAG both amend costs of ABCP in base cases, but usage differs

Committee at ACM1

- Preferred EAG approach of excluding ABCP at 2nd line
- Requested scenario where 7% have ABCP (CDF lead: 6-7% in NHS)

Company

- Incorrect in draft guidance that ABCP not used in FLAURA2 (see appendix)
- 7% ABCP too low
- 8.2% ([redacted]) in updated base case (original base case: [redacted]%)
  - Based on denominator [redacted] osimertinib 'new patients' from internal AstraZeneca data and numerator [redacted] patients having atezolizumab from SACT

EAG comments

- Should include cost of ABCP 2nd line in model
- Unable to adjust overall survival to reflect ABCP; outstanding uncertainty
- Unable to verify company calculations without internal company data
- Scenario with 7% ABCP used in updated base case (see appendix)

What is the most appropriate % of people having ABCP?

Abbreviations: ABCP, Atezolizumab + bevacizumab + carboplatin + paclitaxel; CDF, cancer drugs fund; ICER, incremental cost-effectiveness ratio; SACT, systemic anti-cancer therapy

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Summary - company and EAG base case assumptions

Differences remain

Assumption	Company base case	EAG base case
OS extrapolations	2-knot spline normal models for both treatments	1-knot odds spline for osimertinib monotherapy 2-knot odds spline for osimertinib +chemo
Osimertinib monotherapy extrapolating TTD	Gamma	Average Gompertz/Gamma
Utility value progression free	[redacted]	0.794
Disutility for chemotherapy	[redacted] for duration of adverse events	[redacted] for entire PFS health state
2nd line % ABCP use	8.2%	7%

Abbreviations: ABCP, Atezolizumab + bevacizumab + carboplatin + paclitaxel; OS, overall survival; PFS, progression -free survival; TTD, time to treatment discontinuation

Cost-effectiveness results

Neither company nor EAG suggest osimertinib + chemotherapy value for money

- All ICERs reported in non-public PART 2 as they include confidential discounts
- Company base case above range normally considered cost-effective
- All scenarios from EAG increase estimates of cost-effectiveness
- EAG base case significantly above range normally considered cost-effective

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Abbreviations: ICER: Incremental cost effectiveness ratio

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Equality considerations

Comments from stakeholders

- EGFR Positive UK: EGFR more prevalent in women and in Asian populations; essential to ensure access to treatment and information to these groups
- Asian population discussed at 1st committee meeting, but not considered equalities issue as recommendation does not restrict access to treatment some people over others
- No other equalities issues raised by stakeholders

Is the increased prevalence in women an equalities issue?

Abbreviations: EGFR+, epidermal growth factor receptor positive

Managed access criteria for a recommendation

Committee can make a recommendation with managed access if:

- Cannot recommend technology because evidence too uncertain
- Technology has **plausible potential** to be cost effective at **currently agreed price**
- Expect new evidence that could **sufficiently support the case for recommendation** from ongoing or planned clinical trials, or people having the technology in clinical practice
- Could feasibly collect data within reasonable timeframe (**max 5 years**) without **undue burden**

Committee conclusion at 1st committee meeting

- Company did not submit managed access proposal
- Company stated FLAURA2 unlikely to report further TTD data
- Managed access unlikely to resolve all key uncertainties

Has committee heard anything to change its decision?

- Would another overall survival analysis when 60% have died (next planned data cut) decrease uncertainty?

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Abbreviations: TTD, time to treatment discontinuation

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Key issues

Issue	ICER impact	Slide
Extrapolating overall survival	Large	Slide 14
Extrapolating time to treatment discontinuation	Large	Slide 18
Progression free health state utility	Moderate	Slide 21
Disutility with chemotherapy	Moderate	Slide 22
Assumption 2nd-line treatments	Small	Slide 23

Osimertinib with pemetrexed and platinum-based chemotherapy for untreated EGFR mutation-positive advanced non-small-cell lung cancer

Supplementary appendix

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Patient perspectives (1st committee meeting)

Submissions from Roy Castle Lung Cancer Foundation and a carer

- EGFR mutation patients tend to be diagnosed later, as they do not fit the 'typical' lung cancer patient profile
- Targeted therapies, such as osimertinib, have been a major step forward in the treatment of lung cancer, and a great source of hope for patients. However, disease progression is likely to occur eventually
- Progression free survival appears to be longer when osimertinib is in combination with pemetrexed and platinum-based chemotherapy
- Osimertinib side effects can be debilitating, adding chemotherapy will likely decrease the quality of life of people receiving treatment
- Osimertinib is an oral therapy, so can be acquired from pharmacies. Adding chemotherapy will require IV treatment and more time spent at hospitals

Abbreviations: IV, intravenous; EGFR, epidermal growth factor receptor

Key issues resolved at 1st meeting and company's updated based case with committee preferences from 1st committee meeting (ACM1)

Key Issue	Committee-preferences reflected in company updated base case

• Subgroup - presence or absence of central nervous system metastases at diagnosis:
  • treatment appeared more effective in people with brain metastases
  • Screened in trial, but not in NHS
  • Recognised by company
	• Progressed disease health state utility
	• Measurements of resource use
	• Average starting age in the model
	• Distribution of platinum chemotherapy
	• RDI of chemotherapy
	• Resource costs

Abbreviations: PSSRU, Personal Social Services Research Unit; RDI: relative dose intensity

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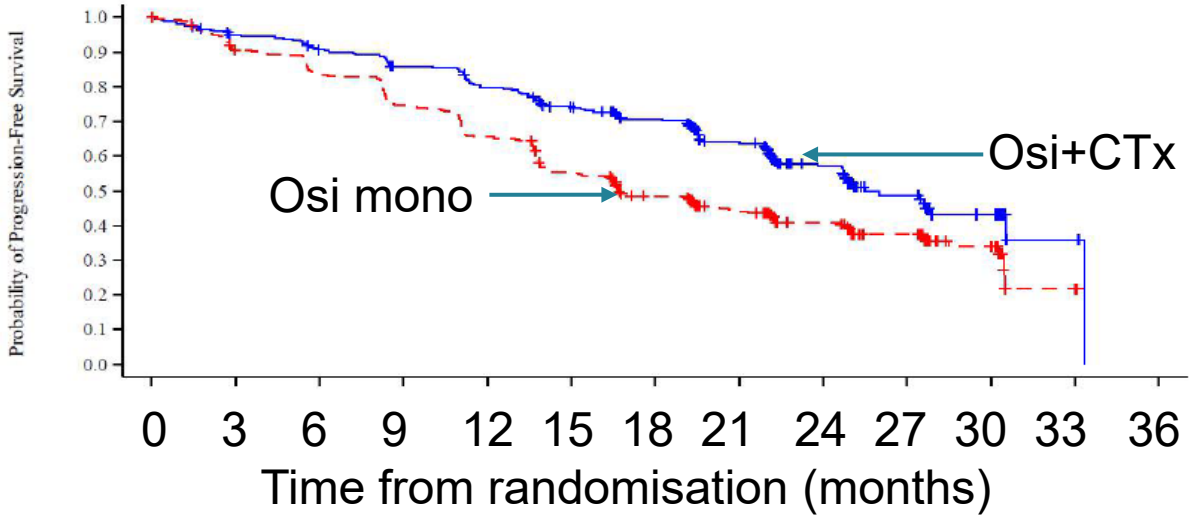
Key clinical trial results – FLAURA2

Osimertinib+chemo (n=279) improves PFS and OS compared to osimertinib mono (n=278)

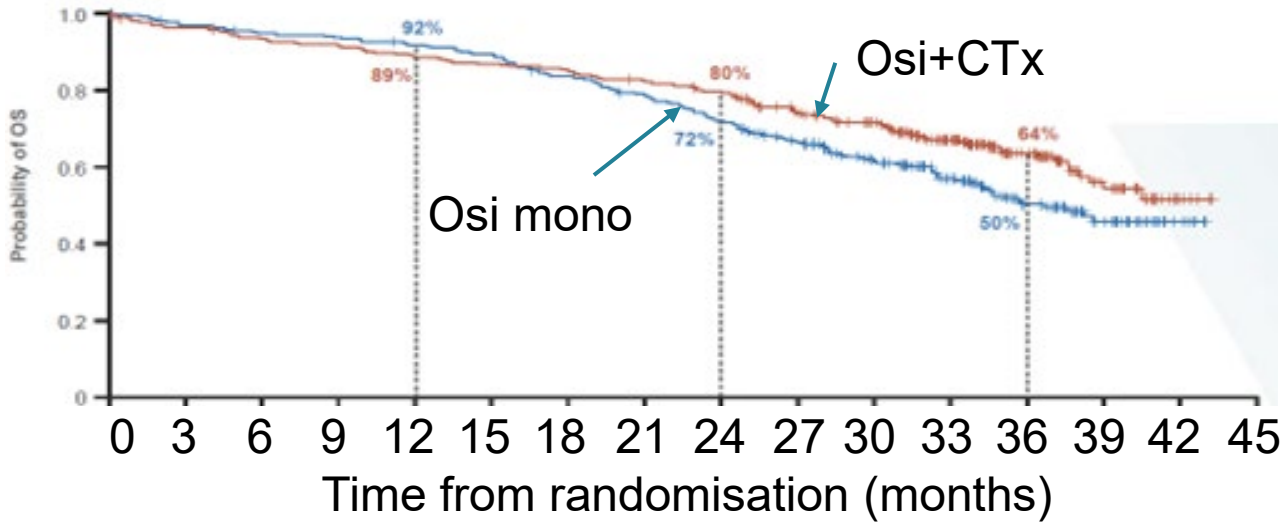
Osimertinib+chemo vs osimertinib mono – PFS April 2023 primary analysis point - FAS



CTx	279	254	241	225	207	187	165	133	84	42	21	3	0
Mono	278	246	227	203	178	148	119	94	67	48	21	1	0

HR (95% CI; p-value)	0.62 (0.49, 0.79) p<0.0001

Osimertinib+chemo vs osimertinib mono – OS January 2024 DCO



CTx	279	267	258	253	245	240	236	226	218	190	169	121	71	31	5	0
Mono	278	267	260	257	251	244	228	213	195	170	142	102	64	34	7	0

HR (95% CI)	0.75 (0.57, 0.97)

NICE Abbreviations: CI, confidence interval; CTx, chemotherapy; DCO, data cut off; FAS, full analysis set; HR, hazard ratio; OS, overall survival; PFS, progression free survival

Key issue: Extrapolating overall survival

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Company and EAG disagree on appropriate extrapolation; considerable uncertainty remains

Osimertinib monotherapy

	Mean	Med	1 year	2 years	3 years	5 years	10 year	15 years
Observed	-	36.5 months	92.0%	72.1%	50.3%	-	-	-
Pred (2 knot normal - company)	46.2 months	36.5 months	89.8%	72.5%	52.2%	24.8%	4.4%	1.1%
Pred (1 knot odds - EAG)	49.7 months	36.5 months	89.8%	72.4%	52.2%	25.9%	6.8%	2.8%

Osimertinib plus chemo

	Mean	Med	1 year	2 years	3 years	5 years	10 year	15 years
Observed	-	-	88.8%	79.7%	63.7%	-	-	-
Pred (2 knot normal - company)	53.3 months	43.4 months	88.7%	78.9%	61.8%	32.6%	6.8%	1.8%
Pred (2 knot odds - EAG)	54.8 months	42.4 months	88.7%	78.9%	61.9%	32.0%	7.8%	3.0%

Abbreviations: Med, median; OS, overall survival; pred, predicted

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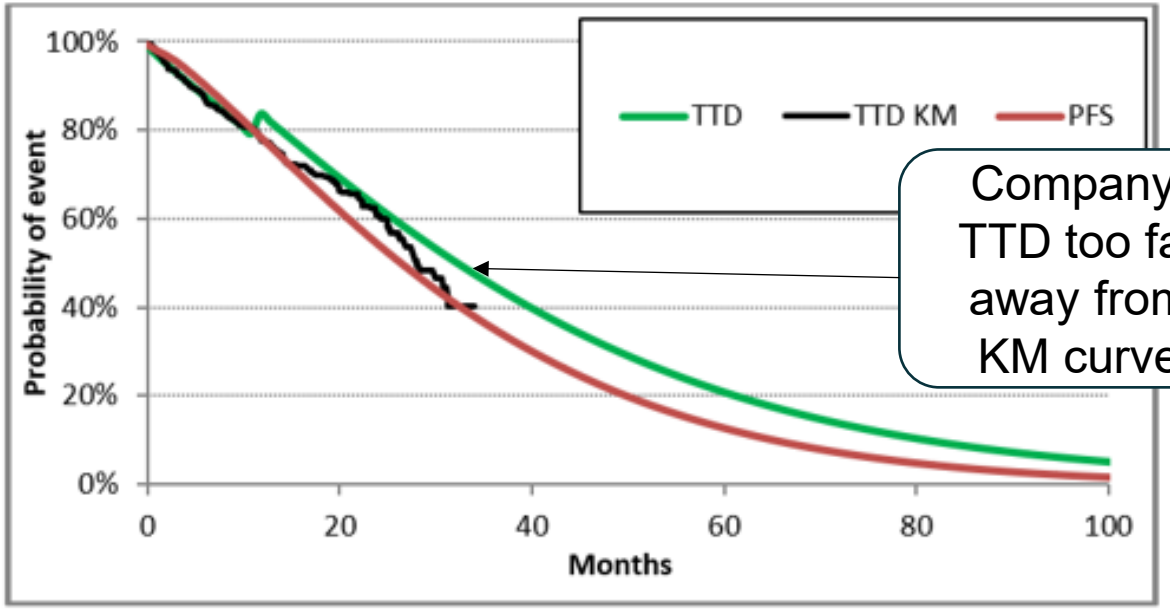
Key Issue: Extrapolation of time to treatment discontinuation

Company scenario modelling same TTD and PFS gap in both arms: consider implausible

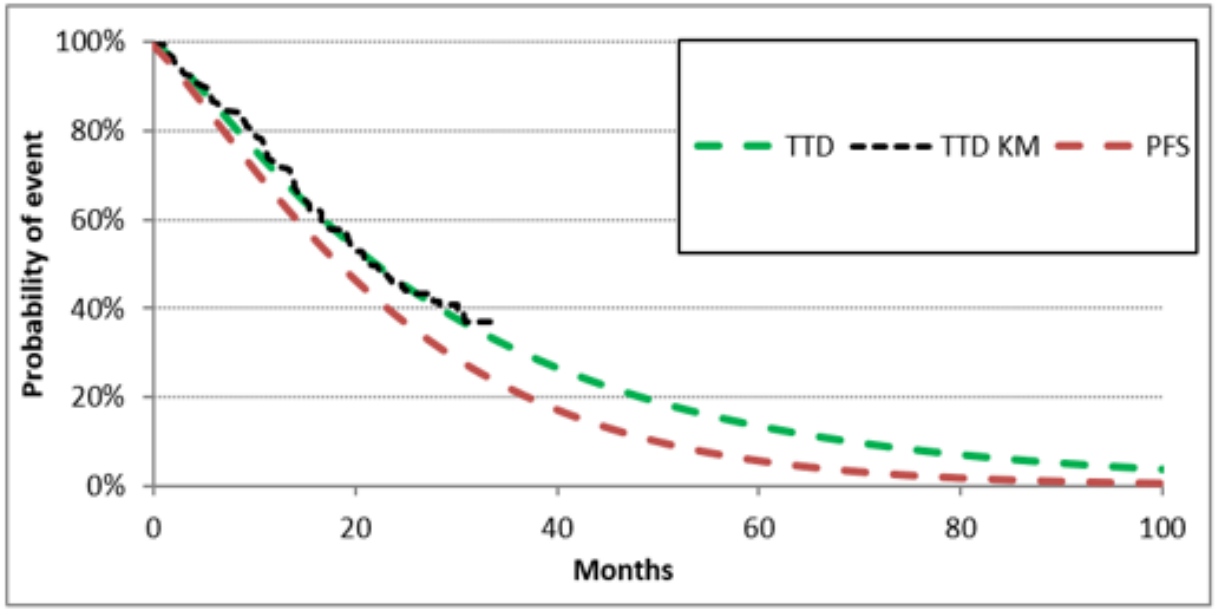
Difference between PFS and TTD curve in osimertinib monotherapy arm added to PFS curve for osimertinib + chemotherapy arm at point where pemetrexed stopped

EAG: Agree results implausible

Osimertinib plus chemotherapy



Osimertinib monotherapy



Abbreviations: KM, Kaplan-Meier; TTD, time to treatment discontinuation

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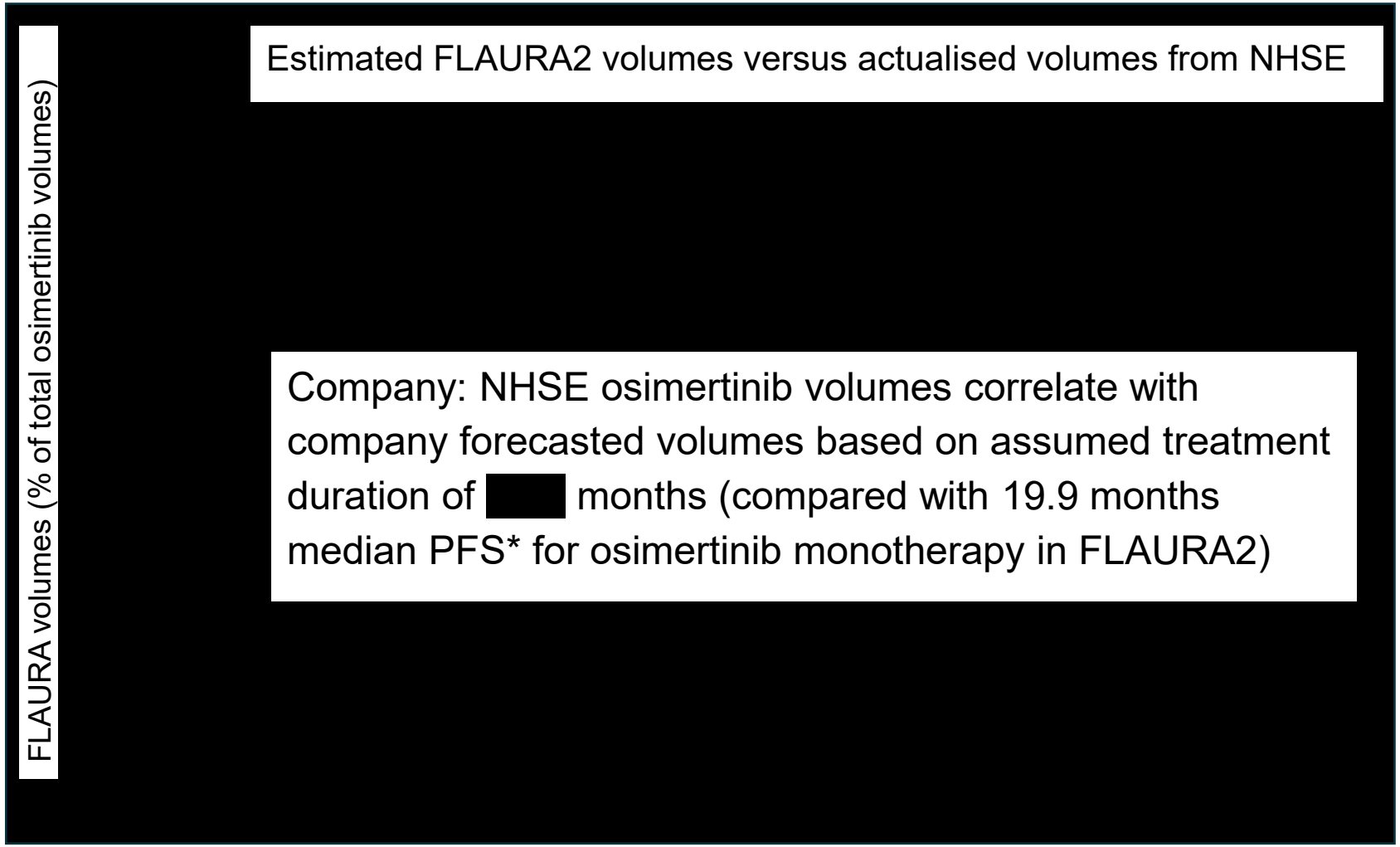
Key Issue: Extrapolation of time to treatment discontinuation

Company present data to support treatment beyond progression in FLAURA2

Company

- Provide evidence to support longer osimertinib TTD than PFS (table) and that FLAURA2 reflects treatment duration of osimertinib in NHS (graph)

Source of evidence for osi mono	Median TTD (months)	Median PFS (months)
FLAURA2	21.2	16.7*
FLAURA	20.8	18.9
Lorenzi et al 2022	25.3	18.9



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* Investigator-assessed PFS was primary outcome; company report median PFS by blinded independent central review was 19.9 months. Abbreviations: NHSE, NHS England; PFS, progression-free survival; TTD, time to treatment discontinuation

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Key Issue: Utility in progression-free health state

Health state (source)	Utility value	
	Osi+chemo	Osi mono
Baseline (FLAURA2)	[redacted]	[redacted]
Progression-free (FLAURA2)	[redacted]	[redacted]
Difference baseline to mean progression-free (FLAURA2)	[redacted]	[redacted]
Progression-free (TA654)	0.794	

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Key Issue: Utility in progression-free health state

Company scenario: different treatment-specific utility values during chemo to calculate decrement

Company

- Scenario: treatment-specific disutility for duration of chemotherapy
- Values derived using MMRM applied to intention-to-treat data from FLAURA2 with 16-week follow-up data cut-off (as in submission)
- Treatment and progression status covariates
- Based on analysis, [redacted] decrement used for osimertinib + chemotherapy arm during chemotherapy

Parameter	Estimate	SE	p-value	95% CI
Intercept	[redacted]	[redacted]	[redacted]	[redacted]
Osimertinib + chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Post progression	[redacted]	[redacted]	[redacted]	[redacted]

State	Utility value: marginal means (95% confidence interval)
Progression -free (osimertinib plus chemotherapy)	[redacted]
Progression -free (osimertinib)	[redacted]
Post-progression (osimertinib plus chemotherapy)	[redacted]
Post progression (osimertinib monotherapy)	[redacted]

Abbreviations: MMRM, mixed models for repeated measures

Key Issue: Assumptions on treatments at 2nd line

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Difficult to determine exact ABCP usage in trial as reported for each component separately

Post-treatment anti-cancer therapy in FLAURA2 in full analysis set

Post-treatment anti-cancer therapy – percentage (n)	Osi + chemo (N=279)	Osimertinib monotherapy (N=278)
Cytotoxic chemotherapy (all)	15% (41)	81 (29.1)
Cytotoxic chemotherapy: platinum compounds	7% (19)	78 (28.1)
Cytotoxic chemotherapy: folic acid analogues (pemetrexed)	3% (8)	55 (19.8)
Cytotoxic chemotherapy: taxanes	9% (26)	14% (39)
EGFR-TKI (all)	7% (18)	14% (39)
1st or 2nd generation EGFR-TKI	4% (12)	8% (22)
3rd generation EGFR-TKI (all)	2% (6)	8% (22)
3rd generation EGFR-TKI: osimertinib	2% (6)	7% (19)
3rd generation EGFR-TKI: aumolertinib	0	1% (3)
VEGF inhibitor – monoclonal antibody	5% (14)	14% (38)
PD-1/PD-L1 inhibitor – immunotherapy	4% (10)	8% (22)
Other	4% (11)	7% (19)

NICE

Abbreviations: ABCP, Atezolizumab + bevacizumab + carboplatin + paclitaxel; PDC, Platinum Doublet Chemotherapy; EGFR+, epidermal growth factor receptor positive

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Key Issue: Assumptions on treatments at 2nd line

Company and EAG both amend costs of ABCP in base cases, but usage differs

Company updated base case of distribution of 2nd line treatments in patients who received them

From ↓To →	PDC	Pemetrexed	Docetaxel	ABCP
Osimertinib + chemotherapy	[redacted]	[redacted]	[redacted]	[redacted]
Osimertinib	[redacted]	[redacted]	[redacted]	[redacted]

EAG-corrected company base case of distribution of 2nd line treatments in patients who received them*

From ↓To →	PDC	Pemetrexed	Docetaxel	ABCP
Osimertinib + chemotherapy	[redacted]	[redacted]	[redacted]	8.2%
Osimertinib	[redacted]	[redacted]	[redacted]	8.2%

* Company fixed 8.2% for all patients on osimertinib. EAG conditional on those who received 2nd line treatments

EAG updated base case of distribution of 2nd line treatments in patients who received them

From ↓To →	**PDC**	Pemetrexed	Docetaxel	ABCP
Osimertinib + chemotherapy	[redacted]	[redacted]	[redacted]	7%
Osimertinib	[redacted]	[redacted]	[redacted]	7%

Abbreviations: ABCP, Atezolizumab + bevacizumab + carboplatin + paclitaxel; PDC, platinum doublet chemotherapy