Public observer slides

AIC and CIC redacted

NICE National Institute for Health and Care Excellence

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection

Lead team presentation

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ERG: ScHARR

Technical team: Gary McVeigh, Laura Coote & Samuel Harper, Caron Jones, Ross Dent

Company: AstraZeneca

ACM1 date: 14th July 2021

Key issues

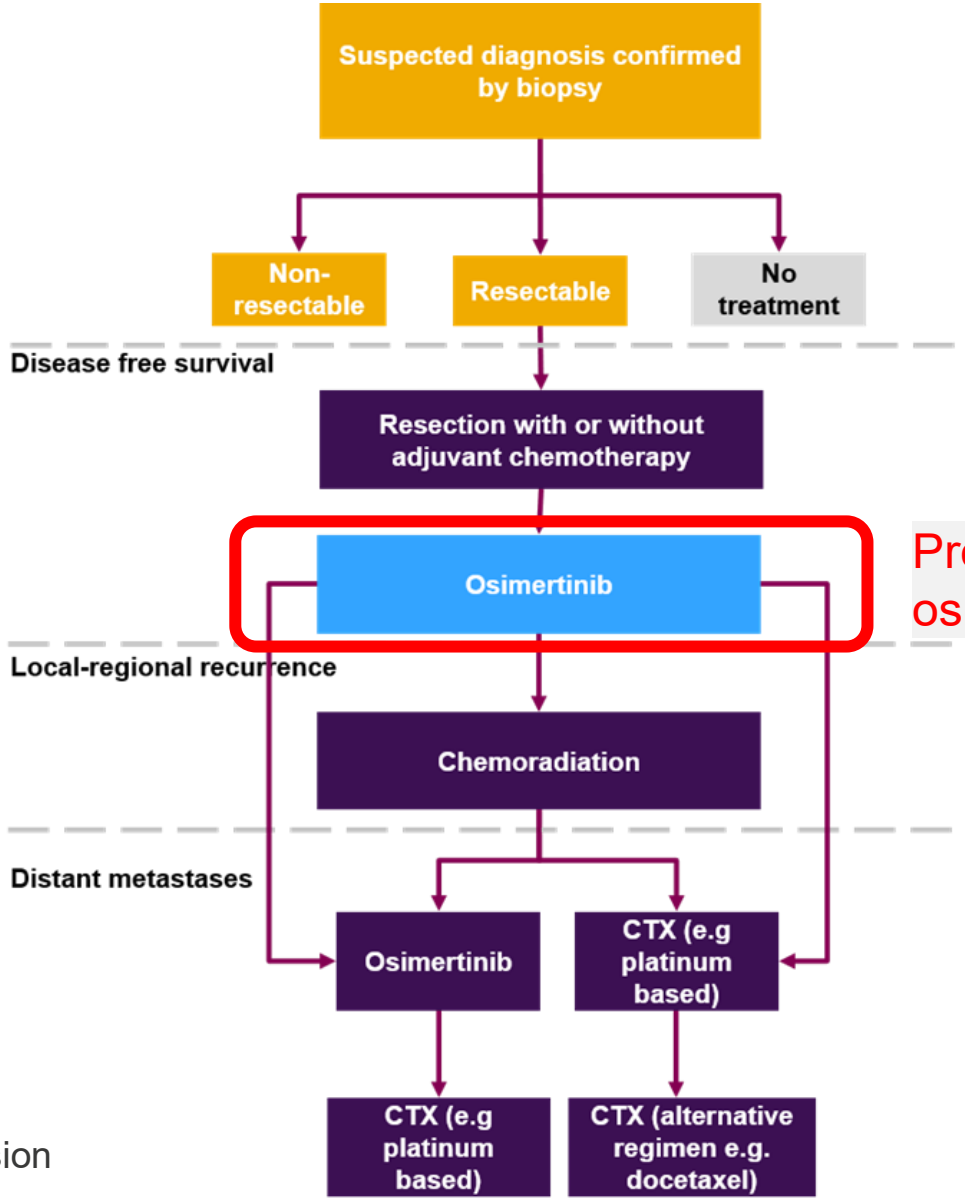
- **Issue 1:** Is a statistically significant disease free survival (DFS) benefit likely to translate into a significant overall survival (OS) benefit?
- **Issue 3:** What should be the timing of the cure assumption under current practice (active monitoring)? Will adjuvant osimertinib prevent, or only delay, disease recurrence beyond this timepoint?
- **Issue 2:** What are the downstream treatment pathways with or without adjuvant osimertinib?
- **Issue 4:** Should re-treatment with osimertinib be permitted?
- **Issue 5:** Given the lack of evidence, is the exploration of the utility values for EGFRm-positive NSCLC acceptable?
- **Issue 6:** Should the model include subgroup analyses for patients with stage IB NSCLC?
- **Cancer Drugs Fund (CDF):** Should osimertinib be considered for the CDF?

DFS = Disease free survival; OS = Overall survival; EGFRm = Epidermal growth factor receptor mutation; NSCLC = Non-small cell lung cancer

Disease background

- Lung cancer is 3rd most common cancer and the most common cause of cancer death in UK. Up to 85% of lung cancers are non-small-cell lung cancers (NSCLC)
- Among the mutations observed in NSCLC, epidermal growth factor receptor mutations (EGFRm) are common , found in 10% of patients with adenocarcinoma
- Surgical removal of tumours is the preferred treatment for many patients with early-stage NSCLC due to its curative potential. Despite the curative intent of complete resection, 45% of patients with stage IB, 62% with stage II, and 76% with stage III disease experience disease recurrence within approximately 5 years of surgery
- Resectable NSCLC imposes a clinical and humanistic burden, which may include disease symptoms and poor mental health, and reduced quality of life (QoL)
- Disease recurrence occurs at distant sites in almost 70% of patients with post-resection recurrence, with brain metastases most frequent
- Due to disease recurrence, post-resection mortality rates are 38–70% in stage IB–III disease over an approximate 5-year follow-up
- Prevention of recurrence – especially distant and central nervous system (CNS) recurrence – is critical to improve survival and avoid high-burden metastases.

Positioning in treatment pathway



Proposed positioning of osimertinib as adjuvant treatment

Source: Company submission
Part B, Figure 4

Abbreviations: CTX, chemotherapy; EGFRm, epidermal growth factor receptor mutation; EGFR TKI, epidermal growth factor receptor tyrosine kinase inhibitor; NSCLC, non-small cell lung cancer.

Osimertinib (Tagrisso, AstraZeneca)

Marketing authorisation	Osimertinib as adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA non-small cell lung cancer (NSCLC) whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
Mechanism of action	Osimertinib is a selective, small molecule tyrosine kinase inhibitor that targets the sensitising (exon 19 deletions and exon 21 L858R point mutations) and T790M mutant forms of the EGFR-TK, while having minimal activity against wild-type EGFR
Administration	Orally at a dose of 80mg once daily. The model includes a stopping rule for osimertinib at 3 years based on the design of the ADAURA trial. The SmPC states that *'patients in the adjuvant setting should receive treatment until disease recurrence or unacceptable toxicity. Treatment duration for more than 3 years was not studied'*
Cost (list price)	The list price for 30 tablets is £5,770. At list price, the total cost is approximately £210,000 per patient (36 months treatment duration). Commercial access arrangements are in place for osimertinib (as a downstream treatment) and XXXX

Background

Clinical trial: ADAURA	Phase III, randomised, double-blind, multicentre study
Comparators	Active monitoring (placebo in ADAURA trial)
Population and subgroups	**Overall:** Adults with fully resected, stage IB-IIIA EGFRm-positive NSCLC **Subgroups**: Stage IB and stage II-IIIA EGFRm-positive NSCLC
Key results for the overall population (interim results: data cut-off from 17 January 2020)	OS: HR [redacted] DFS: HR 0.20 (99.12% CI 0.14, 0.30; p<0.001) CNS: HR: 0.18 (95% CI: 0.10, 0.33; p<0.0001) ADAURA study was unblinded 2 years early due to overwhelming efficacy. OS results have [redacted] maturity
Model	State transition (semi-Markov) approach. Five health states: (i) disease-free (DF); (ii) loco-regional recurrence (LRR); (iii) first-line treatment for distant metastases (DM1); (iv) second-line treatment for distant metastases (DM2), and (v) dead
Company base case ICERs*	Probabilistic: £11,314 per QALY gained Deterministic: £11,136 per QALY gained
ERG base case ICERs**	Optimistic: £9,838 per QALY gained (probabilistic) Pessimistic: £20,301 per QALY gained (probabilistic)

*[redacted]

**[redacted]

Patient and carer perspectives

Views from EGFR Positive UK Lung Cancer Charity and one patient

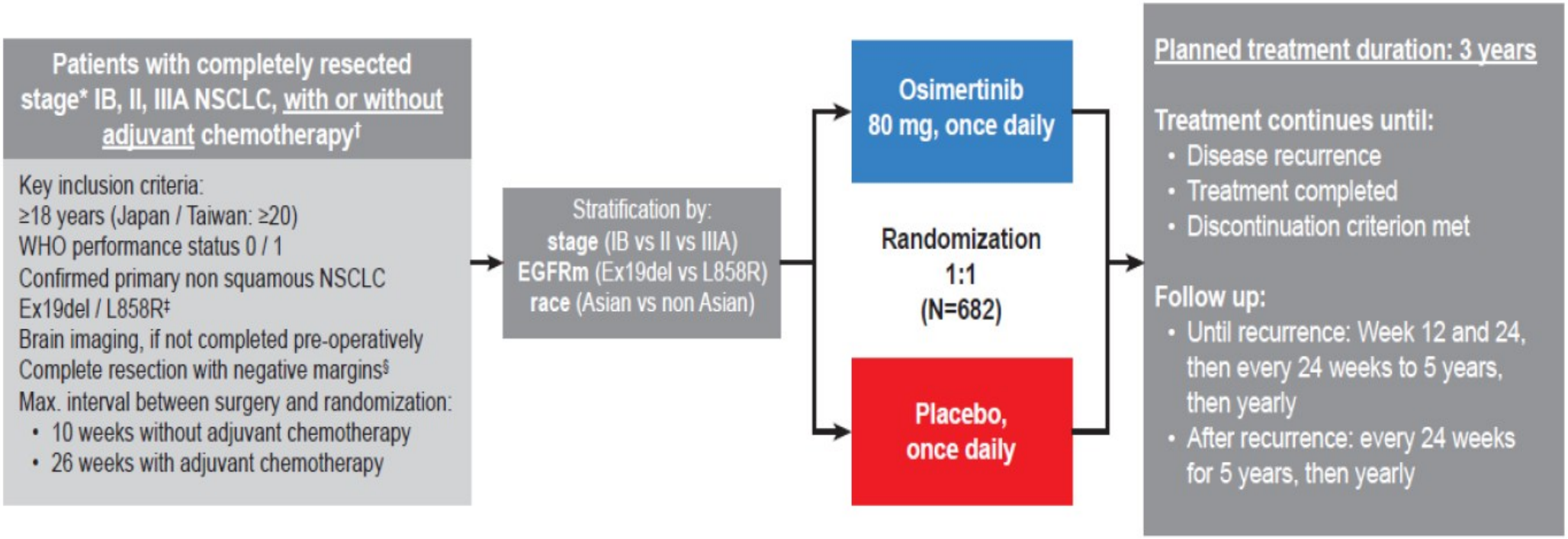
- *"Psychologically, socially, and economically, life can be extremely challenging."*
- There are few options once resistance to TKIs develop
- An adjuvant treatment to prevent/delay progression would be welcomed by patients
- Taking a single daily tablet is easy and means less time in hospital
- Osimertinib is a well-tolerated drug, with a low toxicity profile. It is important that this option is available
- *"Most fellow patients with EGFR dread the move to chemo"*
- *"Continued use of osimertinib after 3 years is not recommended. Why? If the patient is doing well what would be the recommended replacement treatment?"*
- If osimertinib is prescribed in the adjuvant setting it may not be available as a later treatment / re-challenge. This would mean some patients lose out on a potentially beneficial later treatment
- *"Taking a daily TKI has minimal impact on me or my family and enables this patient to live a full and active life"*

Clinical expert perspectives

Views from Royal College of Pathologists and 4 clinical specialists:

- Significant unmet need
- Variation in how and when EGFR testing for NSCLC is performed, and in the use of adjuvant chemotherapy in the UK
- This technology may result in an increased demand to test NSCLC tumours for EGFR mutations. These costs have already been recognised and addressed by the ERG in their analysis.
- The clinical trials broadly reflect current UK clinical practice.
- In UK, frequency of EGFR mutation positive patients after lung cancer resection is likely to be much lower (<5%) than the ADAURA cohort.
- Potential equality issue - EGFR mutation positive tend to occur more in women and Chinese people.
- Most important outcomes: Disease free survival (DFS), intracranial DFS, overall survival, health-related quality of life

ADAURA trial information



*AJCC 7th edition. †Prior, post, or planned radiotherapy was not allowed. ‡Centrally confirmed in tissue, prior to randomisation during the screening period (maximum 4 weeks). §Patients received a CT scan after resection and within 28 days prior to treatment.
Abbreviations: AJCC, American Joint Committee on Cancer; CT, computed tomography; EGFRm, EGFR mutation positive; Ex19del, exon 19 deletion; NSCLC, non-small cell lung cancer; WHO, World Health Organization.
Source: Wu et al, 2020.

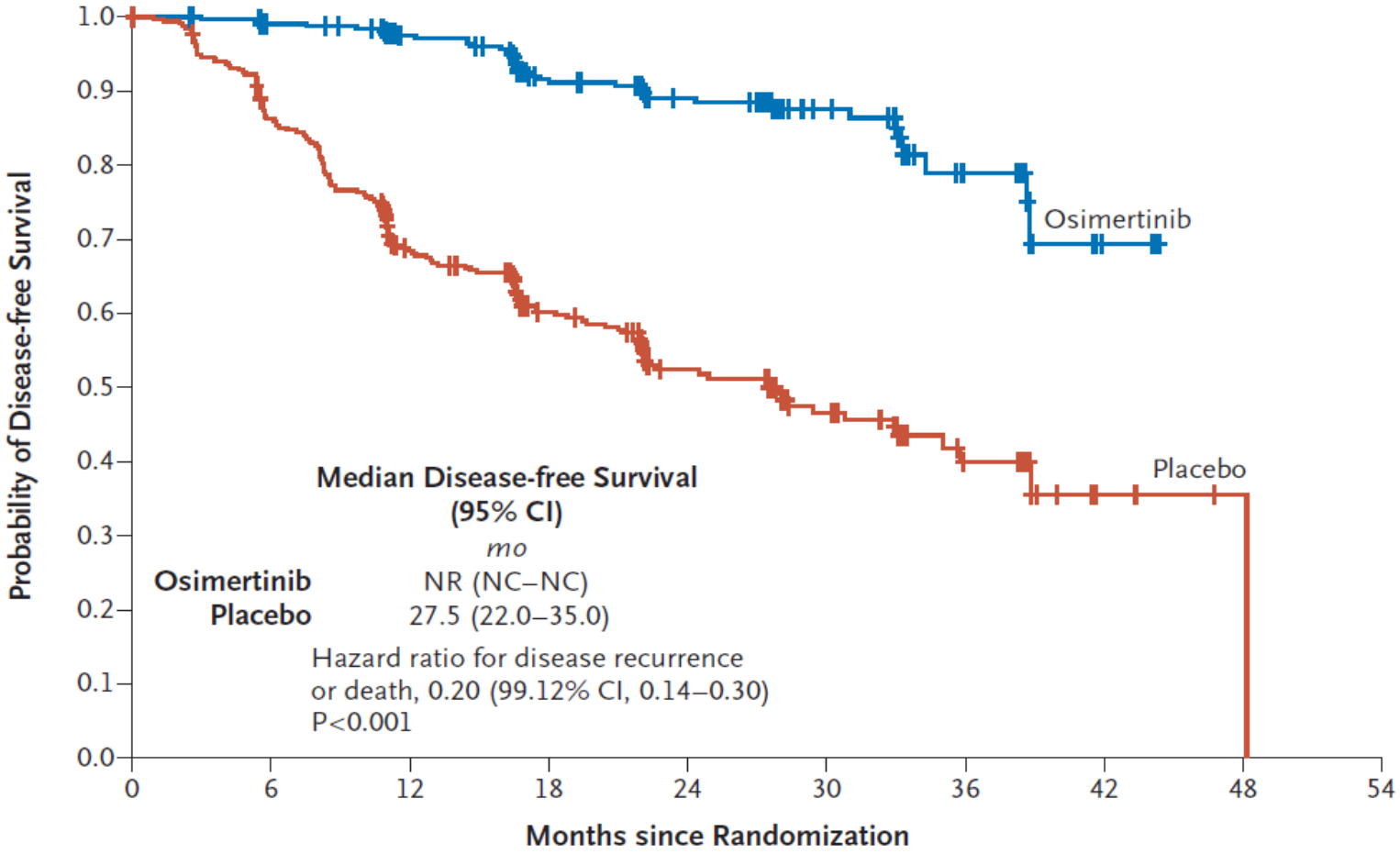
NICE Source: Company submission Part B, Figure 5

Key trial results

	Key outcomes*	Osimertinib	Placebo
	Number in study (n)	339	343
Overall population (stage IB-IIIA)	Median DFS (months)	Not reached	27.5
	DFS benefit	HR: 0.20; 99.12% CI: 0.14, 0.30; p<0.001	
	Proportion of patients alive and disease free at 24 months (%)	89.1 (95% CI: 84.5, 92.4)	52.4 (95% CI: 46.4, 58.1)
	Median OS (months)	XXXX	XXXX
	CNS recurrence	4 patients (1.2%)	33 patients (9.6%)
	Number in study (n)	233	237
Subgroup (stage II–IIIA	Median DFS (months)	Not reached	19.6
	DFS benefit	HR: 0.17; 99.06% CI: 0.11, 0.26; p<0.001	
	Proportion of patients alive and disease free at 24 months (%)	89.5 (95% CI: 84.0, 93.2)	43.6 (95% CI: 36.5, 50.6)
	Median OS (months)	Not calculable	Not calculable
	CNS recurrence	XXXX	XXXX

NICE *Interim results: data cut-off from 17 January 2020

Kaplan-Meier plot of DFS in ADAURA - Overall population



No. at Risk										
Osimertinib	339	313	272	208	138	74	27	5	0	
Placebo	343	287	207	148	88	53	20	3	1	0

CI - confidence interval; DFS - disease-free survival; NC - not calculable; NR - not reached. Tick marks indicate censored data.

Original source: Wu Y-L, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non–small-cell lung cancer. N Engl J Med 2020;383:1711-23. DOI: 10.1056/NEJMoa2027071

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Source: Company submission Part B, Figure 7

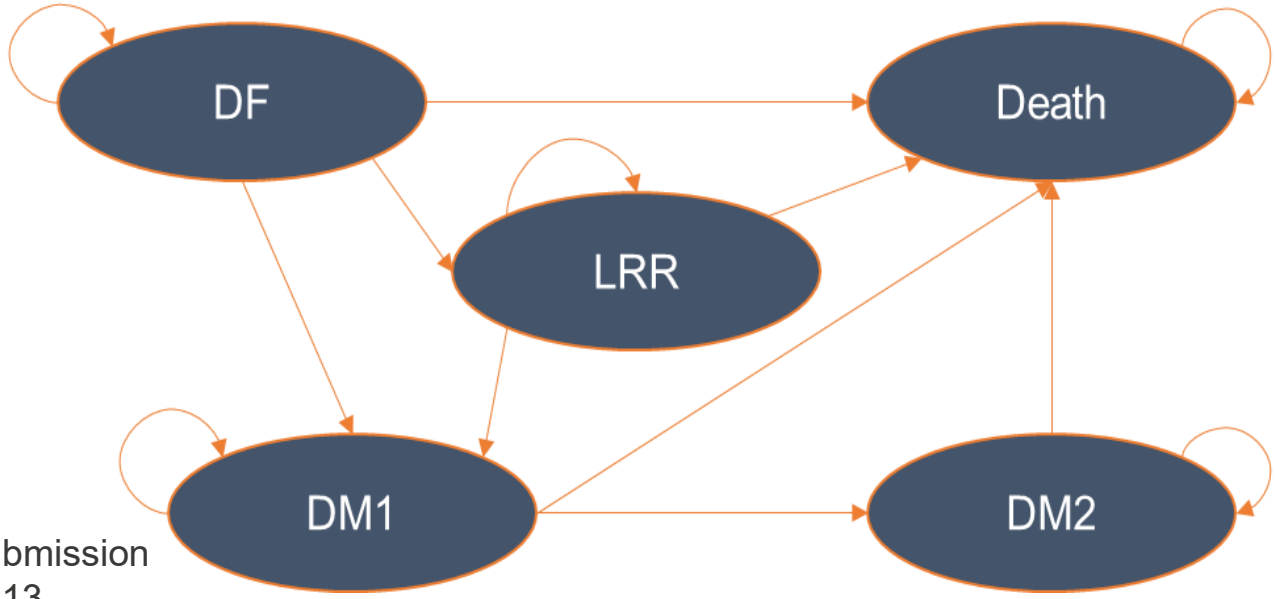
Kaplan-Meier plot of OS in ADAURA - Overall population

Source: Company submission Part B, Figure 10

Observed and model-predicted OS, based on ADAURA & company model (re-drawn by ERG using company's updated model)

NICE Source: ERG Post-FAC Report, Figure 21

Model structure:



Source: Company submission Part B, Figure 13

Structure	Semi-Markov model with 5 health states: 'Disease-free (DF)', 'Locoregional recurrence (LRR)', '1st line treatment for distant metastatic NSCLC (DM1)', '2nd line treatment for distant metastatic NSCLC (DM2)', and 'Death'
Time horizon	37 years
Cycle length	4 weeks (28 days)
Half-cycle correction	Yes
Stopping rule	3 years for osimertinib based on the design of the ADAURA trial
Discount rate	3.5%
Perspective	NHS and Personal Social Services

Model transition rates

Parameter group	Source
Transitions from DF to LRR and DM1 (TP1, TP2)	Adjuvant osimertinib group: ADAURA, osimertinib group Active monitoring group: ADAURA, placebo group
Cure assumption (assumed reduction in risk of relapse and associated timepoint)	Assumed reduction in risk based on company's assumption; timepoint for reduction in risk based on input from clinical experts
Transition from LRR to DM1 (TP4)	Both groups: CancerLinQ

Transitions between DM1, DM2 and dead (TP6, TP7, TP8)	• Adjuvant osimertinib group
	  ○ no re-treatment: FLAURA TKI arm with HR adjustment from a published meta-analysis to reflect chemotherapy outcomes
	  ○ re-treatment: FLAURA osimertinib arm
	• Active monitoring group: FLAURA osimertinib arm
	• DM1 to dead (TP7) for both groups based on pooled TKI and osimertinib data from FLAURA

Re-treatment probability	Company's assumption, ratified by clinical experts
Transitions from DF and LRR to dead (TP3, TP5)	ONS life tables

TP - transition probability; DF - disease-free; LRR - loco-regional recurrence; DM1 - first-line treatment for distant metastases; DM2 - second-line treatment for distant metastases

NICE Source: ERG Post-FAC Report, Table 20

Outstanding issues after technical engagement

Issue	Impact	Slides
Issue 1: Uncertainty surrounding whether a benefit in disease-free survival (DFS) will translate to a benefit in overall survival (OS)		17-18
Issue 3: Uncertainty surrounding company's cure assumptions and OS predictions		19-20
Issue 2: Uncertainty surrounding downstream treatment pathways with or without adjuvant osimertinib		21-22
Issue 4: Uncertainty regarding re-treatment with osimertinib		23
Issue 5: Limitations of available utility values for EGFRm-positive NSCLC		24
Issue 6: Absence of subgroup analyses for patients with stage IB NSCLC		25-26
CDF: Should osimertinib be considered for the CDF?		29

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Model driver


Unknown impact


Small/Moderate impact

Issue 1: Uncertain whether a benefit in disease-free survival (DFS) will translate to a benefit in overall survival (OS)

Background: ADAURA trial was unblinded at trial level 2 years early due to overwhelming efficacy with osimertinib for DFS. OS and DFS data are therefore immature.
Median duration of treatment : 22.5 months in osimertinib arm and 18.7 months in placebo arm.

ERG comments:

- OS data were immature. Therefore, it is uncertain whether the statistically significant DFS benefit will translate into a significant OS benefit.
- ERG has done exploratory analyses which assess the impact of making optimistic and pessimistic assumptions regarding how DFS translates to OS in the model.

Company TE response: Even though OS data from ADAURA is highly immature, a numerical benefit was observed in the overall population for osimertinib vs placebo. Adjuvant osimertinib is expected to translate into long-term survival benefit due to the unprecedented magnitude of the DFS benefit, the significant reduction in CNS metastases and the consistent OS benefit observed in the metastatic setting.

[redacted]

- [redacted]
- [redacted]
- [redacted]

Issue 1: Uncertain whether a benefit in disease-free survival (DFS) will translate to a benefit in overall survival (OS)

Response from clinical experts:

- DFS is a clinically significant and meaningful endpoint.
- OS outcome data remains immature, so uncertainty remains around the extent to which adjuvant osimertinib prevents disease recurrence versus delays disease recurrence.

ERG critique of company TE response:

- The ERG agrees that DFS is a clinically relevant endpoint and that there is value in extending DFS in patients with resected EGFRm NSCLC.
- Due to the immaturity of OS data from ADAURA, the magnitude of any OS benefit is uncertain. The impact of this uncertainty has been explored. See key issue 3. (ERG report, Section 5.4).
- The company's technical engagement response does not present any additional evidence which addresses this uncertainty.

Technical team:

- DFS data in ADAURA are immature and its uncertain how DFS benefit will evolve with further follow up.
- There is uncertainty surrounding how DFS benefit will translate to OS benefit:
  - Uncertainty over transitions from loco-regional recurrence to metastatic stage (based on CancerLinQ data) .
  - Uncertainty over the transitions in the metastatic stage.

Question: Is a statistically significant DFS benefit likely to translate into a significant OS benefit?

Issue 3: Uncertainty surrounding company's cure assumptions and OS predictions

Background: The predicted OS gain is a function of all transitions included in the model, most of which are informed by external data, and the company's structural cure assumption (risks of transitioning from disease free (DF) to Loco-regional recurrence (LRR) and first-line treatment for distant metastatic NSCLC (DM1) are reduced by 95% from 5 years onwards).

ERG comments:

- Timing of cure assumption under current practice (active monitoring) and whether adjuvant osimertinib will prevent, or only delay, disease recurrence beyond this timepoint uncertain.
- The ERG's preferred pessimistic analysis applies a later timepoint for cure in the adjuvant osimertinib group of 8 years → 8 years = 5-year cure timepoint in the active monitoring group plus the 3-year osimertinib treatment period.
- Sensitivity analysis exploring the impact of applying less favourable parametric survival models for transitions out of the DF health state in the adjuvant osimertinib group was undertaken.

Company TE response:

- XXXX
- ERG's pessimistic analysis is overly pessimistic and clinically implausible due to the suggested change in survival probabilities being equal at the relative cure points. This contradicts the DFS benefit displayed in the ADAURA trial and clinical opinion.
- A 6-year cure timepoint for osimertinib is supported by UK clinical opinion.

Issue 3: Uncertainty surrounding company's cure assumptions and OS predictions

Response from clinical experts:

- The magnitude of benefit will be greater in the real world for patients than that presented.
- Given relatively longer active treatment phase (3 years), 5-year timepoint may be less applicable

ERG critique of company TE response:

- ERG's views unchanged – company's cure assumptions and magnitude of additional OS benefit uncertain.
- ERG report presents a range of scenarios which explore this uncertainty; the most pessimistic scenario is a potentially helpful marker to be interpreted as a worst-case scenario.
- The ERG does not believe that the company's updated economic analyses fully represent the uncertainty surrounding the available OS data from ADAURA or the extent to which adjuvant osimertinib will lead to cure and extended OS.

Technical team:

- Assumption on cure timepoint is based on clinical opinion rather than data.
- Uncertain whether adjuvant osimertinib will leave the number of people cured following resection unchanged and just delay recurrence in uncured patients, or whether osimertinib will eliminate micro-metastases in some patients and so increase the cured proportion.

Question: What should be the timing of the cure assumption under current practice? Will adjuvant osimertinib prevent or delay disease recurrence beyond this?

Issue 2: Uncertainty surrounding downstream treatment pathways with or without adjuvant osimertinib

Background: Within the intervention group, all patients who develop distant metastases within 5 years of starting adjuvant osimertinib treatment are assumed to have pemetrexed plus cisplatin (PDC) followed by docetaxel. After this 5-year timepoint, 50% of patients who develop distant metastases are assumed to be re-treated with osimertinib as first-line therapy followed by PDC, with the remaining 50% receiving PDC followed by docetaxel.

ERG comments:

- ERG prefers to include atezolizumab, bevacizumab, carboplatin and paclitaxel (ABCP) as a 2nd-line treatment in both groups and exclude re-treatment in the adjuvant osimertinib group.
- NICE has recently recommended osimertinib for metastatic disease and it is expected that the use of this drug will increase.
- The company's clarification response and the ERG's exploratory analyses each include additional scenarios in which other TKIs are used.
- If re-treatment is not permitted, the company's model assumes that a patient who has adjuvant osimertinib and subsequently develops distant recurrence will go on to have PDC followed by docetaxel. It is unclear whether this pathway is appropriate.

Company TE response:

- Osimertinib represents the mainstay treatment option and is considered the current standard of care in 1L locally advanced/metastatic EGFRm NSCLC.

Issue 2: Uncertainty surrounding downstream treatment pathways with or without adjuvant osimertinib

Response from clinical experts:

- Patients who progress *during* treatment with osimertinib are likely to have chemotherapy or a combination of atezolizumab, bevacizumab, carboplatin and paclitaxel (ABCP).
- Patients who progress *after* treatment with osimertinib, should be treated like other patients newly presenting with metastatic disease and would be offered osimertinib if they meet the criteria.
  - It would be unethical not to offer rechallenge of osimertinib to these patients.

ERG critique of company TE response:

- ERG's preferred analyses assume patients in the active monitoring group who develop distant metastases will receive 1st-line treatment with osimertinib, consistent with company's base case.
- ERG report includes an additional sensitivity analysis (ASA3) which assumes that a mix of TKIs is used as prescribing data show that currently not everyone with distant metastases gets osimertinib.

Question: What are the downstream treatment pathways with or without adjuvant osimertinib?

Issue 4: Uncertainty regarding re-treatment with osimertinib

Background: In the model some patients who have adjuvant osimertinib and subsequently develop distant metastases go on to have osimertinib as 1st-line treatment in the metastatic setting.

ERG comments: ERG's exploratory analyses exclude re-treatment following personal communication from NHSE. If re-treatment is permitted, it may be appropriate to consider further scenarios in which effectiveness is assumed lower than observed in FLAURA.

- Longer-term follow-up from ADAURA may help to resolve uncertainty surrounding the plausibility of the company's cure assumptions and the modelled OS predictions.
- This would not affect the ICER in the optimistic scenario because the re-treatment time point coincides with the cure time point. However, it will have more impact in the pessimistic scenario as the cure and re-treatment time points no longer coincide.

Company TE response: Re-treatment with osimertinib is supported by UK clinical opinion.

ERG critique of company TE response:

- The ERG believes that this issue is a matter for NHSE to address.
- Whilst the ERG's preferred analyses assume that re-treatment is not permitted, the ERG report includes an additional sensitivity analysis (ASA7) in which re-treatment is permitted. This analysis indicates that including re-treatment has a limited effect on the ICER for adjuvant osimertinib.

Question: Should re-treatment with osimertinib be permitted?

Issue 5: Limitations of available utility values

Background: utility values are based on EQ-5D-3L estimates from ADAURA (mapped from the SF-36), EQ-5D-3L estimates from FLAURA (mapped from the EORTC QLQ-C30) and published EQ-5D-3L estimates from the literature (Labbé *et al*). Disutilities associated with AEs are based on published literature (Nafees *et al*, standard gamble) and TA653.

ERG comments - concerns with the utility values applied in the company's original model:

- Utility value applied in the disease free (DF) and loco-regional recurrence (LRR) health states is higher than for the age and sex matched population – n.b. now capped at general population level
- Utility value applied in the first-line treatment for distant metastases (DM1) state (0.794) may be implausibly high
- The model does not include HRQoL decrements for late effects of adjuvant treatment or downstream AEs
- The ERG has conducted sensitivity analyses which use alternative utility values from Andreas *et al.* and which include longer-term QALY losses associated with AEs

Company TE response:

- Updated utility value for DFS (and therefore LRR) to be equal to general population estimates
- Agree that patients with LRR will likely not have the same level of quality of life as those who are disease-free in clinical practice

ERG critique of company TE response:

- ERG's exploratory analyses include an additional sensitivity analysis using utility values from *Andreas et al.;* limited impact on the ICER. No further comments.

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Question: Given the lack of evidence, are the utility values in the model acceptable for decision-making?

Issue 6: No subgroup analyses for patients with stage IB NSCLC

Background: The model reflects the overall population of ADAURA and does not report an economic subgroup analysis for patients with stage 1B NSCLC.

ERG comments:

- The final NICE scope states that *"If the evidence allows, subgroups based on NSCLC stage (IB versus II-IIIA) may be considered."*
- Company stated that available data are limited for the stage 1B subgroup and that the study was not powered to assess the efficacy of osimertinib by stage of disease
- Subgroup analysis presented for patients with stage II-IIIA NSCLC, resulted in a lower ICER that that for the overall population → implies osimertinib is likely to be less cost-effective in the stage 1B subgroup
- ERG would prefer to see an economic subgroup analysis for patients with stage 1B NSCLC; however, data are currently very limited

Company TE response:

- Osimertinib has demonstrated a significant DFS benefit in stage IB
- Osimertinib as adjuvant treatment for stage IB will be cost-effective use of NHS resources
- Inappropriate to consider an analysis by subgroup

Issue 6: No subgroup analyses for patients with stage IB NSCLC

Response from clinical experts:

- The comparison should simply be between the effectiveness of osimertinib versus placebo in the stage IB group.
- The improvement in DFS appears to extend to stage IB patients and therefore is appropriate to include within these patients for a final recommendation.

ERG critique of company TE response:

With respect to the company's argument that it is inappropriate to consider subgroup analyses, the ERG disagrees for several reasons:

- The stage IB subgroup is identifiable
- The inclusion of subgroup analyses by stage was listed in the "Other considerations" section of the final NICE scope
- There is uncertainty regarding whether adjuvant osimertinib might represent a good use of NHS resources in the stage IB subgroup.

Question: Should the model include subgroup analyses for patients with stage IB NSCLC?

Summary of ERG base cases

Summary of key differences ERG base cases

ERG base case - optimistic	ERG base case - pessimistic
EA1: Correction of model errors	
EA2: Re-treatment not permitted	
EA3: 5-year treatment effect for metastatic osimertinib DM1 to DM2	
EA4: Update unit costs for administration of chemotherapy and docetaxel drug acquisition	
EA5: Inclusion of wastage for osimertinib (0.50 packs)	
EA6: Inclusion of ABCP treatment option	
	EA7: 8-year cure point applied
ERG preferred optimistic analysis (EA1-EA6 combined)	**ERG preferred pessimistic analysis (EA1-EA7 combined)**

Cost-effectiveness results

All cost-effectiveness results are reported in private PART 2 slides because they include confidential PAS discounts for other treatments

Cancer Drugs Fund

Committee decision-making criteria:

ADAURA trial is currently congoing. Next data cut XXXX with study completion expected XXXX

Proceed down if answer to each question is yes

Starting point: drug not recommended for routine use due to **clinical uncertainty**

1. Is the model structurally robust for decision making? (omitting the clinical uncertainty)

2. Does the drug have plausible potential to be cost-effective at the offered price, taking into account end of life criteria?

3. Could further data collection reduce uncertainty?

4. Will ongoing studies provide useful data?

and

5. Is CDF data collection via SACT relevant and feasible?

Consider recommending entry into CDF (invite company to submit CDF proposal)

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

Other Considerations

Innovation:

- Osimertinib is recognised as an innovative therapy in the adjuvant setting and therefore the ADAURA indication has been reviewed as part of Project Orbis.

Equality:

- No case for end of life has been made
- EGFR mutation positive tend to occur more in women and Chinese people – issues of different disease prevalence cannot be addressed in a TA

- **Is osimertinib innovative?**
- **Are there any benefits that have not been adequately captured in the economic model?**
- **Are there any more equality issues relevant to this appraisal?**

Key Issues

- **Issue 1:** Is a statistically significant disease free survival (DFS) benefit likely to translate into a significant overall survival (OS) benefit?
- **Issue 3:** What should be the timing of the cure assumption under current practice (active monitoring)? Will adjuvant osimertinib prevent, or only delay, disease recurrence beyond this timepoint?
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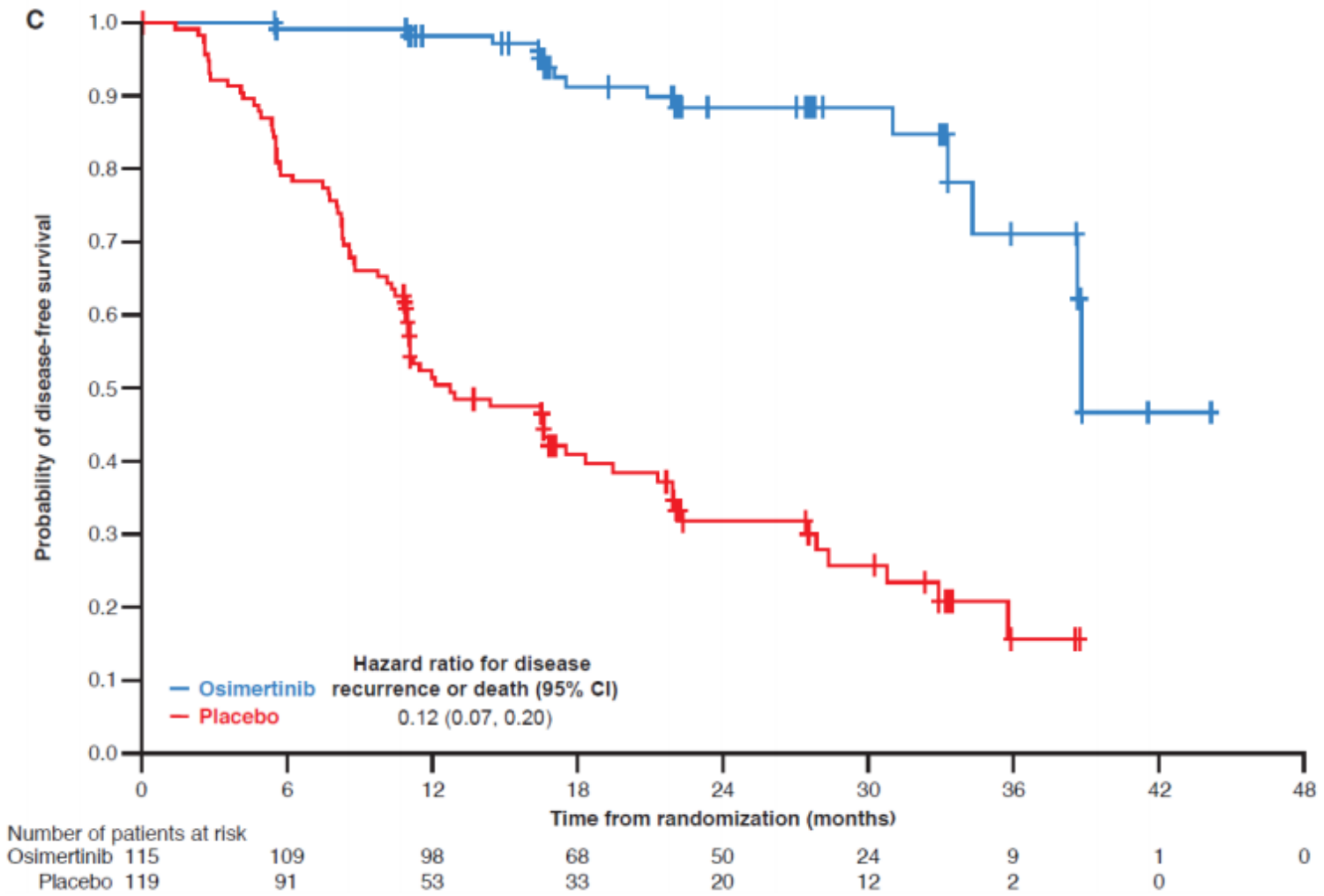
- **Issue 6:** Should the model include subgroup analyses for patients with stage IB NSCLC?
- **Cancer Drugs Fund (CDF):** Should osimertinib be considered for the CDF?

DFS = Disease free survival; OS = Overall survival; EGFRm = Epidermal growth factor receptor mutation; NSCLC = Non-small cell lung cancer

Back-up

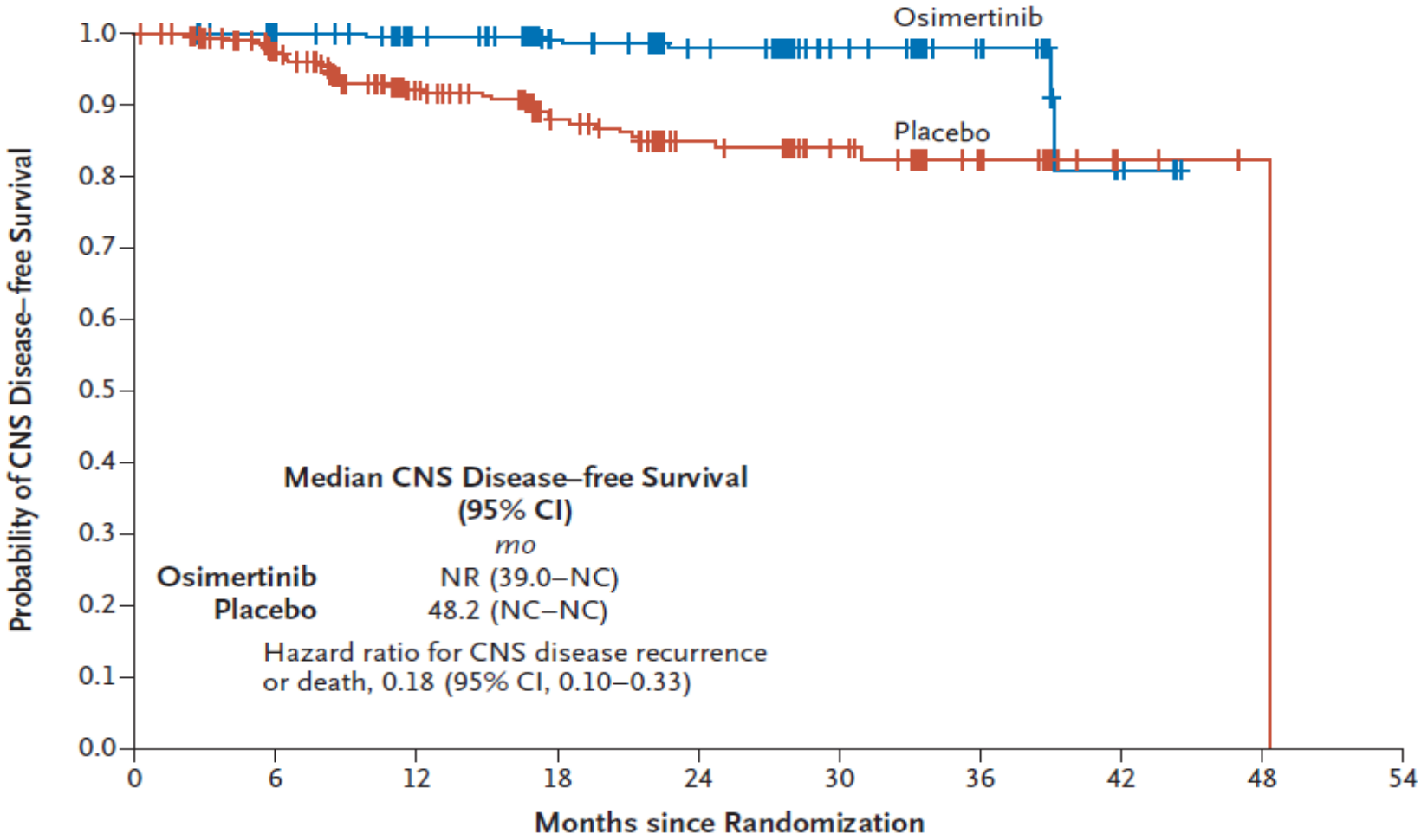
DFS by stage of disease: stage IIIA



CI - confidence interval. Tick marks indicate censored data.

Source: Supplement to: Wu Y-L, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non–small-cell lung cancer. N Engl J Med 2020;383:1711-23. DOI: 10.1056/NEJMoa2027071.

Kaplan-Meier plot of CNS DFS in ADAURA - Overall population



No. at Risk										
Osimertinib	339	313	272	209	138	74	28	5	0	
Placebo	343	288	208	149	88	53	20	3	1	0

CI - confidence interval; CNS - central nervous system; DFS - disease-free survival; NC - not calculable; NR - not reached.

Source: Wu Y-L, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non–small-cell lung cancer. N Engl J Med 2020;383:1711-23. DOI: 10.1056/NEJMoa2027071.

NICE Source: Company submission
Part B, Figure 12