NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance

Osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (review of TA761)

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using osimertinib in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Issue date: June 2024

Note that this document is not NICE's final guidance on osimertinib. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using osimertinib in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 18 July 2024
- Second evaluation committee meeting: 7 August 2024
- Details of the evaluation committee are given in section 4

1. Recommendations

1.1 Osimertinib is not recommended, within its marketing authorisation, for the adjuvant treatment of stage 1b to 3a non-small-cell lung cancer (NSCLC) after complete tumour resection in adults whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.

1.2 This recommendation is not intended to affect treatment with osimertinib that was funded by the Cancer Drugs Fund before final guidance was published. If this applies, when that funding ends osimertinib will be funded by the company. Osimertinib should be stopped at 3 years, or earlier if there is disease recurrence, unacceptable toxicity or the patient and their NHS healthcare professional consider it appropriate to stop.

Why the committee made these recommendations

This evaluation reviews the evidence for osimertinib for treating NSCLC after complete tumour resection (NICE technology appraisal guidance 761). It also reviews new evidence collected as part of the managed access agreement, which includes evidence from a clinical trial and from people having treatment in the NHS in England.

People with EGFR mutation-positive NSCLC whose tumour has been surgically removed (complete resection) have the option of then having chemotherapy. There are no other options to have in addition to chemotherapy, so if a person does not have osimertinib they would have active monitoring.

A clinical trial comparing osimertinib with placebo shows that people who have osimertinib have less chance of their cancer coming back or getting worse, and live longer. But in the long term it is uncertain whether osimertinib is a cure or just delays the cancer coming back.

Because of the uncertainty in the long-term clinical effectiveness, the most likely cost-effectiveness estimates are above the range that NICE normally considers an acceptable use of NHS resources. So, osimertinib is not recommended for routine use in the NHS.

2. Marketing authorisation indication

2.1 Osimertinib (Tagrisso, AstraZeneca) is indicated for 'adjuvant treatment following complete tumour resection in adults with stage IB to IIIA NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for osimertinib.

Price

2.3 The list price for osimertinib is £5,770 per 30 pack of 80-mg tablets (NICE BNF, June 2024). The company has a commercial arrangement (simple discount patient access scheme). This makes osimertinib available to the NHS with a discount. The size of the discount is commercial in confidence.

3. Committee discussion

The evaluation committee considered evidence submitted by AstraZeneca, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Epidermal growth factor receptor mutation-positive non-small-cell lung cancer

3.1 Non-small-cell lung cancer (NSCLC) accounts for around 80% to 85% of all lung cancers. People with an epidermal growth factor receptor (EGFR) mutation are at increased risk of recurrence, with particular risk of brain metastases. People with EGFR mutation-positive NSCLC tend to be younger than people with other types of NSCLC, so a treatment that delays or prevents recurrence or central nervous system (CNS) metastases is important. Around 8% to 16% of people with early-stage (1b to 3a) NSCLC have cancer that is EGFR mutation-positive. The patient experts outlined how earlier stage NSCLC can be asymptomatic for years with a wide range of symptoms developing later (such as cough, chest pain, difficulty breathing, weight loss, fatigue and bone pain). They explained that the fear of their cancer returning or spreading is a major source of anxiety and that the consequences of this happening can be devastating. They also highlighted that brain metastases can have particularly pronounced effects on their quality of life and can mean they must stop driving, limiting their ability to attend appointments. The committee agreed that people with EGFR mutation-positive NSCLC and their families would welcome new, effective treatments that reduce the risk of recurrence.

Clinical management

Existing treatment pathway

3.2 Complete tumour resection is the preferred treatment for many people with early-stage EGFR mutation-positive NSCLC because it is potentially a cure. Following complete tumour resection, people have the option of having adjuvant chemotherapy, which provides a small benefit in overall survival (OS). The patient experts advised that the side effects of

chemotherapy can be very difficult to manage and that people often dread this option. But they added that the thought of doing nothing following surgery and their cancer returning can cause significant anxiety and panic. They also advised that monitoring can help to reduce anxiety, but because the frequency of scans varies between stages of disease, some people benefit less from this reassurance. There are no other options in the adjuvant setting. If people develop distant metastases after surgical resection, treatment options include chemotherapy or a tyrosine kinase inhibitor. The committee agreed that osimertinib as an adjuvant treatment may address an unmet need for people with EGFR mutation-positive NSCLC who have had a resection.

Active monitoring is an appropriate comparator

3.3 Osimertinib is a tyrosine kinase inhibitor that targets and kills cancerous cells that have EGFR mutations, but has minimal activity against cells without these mutations. Clinical experts advised that osimertinib is an improvement in the management of EGFR mutation-positive disease. They expressed that osimertinib extends disease-free survival (DFS) and OS and is tolerable, with limited side effects that are unlikely to lead to discontinuation of treatment. The patient experts agreed that osimertinib is a valuable, tolerable option and combined with frequent monitoring can reduce some of the anxieties surrounding recurrence. They agreed that there are fears surrounding stopping osimertinib after 3 years and uncertainty about what this means for their risk of recurrence. The company outlined how osimertinib is not intended to displace adjuvant chemotherapy but instead be used in this setting with or without chemotherapy. There is therefore no alternative to osimertinib in this treatment space and the relevant comparator is active monitoring. The committee concluded that active monitoring was the relevant comparator in this appraisal.

Clinical effectiveness

Osimertinib data sources

3.4 In the original evaluation (NICE technology appraisal guidance 761), the main clinical-effectiveness evidence for osimertinib came from the ADAURA trial, a phase 3 randomised, double-blind, placebo-controlled, multicentre trial. ADAURA compared adjuvant osimertinib 80 mg (n=339) with placebo (n=343) for adjuvant treatment of stage 1b to 3a EGFR mutation-positive NSCLC after complete tumour resection in adults. Following a recommendation in the Cancer Drugs Fund (CDF; NICE technology appraisal guidance 761), new evidence was collected as part of the managed access agreement. The current submission relies mainly on an updated data-cut of the ADAURA trial providing an additional 2 years of data for DFS and 3 years of data for OS. Additionally, the Systemic Anti-Cancer Therapy (SACT) dataset collected data on people who had osimertinib in the NHS during its availability in the managed access period.

Clinical effectiveness in the osimertinib study

3.5 Evidence from ADAURA showed that, compared with placebo, osimertinib led to improvements in key clinical outcomes, including DFS and OS. The median DFS in the osimertinib arm was 65.8 months, while in the placebo arm it was 28.1 months (hazard ratio [HR] was 0.27; 95% confidence intervals [CI] 0.21 to 0.34). Median OS was not reached in the osimertinib arm or the placebo arm, but 5-year OS rates were 88% and 78%, respectively (HR was 0.49; 95% CI 0.34 to 0.70). Long-term effectiveness was a key uncertainty in the original appraisal and the EAG noted that there is still uncertainty in long-term DFS and OS. This is because of the low number of events in the osimertinib arm. It is therefore possible that the gap between the osimertinib and placebo DFS curves will decrease over time. Maturity rates (percentage of people experiencing the event) for osimertinib were 28% for DFS and 12% for OS. One expert advised that

although osimertinib will only slow recurrence for some people, this is still a meaningful benefit. The trial also reported data on CNS-specific DFS, in which osimertinib showed a significant improvement compared with placebo (HR was 0.36; 95% CI 0.23 to 0.57). The committee agreed that osimertinib improves key outcomes compared with placebo, but that there was uncertainty around the extent to which the DFS benefit would continue beyond 6 years.

Subgroup clinical effectiveness in the osimertinib study

3.6 ADAURA reported evidence for stage 1b and stages 2 to 3a subgroups. The committee noted that for stages 2 to 3a, results were broadly similar to the overall population. But there was some uncertainty for the stage 1b subgroup, the benefit in DFS was smaller and rates of CNS-specific DFS were not reported. The EAG also expressed concern that subgroups were not included in the economic modelling. The committee agreed that it would have been useful to include subgroups in the economic modelling but that it was appropriate to use the overall population for decision making.

SACT dataset

3.7 The SACT dataset collected data on 143 people who had osimertinib between November 2021 and December 2022. The NHS England CDF clinical lead (from here, CDF lead) outlined that the population in SACT was older (median age 70 years) than the population in the ADAURA trial (median age 64 years). The number of people who had had prior chemotherapy was also much lower in the SACT dataset (27% compared with 60% in ADAURA). The EAG advised that this suggests some people may be being offered osimertinib instead of adjuvant chemotherapy. One clinical expert advised that some people would never have been offered chemotherapy, such as people who were too unwell to tolerate its side effects. Additionally, people with stage 1b NSCLC would not be offered cytotoxic chemotherapy and people with additional needs (such as

needing renal function monitoring) could be more likely to be offered osimertinib. But, people would typically still be offered chemotherapy if they are young and fit enough to tolerate it. The experts also advised that the option of osimertinib may mean that chemotherapy is stopped sooner if there are signs of cytotoxicity. The OS data maturity in SACT was only 6.2% by the April 2023 data cutoff. OS rates at 12 months were 92%, which is lower than those seen in ADAURA (95% at 36 months). The percentage of people on treatment was also lower in SACT than ADAURA at 12 months (75% compared with 96%) suggesting higher rates of people stopping treatment early. The committee discussed whether the data from SACT suggested osimertinib outcomes were more pessimistic in the real-world, but concluded that the data was too immature to make certain conclusions around this yet.

Economic model

Company's modelling approach

3.8 The company used a semi-Markov economic model for osimertinib and active monitoring that included 5 states:

- disease-free
- locoregional recurrence (LRR)
- distant metastases first-line
- second-line distant metastases, and
- death.

The model had a 37-year time horizon. The model assumed that people had active treatment on entry to the LRR or distant metastases health states. It also assumed that retreatment with first-line osimertinib in the distant metastases first-line health state is possible after 4 years (1 year after the maximum of 3 years on osimertinib treatment). It also included a cure assumption (see section 3.13). The committee concluded that the

model structure was appropriate for decision making but that there were concerns with the modelling of the cure assumption.

Extrapolating DFS and OS

3.9 The company used different distributions and different sources of data to inform the probability of transitions between the health states in the model. ADAURA DFS data was used to inform the choice of distribution for moving from the disease-free state to the LRR or distant metastases first-line health states. The FLAURA trial, which assessed the use of osimertinib in the metastatic setting, was used to inform the risk of mortality in the distant metastases health states (first- and second-line). The risk of mortality was constrained by general population rates in the UK. Risk of mortality in the disease-free and LRR health states was assumed to be the same as the UK age- and sex-matched general population. The EAG had concerns that the predicted data was not a good match for the data observed in the ADAURA trial. They suggested that alternative choices of distributions would improve this to an extent, but a key limitation was the choice of model form. The EAG explained that the model form selected by the company was very rigid and could not account for the complexities seen in the ADAURA data. For example, ADAURA hazards for the risk of developing LRR suggested 2 turning points for people having osimertinib, but the model only allowed for 1. Also, for people having active monitoring, none of the distributions provided a good fit to the data for transitioning between the disease-free and distant metastases first-line health states. For osimertinib, the EAG argued that alternative distribution choices offer better matches to the observed data. But the company argued that these alternative choices are overly influenced by longer-term trial data, which is very uncertain because of the small number of people still at risk of recurrence and being followed up. The committee were concerned that these limitations lead to uncertainty in the modelling of long-term outcomes and could introduce

inaccuracy. It concluded that this uncertainty was largely unresolvable without longer-term data.

Retreatment with osimertinib

3.10 The company model assumed that retreatment with osimertinib was possible but only from 4-years after starting treatment and that 50% of people who have a distant recurrence after this point would have osimertinib. The company also assumed that 83% of people who have a distant recurrence after being assigned to the active monitoring arm would have osimertinib. The EAG base case has the same assumptions but advised that it is likely a much higher percentage of people would have retreatment and that their clinical advisers suggested the vast majority would. The EAG conducted scenario analyses varying the rates of retreatment. Increasing the percentage of people having retreatment consequentially increases the incremental cost-effectiveness ratio (ICER). Data on retreatment was not collected in the SACT dataset. But, the CDF lead advised that despite osimertinib only having been available in the CDF for 3 years, around 7% (33 people) of those who had osimertinib have already had retreatment. They advised that this suggests that retreatment is happening before 4 years, and noted that retreatment was only allowed if a person did not progress on osimertinib previously. One clinical expert agreed that it is likely that the vast majority of people would have retreatment. They added that retreatment is particularly likely if the person stops treatment early or has low level toxicity. But people with adverse reactions to treatment or those with brain metastases may be less likely to have retreatment. The company outlined that in ADAURA, 41% of people in the osimertinib arm who had any subsequent treatment had osimertinib. But, the EAG advised that it was unclear how many of these people had previously progressed on osimertinib. The committee also noted that it was unclear whether osimertinib was available in the metastatic setting in all of the countries where the ADAURA trial was conducted. It added that the trial did not initially allow people in the active

monitoring group to have subsequent osimertinib. The committee agreed that it is likely that much more than 50% of people would have osimertinib as a retreatment in the metastatic setting. The committee agreed that 70% would be a more reasonable estimate. It also agreed that it was implausible that retreatment would only be started after 4 years (after first starting osimertinib), noting evidence from the CDF lead. The committee concluded that the model should allow retreatment from 3 years and that 70% of people having treatment in the metastatic setting who previously had osimertinib would be offered retreatment.

3-year stopping rule

3.11 The original appraisal included a 3-year treatment stopping rule in its model and this was again included in the company modelling. This is based on the trial design of ADAURA, where the maximum possible treatment duration was 3 years. It is also stated in the summary of product characteristics that treatment for more than 3 years was not studied. The clinical experts said that adjuvant treatment could not be indefinite and that the 3-year time period is appropriate. They also noted that some people would stop sooner in cases of high toxicity but noted that in their experience these people often respond well to treatment with osimertinib. They added that these risks and rewards must be balanced against each other. The committee noted that in ADAURA, 13% of people on osimertinib stopped because of toxicity compared with 3% in the placebo group. The patient expert explained that some people would find stopping treatment difficult because they would fear the disease coming back. The committee concluded that a 3-year treatment stopping rule was acceptable.

Starting age

3.12 The committee recalled that people in the SACT dataset were, on average, 6 years older than the people in ADAURA (see section 3.7). The company modelling used 63 years as the starting age upon entry to the

model, based on ADAURA. The committee were concerned that this might underestimate the average age of people having treatment. This has implications for cost-effectiveness estimates because a starting age of 70 years would mean that the average remaining life expectancy would be reduced. It agreed that a starting age of 70 years would be more reflective of what would be expected in the NHS because this is what was seen in SACT. The committee concluded that the economic model should use a starting age of 70 years, which would also reduce the time horizon of the model by 7 years (to 30 years). The committee requested analyses from the EAG to understand the impact of this change on the ICER.

Cure assumptions

Company and EAG approaches

3.13 The company applied a cure timepoint in the model. This meant that people only had a 5% chance of local or distant recurrence if they were in the disease-free health state for:

- 5 years in the active monitoring arm, or
- 8 years in the osimertinib arm.

The company advised that the difference in these final cure points was to account for the additional 3 years during which the person would have osimertinib. This was also the preferred assumption of the committee in the original appraisal. The company included a 'warm-up' period beginning after 4 years for both groups, in which the chance of having a recurrence decreases roughly linearly until the final cure-point (see section 3.14). The EAG commented that the company approach to modelling cure was unconventional. They noted that typically a mixture-cure model is used in which a 'cured' group is exposed to different risks of recurrence to a 'non-cured' group, after a specific timepoint. In the absence of an alternative model structure, the EAG base case was the same as the company's, but with no warm-up period. The EAG also

presented scenario analyses in which the osimertinib cure-point was reduced to 7 years and to be equivalent to how long someone is on treatment plus 5 years. But, neither of these scenarios had a warm-up period. The committee was concerned with the model structure used by the company, agreeing with the EAG that it was unconventional to model cure this way. But it agreed that decisions surrounding cure should be made using this model structure, in the absence of an alternative. It concluded that decisions had to be made on:

- whether there is evidence of cure in the data for either osimertinib or active monitoring (or both)
- the timepoint from which this cure should be applied (if at all), and
- whether a warm-up period should be applied.

Warm-up period

3.14 The company included a warm-up period because without it, people in the model would reach the final cure-point (see section 3.13) and suddenly have a huge drop in risk of recurrence, which is not plausible. It suggested that although the 4-year timepoint (from which a person's risk begins to decrease after remaining in the disease-free state) is arbitrary, it is more logical than a sudden drop. One clinical expert advised that a warm-up period should be included. They explained that this is because follow up in clinical practice is often only 5 years. By this timepoint, the risk of recurrence is low, the number of subsequent events is small, and a durable response is expected. But they added that the timepoint from which a warm-up period would begin is unclear. The EAG noted that the ADAURA trial shows that for active monitoring the risk of recurrence starts high and decreases over time, but for osimertinib it starts lower and increases. The committee agreed that this suggests that for some people osimertinib only slows recurrences compared with active monitoring. It is also possible that there is a rebound effect in which recurrence risk increases after stopping treatment. The EAG advised that although it is

not impossible that a plateau would emerge for osimertinib, the data does not show a clear cure-point in the hazards for recurrence. So a warm-up period from 4 years is unlikely. Additionally, the company noted that a warm-up period had been considered in the NICE technology appraisal for trastuzumab emtansine for adjuvant treatment of HER2-positive early breast cancer. The EAG advised that in that appraisal, the warm-up period assumption had a relatively small impact on the ICER and the cure points for the treatment and comparator was the same. But for this appraisal it has a much bigger impact and the cure time-points are different between treatments. The committee noted that applying a warm-up period has implications for long-term modelling of outcomes, creating a substantial gap in DFS between osimertinib and placebo that extends decades into the future. It agreed that a sharp drop in risk had been seen in the DFS curves for previous tyrosine kinase inhibitors and had concerns with applying a warm-up period to the modelling. It noted that there was a lack of support for this in the observed data and that the warm-up period started after 4 years for both treatment groups. This is despite osimertinib having a longer final cure-point and the fact many people in that group will only just have finished treatment. The committee agreed that the company's approach to modelling cure had considerable limitations. It concluded there was uncertainty about DFS modelling and that a warm-up period should not be applied. But, the committee noted that this results in more conservative DFS outcomes and substantially increased the ICER.

Final cure timepoint

3.15 The company submission included a cure at 5 years for active monitoring and 8 years for osimertinib. The company stated that ADAURA DFS data shows a plateau forming after 48 months for people having placebo, suggesting a very small remaining risk of recurrence after this point. The company advised that a plateau is also expected for osimertinib at a later timepoint. But interpretation of the trial data beyond 48 months is limited

by the small number of people who are still being followed up. The EAG highlighted that there is insufficient evidence to apply a cure for osimertinib. It noted that the risk of recurrence for people who had osimertinib was still increasing at 5 years in the ADAURA trial. The EAG used individual patient data from ADAURA to create mixture-cure models to test the plausibility of cure in each group. It found that for active monitoring, a cure could be modelled using most distributions. But for osimertinib, most distributions failed to model a cure, suggesting insufficient DFS data to support this assumption. Clinical experts advised that the 5-year timepoint is a pragmatic choice. This is because it coincides with the timepoint in clinical practice from which routine follow-up can be stopped because the risk of subsequent events is sufficiently low. One expert agreed that an 8-year timepoint for osimertinib is also reasonable because it contains the 5-year follow up plus the 3-year treatment duration. The clinical experts agreed that for some people it would only slow recurrence, but it is also plausible that it would reduce the recurrence rate overall compared with active monitoring. But, it is also plausible that some people will not have recurrence and that most recurrences would be expected in the first few years after stopping osimertinib. The committee agreed that there was uncertainty surrounding when, if at all, people who had osimertinib could be considered cured. This is because it is unclear whether, in the long term, DFS rates for people having osimertinib would gradually increase to the same rate as those assigned to active monitoring. The committee recalled their preference to not apply a warm-up period (see section 3.14). It considered a scenario in which no warm-up period was applied with a cure timepoint for osimertinib at 8 years. This generated DFS outcomes that implied no increase in the long-term proportion of people cured after having osimertinib. The committee agreed this was a conservative assumption. So it considered an EAG scenario in which the timepoint was reduced to less than 8 years (5 years plus the model estimate of time on treatment). This was to reflect that not all people completed a full 3 years on

treatment. The committee felt that this scenario generated DFS outcomes that were more plausible and noted that it reduced the ICER. The committee concluded that this should be included in the model because using the 8-year timepoint without warm-up would be too conservative. The committee noted the uncertainty surrounding this assumption and that an alternative model structure would have been preferred.

Other factors

EGFR testing

3.16 The company did not include the costs associated with testing for EGFR mutations in their economic model. It argued that these mutations are already routinely tested for in the NHS by next generation sequencing panel tests, so the tests do not represent additional costs for osimertinib. One clinical expert advised that people with EFGR-positive cancer would not be offered neoadjuvant treatment. So EGFR status would typically be tested for in addition to other mutations before any treatment is given. The CDF lead advised that because people with stage 1b disease are not eligible for neoadjuvant treatment, these people may not be tested routinely. They advised that some of the testing costs for EGFR should be included in the model, though the appropriate proportion to apply costing to is unclear. The committee concluded that additional costs associated with EGFR testing should be included in the model.

Equality

3.17 It was noted that EGFR mutations are more common in younger people, Asian populations and females. The committee noted that the issue of different disease prevalence cannot be addressed in a technology appraisal.

Uncaptured benefits

3.18 The committee recognised that osimertinib represents an effective treatment option for people with EGFR mutation-positive NSCLC who have undergone complete resection, who would otherwise have limited options. The evidence showed that it is associated with improvements in key clinical outcomes. But, the committee concluded that all benefits of treatment with osimertinib were captured within the model.

Severity

3.19 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a severity modifier (a greater weight to quality-adjusted life years [QALYs]) if technologies are indicated for conditions with a high degree of severity. Neither the EAG nor the company made a case for a higher-than-normal severity modifier to be applied to this disease area. So, the committee concluded that a severity weight of 1.0 applied to the QALYs was appropriate.

Cost-effectiveness estimates

Acceptable ICER

3.20 NICE's manual on health technology evaluations notes that, above a most plausible ICER of £20,000 per QALY gained, decisions about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. The committee noted several uncertainties, specifically regarding:

- long-term DFS and OS (and uncertainty around cure)
- rates of retreatment and time from which retreatment occurs.

Because of the uncertainty in the cost-effectiveness estimates, the committee agreed that an acceptable ICER would be around £20,000 per QALY gained when compared with active monitoring.

Committee's preferred assumptions

3.21 The committee's preferred model assumptions were:

- using the EAG's corrections for model and costing errors (including having EGFR testing costs)
- no warm-up period prior to cure
- cure-point of 5 years for active monitoring
- cure-point of 5 years plus time on treatment (1 minus time to treatment discontinuation function) for osimertinib
- retreatment allowed from 3 years after starting osimertinib
- 70% of people in the osimertinib group who develop distant metastases will have osimertinib in the first-line setting
- starting age of 70 years in the economic model.

The company's base-case ICERs for osimertinib compared with active monitoring were below £20,000 per QALY gained (because of confidential discounts, the exact ICERs are confidential and cannot be reported here). The ICERs were substantially above this threshold when the committee's preferred assumptions were taken into account.

Conclusion

Recommendation

3.22 The clinical-effectiveness evidence showed that osimertinib improved key outcomes in people with EGFR mutation-positive NSCLC. The committee concluded that the ICER that included its preferred assumptions was above the range that NICE considers an acceptable use of NHS resources (see section 3.19). So, osimertinib is not recommended for routine commissioning.

4. Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee D.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Megan John
Chair, technology appraisal committee D

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Tom Jarratt
Technical lead

Christian Griffiths
Technical adviser

Kate Moore and Louise Jafferally
Project manager

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