NICE National Institute for Health and Care Excellence

NICE

guidance

Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer

Technology appraisal guidance
Published: 28 September 2022

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Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1   Recommendations

1.1   Atezolizumab is recommended for use within the Cancer Drugs Fund as an option for adjuvant treatment after complete tumour resection in adults with stage 2 to 3a non-small-cell lung cancer (NSCLC) whose:

- tumours have the programmed cell death ligand-1 (PD-L1) biomarker expression on 50% or more of their tumour cells and

- whose disease has not progressed after platinum-based adjuvant chemotherapy.

  It is recommended only if the company provides atezolizumab according to the managed access agreement.

1.2   This recommendation is not intended to affect treatment with atezolizumab that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

There are no immunotherapy treatments available in England for NSCLC after complete tumour resection.

Clinical trial evidence shows that compared with active monitoring, atezolizumab reduces the risk of the disease coming back. It may also lower the risk of death. However, this evidence is uncertain because the available data is still immature. Also, the company's model structure did not fully capture expected outcomes from more advanced disease health states.

Because of this, the cost-effectiveness estimates for atezolizumab are also uncertain. It has the potential to be cost effective, but more evidence is needed to address these uncertainties before it can be recommended for routine use.

Because more data is being collected that addresses these uncertainties, atezolizumab is recommended for use in the Cancer Drugs Fund.

2 Information about atezolizumab

Marketing authorisation indication

2.1 Atezolizumab (Tecentriq, Roche) is indicated for 'adjuvant treatment following complete resection for adult patients with stage II to IIIA (7th edition of the UICC/AJCC-staging system) non-small-cell lung cancer (NSCLC) whose tumours have programmed cell death ligand-1 (PD-L1) expression on $\geq$50% of tumour cells and whose disease has not progressed following platinum-based adjuvant chemotherapy'.

Dosage in the marketing authorisation

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

Price

2.3 The list price is £3,807.69 for a (1,200 mg) 20-ml vial and £2,665.38 for a (840 mg) 14-ml vial (excluding VAT; BNF online accessed July 2022).

2.4 The company has a commercial arrangement. This makes atezolizumab available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The [appraisal committee](#) considered evidence submitted by Roche, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

New treatment option

People with early-stage non-small-cell lung cancer would welcome new effective treatments that reduce the risk of recurrence

3.1   Surgical removal of tumours is the preferred treatment for many people with early-stage non-small-cell lung cancer (NSCLC) because it is potentially a cure, and can be followed by adjuvant chemotherapy. But despite the curative intent of complete resection, recurrence rates in people with early NSCLC (stage 1 to 3) remain high. The disease comes back within about 5 years of surgery in 17% to 29% of people with stage 1, 38% to 46% of people with stage 2, and 47% to 64% of people with stage 3, regardless of using adjuvant chemotherapy. Clinical experts stated that outcomes after surgical resection remain poor, and this highlights the need to reduce the incidence of recurrence after surgery and improve outcomes for people with early-stage NSCLC in this potentially curative setting. The clinical experts stated that the availability of atezolizumab would be welcomed by people with early-stage NSCLC, because it addresses a high unmet need. The committee concluded that new, effective treatments that reduce the risk of recurrence would be welcomed.

Treatment pathway

Atezolizumab is the first immunotherapy available at this point in the pathway

3.2   The only treatment routinely available in England as adjuvant therapy for NSCLC after complete resection is chemotherapy (platinum-based combination therapy), which provides a small benefit in overall survival. NICE's technology appraisal on osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer recommends it for use through the Cancer Drugs Fund, but epidermal growth factor receptor (EGFR) mutation-positive NSCLC only accounts for a small subset of people with NSCLC. After adjuvant chemotherapy, standard care is active monitoring. The clinical experts stated that adjuvant atezolizumab after chemotherapy could prevent or delay disease recurrence in people with programmed cell death ligand-1 (PD-L1) positive early-stage NSCLC, increasing the number of people whose disease is considered cured. The committee concluded that atezolizumab is the first immunotherapy at this point in the pathway for adjuvant treatment of people with PD-L1 positive NSCLC after chemotherapy.

Retreatment with atezolizumab would be offered to some people whose disease has progressed

3.3   At the first committee meeting, the company assumed that people who have adjuvant treatment with atezolizumab and develop metastatic disease recurrence, would not have any subsequent immunotherapy treatment. The Cancer Drugs Fund clinical lead explained that if disease relapsed after treatment with atezolizumab was stopped, then retreatment with an immunotherapy would be commissioned in the NHS. They explained that this would depend on the time since finishing atezolizumab and the onset of metastatic disease. If this time gap was short, then retreatment would be unlikely to provide significant benefit. The ERG provided an analysis which assumed the same treatments would be given after metastatic disease recurrence in both the atezolizumab and active monitoring groups. The ERG explained that this scenario was likely to be appropriate because of the 1-year treatment

stopping rule for atezolizumab. This is because only a minority of people had experienced disease progression in the IMpower010 trial in the atezolizumab group while either having treatment or shortly after stopping treatment. The committee agreed that the ERG's retreatment scenario should be considered in its decision making but acknowledged that it may assume a slightly higher rate of immunotherapy retreatment than may happen in NHS clinical practice. At the second committee meeting, the company updated its analysis to include the assumption of immunotherapy retreatment in line with comments from the Cancer Drugs Fund clinical lead at the first meeting. The committee concluded that retreatment with atezolizumab would be offered to some people whose disease has progressed after having atezolizumab as an adjuvant treatment.

Clinical evidence

The clinical evidence for atezolizumab is from IMpower010, a phase 3, randomised, placebo-controlled trial

3.4   The clinical-effectiveness evidence for atezolizumab came from the IMpower010 trial. This is a phase 3, multicentre, open-label, clinical trial comparing atezolizumab with active monitoring after resection and cisplatin-based adjuvant chemotherapy in adults with completely resected stage 1b to 3a NSCLC. IMpower010 compared adjuvant atezolizumab treatment for up to approximately 1 year with active monitoring which comprised regular observations and scans for disease recurrence. The trial population which was covered by the marketing authorisation were those people with stages 2 to 3a and PD-L1 positive (tumour expression of 50% or more) NSCLC. This reduced the number of people included in the analysis to 115 for atezolizumab and 114 for active monitoring. The unstratified clinical trial results showed that atezolizumab reduces the relative risk of experiencing disease recurrence or death (disease-free survival) by 57% compared with active monitoring (hazard ratio (HR) 0.43, 95% confidence interval [CI] 0.27 to 0.68). Median disease-free survival was 35.7 months for the active monitoring group but it was not reached for the atezolizumab group. The overall survival results are immature as few events happened in the

interim trial data, but suggested a survival benefit in favour of atezolizumab (HR 0.37, 95% CI 0.18 to 0.74). The committee concluded that data from IMpower010 suggests that atezolizumab could be clinically effective. However, the disease-free survival data is immature and there have been very few events from which to calculate overall survival.

It is not certain to what extent disease-free survival improves overall survival

3.5   The company stated that although overall survival data from IMpower010 was not mature and very limited number of events had happened, atezolizumab was likely to increase survival based on the improvements seen in disease-free survival. The committee was aware that overall survival data would take longer to mature because of the nature of early-stage NSCLC. The overall survival results from IMpower010 showed that atezolizumab was associated with a relative risk reduction of death compared with active monitoring (the exact results are confidential and cannot be reported here). The ERG explained that although these results seem encouraging, they should be interpreted with caution given that median overall survival was not reached in either arm and a very low number of deaths had happened in the interim trial data. The clinical experts noted that while data on overall survival was not robust, the improvements in disease-free survival were significant and clinically important. The company explained that further analysis including more data on both disease-free and overall survival will become available from IMpower010. After the first committee meeting, the company provided an updated analysis of IMpower010 overall survival data for people with stages 2 to 3a and PD-L1 positive (tumour expression of 50% or more) NSCLC (the exact results are confidential and cannot be reported here). However, it did not provide a corresponding updated analysis of disease-free survival data since it will not be available until 2023. The committee concluded that data from IMpower010 is still immature and it was not certain to what extent disease-free survival improves overall survival.

The company's economic model

The company's original economic modelling approach was not appropriate for decision making

3.6 The company used a cohort-level, discrete-time model. The model includes 8 disease-free survival health states: locoregional recurrence; first metastatic recurrence; second metastatic recurrence; and death. The locoregional and metastatic recurrence health states included both on and off active treatment states. In the model, people enter the disease-free survival state. The proportion of individuals in each health state model cycle varies with time as per the extrapolations of the disease-free survival Kaplan–Meier data from people with stage 2 or 3a PD-L1 positive (tumour expression of 50% or more) NSCLC in IMpower010, and adjustments to these extrapolations (see section 3.9). The ERG explained that using a cohort-level analysis meant it was difficult to track events that usually vary with time. This meant that most of the transitions in the model were assumed to be constant. The ERG also noted that the model transitions were mostly informed by external sources rather than IMpower010 data. It explained that some of these sources covered heterogenous populations and some were based on small numbers within the studies. The company highlighted that the model structure was consistent with that used in NICE's technology appraisal guidance on osimertinib for adjuvant treatment of EGFR mutation-positive non-small-cell lung cancer after complete tumour resection (TA761). The ERG noted that the company's model was comparable to the model used in TA761 in terms of model health states. However, it relied on stronger assumptions than the model used in TA761. This is because the model used in TA761 allowed the risk of having locoregional and distant metastasis health states to be varied with time, by tracking the time that people have been in a particular health state in the model. The ERG also noted that the company's model did not allow transitions between locoregional recurrence and metastatic recurrence. The committee was aware that the modelled overall survival estimates were affected by a combination of all transitions in the model. It noted that the projected overall survival outcomes in the company's base case appeared to be underestimated when compared with IMpower010 trial

data in both treatment groups. The ERG highlighted that the company's model did not appear to capture the expected outcomes from the metastatic disease recurrence states, because the incremental quality-adjusted life years (QALYs) accrued in these states were lower than in previous NICE technology appraisal guidance on pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA531), atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (TA584), pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (TA683) and atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (TA705) at this part of the treatment pathway. The committee concluded that the company's original model was not appropriate for decision making and it needed further analyses after the first committee meeting.

The company's updated economic modelling approach is acceptable for decision making

3.7   At the second committee meeting, the company updated its economic modelling approach to align with previous NICE technology appraisal guidance (TA531, TA584, TA683 and TA705). It adjusted the post disease-free survival transition probabilities to better fit the modelled overall survival data to the observed overall survival data in IMpower010. The ERG stated that making the post disease-free survival transitions match 1 arm's Kaplan–Meier overall survival curve did not produce a good visual fit to the other arm's Kaplan–Meier overall survival curve. The committee was concerned that the model may not represent observed disease-free survival and overall survival data by making the trial data fit the model. The survival benefit seems to be maintained but this is uncertain owing to a lack of data. The company provided a further scenario which allows people with PD-L1 positive early-stage NSCLC to enter the first metastatic disease recurrence state after cycle 1. It compared the resulting QALYs with metastatic NSCLC models which were previously submitted to NICE. In addition, the company presented additional evidence including justification of external resources for transitions in the model and the risk of having a locoregional recurrence state. The ERG noted that the company's updated approach to explore the consistency of the model with previous NICE appraisal guidance on

treatments for metastatic lung cancer was useful. However, the approach is likely to underestimate the benefits of immunotherapy for metastatic lung cancer. The committee concluded that the company's updated economic modelling approach was acceptable for decision making.

There is uncertainty about the company's cure assumptions

3.8   In its original model, the company used a study by Sonoda et al. (2019) to assume that 91.5% of people who were in the disease-free survival health state at 5 years could be assumed to be cured and no longer at risk of disease recurrence. The ERG explained that this study used data from a single Japanese hospital between 1990 and 2006, and included 53% of people with stage 1a disease. It queried the appropriateness of the source to inform a cure assumption. The ERG provided analysis which assumed a longer time before a cure was assumed (8 years in both model arms). One of the clinical experts stated that the higher proportion of early-stage lung cancer in Sonoda et al. (2019) may not be an issue as these people tend to experience disease recurrence later, and therefore may give a good estimate on long-term recurrence. The committee noted that it would have preferred to have seen a more recent study which more closely aligned to the population in this appraisal. The clinical experts stated that in clinical practice people are followed up for 5 years after surgery. The committee agreed that while a cure assumption may be plausible, the point at which this should be applied in the model was uncertain. After the first committee meeting, the committee requested that the company explore other sources of literature reporting the proportion cured after resection and do a sensitivity analysis of the cure assumptions. In response, the company included 2 more studies (Shin 2021 and Maeda 2010a) to inform the cure assumptions, but they also had similar issues to Sonoda et al. (2019) around applicability to UK clinical practice. Therefore, the committee agreed that assuming a cure proportion from either Sonada et al. (2019), Shin (2021) or Maeda (2010a) was uncertain because the 2 new studies provided no better information. The committee noted the uncertainty around the proportion of people who could be assumed to be effectively cured as well as the cure timepoint because of the limitations of the data. It agreed that it was appropriate to have differential cure timepoints between the 2 arms. The Cancer Drugs Fund clinical lead suggested that

1 to 2 years difference is plausible because most disease relapses occur after 12 months or at most after 18 months after the surgery and adjuvant treatment. Therefore, a cure timepoint of 6 years or 7 years for atezolizumab and a cure timepoint of 5 years for active monitoring was a reasonable assumption. The ERG provided analyses which assumed these alternative cure timepoints. The committee concluded that there was significant uncertainty about the company's cure assumptions, and it would consider both of the ERG's approaches in its decision making.

Some of the company's adjustments to the disease-free survival extrapolation are not appropriate

3.9   The company's original base-case analysis made several adjustments to the disease-free survival curves. The company applied a linearly increasing cure rate from 0% to 91.5% between years 3 and 6, to account for the effect of the 5-year cure assumption on the disease-free survival curve (see section 3.8). The ERG believed that this adjustment was not appropriate because it was not justified by the company, and removed it in its analysis. In addition, the company applied a treatment effect limitation, in which the probability of an event in the atezolizumab arm equalled that of the active monitoring arm at 5 years. The ERG noted that this improved the cost effectiveness of atezolizumab because the Kaplan–Meier data initially separates between the trial arms but this trend starts to reverse. The company also assumed a different proportion of transitions from the disease-free survival health state to locoregional and first-line metastatic health states between the atezolizumab and active monitoring arms based on data from IMpower010. The ERG highlighted that this assumption was based on a post-hoc analysis and was not justified by the company. The clinical experts stated that they were not aware of a biologically plausible explanation of why the proportion of people experiencing either a locoregional or first-line metastatic recurrence would differ between treatment arms. The committee agreed with the ERG and did not consider these assumptions in its preferred assumptions (see section 3.14). After the first committee meeting, the committee requested that the company provide analyses and commentary on alternative extrapolations of disease-free survival. In response, the company provided justification for the disease-free survival extrapolation and presented scenario analyses using different

parametric models. The ERG noted that the company fitted the data from each trial arm separately to the parametric models. The projections in each parametric model had a tendency to converge across arms because of the different shapes of the Kaplan–Meier curves across arms. The 5-year disease-free survival estimates the company assumed were broadly consistent with the 5-year estimates from all parametric survival models of active monitoring tested, except the generalised gamma model. Therefore, the ERG was concerned about the long-term benefit of disease-free survival provided by adjuvant atezolizumab from the variations of different structural parametric model assumptions. The committee concluded that some of the company's adjustments to the disease-free survival extrapolation are not appropriate.

Using a log-logistic, Weibull or log-normal distribution to model disease-free survival may be plausible but the data is limited

3.10   The company stated that it had followed the advice outlined in NICE Decision Support Unit Technical Support Document 14 (TSD14) when selecting which distribution to use to extrapolate disease-free survival. It highlighted that there was no clearly best fitting model for extrapolating disease-free survival. The company explained that it chose the log-logistic distribution because the outcomes produced by this curve were validated by its clinical experts and reflected outcomes seen in Pignon et al. (2008). The ERG noted that the Weibull distribution was also a potentially plausible choice and provided a scenario analysis using this distribution. It also noted that Pignon et al. (2008) included 38% of people with stage 1a or stage 1b NSCLC, which raised generalisability issues. The committee agreed that because the disease-free survival data was limited and many distributions could potentially be used to extrapolate, this increased the uncertainty in the cost-effectiveness results. At the second committee meeting, the company updated its analyses to include the log-normal extrapolation with cure adjustments for disease-free survival modelling, but they did not use either log-logistic or Weibull distributions from the ERG preferred analyses. The committee noted that the log-normal extrapolation from the company was no better fit than other distributions. The company explained that it researched the plausibility of different distributions systematically and chose the log-normal distribution by statistical ranking compared with

other distributions. The committee noted that using the log-normal distribution to model disease-free survival generated better results compared with log-logistic and Weibull distributions which were used in ERG preferred analyses, but the results are highly uncertain because of the limitations of the evidence. It noted that varying structural parametric model assumptions leads to uncertainties around cost-effectiveness results. The committee concluded that using either a log-logistic, Weibull or log-normal distribution to model disease-free survival may be plausible but the data informing this choice is limited.

The ERG's approach to the treatment pathway is more appropriate

3.11   In the company's model, a proportion of people were assumed to have further treatment after metastatic disease progression. The company assumed these people would have subsequent treatments based on clinical expert input. The ERG considered that the company's approach did not reflect the complexity of the treatment pathway, and the ERG exploratory analysis updated the assumed treatment pathway informed by their clinical expert and an NHS treatment algorithm. In the second committee meeting, the company included immunotherapy retreatment in its analysis but did not reflect other aspects noted by the ERG in the treatment pathway. The committee considered that the ERG's approach was more appropriate and concluded that it would use this analysis for decision making.

Some of the costs in the company's analysis are not appropriate

3.12   The ERG did not agree with some aspects of the company's cost analysis. In particular, it queried the following company assumptions:

- No treatment discontinuation in metastatic recurrence health states, except for assuming a 2-year stopping rule for pembrolizumab.

- Only people who experience a disease-related death incur a terminal care cost.

- A lower adjuvant atezolizumab NHS and patient treatment burden is assumed than expected by the ERG's clinical expert.

- Double counting of some intravenous treatment administration costs and assuming no atezolizumab batch remakes.

In its analysis, the ERG preferred to assume that people would stay on treatment for half of the time until disease progression or death. It also included terminal care costs for all patients and included additional resource costs for adjuvant atezolizumab. The committee agreed with the ERG's costing analysis but noted the company had stated that the cost of any atezolizumab batch remakes would be covered by the company. At the second committee meeting, the company's updated base-case analysis included terminal care costs and removed the double administration costing for combination treatments. It did not explain the reason why the rest of the ERG preferred costing assumptions were not included. The committee concluded that some of the costs in the company's analysis are not appropriate and it preferred the ERG's assumptions.

There are still uncertainties in the company's updated analyses because of the immaturity of the trial data

3.13   At the first committee meeting, the committee noted that the model had several limitations which increased the uncertainty in the cost-effectiveness results. Using exponential models to inform health state transitions was not properly justified (and unlikely to be appropriate, see section 3.6). In addition, using external sources to inform model transitions increased uncertainty in the post disease-free survival model state transitions (see section 3.6). The QALY gains from health states post disease-free survival and the time to stopping treatment in these health states were lower than those seen in recent NICE technology appraisal guidance in this part of the treatment pathway (see section 3.6). In addition, the committee noted there were other uncertainties in the analysis, including the cure assumption implemented in the analysis (see section 3.8) and the limited data on disease-free and overall survival (see section 3.4). After the first appraisal committee meeting, NICE requested that the company provide additional analyses to improve its modelling approaches. In response, the company updated its analyses to include a scenario in which people were retreated with atezolizumab 3 months after stopping treatment. It also updated the approach to post disease-free survival by adjusting the transition

probabilities, comparing metastatic health state QALY gains with previous NICE appraisals and converting the model to a metastatic model (see section 3.7). The company updated its cure assumptions (see section 3.8) but the committee noted that the company's updated cure proportions and cure timing assumptions are still uncertain.This may be because there is limited data and evidence existing in this area. The committee recognised that the updated analyses done by the company may address some of the concerns around the company's original economic model but there still were some uncertainties around its approach. The committee concluded that in the absence of an alternative model, the company's updated model could be used for decision making. However, it noted that the model added uncertainty because of the immaturity of the trial data.

Cost-effectiveness estimate

The most plausible incremental cost-effectiveness ratios are highly uncertain

3.14 Because of confidential discounts for subsequent treatments, the cost-effectiveness results are commercial in confidence and cannot be reported here. The ERG's optimistic base case included a cure assumption of 5 years for both the atezolizumab and active monitoring groups and a log-logistic distribution to model disease-free survival. The ERG's alternative base case included a cure assumption of 8 years for both the atezolizumab and active monitoring groups and a Weibull distribution to model disease-free survival. Both analyses produced incremental cost-effectiveness ratios (ICERs) below £20,000 per QALY gained. The committee considered several assumptions were plausible:

- A cure assumption of 6 years in the atezolizumab arm and 5 years in active monitoring arm.

- A cure assumption of 7 years in the atezolizumab arm and 5 years in active monitoring arm.

- Including retreatment with atezolizumab at 3 months after stopping treatment.

  The committee considered these assumptions when applied to the updated analysis from the company (which included a log-normal distribution to model disease-free survival), the ERG's optimistic and alternative base cases. Combining any of these assumptions with the ERG's optimistic base case resulted in ICERs of below £20,000 per QALY gained. However, combining them with the ERG's alternative base case at cure point of 7 years in the atezolizumab arm resulted in ICERs above £30,000 per QALY gained. Using these preferred assumptions, the committee considered that the most plausible ICERs for atezolizumab were in the range of less than £20,000 per QALY gained to more than £30,000 per QALY gained. The committee concluded that the most plausible ICER range may be within or above the range usually considered a cost-effective use of resource, but it is associated with high uncertainty because of the immaturity of the current trial data.

Atezolizumab is not recommended for routine use in the NHS

3.15   The committee recognised that disease-free survival and overall survival data for atezolizumab from IMpower010 was immature. It also noted that the most plausible ICER range may be within or above the range considered cost effective for routine use in the NHS (see section 3.14). After considering the uncertainty of the clinical evidence along with its preferred assumptions, the committee agreed that the additional data being collected from IMpower010 may reduce the uncertainties around the modelling. The committee concluded it could not recommend atezolizumab for the adjuvant treatment of stage 2 to 3a NSCLC after complete resection in adults whose tumours have PD-L1 expression on 50% or more of their tumour cells and whose disease has not progressed after platinum-based adjuvant chemotherapy for routine use in the NHS.

Atezolizumab is recommended for use in the Cancer Drugs Fund

3.16   Having concluded that atezolizumab could not be recommended for routine use, the committee then considered if it could be recommended for treating stage 2 to 3a NSCLC within the Cancer Drugs Fund. The committee discussed the arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting NICE's Cancer Drugs

Fund methods guide (addendum). The committee acknowledged that the disease-free survival and overall survival data from IMpower010 was not mature and the evidence is limited to prefer either the log-logistic, Weibull or log-normal curves for disease-free survival extrapolations, so that further data collection may help address uncertainty. In addition, there are still many limitations with the approaches in the company's economic modelling. The committee considered that an updated model from the company is needed to address the modelling issues. The committee was aware that, although a period of time in the Cancer Drugs Fund may not produce enough mature overall survival and disease-free survival data for the modelling, there will still be benefits:

- The disease-free survival data and overall survival data will be more mature.

- More data will be available to estimate the extent of the cure proportion and cure timing assumption.

  The committee considered that further data collection in the Cancer Drugs Fund could address some of the uncertainty in the cost-effectiveness estimates. Most analyses resulted in ICERs showing that atezolizumab was cost effective within and above the range normally considered a cost-effective use of NHS resources. However, the uncertainties around the ICERs are high. The committee concluded that atezolizumab met the criteria to be considered for inclusion in the Cancer Drugs Fund. It recommended atezolizumab for use within the Cancer Drugs Fund as an option for people with stage 2 to 3a NSCLC after complete resection in adults whose tumours have PD-L1 expression on 50% or more of their tumour cells and whose disease has not progressed after platinum-based adjuvant chemotherapy, if the conditions in the managed access agreement are followed. When the guidance is next reviewed the company should use the committee's preferred assumptions and provide an updated model (unless new evidence indicates otherwise), as set out in section 3.13.

Innovation

Atezolizumab is an innovative treatment for people with PD-L1 positive early-stage NSCLC in the adjuvant setting

3.17 The company stated that atezolizumab is innovative because there has been little innovation in adjuvant treatment for early NSCLC. It highlighted that there are no treatment options for most people at this part of the treatment pathway apart from adjuvant chemotherapy, which has shown to provide limited benefits. The clinical experts considered atezolizumab is a step change in the management of early-stage NSCLC with PD-L1 expression on 50% or more of their tumour cells and represents a significant improvement in outcomes for this population. The committee was aware that atezolizumab has been reviewed as part of Project Orbis because it is considered an innovative adjuvant treatment. In addition, atezolizumab has been granted an 'Innovation Passport' through the Medicines and Healthcare products Regulatory Agency's Innovative Licensing and Access Pathway (ILAP). The committee considered that atezolizumab was an innovative treatment for people with PD-L1 positive early-stage NSCLC but considered that all related health benefits had been captured in the model.

Other factors

3.18 No equality or social value judgement issues were identified.

3.19 NICE's advice about life-extending treatments for people with a short life expectancy did not apply.

Conclusion

3.20 The committee recognises that atezolizumab is a promising treatment option at this point in the pathway. However, there is not enough clinical and cost-effectiveness evidence to recommend it for routine use in the NHS. Therefore, atezolizumab is recommended for use in the Cancer Drugs Fund as an adjuvant treatment of stage 2 to 3a NSCLC after complete tumour resection, in adults whose tumours have PD-L1

expression on 50% or more of their tumour cells and whose disease has not progressed after platinum-based adjuvant chemotherapy. The committee recognised that the IMpower010 trial used American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) TNM 7th edition lung cancer staging criteria and that this evidence underpinned the marketing authorisation. It was aware that these criteria had been recently updated and that the 8th edition is also now used in NHS clinical practice. It understood from the Cancer Drugs Fund clinical lead that the population as per 7th edition (stages 2 to 3a – as specified in the marketing authorisation) corresponds to stages 2 to N2 only stage 3b in the 8th edition. It also understood that the Cancer Drugs Fund would ensure patient access in accordance with this translation from the 7th to the 8th edition lung cancer staging criteria.

4 Implementation

4.1 When NICE recommends a treatment as an option for use within the Cancer Drugs Fund, NHS England will make it available according to the conditions in the managed access agreement. This means that, if a person has fully resected, stage 2 to 3a non-small-cell lung cancer (NSCLC) whose tumours have programmed cell death ligand-1 (PD-L1) expression on 50% or more of their tumour cells and whose disease has not progressed after platinum-based adjuvant chemotherapy and the doctor responsible for their care thinks that atezolizumab is the right treatment, it should be available for use, in line with NICE's recommendations and the Cancer Drugs Fund criteria in the managed access agreement. Further information can be found in NHS England's Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry.

4.2 Chapter 2 of Appraisal and funding of cancer drugs from July 2016 (including the new Cancer Drugs Fund) – A new deal for patients, taxpayers and industry states that for those drugs with a draft recommendation for use in the Cancer Drugs Fund, interim funding will be available (from the overall Cancer Drugs Fund budget) from the point of marketing authorisation, or from release of positive draft guidance, whichever is later. Drugs that are recommended for use in the Cancer Drugs Fund will be funded in line with the terms of their managed access agreement, after the period of interim funding. The NHS England and NHS Improvement Cancer Drugs Fund list provides up-to-date information on all cancer treatments recommended by NICE since 2016. This includes whether they have received a marketing authorisation and been launched in the UK.

4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance when the drug or treatment, or other technology, is approved for use within the Cancer Drugs Fund. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, for use within the Cancer Drugs Fund, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document or

agreement of a managed access agreement by the NHS in Wales, whichever is the later.

5 Appraisal committee members and NICE project team

Appraisal 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 to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

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

NICE project team

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

Alan Moore and Ziqi Zhou
Technical leads

Sally Doss
Technical adviser

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Project managers

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