NICE National Institute for Health and Care Excellence

NICE guidance

Avelumab with axitinib for untreated advanced renal cell carcinoma

Technology appraisal guidance
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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 Avelumab with axitinib is recommended for use within the Cancer Drugs Fund as an option for untreated advanced renal cell carcinoma in adults. It is recommended only if the conditions in the managed access agreement for avelumab with axitinib are followed.

1.2 This recommendation is not intended to affect treatment with avelumab plus axitinib 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

Treatment for untreated advanced renal cell carcinoma includes sunitinib, pazopanib, tivozanib or cabozantinib.

Clinical trial evidence shows that, for people with untreated advanced renal cell carcinoma, avelumab plus axitinib increases how long people live without their disease getting worse compared with sunitinib. Early trial results suggest that avelumab plus axitinib also increases how long people with the disease live. But this is uncertain because the final trial results are not available yet. There are no trials comparing avelumab plus axitinib with tivozanib, pazopanib or cabozantinib directly. So, it is uncertain how it compares with these drugs.

Avelumab plus axitinib has the potential to be cost effective, but more evidence is needed:

- Longer-term follow up of patients in JAVELIN Renal 101 would help to address the uncertainties about how long people live, and how long they live without their disease getting worse.
- The economic model should reflect the treatment patients in the NHS would have after avelumab plus axitinib.

Therefore, avelumab plus axitinib is recommended through the Cancer Drugs Fund

while further data are collected, and the economic model is updated.

2 Information about avelumab with axitinib

Marketing authorisation indication

2.1 Avelumab (Bavencio, Merck-Pfizer) with axitinib (Inlyta, Pfizer) 'is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma'.

Dosage in the marketing authorisation

2.2 The dosage schedules are available in the avelumab summary of product characteristics and the axitinib summary of product characteristics.

Price

2.3 Avelumab is available at a list price of £768.00 per 200-mg vial or £3,072.00 per 800-mg fixed dose (excluding VAT; companies' submission).

2.4 Axitinib is available in 4 strengths, which all come in packs of 56 tablets. The list prices are: £703.40 for 1-mg tablets, £2,110.20 for 3-mg tablets, £3,517.00 for 5-mg tablets and £4,923.80 for 7-mg tablets (excluding VAT; companies' submission).

2.5 There is a commercial arrangement for avelumab plus axitinib. This makes avelumab plus axitinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the companies' responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by 2 companies: Merck KGaA and Pfizer Ltd, a review of this submission by the evidence review group (ERG), and the technical report developed through engagement with stakeholders. See the committee papers for full details of the evidence.

The appraisal committee was aware that 1 issue was resolved during the technical engagement stage. It agreed that, in the comparison with tivozanib, survival estimates for avelumab plus axitinib in the model should be based on trial data rather than on network meta-analyses.

It recognised that there were remaining areas of uncertainty associated with the analyses presented (see technical report, table 3, page 35), and took these into account in its decision making.

Treatment pathway

Comparators include pazopanib, sunitinib, tivozanib and cabozantinib

3.1 First-line treatment options in clinical practice for people with advanced renal cell carcinoma include pazopanib, sunitinib, tivozanib and, for people with disease classified as intermediate or poor risk, cabozantinib. Nivolumab with ipilimumab and pembrolizumab with axitinib cannot be comparators in this appraisal because they are not established clinical practice. Nivolumab with ipilimumab is recommended through the Cancer Drugs Fund (and so is not routinely commissioned) and pembrolizumab with axitinib is being appraised by NICE. Later-line treatments include axitinib alone, nivolumab, cabozantinib, lenvatinib with everolimus, and everolimus alone.

Having avelumab plus axitinib affects which treatments people have later

3.2 The Cancer Drugs Fund clinical lead and the clinical experts explained that, if people were to have first-line treatment with avelumab (a checkpoint inhibitor) plus axitinib (a tyrosine kinase inhibitor), they would not be eligible in the NHS for nivolumab (another checkpoint inhibitor) or axitinib monotherapy later in the treatment pathway. The committee noted that any disease model should reflect this, but the current model does not. The clinical experts also explained that they would value being able to offer the most effective treatments at first line. The Cancer Drugs Fund clinical lead and the clinical experts stated that, if patients have avelumab plus axitinib first line, there would be interest from patients and clinicians in using current first-line treatments such as sunitinib in the second-line setting. The committee concluded that patients and clinicians should have the opportunity to choose between the most effective treatment options as early in the pathway as possible, and that the modelled treatment pathway should reflect both the costs and benefits of NHS care.

Clinical trial evidence

The key evidence comes from the JAVELIN Renal 101 trial

3.3 The companies presented evidence from JAVELIN Renal 101, a phase 3 randomised controlled trial of avelumab plus axitinib (442 patients) compared with sunitinib (444 patients) in advanced renal cell carcinoma. The original primary objective was to show the superiority of avelumab plus axitinib in prolonging progression-free survival in all patients in the trial. However, the investigators amended the protocol during the trial. The primary objective was changed to show superiority either on progression-free or overall survival in a subpopulation (that is, people with PD-L1 positive tumours). The companies stated that this had changed because results from other trials suggested that avelumab plus axitinib may improve overall survival in the PD-L1 subpopulation, and it improved effectiveness compared with the subpopulation whose tumours do not express PD-L1. However, the European Medicines

Agency ultimately granted the licence for the whole population. The clinical experts explained that NHS clinicians do not measure PD-L1 in renal cell carcinoma. The committee was satisfied that it could take the results of the main population into account in its decision making.

Avelumab plus axitinib is more effective than sunitinib for prolonging progression-free survival, but overall survival benefit is uncertain

3.4 The companies explained that the first interim analysis of JAVELIN Renal 101 showed a benefit for progression-free survival of avelumab plus axitinib over sunitinib, and that the companies continued the trial to evaluate overall survival. The companies submitted 2 data cuts from the trial: interim analysis 1 (June 2018) and interim analysis 2 (January 2019). The committee noted that avelumab plus axitinib was more effective in improving progression-free survival compared with sunitinib at the first interim analysis (hazard ratio [HR] 0.69, 95% confidence interval [CI] 0.56 to 0.84). The committee also noted that the results for overall survival from JAVELIN Renal 101 were immature (fewer than half of the 535 deaths needed for the planned final analysis had occurred at the January 2019 data cut) and the results showed a hazard ratio of 0.80 (95% CI 0.62 to 1.03). The clinical experts explained that people are likely to live longer if they take avelumab plus axitinib, which combines an immune-oncology drug (avelumab) and a tyrosine kinase inhibitor (axitinib), than if they take only a tyrosine kinase inhibitor (sunitinib). The committee concluded that avelumab plus axitinib prolongs progression-free survival compared with sunitinib. However, it added that the companies' immature data meant that uncertainty remained about whether avelumab plus axitinib prolongs overall survival compared with sunitinib and, if so, by how much

There are no data to inform the long-term effects of avelumab plus axitinib

3.5 Given the absence of mature trial data for overall survival, the committee considered whether there were other data to inform effectiveness over time:

- The clinical experts explained that there is no evidence to inform the long-term survival outcomes of either avelumab plus axitinib or any other checkpoint inhibitor in advanced renal cell carcinoma. They noted that, from their experience with checkpoint inhibitors, many patients do well in the longer term. The patient expert said that he was grateful to take part in an avelumab and axitinib trial. One clinical expert considered it plausible that 20% of patients would be alive at 5 years and 15% at 10 years.
- The committee noted that there had been a previous avelumab plus axitinib trial (JAVELIN Renal 100). It included only 55 patients, but the committee thought that it could inform the treatment effect of avelumab plus axitinib over a longer time period.

  The committee agreed that any additional data would likely inform the longer-term overall survival effects of avelumab plus axitinib.

The dosing in the marketing authorisation differs from that in JAVELIN Renal 101

3.6 The committee highlighted that a weight-based dose for avelumab was used in JAVELIN Renal 101, whereas the licence specifies a fixed dose. The companies explained that they derived the fixed dose using pharmacokinetic and pharmacodynamic data, and taking into account similar approaches used historically. The Cancer Drugs Fund clinical lead advised that this approach was taken with other drugs for this disease area. The committee was aware that it could appraise drugs only within their marketing authorisation. It accepted that the licensed fixed dose would have similar effectiveness to the weight-based dose, and concluded that it would use the licensed dose in making decisions.

There is little evidence for avelumab plus axitinib in non-clear-cell renal cell carcinoma, as with other first-line treatments

3.7 The committee noted that most patients in JAVELIN Renal 101 had clear-cell disease, but in NHS practice some have non-clear-cell disease. The clinical experts stated that there is no evidence that the results in people with cancers characterised by clear-cell histology would be generalisable (or not) to people with disease characterised by non-clear-cell histology.

Therefore, there might be an argument to limit avelumab plus axitinib to people with clear-cell disease only. However, the clinical experts noted, and the committee agreed, that the situation is similar with other first-line treatments for advanced renal cell carcinoma. The committee agreed that this was an area in need of further research. It suggested that data should be collated by histology in the Cancer Drugs Fund, to monitor whether there is a difference in effectiveness.

Indirect treatment comparison

An indirect comparison is needed to compare avelumab plus axitinib with comparators other than sunitinib

3.8 There are no head-to-head trials of avelumab plus axitinib compared with tivozanib, pazopanib or cabozantinib. The companies therefore indirectly compared avelumab plus axitinib with these comparators by network meta-analyses for progression-free and overall survival. The companies constructed networks for:

- the whole population across the range of risk (and which included the treatments avelumab plus axitinib, sunitinib, tivozanib and pazopanib) and
- the population with intermediate- or poor-risk disease (which included the treatments avelumab plus axitinib and cabozantinib).

The committee agreed that, for the economic modelling, pazopanib had the same effectiveness as sunitinib, which the committee had accepted in NICE's technology appraisal guidance on tivozanib for treating advanced renal cell carcinoma and nivolumab with ipilimumab for untreated advanced renal cell carcinoma.

Comparisons with sunitinib and pazopanib are the most relevant for decision making

3.9 There were several issues with using the network meta-analyses to compare avelumab plus axitinib with tivozanib:

- To estimate overall survival, the companies used sunitinib and sorafenib as links in the network. The 2 trials comparing sunitinib with sorafenib (Eichelberg et al. 2015 and Tomita et al. 2017) had a randomised sequential design (that is, patients were randomised to have sunitinib followed by sorafenib, or sorafenib followed by sunitinib). The overall survival data were available in these trials only at the end of each treatment sequence. Therefore, these trials did not directly compare sorafenib with sunitinib for overall survival. The ERG noted that this invalidated the network.

- The trial comparing tivozanib with sorafenib (Motzer et al. 2013) allowed crossover from sorafenib to tivozanib on disease progression (61% of patients who progressed on sorafenib crossed over to tivozanib).

- A large proportion of the patients in all the trials included in the network had subsequent treatments after progression, which may not have reflected NHS practice, and which may have extended their lives.

  The ERG explained that a 'disconnected network' would be an alternative approach to estimate the effectiveness of avelumab plus axitinib compared with tivozanib. The committee noted that, in previous tivozanib technology appraisal guidance, it had concluded that tivozanib was 'at best' similar to sunitinib or pazopanib. This was based on tivozanib being less effective, but less expensive, than sunitinib. In comments received during the technical engagement stage for this appraisal, clinical experts noted that sunitinib and tivozanib are likely similarly effective, although a patient organisation argued that it was not appropriate to assume equal efficacy. The committee agreed that the network estimating overall survival comparing avelumab plus axitinib with tivozanib was not valid, so the effectiveness of tivozanib compared with other treatments is uncertain. However, the committee also heard from the Cancer Drugs Fund clinical lead that tivozanib was less commonly used than the other comparators in clinical practice. It therefore concluded that it would prioritise comparisons with sunitinib and pazopanib.

The companies' network meta-analyses either relying on or not relying on proportional hazards both have high levels of uncertainty

3.10 The companies stated that some of the trial results in the networks

appeared to violate the assumption of proportional hazards. They therefore did 2 sets of network meta-analyses. One set was a standard Bayesian network meta-analysis, which assumed proportional hazards. The output of this was a hazard ratio for avelumab plus axitinib compared with each comparator in the scope. In the other set, the companies did not assume proportional hazards. Instead, parametric curves were fitted to data from each treatment arm of each trial in the network to estimate time-varying treatment effects. This generated estimates of the probabilities of progression-free and overall survival at 1, 2 and 10 years for each treatment in the model. The companies chose the latter approach for their base case. The ERG was satisfied with the methods and rationale for both approaches. It noted that it was useful to see both approaches, as 1 generates a hazard ratio and the other a parametric curve over time. However, the ERG outlined that the concerns it had already highlighted with the network meta-analysis (see section 3.9) applied to both approaches. The committee concluded that methodological concerns and the immature data informing the model made these results uncertain.

Assumptions in the economic model

The model type is appropriate

3.11 The companies used a partitioned-survival economic model that included 3 health states: pre-progression, post-progression and death. Patients could have first-line treatment with avelumab plus axitinib, sunitinib, pazopanib or tivozanib. The population with intermediate and poor risk could have avelumab plus axitinib or cabozantinib. If disease progressed, patients could move on to several other subsequent treatments, depending on which treatment they had first line. The committee concluded that the model type was appropriate and consistent with the approach used in other appraisals for renal cell carcinoma.

The committee would have preferred to see the effects of subsequent treatments explored further

3.12 In JAVELIN Renal 101, people in both treatment arms could have nivolumab after disease progression on first-line treatment. The committee noted that this differed from NHS practice in which only people having sunitinib would be eligible to have second-line nivolumab or axitinib in NHS practice. The committee appreciated that the results of JAVELIN Renal 101 reflected the effect of treatments offered second line and beyond (see section 3.1). The companies stated that this had biased the trial results against avelumab plus axitinib because a substantially higher proportion of patients had nivolumab in the sunitinib arm than in the avelumab plus axitinib arm. The companies also claimed that the proportion of patients in the trial having nivolumab after disease progression on sunitinib was higher than would be expected in NHS practice. To explore the effect of this, the companies adjusted the trial results using the rank preserving structural failure time method. The committee noted that the companies did not provide details of this method or the assumptions needed for it. Also, they did not justify their choice of this method over others. The committee was aware that, in the NHS, some patients would be expected to have nivolumab after sunitinib, whereas no patients would be expected to have nivolumab after avelumab plus axitinib. Therefore, the companies' adjustment was not appropriate. The committee concluded that it would have preferred to see the companies adjusting for any life-extending follow-on treatments offered in the trial that would not form part of a routine NHS treatment pathway, using an appropriate adjustment method.

The committee would have preferred to see the costs of subsequent treatments explored further

3.13 The companies applied the costs of subsequent treatments using a one-off cost, which depended on the treatment offered first line. For avelumab plus axitinib, and for sunitinib, the treatment patients had in the model was estimated from the subsequent treatments given in the relevant treatment arm in JAVELIN Renal 101. All other first-line treatments in the model were assumed to be the same as sunitinib. The committee recognised that it was important to know all the treatments

offered in the trial that are proven to extend life, but are not routinely commissioned in the NHS. However, the companies' model accounted only for the subsequent treatments taken by more than 10 people in either treatment arm of JAVELIN Renal 101. These treatments were cabozantinib, everolimus, axitinib, sunitinib, nivolumab, lenvatinib plus everolimus, and pazopanib. The companies confirmed that the trial had included some treatments that are not available in the NHS, such as durvalumab. As discussed (see section 3.12), a small proportion of patients in the model having avelumab plus axitinib went on to have other checkpoint inhibitors or axitinib after progression. The committee noted that although this likely had little effect on the cost-effectiveness estimates, given the small proportion of patients, it did not reflect clinical practice in England. The committee agreed that it would have liked to have seen base-case modelling that adjusted the trial data to reflect both the effects and costs of subsequent treatments offered in NHS practice.

Overall survival extrapolations

There are high levels of uncertainty when extrapolating overall survival

3.14 In the economic model, the companies used parametric distributions to extrapolate the data on overall survival from JAVELIN Renal 101. The committee noted several uncertainties with modelled overall survival:

- The short-term data informing the model (median follow up was 12 months or less) meant that survival estimates varied widely depending on the choice of extrapolation curve. For example, in the companies' model at 5 years, the proportion of patients alive who had treatment with avelumab plus axitinib could be:
  - 16% using a Gompertz function
  - 57% using a log-normal function.
- The companies fitted the parametric curves independently to the survival data of each comparator, but did not explicitly present the hazard plots, so the

committee could not see the implied treatment effect over the time horizon of the model.

- Using either a log-normal or a log-logistic function (as used in the companies' base case) or an exponential function (as preferred by the ERG) may have generated clinically implausible results for overall survival, with mortality rates for patients who had treatment with avelumab plus axitinib falling below those of the general population after 18 to 20 years.

  The committee recognised that using an exponential curve assumes that the treatment benefit remains constant over time. This is because the relative hazards stay constant, which may be more likely to reflect clinical experience with checkpoint inhibitors. However, the clinical experts explained that, in other cancers, for a small group of patients, their disease continues to have a lasting response to checkpoint inhibitors (and so the relative hazard may change over time). The committee noted this, but was also aware that observations in 1 type of cancer are not necessarily generalisable to another type of cancer. The committee concluded that all extrapolations were fundamentally uncertain because of the lack of data on long-term survival, and that only longer-term data on overall survival could address this. It also agreed that it would have preferred the companies to present the modelled treatment effect for overall survival over time explicitly.

The latest data cut for overall survival and progression-free survival should be modelled

3.15 The companies based the cost-effectiveness estimates on the results from the June 2018 data cut, even though they had presented clinical results using the January 2019 data cut. The companies stated that this was because the first data cut was:

- a complete data set
- available at the time of economic modelling
- reflecting the same time periods.

The companies explained that the first interim analysis showed a progression-free survival benefit and the trial continued to evaluate overall survival. The

committee concluded that, although the most mature data available for overall and progression-free survival would be useful, they would likely not reduce the uncertainty substantially (see section 3.14).

It is not appropriate to include a stopping rule

3.16 In the economic model, the companies originally assumed that clinicians stop treatment with avelumab plus axitinib after 2 years of treatment, whether or not a patient's disease has progressed. After this, and despite stopping treatment, the companies assumed that:

- two-thirds of patients would continue to have a lifetime treatment benefit
- the other third would gradually assume the progression and mortality hazards of the comparator treatment over 2 years.

The committee noted that the JAVELIN Renal 101 protocol and the marketing authorisation did not include stopping treatment. The Cancer Drugs Fund clinical lead confirmed that, if a stopping rule was accepted, retreatment with avelumab plus axitinib or a second-line checkpoint inhibitor would not be available for patients who had previous treatment with avelumab plus axitinib. The clinical experts stated that stopping treatment after 2 years might be reasonable for some patients. This is because clinical experience with other cancers shows that, for a small group of patients, their disease continues to have a lasting response to checkpoint inhibitors. However, the committee understood that this had not yet been shown in renal cell carcinoma and it was not appropriate to generalise from 1 cancer to another. It also recognised that currently there is no clear way of identifying these patients. The committee understood that if patients relapsed after stopping treatment, they would not be able to have the treatment again. The patient expert stated that he had had 4 years of treatment so far. He would be reluctant to abide by an arbitrary stopping rule for fear of losing benefit, and then not be able to have treatment again. The committee concluded that there was no evidence to support a stopping rule and that it should not be in the model. For its second meeting, the committee understood that the companies removed this assumption from their base case.

It is not appropriate to include the approach chosen by the

companies to address treatment waning

3.17 Related to the stopping rule, the companies assumed that two-thirds of patients who stopped treatment would have a treatment benefit over their lifetimes, and one-third would have waning of the treatment effect (that is, over 2 years, the effect of treatment would decrease to that of the comparator). The ERG presented scenarios exploring the effect of removing the treatment waning effect (that is, all patients maintained a full treatment effect in the absence of treatment). However, the committee was not clear how the ERG had implemented removing the treatment waning effect and the stopping rule (see section 3.15). The committee concluded that there was no evidence to support what proportion of patients would have a long-term treatment effect after stopping treatment. Therefore, the modelling should have accounted for a range of potential options, including the potential for no patients to have a long-term treatment effect after stopping treatment. At the second meeting, the committee was aware that the companies had removed the stopping rule, so the model now excluded treatment waning (that is, because treatment now continued in the model, there was no need to apply assumptions around what happens to the treatment effect after stopping treatment at a set time period, rather than for adverse events or progression). The committee agreed this was appropriate.

Cost-effectiveness estimates

Avelumab plus axitinib cannot be recommended for routine use

3.18 The cost-effectiveness results are commercial in confidence and cannot be reported here. The committee agreed that some of the original assumptions in the companies' base-case model were implausible. The committee went on to review the exploratory scenarios presented by the ERG, some (but not all) of which had used some of the committee's preferred assumptions:

- no stopping rule
- removed treatment waning effect as modelled

- a range of overall survival extrapolations, including the exponential curve.

The cumulative effect of the committee's preferred assumptions increased the companies' base case above what is considered to be a cost-effective use of NHS resources. The committee concluded that avelumab plus axitinib cannot be recommended for routine use.

Cancer Drugs Fund

The companies propose including avelumab plus axitinib in the Cancer Drugs Fund while more data are collected from JAVELIN Renal 101

3.19 Having concluded that avelumab plus axitinib could not be recommended for routine use, the committee then considered whether it could be recommended for treating advanced renal cell carcinoma within the Cancer Drugs Fund. It 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 noted that the key uncertainties were:

- the immaturity of the overall survival data and the companies' approach to modelling overall survival over the long term
- the lack of data on whether the treatment is effective for non-clear-cell disease and
- the companies' methods for adjusting both the costs and benefits of subsequent treatments to reflect NHS practice.

The committee agreed that the first 2 uncertainties could be resolved by collecting further data. It considered a proposal by the companies for including avelumab plus axitinib in the Cancer Drugs Fund as part of a managed access agreement. In this, the companies would collect further data from clinical trials, and would provide avelumab plus axitinib at a discounted price to the NHS for the duration of the managed access agreement. The committee agreed that avelumab plus axitinib showed plausible potential for cost effectiveness, but only if the companies address the committee's concerns about the modelling

(see section 3.20) when there are mature data and the guidance is reviewed. The committee was satisfied that, until then, the proposed pricing arrangement compensates for the clinical uncertainty about survival while avelumab plus axitinib is in the Cancer Drugs Fund.

Avelumab plus axitinib is recommended for use within the Cancer Drugs Fund

3.20 Based on the considerations in section 3.19, the committee considered that it could recommend avelumab plus axitinib for use in the Cancer Drugs Fund. The committee agreed that, at the end of the period in the Cancer Drugs Fund, when the guidance is reviewed, the updated model should include these preferred assumptions (unless new evidence indicates otherwise):

- no stopping rule (see sections 3.16 and 3.17)
- trial evidence and costs adjusted to reflect subsequent treatments used in NHS practice, including adjusting for life-extending treatments used in the trial not available in the NHS (see sections 3.12 and 3.13) and justifying the methods used to adjust for follow-on treatments (see section 3.12)
- a range of overall survival extrapolations explored, including the exponential curve (see section 3.14)
- the modelled overall survival treatment effect over comparators over time, explicitly presented (see section 3.14).

Other factors

Avelumab plus axitinib did not meet the criteria for end of life

3.21 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. It recognised that the companies did not submit evidence to support avelumab plus axitinib as an end-of-life therapy. It noted that the lower confidence interval boundary of median overall survival exceeded 24 months. The committee noted the comments from

the companies in their submission that, in pivotal trials of the NICE-recommended first-line monotherapies for acute renal cell carcinoma (sunitinib, pazopanib, tivozanib and cabozantinib), median overall survival ranged from 21.8 to 30.3 months. As such, avelumab plus axitinib does not meet the criteria for consideration as a life-extending treatment at the end of life for patients with acute renal cell carcinoma with favourable- to poor-risk status. The committee concluded that avelumab plus axitinib does not meet the criteria for end of life.

Innovation

Benefits are likely captured in the quality-adjusted life year calculations

3.22 The clinical experts stated they considered avelumab plus axitinib to be innovative because it is the first combination of a checkpoint inhibitor plus a tyrosine kinase inhibitor licensed for use in patients with untreated advanced renal cell carcinoma. The committee considered that this does not make the treatment innovative. It also concluded that the associated benefits of treatment are likely captured in the quality-adjusted life year calculations.

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 patient has untreated advanced renal cell carcinoma and the doctor responsible for their care thinks that avelumab plus axitinib 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 B.

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.

Iordanis Sidiropoulos
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