NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avelumab with axitinib for untreated advanced or metastatic renal cell carcinoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of avelumab in combination with axitinib within its marketing authorisation for untreated, advanced or metastatic renal cell carcinoma.

Background

Renal cell carcinoma (RCC) is a cancer that usually originates in the lining of the tubules of the kidney (the smallest tubes inside the nephrons) that help filter the blood and make urine. RCC is the most common type of kidney cancer (more than 80% of the cases).[1] There are several types of RCC. The main ones are clear cell (accounting for approximately 75% of cases), papillary and chromophobe.[1]

Early small RCC tumours are usually asymptomatic; the diagnosis of early RCC is often incidental after abdominal scans for other reasons. The most common presenting symptoms of advanced RCC are blood in the urine (haematuria), a palpable mass in the flank or abdomen and abdominal pain. Other non-specific symptoms include fever, night sweats, malaise and weight loss. RCC is graded into stages I to IV. Stage III denotes disease that is locally advanced and/or has spread to regional lymph nodes. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is defined as stage IV. Localised radical approaches including nephron-sparing surgery, radical nephrectomy and ablative therapies may be curative in people with localised tumours. However, around half of those who have surgery develop advanced disease later on.

In 2016, 10,609 new kidney cancer cases were diagnosed in England.[2] In 2015, approximately 44% of people diagnosed with kidney cancer had stage III or IV disease and 25% to 31% had metastases.[3] The 5-year relative survival rate for stage IV RCC is approximately 6%.[4]

The aim of treatment is to prevent the growth and survival of cancer cells within the tumour. In untreated RCC, NICE technology appraisal guidance 169 recommends sunitinib as a ‘first-line treatment option for people with advanced and/or metastatic renal cell carcinoma who are suitable for immunotherapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1.’ NICE technology appraisal guidance 215

recommends pazopanib as a 'first-line treatment option for people with advanced renal cell carcinoma who have not received prior cytokine therapy and have an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1'. NICE technology appraisal guidance 512 recommends tivozanib for treating advanced renal cell carcinoma in adults who have had no previous treatment. NICE technology appraisal guidance 542 recommends cabozantinib for untreated advanced renal cell carcinoma that is intermediate- or poor-risk as defined in the International Metastatic Renal Cell Carcinoma Database Consortium criteria.

The technology

Avelumab (Bavencio, Merck-Pfizer) is an anti-PD-L1 monoclonal antibody with a dual mechanism of action. It aims to bind and block the inhibitory signalling through PD-1/PD-L1 resulting in the activation of T-cells and cell-mediated immune responses against tumour cells or pathogens. Avelumab is administered by intravenous infusion.

Axitinib (Inlyta, Pfizer) is an oral multi-targeted kinase receptor inhibitor with anti-tumour activity. Axitinib inhibits vascular endothelial growth factor receptor (VEGFR) -1, -2 and -3, platelet-derived growth factor receptor (PDGFR), and c-kit, which may result in inhibition of angiogenesis in tumours.

Avelumab does not currently have a marketing authorisation in the UK for untreated, advanced or metastatic RCC. It has been studied in clinical trials, in combination with axitinib, compared to sunitinib, in adults with untreated, advanced or metastatic RCC with clear cell component.

Axitinib monotherapy has a marketing authorisation for treating adults with advanced renal cell carcinoma after failure of previous treatment with sunitinib or a cytokine.

Intervention(s)	Avelumab with axitinib
Population(s)	Adults with untreated locally advanced or metastatic renal cell carcinoma

Comparators	• Pazopanib • Sunitinib • Tivozanib • Cabozantinib (only for intermediate- or poor-risk disease as defined in the International Metastatic Renal Cell Carcinoma Database Consortium criteria) • Nivolumab with ipilimumab (only for intermediate- or poor-risk disease as defined in the International Metastatic Renal Cell Carcinoma Database Consortium criteria; subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related Technology Appraisals:** Cabozantinib for untreated advanced renal cell

and NICE Pathways	carcinoma (2018). NICE technology appraisal 542. Review date October 2021. Tivozanib for treating renal cell carcinoma (2018). NICE technology appraisal 512. Review date March 2021. Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (2009). NICE Technology Appraisal 169. Guidance placed on static list. Pazopanib for the first-line treatment of advanced renal cell carcinoma (2011). NICE Technology Appraisal 215. Guidance placed on static list. Bevacizumab (first-line), sorafenib (first- and secondline), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma. Guidance placed on static list **In development** Pembrolizumab with axitinib for untreated metastatic renal cell carcinoma ID1426. Expected publication date: 27 May 2020 Nivolumab in combination with ipilimumab for untreated advanced or metastatic renal cell carcinoma'. NICE technology appraisal [ID1182]. Publication date to be confirmed. **Related NICE Pathways:** Renal cancer (2017) NICE pathway http://pathways.nice.org.uk/pathways/renal-cancer
Related National Policy	NHS England (2018/2019) Section 105. NHS manual for prescribed specialist services (2018/2019) https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Independent Cancer Taskforce (2015) Achieving world class cancer outcomes: a strategy for England 2015-2020 http://www.cancerresearchuk.org/about-us/cancerstrategy-in-england NHS England (2013) B14. Cancer: Specialised kidney,

	bladder and prostate cancer services (Adult). NHS Standard Contract. https://www.england.nhs.uk/wp-content/uploads/2013/06/b14-cancr-kidney-blad-pros.pdf

Questions for consultation

Have all relevant comparators for avelumab with axitinib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated advanced renal cell carcinoma?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom avelumab with axitinib is expected to be more clinically effective and cost effective that should be examined separately?

Where do you consider avelumab with axitinib will fit into the existing Renal Cancer NICE pathway?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which avelumab with axitinib will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider avelumab with axitinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of avelumab with axitinib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Cancer Research UK (2016) Types of kidney cancer. Accessed January 2019.

2. Office for National Statistics (2016) Cancer Registration Statistics. Accessed January 2019.

3. Cancer Research UK (2017) Kidney cancer incidence statistics. Accessed January 2019.

4. Cancer Research UK (2016) Kidney cancer survival statistics. Accessed January 2019.