

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Avelumab with axitinib for untreated advanced or metastatic renal cell carcinoma

Final scope

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

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. In final draft guidance nivolumab with ipilimumab is recommended within the Cancer Drugs fund 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 with 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 advanced or metastatic renal cell carcinoma
Comparators	<ul style="list-style-type: none"> • Pazopanib • Sunitinib • Tivozanib • Cabozantinib (only for intermediate- or poor-risk disease as defined in the International Metastatic Renal Cell Carcinoma Database Consortium criteria)

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression free survival • response rates • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
Other considerations	<p>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.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Cabozantinib for untreated advanced renal cell carcinoma (2018). NICE technology appraisal 542. Review date October 2021.</p> <p>Tivozanib for treating renal cell carcinoma (2018). NICE technology appraisal 512. Review date March 2021.</p> <p>Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (2009). NICE Technology Appraisal 169. Guidance placed on static list.</p> <p>Pazopanib for the first-line treatment of advanced renal cell carcinoma (2011). NICE Technology Appraisal 215. Guidance placed on static list.</p> <p>Bevacizumab (first-line), sorafenib (first- and secondline), sunitinib (second-line) and temsirolimus</p>

	<p>(first-line) for the treatment of advanced and/or metastatic renal cell carcinoma. Guidance placed on static list</p> <p>In development</p> <p>Nivolumab in combination with ipilimumab for untreated advanced or metastatic renal cell carcinoma. NICE technology appraisal [ID1182]. Expected publication date: 15 May 2019.</p> <p>Pembrolizumab with axitinib for untreated metastatic renal cell carcinoma ID1426. Expected publication date: 27 May 2020</p> <p>Related NICE Pathways: Renal cancer (2017) NICE pathway http://pathways.nice.org.uk/pathways/renal-cancer</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan 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</p> <p>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</p> <p>Independent Cancer Taskforce (2015) Achieving world class cancer outcomes: a strategy for England 2015-2020 http://www.cancerresearchuk.org/about-us/cancerstrategy-in-england</p> <p>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</p>

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.