

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

Lenvatinib with pembrolizumab for untreated advanced renal cell carcinoma [ID3760]

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of lenvatinib with pembrolizumab within its marketing authorisation for untreated advanced 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, accounting for more than 80% of cases¹. There are several types of RCC. The main ones are clear cell (around 75% of cases¹), papillary and chromophobe.

Early small RCC tumours are usually asymptomatic; the diagnosis of early RCC is often incidental after abdominal scans for other reasons². 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 categorised into stages 1 to 4. Stage 3 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 4. The International Metastatic RCC Database Consortium (IMDC) Risk Score is also widely used in clinical trials to categorise patients into favourable-, intermediate- or poor-risk based on certain criteria. Because of the nature of symptoms, kidney cancer is often diagnosed at an advanced stage. On average 44% of people diagnosed with kidney cancer have stage 3 or 4 disease³. Localised radical approaches including nephron-sparing surgery, radical nephrectomy and ablative therapies may be curative in people with localised tumours. However, around 30% of those who have surgery develop advanced disease later on⁴⁻⁵.

In 2017, 10,759 new kidney cancer cases were diagnosed in England, of which around 8,607 would be new cases of RCC³. The 5-year relative survival rate ranges from around 86-88% at stage 1 to 12-13% at stage 4 for patients diagnosed with kidney cancer⁶.

[NICE technology appraisal guidance 169](#) recommends sunitinib as a first-line treatment option for people with advanced and/or metastatic RCC 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 ECOG performance status of 0 or 1. [NICE technology appraisal guidance 512](#) recommends tivozanib for treating advanced RCC in adults who have had no previous treatment.

Final scope for the appraisal of lenvatinib with pembrolizumab for untreated advanced renal cell carcinoma

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[NICE technology appraisal guidance 645](#) recommends avelumab with axitinib for use within the Cancer Drugs Fund for untreated advanced renal cell carcinoma. [NICE technology appraisal guidance 542](#) recommends cabozantinib for untreated advanced RCC that is intermediate- or poor-risk as defined in IMDC criteria. [NICE technology appraisal guidance 581](#) recommends nivolumab with ipilimumab for use within the Cancer Drugs Fund as an option for adults with untreated advanced RCC that is intermediate- or poor-risk as defined in the IMDC criteria. [NICE technology appraisal 650](#) does not recommend pembrolizumab with axitinib for untreated advanced RCC.

The technology

Lenvatinib (Kisplyx, Eisai) is a multiple receptor tyrosine kinase inhibitor that selectively inhibits vascular endothelial growth factor (VEGF) receptors and other receptor tyrosine kinases that are involved in the growth of blood vessels to the tumour and tumour proliferation. It is administered orally. Lenvatinib has a marketing authorisation in the UK in combination with everolimus for the treatment of adult patients with advanced RCC following prior vascular endothelial growth factor (VEGF)-targeted therapy.

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as 'programmed death 1' (PD-1). The PD-1 protein is part of the immune checkpoint pathway and blocking its activity may promote an anti-tumour immune response. It is administered intravenously.

Lenvatinib with pembrolizumab does not currently have a marketing authorisation in the UK for untreated advanced RCC. It has been studied in a randomised clinical trial, compared with sunitinib, in adults with untreated advanced RCC.

Intervention(s)	Lenvatinib with pembrolizumab
Population(s)	People with untreated advanced 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 IMDC criteria) • Nivolumab + ipilimumab (only for intermediate- or poor-risk disease as defined in the IMDC criteria) - subject to ongoing appraisal

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. The availability of any managed access arrangement for the intervention will be taken into account.</p>
Other considerations	<p>If the evidence allows the following subgroups will be considered. These include:</p> <ul style="list-style-type: none"> • People with advanced RCC that is intermediate- or poor-risk as defined in IMDC criteria <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>Pembrolizumab with axitinib for untreated metastatic renal cell carcinoma (2020) NICE technology appraisal guidance 650. Review date 2023.</p> <p>Avelumab with axitinib for untreated advanced renal cell carcinoma (2020) NICE technology appraisal guidance 645. Review date TBC.</p> <p>Nivolumab with ipilimumab for untreated advanced renal cell carcinoma (2019) NICE technology appraisal guidance 581. Review date 2021.</p> <p>Cabozantinib for untreated advanced renal cell carcinoma</p>

	<p>(2018) NICE technology appraisal guidance 542. Review date 2021.</p> <p>Tivozanib for treating renal cell carcinoma (2018) NICE technology appraisal guidance 512. Review date 2021.</p> <p>Pazopanib for the first-line treatment of advanced renal cell carcinoma (2011, updated 2013) NICE technology appraisal guidance 215. Static list.</p> <p>Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (2009, updated 2017) NICE technology appraisal guidance 169. Static list.</p> <p>Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma (2009, updated 2017) NICE technology appraisal guidance 178. Static list.</p> <p>Appraisals in development:</p> <p>Nivolumab with cabozantinib for untreated advanced or metastatic renal cell carcinoma [ID1625]. NICE technology appraisal guidance. Publication expected 16 June 2021.</p> <p>Related guidelines:</p> <p>Suspected cancer: recognition and referral (2015 updated 2017) NICE guideline NG12. Static list.</p> <p>Related NICE Pathways:</p> <p>Renal cancer (2017) NICE pathway http://pathways.nice.org.uk/pathways/renal-cancer</p>
<p>Related National Policy</p>	<p>NHS England (2019) The NHS long term plan</p> <p>NHS England (2019) Specialised kidney, bladder and prostate cancer services (Adults). Service specification. Reference: 170114S</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 15 adult specialist renal services. Chapter 105 specialist cancer services (adults).</p> <p>Department of Health (April 2016) NHS Outcomes Framework 2016-2017: Domain 1.</p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). Service specification. Ref:</p>

References

- 1 Cancer Research UK (2020). [Types of kidney cancer](#). Accessed August 2020.
- 2 Petejova N, Martinek A. Renal cell carcinoma: Review of etiology, pathophysiology and risk factors. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2016 Jun;160(2):183-94. Available from: <https://doi.org/10.5507/bp.2015.050>
- 3 Cancer Research UK (2020). [Kidney cancer incidence statistics](#). Accessed August 2020.
- 4 Leibovich, B.C., Blute, M.L., Cheville, J.C., Lohse, C.M., Frank, I., Kwon, E.D., Weaver, A.L., Parker, A.S. and Zincke, H. (2003), Prediction of progression after radical nephrectomy for patients with clear cell renal cell carcinoma. Cancer, 97:1663-1671. Available from: <https://doi.org/10.1002/cncr.11234>
- 5 Ljungberg, , Alamdari, , Rasmuson, and Roos, (1999), Follow-up guidelines for nonmetastatic renal cell carcinoma based on the occurrence of metastases after radical nephrectomy. BJU International, 84: 405-411. Available from: <https://doi.org/10.1046/j.1464-410x.1999.00202.x>
- 6 Cancer Research UK (2019). [Kidney cancer survival statistics](#). Accessed August 2020.