

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab with ipilimumab for untreated metastatic renal cell carcinoma
(CDF review of TA581) [ID3880]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab in combination with ipilimumab within its marketing authorisation for untreated, intermediate or poor risk, 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),¹ papillary and chromophobe.

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. 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. 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 2015, 10,507 new kidney cancers were diagnosed in England.² In 2014, 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’.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a fully humanised IgG4 monoclonal antibody which targets and blocks the programmed cell death-1 receptor (PD-1), to promote an anti-tumour immune response. It is administered intravenously.

Ipilimumab (Yervoy, Bristol-Myers Squibb) is a recombinant human anti-CTLA-4 monoclonal antibody which blocks the effects of CTLA-4 to enhance T-cell mediated immune responses to tumour cells. It is administered intravenously.

Nivolumab does not currently have a marketing authorisation in the UK for untreated RCC. Ipilimumab does not currently have a marketing authorisation in the UK for untreated RCC. Nivolumab in combination with ipilimumab has been studied in a clinical trial, compared with sunitinib, in adults with untreated, advanced or metastatic RCC.

Nivolumab has a marketing authorisation in the UK for treating advanced RCC after prior therapy, and this indication has already been appraised in NICE Technology appraisal 417.

Intervention(s)	Nivolumab in combination with ipilimumab
Population(s)	People with untreated, intermediate or poor risk (as per International Metastatic Renal Cell Carcinoma Database Criteria), advanced or metastatic renal cell carcinoma
Comparators	<ul style="list-style-type: none"> • Pazopanib • Sunitinib
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>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies</p>

	<p>recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.</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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<p>Other considerations</p>	<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>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>‘Nivolumab for previously treated advanced renal cell carcinoma’ (2016). NICE Technology Appraisal 417. Review date November 2019.</p> <p>‘Pazopanib for the first-line treatment of advanced renal cell carcinoma’ (2011). NICE Technology Appraisal 215. Static list.</p> <p>‘Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma’ (2009). NICE Technology Appraisal 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). NICE Technology Appraisal 178. Static list.</p> <p>Appraisals in development:</p> <p>‘Tivozanib for treating renal cell carcinoma’ NICE technology appraisal guidance [ID591]. Publication date to be confirmed.</p> <p>‘Cabozantinib for untreated locally advanced or metastatic renal cell carcinoma’ NICE technology appraisal guidance [ID1208]. Publication expected October 2018.</p>

	<p>Related NICE Pathways:</p> <p>Renal cancer (2017) NICE pathway</p> <p>http://pathways.nice.org.uk/pathways/renal-cancer</p>
Related National Policy	<p>NHS England (May 2016) Manual for prescribed specialised services. Section 105.</p> <p>https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</p> <p>Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1.</p> <p>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</p> <p>http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report</p> <p>NHS England (2013) B14. Cancer: Specialised kidney, bladder and prostate cancer services (Adult). NHS Standard Contract.</p> <p>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 July 2017.
2. Office for National Statistics (2017) [Cancer Registration Statistics](#). Accessed July 2017.
3. Cancer Research UK (2017) [Kidney cancer incidence statistics](#). Accessed July 2017.
4. Cancer Research UK (2016) [Kidney cancer survival statistics](#). Accessed July 2017.