NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for adjuvant treatment of renal cell carcinoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for adjuvant treatment of renal cell carcinoma after nephrectomy.

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). 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 I and II includes tumours which are localised to the kidney. 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

In 2017, 10,759 new kidney cancer cases were diagnosed in England. The incidence rate of kidney cancer increases with age and is highest in people over 85 years of age[1].

Treatment options for localised tumours include laproscopic or open surgery (nephrectomy), which can be partial (nephron sparing) or total, and ablation techniques including radiofrequency ablation and cryoablation (nephrectomy). These are performed with curative intent. NICE cancer service guideline 2, 'Improving outcomes in urological cancer' recommends that surgery can also be considered when there is metastatic disease. After surgery, the disease may relapse and spread to other parts of the body. The aim of adjuvant treatment is to reduce the number of people whose disease relapses. NICE has not appraised a treatment to reduce the risk of recurrence after surgery for renal cell carcinoma before.

The technology

Pembrolizumab (Keytruda, MSD) is a humanised monoclonal anti-programmed cell death-1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK as an adjuvant treatment for renal cell carcinoma. It has been studied in a randomised placebo-controlled trial in people who have had nephrectomy and have intermediate-high risk, high risk or M1 no evidence of disease (M1 NED) renal cell carcinoma with clear cell component. This included people with localised tumours in the kidney and people with solid, isolated, soft tissue metastases that could be surgically removed at the same time or within 1 year of nephrectomy. People with bone or brain metastases were not included in the trial.

Pembrolizumab in combination with axitinib has a marketing authorisation for the first-line treatment of advanced renal cell carcinoma in adults.

Intervention(s)	Pembrolizumab
Population(s)	People with renal cell carcinoma who have had nephrectomy
Comparators	Established clinical management without pembrolizumab
Outcomes	The outcome measures to be considered include: • overall survival • disease-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. The availability of any managed access arrangement for the intervention 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 and NICE Pathways	Related Technology Appraisals: Pembrolizumab with axitinib for untreated advanced renal cell carcinoma (2020) NICE technology appraisal guidance 650 Cabozantinib for untreated advanced renal cell carcinoma (2018) NICE technology appraisal 542 Lenvatinib with everolimus for previously treated advanced

	renal cell carcinoma (2018) NICE technology appraisal guidance 498 Tivozanib for treating renal cell carcinoma (2018) NICE technology appraisal guidance 512 Cabozantinib for previously treated advanced renal cell carcinoma (2017) NICE technology appraisal guidance 463 Everolimus for advanced renal cell carcinoma after previous treatment (2017) NICE technology appraisal guidance 432 Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment (2015) NICE technology appraisal guidance 333 Pazopanib for the first-line treatment of advanced renal cell carcinoma (updated 2013) NICE technology appraisal guidance 215 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 guidance 178 Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma (2009) NICE technology appraisal 169 Appraisals in development (including suspended appraisals) Lenvatinib with everolimus or pembrolizumab for untreated advanced renal cell carcinoma [ID3760] NICE Technology appraisal guidance. Publication date to be confirmed Sunitinib for the adjuvant treatment of early renal cell carcinoma. NICE technology appraisal. Publication date to be confirmed (suspended appraisal). Related Guidelines: Suspected cancer: recognition and referral (2015 updated 2017) NICE guideline NG12 Improving outcomes in urological cancers (2002) Cancer service guideline CSG2 Related Interventional Procedures: Irreversible electroporation for treating renal cancer (2013) NICE interventional procedures guidance 443 Single-port laparoscopic nephrectomy (2011) NICE

	interventional procedures guidance 414 Laparoscopic cryotherapy for renal cancer (2011) NICE interventional procedures guidance 405 Percutaneous cryotherapy for renal cancer (2011) NICE interventional procedures guidance 402 Percutaneous radiofrequency ablation for renal cancer (2010) NICE interventional procedures guidance 353 Laparoscopic partial nephrectomy (2006) NICE interventional procedures guidance 151 Laparoscopic nephrectomy (including nephroureterectomy) (2005) NICE interventional procedures guidance 136 Related NICE Pathways: Renal cancer (updated 2018) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) Chapter 105 NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,3,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2019) Specialised kidney, bladder and prostate cancer services (Adults). Service specification. Reference: 170114S NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). Service specification. Ref: B15/S/a. NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). Service specification. Ref: B01/S/a. Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance

Questions for consultation

Population

- Would pembrolizumab be used as an adjuvant treatment for people:
    - who had partial nephrectomy?
    - who had nephrectomy of their renal cell carcinoma but also had metastases?
- Is nephrectomy ever carried out in people who are taking drug treatments for advanced renal cell carcinoma?

Comparators

- Have all relevant comparators for pembrolizumab been included in the scope
- What is established clinical management without pembrolizumab for people who have had nephrectomy?
    - Does this vary by stage of disease, and if so, how?

Outcomes

- Are the outcomes listed appropriate?

Subgroups

Are there any subgroups of people in whom pembrolizumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab will fit into the existing NICE pathway, Renal cancer

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 pembrolizumab 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 pembrolizumab 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 pembrolizumab 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 Kidney cancer types and grades. Accessed October 2020

[2] Cancer Research UK Kidney cancer incidence statistics. Accessed October 2020.