NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Everolimus for the second-line treatment of advanced and/or metastatic renal cell carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of everolimus within its marketing authorisation for previously treated advanced or metastatic renal cell carcinoma.

Background

Renal cell cancer (RCC) refers to 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 (approximately 90% of the cases)[1]. There are several different types of RCC, with the main ones divided into 5 categories: clear cell, papillary (Types 1 and 2), chromophobe, oncocytic and collecting duct carcinoma. Clear cell is the most common form of RCC accounting for approximately 80–90% of cases.[2]

The tumour node metastases system is used to grade RCC into stages I to IV. Advanced RCC, in which the tumour is either locally advanced and/or has spread to regional lymph nodes, is generally defined as stage III. Metastatic RCC, in which the tumour has spread beyond the regional lymph nodes to other parts of the body, is generally defined as stage IV.

Early, small RCC tumours are usually asymptomatic; the diagnosis of early RCC is often incidental after abdominal scans for other indications. The most common presenting symptoms of metastatic and/or 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. Nephron sparing surgery may be curative in people with localised tumours. However, around half of those who have curative resection for earlier stages of the disease also go on to develop advanced and/or metastatic disease later on.

In 2012, 8638 new kidney cancer cases were diagnosed in England.[3] In 2013, approximately 46% of people diagnosed with kidney cancer had stage III or IV disease and 27% had stage IV disease.[3] The 5-year survival rate for metastatic RCC is approximately 10%.[4]

The aim of treatment is to stop the growth of new blood vessels within a tumour. After failure of prior systemic treatment with a tyrosine kinase inhibitor or cytokine, NICE technology appraisal guidance 333 recommends axitinib. Because the remit referred to NICE by the Department of Health for axitinib

only includes adults who have been previously treated with sunitinib, the use of axitinib after treatment with other tyrosine kinase inhibitors is not subject to statutory funding. Everolimus, sorafenib and sunitinib are not recommended after initial therapies had failed in NICE guidance (NICE technology appraisal guidance 178 and 219); however, everolimus is available in England for metastatic RCC through the Cancer Drugs Fund for some patients.

The technology

Everolimus (Afinitor, Novartis) is a protein kinase inhibitor. It has a marketing authorisation in the UK for the treatment of people with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy. Everolimus is given orally.

Intervention(s)	Everolimus
Population(s)	People with advanced renal cell carcinoma, whose disease has progressed on or after treatment with VEGF-targeted therapy.
Comparators	• Axitinib • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 patient access schemes for the intervention or comparator technologies will be taken into account.

Other considerations	If the evidence allows the following subgroups will be considered. These include: • previous treatment • prognostic score (for example, ECOG or Motzer). 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: 'Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment' (2015). NICE Technology Appraisal 333. '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. 'Pazopanib for the first-line treatment of advanced renal cell carcinoma' (2011). NICE Technology appraisal 215. Review date tbc. 'Sunitinib for the first-line treatment of advanced and/or metastatic renal cell carcinoma' (2009). NICE Technology appraisal 169. On static list. Appraisals in development 'Pazopanib for the second line treatment of metastatic renal cell carcinoma (discontinued)' NICE technology appraisals guidance [ID70]. Related Guidelines: 'Referral guidelines for suspected cancer' (2005). NICE guideline CG27. Review date June 2015. 'Improving outcomes in urological cancers (2002). NICE Guideline CSGUC. Review date tbc. Related Interventional Procedures: 'Irreversible electroporation for treating renal cancer (2013). NICE Interventional Procedure 443. 'Laparoscopic cryotherapy for renal cancer' (2011). NICE Interventional Procedure 405. 'Percutaneous cryotherapy for renal cancer' (2011). NICE Interventional Procedure 402. 'Percutaneous radiofrequency ablation for renal cancer'

	(2010). NICE Interventional Procedure 353. Related NICE Pathways: Renal Cancer (2015) NICE pathway
Related National Policy	NHS England (January 2014) Manual for prescribed specialised services. Section 105 (p236) http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf NHS England: B14. Specialised Urology. NHS Care and Clinical Reference Groups. Link accessed: 26th February 2015 http://www.england.nhs.uk/commissioning/spec-services/npc-crg/group-b/b14/ Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health (2014) The national cancer strategy: 4th annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report

References

1. American Cancer Society - Kidney Cancer (Adult) - Renal Cell Carcinoma. Accessed January 2016
2. Patient.co.uk – Renal Cancer. Accessed January 2016
3. Cancer Research UK (2011) Kidney cancer incidence statistics. Accessed January 2016
4. GP Notebook - Clear Cell Cancer Accessed January 2016