NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Nivolumab for treating metastatic or unresectable urothelial cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating metastatic or unresectable urothelial cancer in adults whose disease has progressed after prior platinum-containing chemotherapy.

Background

Urothelial carcinoma is cancer of the transitional cells which form the inner lining of the bladder, urethra, ureter, or renal pelvis. Urothelial carcinoma is most common in the bladder, and accounts for 90% of bladder cancers[1]. Transitional cell cancers can be split into papillary carcinomas and flat carcinomas. Papillary carcinomas often grow towards the centre of the bladder, without going into deeper layers (non-invasive) but sometimes these can grow deeper into the bladder wall and are more likely to spread (invasive). Flat carcinomas do not grow toward the hollow part of the bladder and remain in the inner layers (non-invasive). Other types of bladder cancers include squamous cell carcinoma (beginning in thin flat cells) and adenocarcinoma (beginning in cells which make and release mucus and other fluids). These types of bladder cancer arise as a result of chronic irritation and inflammation.

There were 10,300 diagnoses of bladder cancer in 2013, accounting for 1 in every 30 new cases of cancer each year[2, 3]. Overall incidence is 11.4 per 100,000 and is more common in men than women (3:1)[2]. The majority of cases are in those over the age of 60 but can also affect young people too[3, 4]. Smoking is major factor in the cause of bladder cancer[4].

Patients with metastatic or advanced urothelial cancer may receive treatment with surgery and/or radiotherapy. Chemotherapy may be given before (neoadjuvant) or after surgery and/or radiotherapy in an attempt to improve cure rates. If the urothelial cancer is too advanced for surgery/radiotherapy or has recurred after these treatments, chemotherapy can be used to improve quality of life and survival. NICE guideline NG2 recommends cisplatin-based regimens (such as gemcitabine plus cisplatin or accelerated methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]) for untreated disease or after one prior therapy. In addition, carboplatin plus gemcitabine maybe considered for untreated disease and carboplatin or gemcitabine plus paclitaxel may be considered after one prior therapy. For people whose disease has progressed after platinum-based

chemotherapy, a taxane such as docetaxel or paclitaxel may be given. Vinflunine is not recommended for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract that has progressed after treatment with platinum-based chemotherapy (NICE technology appraisal 272).

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a fully humanised monoclonal antibody that specifically binds to anti-programmed cell death-1 (PD-1) receptor on the surface of immune cells and restores T-cell activity by blocking the inhibitory pathway with PD-L1. It is administered intravenously.

Nivolumab does not currently have a marketing authorisation in UK for treating urothelial carcinoma after treatment with platinum-based chemotherapy. It is being studied in a non-comparative phase II clinical trial in adults with locally advanced or metastatic urothelial cancer that has progressed or recurred following platinum-containing chemotherapy.

Intervention(s)	Nivolumab
Population(s)	Adults with metastatic or unresectable urothelial cancer whose disease has progressed after platinum-based chemotherapy
Comparators	• Retreatment with 1st line platinum-based chemotherapy (only for people whose disease has had an adequate response) • Docetaxel • Paclitaxel • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-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.
Other considerations	If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices. 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:** 'Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract' (2013) NICE technology appraisal guidance 272. Added to static list November 2015. *Appraisals in development (including suspended appraisals)* 'Atezolizumab for treating metastatic urothelial bladder cancer after platinum-based chemotherapy' NICE technology appraisals guidance (ID939). Publication expected September 2017. 'Durvalumab for treating locally advanced or metastatic urothelial carcinoma' Suspended NICE technology appraisal guidance (ID1172). 'Pembrolizumab for previously treated advanced or metastatic urothelial cancer' NICE technology appraisals guidance (ID1019). Publication expected October 2017. **Related Guidelines:** 'Bladder cancer: diagnosis and management' (2015) NICE guideline NG2. Review date 2019 'Improving outcomes in urological cancers' (2002) NICE cancer service guidance. Review date March 2020.

	Related Interventional Procedures: 'Laparoscopic cystectomy' NICE interventional procedure guidance 287. Published February 2009. 'Electrically-stimulated intravesical chemotherapy for superficial bladder cancer' (2008). NICE interventional procedure guidance 277. 'Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer' (2007). NICE interventional procedure guidance 235. **Related Quality Standards:** 'Bladder cancer' (2015) NICE quality standard. **Related NICE Pathways:** Bladder cancer (2015) NICE Pathway
Related National Policy	Department of Health (2014) NHS outcomes framework 2015-2016 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 Department of Health (2007) Cancer reform strategy

References

1. Transitional cell cancer, Cancer Research UK. Accessed January 2017
2. Bladder Cancer statistics, Cancer Research UK. Accessed January 2017
3. Bladder Cancer, Patient UK. Accessed January 2017
4. The facts about Bladder cancer, Action Bladder Cancer UK. Accessed January 2017