NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for treating resected high-risk invasive urothelial cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for the adjuvant treatment of muscle-invasive urothelial cancer with high-risk of recurrence following surgical resection.

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 approximately 90% of bladder cancers.[1] Urothelial carcinomas can be described as non-invasive or invasive depending on how far the carcinomas invade the tissues. Invasive urothelial cancer is when cancerous cells spread beyond the lining into the surrounding bladder muscle and is normally treated by resection. After the cells are removed, some people are at higher risk of the cancer recurring depending on the size, number, and biological markers of the removed carcinomas.

In 2017, 9974 new invasive urothelial cancers were diagnosed in England[2]. Approximately 25-30% of patients have muscle-invasive urothelial carcinoma at diagnosis, but some non-invasive tumours can become invasive[3]. The majority of new cases are in those over the age of 75 but can also affect young people too. 73% of bladder cancer cases in the UK are in males, and 27% are in females[4]. Smoking is a major factor in the cause of bladder cancer.

People with muscle invasive urothelial cancer may have surgery and/or radiotherapy. Chemotherapy with cisplatin-based regimen may be given before (neoadjuvant) surgery and/or radiotherapy in an attempt to improve cure rates. Surgery consists of radical cystectomy (removal of the bladder) with urinary stoma or a continent urinary diversion. After surgery, some patients with high risk of recurrence (for example positive lymph-node involvement, or for whom neoadjuvant chemotherapy was not suitable) may receive cisplatin-based adjuvant therapy to improve survival. If the cancer has recurred after these treatments, NICE guideline NG2 recommends cisplatin-based regimens (such as gemcitabine plus cisplatin or accelerated [high dose] methotrexate, vinblastine, doxorubicin and cisplatin [MVAC] plus granulocyte stimulating factor [G-CSF]). Carboplatin plus gemcitabine may be considered for untreated disease if cisplatin is unsuitable. In people for whom cisplatin is unsuitable, and their tumours express PD-L1 at a level of 5% or more, NICE technology appraisal 492 recommends atezolizumab within the Cancer Drugs Fund. Where cisplatin is unsuitable and tumours express PD-L1 with a combined positive score of 10 or more, NICE technology appraisal 522 recommends pembrolizumab within the Cancer Drugs Fund.

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 the UK for the adjuvant treatment of invasive urothelial cancer with high-risk of recurrence following surgical resection. It has been studied in clinical trials as monotherapy in adults who have undergone radical surgery for invasive urothelial cancer compared with placebo. Nivolumab has a marketing authorisation as monotherapy for the treatment of locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy.

Intervention	Nivolumab
Population	People with invasive urothelial cancer following radical surgical resection who: • are at high-risk of recurrence • did not receive neoadjuvant cisplatin chemotherapy
Comparators	• Adjuvant chemotherapy (e.g. cisplatin-based regimen) • Best supportive care (monitoring and further treatment at recurrence)
Outcomes	The outcome measures to be considered include: • disease-free survival • overall survival • 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.

Other considerations	If the evidence allows, the following subgroups will be considered. These include PD-L1 status of the resected tumour. 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:** Atezolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (2017). NICE Technology Appraisal 492. Review date: December 2020. Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 525. Review date: June 2021. Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (2018). NICE Technology Appraisal 530. Review date: July 2021. Pembrolizumab for untreated PD-L1-positive locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (2018). NICE Technology Appraisal 522. Review date to be confirmed. Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 519. Review date to be confirmed. Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract (2013). NICE Technology Appraisal 272. Transferred to the static list November 2015. **Appraisals in development (including suspended appraisals):** Atezolizumab for adjuvant treatment of resected high-risk muscle-invasive urothelial cancer. NICE technology appraisal guidance [ID2730] Publication date to be confirmed. Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. NICE technology appraisals guidance [ID1333]. Publication date to be confirmed Durvalumab for treating metastatic urothelial bladder cancer after chemotherapy. Suspended NICE technology appraisals guidance [ID1172]. Durvalumab for untreated PD-L1 positive metastatic urothelial bladder cancer. NICE technology appraisals guidance

	[ID1169]. Publication date to be confirmed. Durvalumab with tremelimumab for untreated PD-L1-positive urothelial bladder cancer. NICE technology appraisals guidance [ID1335]. Publication date to be confirmed. **Related Guidelines:** Bladder cancer: diagnosis and management (2015) NICE guideline NG2. Improving outcomes in urological cancers (2002) NICE cancer service guidance. Published September 2002. **Related Interventional Procedures:** Laparoscopic cystectomy NICE interventional procedure guidance 287. Published February 2009. Electrically-stimulated intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 277. Published November 2008 Transurethral laser ablation for recurrent non-muscle-invasive bladder cancer NICE interventional procedures guidance 656. Published July 2019. Intravesical microwave hyperthermia with intravesical chemotherapy for superficial bladder cancer NICE interventional procedure guidance 235. Published October 2007. **Related Quality Standards:** Bladder cancer NICE quality standard. Published December 2015. **Related NICE Pathways:** Bladder cancer (2019) NICE Pathway.
Related National Policy	NHS England (2019) Specialised kidney, bladder and prostate cancer services (adults) The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for nivolumab been included in the scope?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate?

How is high-risk muscle invasive urothelial cancer defined in clinical practice?

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

Where do you consider nivolumab will fit into the existing NICE pathway, Bladder 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 nivolumab 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 nivolumab 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 nivolumab 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 (2018) Types of bladder cancer. Accessed September 2020.

2. Office for National Statistics (2019) Cancer Registration Statistics, England: 2017. Accessed September 2020.

3. Cumberbatch MGK, Noon AP (2019) Epidemiology, aetiology and screening of bladder cancer. Translational Andrology and Urology. 8(1): 5–11

4. Cancer Research UK (2018) Bladder cancer incidence statistics. Accessed September 2020.

