

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for treating resected high-risk invasive urothelial cancer

Final scope

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 cancers¹. Urothelial cancer can also originate in the upper urinary tract. 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 England². Approximately 25-30% of patients have muscle-invasive urothelial carcinoma at diagnosis, but some non-invasive tumours can become invasive³. 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 females⁴. Smoking is a major factor in the cause of bladder cancer.

People with muscle-invasive urothelial cancer may have surgery or radiotherapy. Chemotherapy with cisplatin-based regimen may be given before (neoadjuvant) surgery 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 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 who are at high-risk of recurrence following radical surgical resection
Comparators	<ul style="list-style-type: none"> • Adjuvant chemotherapy (e.g. cisplatin-based regimen) • Best supportive care (monitoring and further treatment at recurrence)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • disease-free survival • overall survival • 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>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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>

<p>Other considerations</p>	<p>If the evidence allows, the following subgroups will be considered. These include PD-L1 status of the resected tumour.</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>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.</p> <p>Atezolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 525. Review date: June 2021.</p> <p>Nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (2018). NICE Technology Appraisal 530. Review date: July 2021.</p> <p>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.</p> <p>Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy (2018). NICE Technology Appraisal 519. Review date to be confirmed.</p> <p>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.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Atezolizumab for adjuvant treatment of resected high-risk muscle-invasive urothelial cancer. NICE technology appraisal guidance [ID2730] Publication date to be confirmed.</p> <p>Erdafitinib for treating metastatic or unresectable FGFR-positive urothelial cancer. NICE technology appraisals guidance [ID1333]. Publication date to be confirmed</p> <p>Durvalumab for treating metastatic urothelial bladder cancer after chemotherapy. Suspended NICE technology appraisals guidance [ID1172].</p> <p>Durvalumab for untreated PD-L1 positive metastatic urothelial bladder cancer. NICE technology appraisals guidance</p>

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

References

1. Cancer Research UK (2018) [Types of bladder cancer](#). Accessed February 2021.
2. Office for National Statistics (2019) [Cancer Registration Statistics, England: 2017](#). Accessed February 2021.

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 February 2021.