NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Erdafitinib for treating metastatic or unresectable FGFR-altered urothelial cancer [ID1333]

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of erdafitinib within its marketing authorisation for treating metastatic or unresectable fibroblast growth factor receptor (FGFR)-altered urothelial cancer.

Background

Urothelial carcinoma is cancer of the transitional cells which form the inner lining the bladder, urethra, ureter, or renal pelvis. It 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. Non-invasive urothelial carcinomas can be further split into papillary carcinomas or flat carcinomas. Papillary carcinomas often grow towards the hollow part of the organ (for example bladder and ureter), without going into deeper layers. Flat carcinomas remain in the inner layers. Both papillary and flat carcinomas can become invasive.

Fibroblast growth factor receptors regulate cell growth. Genetic alterations in these receptors can promote uncontrolled growth of urothelial carcinoma tumours. Around 15-20% of patients with advanced urothelial carcinoma have alterations in the FGFR gene.[2,3]

In 2021, 18,194 new bladder cancers were diagnosed in England.[4] Bladder cancer is the 11th most common cancer in the UK.[5] The majority of cases are in those over the age of 60 and it is more common among men than women (3 males for every 1 female).[4,5] Bladder cancer has a high recurrence rate, with around 70% of cases returning within 5 years of initial treatment.[6] The most common symptom of bladder cancer is blood in urine, which is usually painless. Smoking is a major factor in the cause of bladder cancer. Urothelial carcinoma has a poor prognosis in the metastatic stage.

Standard care for initial treatment of locally advanced or metastatic cancer is a cisplatin-containing chemotherapy. Where cisplatin is unsuitable, people may be offered carboplatin plus gemcitabine or, if eligible, atezolizumab. People whose disease has progressed after platinum-based chemotherapy (cisplatin or carboplatin) may be offered atezolizumab or further chemotherapy. People whose cancer has not progressed after platinum-based chemotherapy may be offered avelumab as maintenance therapy.

Currently, related NICE guidance includes:

- NICE technology appraisal 525, which recommends atezolizumab for treating locally advanced or metastatic urothelial carcinoma in adults who have had platinum-containing chemotherapy.

- NICE technology appraisal 739, which recommends atezolizumab as an option for untreated locally advanced or metastatic urothelial cancer in adults whose tumours express PD-L1 at a level of 5% or more and when cisplatin-containing chemotherapy is unsuitable.

- NICE technology appraisal 788, which recommends avelumab as an option for maintenance treatment of locally advanced or metastatic urothelial cancer that has not progressed after platinum-based chemotherapy in adults.

The technology

Erdafitinib (Balversa, Janssen) does not currently have a marketing authorisation in the UK for treating urothelial cancer. It is being studied in a phase 3 clinical trial in adults with advanced urothelial cancer that has progressed following 1-2 previous treatments (mostly chemotherapy and/or immunotherapy).

Intervention(s)	Erdafitinib
Population(s)	People with metastatic or unresectable fibroblast growth factor receptor (FGFR)-altered urothelial cancer
Subgroups	If the evidence allows the following subgroups will be considered: • FGFR alteration type • Previous anti-PD-(L) 1 treatment • People with upper tract urothelial cancer

Comparators	• Established clinical management without erdafitinib, including but not limited to:
	  ○ Chemotherapy (including docetaxel, paclitaxel)
	  ○ Atezolizumab
	  ○ Best supportive care

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates (including type and duration of response) • 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 and cost of biosimilar and generic products should be taken into account. The use of erdafitinib is conditional on the presence of FGFR alterations. The economic modelling should include the costs associated with diagnostic testing for FGFR alterations in people with urothelial cancer who would not otherwise have been tested (if applicable). A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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	**Related technology appraisals:** Atezolizumab for untreated PD-L1-positive advanced urothelial cancer when cisplatin is unsuitable. NICE technology appraisal guidance 739. Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract. (2013) NICE technology appraisal guidance 272. Pembrolizumab for locally advanced or metastatic urothelial cancer where cisplatin is unsuitable. NICE technology appraisal guidance 674 (terminated appraisal) Pembrolizumab for previously treated advanced or metastatic urothelial cancer NICE technology appraisal guidance 692 (negative recommendation).

	Nivolumab for treating metastatic or unresectable urothelial cancer after platinum-based chemotherapy. NICE technology appraisal guidance 530 (negative recommendation). Atezolizumab for treating metastatic urothelial cancer after platinum-based chemotherapy. NICE technology appraisal guidance 525. Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy NICE technology appraisal guidance TA788 **Related technology appraisals in development:** Durvalumab with tremelimumab and chemotherapy for treating unresectable or advanced urothelial cancer NICE technology appraisal guidance [ID3855]. Publication date tbc. Sacituzumab govitecan for treating unresectable metastatic urothelial cancer NICE technology appraisal guidance [ID6150]. Publication date tbc. Nivolumab with ipilimumab for untreated unresectable or metastatic urothelial cancer when cisplatin is unsuitable NICE technology appraisal guidance [ID3939] Publication date tbc. Pembrolizumab with enfortumab vedotin for untreated metastatic urothelial cancer NICE technology appraisal guidance [ID6332] Publication date tbc. **Related NICE 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:** Transurethral laser ablation for recurrent non-muscle-invasive bladder cancer (2019) NICE interventional procedures guidance 656 Electrically stimulated intravesical chemotherapy for non-muscle-invasive bladder cancer (2019) NICE interventional procedures guidance 638 Intravesical microwave hyperthermia and chemotherapy for non-muscle-invasive bladder cancer (2018) NICE interventional procedures guidance 628

	Laparoscopic cystectomy (2009) NICE interventional procedures guidance 287 **Related Quality Standards:** Bladder cancer NICE quality standard. Published December 2015
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 105 NHS England (2019) Specialised kidney, bladder and prostate cancer services (adults): Service specification

References

1 Cancer Research UK. Types of bladder cancer. https://www.cancerresearchuk.org/about-cancer/bladder-cancer/types-stages-grades/types Accessed November 2023

2 Xiao, J.F., et al., 2021. Targetable pathways in advanced bladder cancer: FGFR signaling. Cancers, 13(19), p.4891.

3 Kalebasty, A. R., et al. (2023). Outcomes of Patients with Advanced Urothelial Carcinoma after Anti–programmed Death-(ligand) 1 Therapy by Fibroblast Growth Factor Receptor Gene Alteration Status: An Observational Study. European Urology Open Science, 47, 48-57.

4 NHS Digital. Cancer Registrations Statistics, England 2021 https://digital.nhs.uk/data-and-information/publications/statistical/cancer-registration-statistics/england-2021---summary-counts-only Accessed November 2023.

5 Cancer Research UK (2023) Bladder cancer incidence statistics. https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/bladder-cancer#heading-Zero Accessed March 2023.

6 Chamie, K., et al. (2013). Recurrence of high-risk bladder cancer: a population-based analysis. Cancer, 119(17), 3219-3227.