Atezolizumab (Tecentriq) with gemcitabine and carboplatin for advanced bladder cancer

NIHR HSRIC ID: 12884

Lay summary

Atezolizumab is a new drug to treat bladder cancer that has spread to other parts of the body in people who are not suitable for the standard chemotherapy treatment. It is injected directly into the bloodstream and is given alongside two other chemotherapy drugs called gemcitabine and carboplatin.

This briefing is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information.

This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.
TARGET GROUP

- Urothelial carcinoma: untreated locally advanced or metastatic; ineligible for cisplatin-based therapy.

TECHNOLOGY

DESCRIPTION

Atezolizumab (Tecentriq; MPDL-3280A; RG 7446; RO-5541267) is a human monoclonal antibody that targets programme death ligand-1 (PD-L1). In the phase III clinical trial, atezolizumab is administered at 1,200mg via an intravenous (IV) infusion on day 1 of a 21 day cycle in combination with gemcitabine 1,000mg/m² on day 1 and 8 of the 21 day cycle, and with carboplatin area under the curve (AUC) 4.5 IV on day 1 of 21 day cycle1a. Treatment continues as long as the patient continues to experience clinical benefit or until unacceptable toxicity or symptomatic deterioration attributed to disease progression.

Atezolizumab does not currently have Marketing Authorisation in the EU for any indication2.

Atezolizumab is also in phase III clinical trials for breast cancer, colorectal cancer, melanoma, small cell lung cancer, non-small cell lung cancer, renal cancer, prostate cancer, and ovarian, fallopian tube, or primary peritoneal cancer. Atezolizumab is in phase II clinical trials for head and neck cancer, sarcoma, solid tumours and lymphoma.

INNOVATION and/or ADVANTAGES

If licensed, atezolizumab will offer an additional treatment option for locally advanced or metastatic urothelial carcinoma.

DEVELOPER

Roche Products Ltd.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.

PATIENT GROUP

BACKGROUND

The most common symptom of bladder cancer is blood in the urine (haematuria); other symptoms include burning when passing urine, increased urinary frequency or urgency and pain in the lower abdomen or back2. Most bladder cancers occur in people aged over 60 years and the main risk factors are increasing age, smoking and exposure to chemicals in the workplace3.

The involvement of the urogenital tract and the nature of the treatments gives bladder cancer a strong psychological impact, in addition to the physical impact of the disease and its
treatments, which is often profound. The prevalence of the condition and the nature of its management make bladder cancer one of the most expensive cancers for the NHS.

Bladder cancer is categorised into stages that describe the size of the primary tumour and its local or distant spread. The first stage is early, superficial or non-muscle invasive bladder cancer, which describes cancer that is confined to the urothelium. Invasive cancer describes disease that has spread into the muscle of the bladder wall; it may also have spread to the fat layer of the bladder, the prostate, uterus or vagina. Advanced cancer describes disease that has spread to the wall of the abdomen or pelvis, or the lymph nodes. Metastatic cancer involves other parts of the body.

### CLINICAL NEED and BURDEN OF DISEASE

Bladder cancer is the 10th most common cancer in the UK, accounting for 3% of new cases. In 2014 there were 10,063 new diagnoses in UK. In 2014, 24% of people diagnosed with bladder cancer with a known stage had advanced disease and approximately 17% had metastases at diagnosis.

Locally administered BCG is the main treatment modality for non-muscle invasive bladder cancer, however 30-40% of treated patients do not respond to this therapy and another 30-40% of initial responders relapse within 5 years. BCG may only be used in early bladder cancer.

Bladder cancer is more common in men than women, with a male to female ratio of around 27:10. The one-year survival rates are 77% and 62% for men and women respectively. Ten-year survival at diagnosis is 54% and 40% for men and women respectively.

In 2014-15, there were 69,058 hospital admissions in England due to bladder cancer (ICD10: C67), accounting for 73,227 finished consultant episodes and 122,512 bed days. In 2014, 4,776 deaths from malignant neoplasm of bladder (C67) were registered in England and Wales.

### PATIENT PATHWAY

### RELEVANT GUIDANCE

**NICE Guidance**


---

*a Company provided information.*
Horizon Scanning Research & Intelligence Centre

NHS England Policies and Guidance


Other Guidance

- European Society for Medical Oncology. Bladder cancer: ESMO practice guidelines for diagnosis, treatment and follow-up. 2014\textsuperscript{10}.
- European Association of Urology. Guidelines on non-muscle invasive bladder cancer (aT1 and CIS). 2015\textsuperscript{11}.

CURRENT TREATMENT OPTIONS

The recommended treatment plan for muscle-invasive bladder cancer depends on the stage of disease\textsuperscript{12}. In early stages of bladder cancer, cure or long term control are realistic aims for treatment. In advanced or metastatic disease, treatment is typically palliative.

Treatment options for advanced or metastatic disease include surgical resection of the bladder (cystectomy); chemotherapy and/or radiotherapy in conjunction with a radiosensitiser. In all cases, supportive care and end of life palliative care should be considered. This may include procedures that aim to relieve cancer symptoms, such as radiotherapy to treat haematuria or pelvic pain; and urinary diversion, ureteric stents or urinary catheterisation to improve renal function and avoid urinary retention.

EFFECTICITY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>Sponsor</th>
<th>Status</th>
<th>Source of information</th>
<th>Location</th>
<th>Design</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMvigor211, NCT02302807, GO29294, 2014-003231-19; atezolizumab vs chemotherapy; phase III.</td>
<td>Hoffmann-La Roche.</td>
<td>Ongoing.</td>
<td>Trial registry\textsuperscript{1}, manufacturer.</td>
<td>EU (UK), USA, Canada and other countries.</td>
<td>Randomised, active-controlled.</td>
<td>n=932 (planned); aged ≥18 yrs; locally advanced or metastatic urothelial bladder cancer.</td>
</tr>
<tr>
<td>IMvigor010, NCT02450331, WO29636, 2014-005603-25; atezolizumab vs observation; phase III.</td>
<td>Hoffmann-La Roche.</td>
<td>Ongoing.</td>
<td>Trial registry\textsuperscript{13}, manufacturer.</td>
<td>EU (incl UK), USA, Canada and other countries.</td>
<td>Randomised, controlled.</td>
<td>n= 700 (planned); aged ≥18 yrs; muscle-invasive transitional cell carcinoma of the bladder; PD-L1 positive.</td>
</tr>
<tr>
<td>IMvigor130, NCT02807636, WO30070, 2016-000250-35; atezolizumab and chemotherapy vs atezolizumab monotherapy vs placebo; phase III.</td>
<td>Hoffmann-La Roche.</td>
<td>Ongoing.</td>
<td>Trial registry\textsuperscript{14}, manufacturer.</td>
<td>EU (incl; UK), USA, Canada and other countries.</td>
<td>Randomised, placebo-controlled.</td>
<td>n=1,200 (planned); aged ≥18 yrs; locally advanced or metastatic urothelial carcinoma.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to atezolizumab 1,200mg IV on day 1 of 21 day cycle; or chemotherapy (vinflunine 320mg/m² or paclitaxel 175mg/m² or docetaxel 75mg/m² all administered IV on day 1 of 21 day cycle).</td>
<td>Randomised to atezolizumab 1,200mg IV once every 3 wks; or observation once every 3 wks for 16 cycles or 1 yr.</td>
<td>Randomised to atezolizumab 1,200mg IV on day 1 in combination with carboplatin AUC 4.5 mg/mL*min IV on day 1 and gemcitabine 1,000mg/m² IV on days 1 and 8, all given in a 21 day cycle; or placebo IV given on day 1 with carboplatin and gemcitabine at the same dosage and frequency as above; or atezolizumab 1,200mg IV on day 1 of 21 day cycle.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment until disease progression or unacceptable toxicity, follow up 25 mnths.</td>
<td>Active treatment for up to 1 yr, follow-up 6 yrs.</td>
<td>Active treatment until disease progression or loss of clinical benefit, follow-up 44 mnths.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary outcomes</td>
<td>Overall survival (OS).</td>
<td>Disease-free survival.</td>
<td>PFS, OS and AEs.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary outcomes</td>
<td>Objective response; progression-free survival (PFS); duration of response (DOR); adverse events (AEs); anti-therapeutic antibodies (ATAs) to atezolizumab; pharmacokinetics; EORTC QLQ-C30.</td>
<td>OS; disease-specific survival; distant metastasis-free survival; AEs; ATAs to atezolizumab; pharmacokinetics; participant-reported health status in the EuroQol 5-dimension, 5-level version questionnaire.</td>
<td>Overall response; DOR; survival to 1 year; EORTC QLQ-C30; pharmacokinetics; ATAs to atezolizumab.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Study completion date reported as November 2017.</td>
<td>Study completion date reported as April 2022.</td>
<td>Study completion date reported as July 2020.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**COST**

The cost of atezolizumab is not yet known.

Gemcitabine is already marketed in the UK; a 1g vial (1g/25mL) costs £13\(^{15}\). Carboplatin is also already marketed in the UK; a 150mg vial (150/15mL) costs £50.

**IMPACT - SPECULATIVE**

**Impact on Patients and Carers**

- Reduced mortality/increased length of survival
- Reduced symptoms or disability
- Other
- No impact identified

**Impact on Health and Social Care Services**

- Increased use of existing services
- Decreased use of existing services
- Re-organisation of existing services
- Need for new services
- Other
- None identified
Impact on Costs and Other Resource Use

- Increased drug treatment costs
- Reduced drug treatment costs
- Other increase in costs
- Other reduction in costs
- Other
- None identified

Other Issues

- Clinical uncertainty or other research question identified
- None identified

REFERENCES


