

Health Technology Briefing

July 2022

Atezolizumab with cabozantinib for advanced renal cell carcinoma after 1 therapy

Company/Developer

Roche Products Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 29876

NICE ID: 10717

UKPS ID: 661891

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Atezolizumab in combination with cabozantinib is in clinical development for the treatment of advanced renal cell carcinoma (RCC) after prior treatment. RCC (also called kidney cancer) is a disease that affects the lining of tiny tubes within the kidney which filter waste from the blood, making urine. In many cases of RCC there are no obvious symptoms at first, and kidney cancer is found during tests for another reason. RCC is called advanced when the tumour has spread to other parts of the body. Some patients experience drug resistance to existing single drug therapies and require the use of more effective combination therapies.

Atezolizumab is a monoclonal antibody, a type of protein designed to attach to a protein called PD-L1, which is present on many cancer cells. PD-L1 acts to switch off immune cells that would otherwise attack cancer cells. By attaching to PD-L1 and reducing its effects, atezolizumab increases the immune system's ability to attack cancer cells, thereby slowing down progression of the disease. Cabozantinib blocks the activity of enzymes known as tyrosine kinases which reduces the growth and spread of the cancer. If licensed, atezolizumab, administered through intravenous infusion, in combination with cabozantinib, administered orally, would offer an additional treatment option for adult patients with advanced RCC who have been previously treated.

Proposed Indication

Atezolizumab with cabozantinib, for the treatment of adult patients with inoperable, locally advanced or metastatic renal cell carcinoma (RCC) who experienced radiographic tumour progression during or after immune checkpoint inhibitor (ICI) treatment.¹

Technology

Description

Atezolizumab (Tecentriq, MPDL3280A) is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to programmed death-ligand 1 (PD-L1) and provides a dual blockade of the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the antitumour immune response without inducing antibody-dependent cellular cytotoxicity. Atezolizumab spares the PD-L2/PD-1 interaction allowing PD-L2/PD-1 mediated inhibitory signals to persist.²

Atezolizumab in combination with cabozantinib is currently in phase III clinical development for the treatment of adult patients (18 years and older) with previously treated inoperable, locally advanced or metastatic RCC. In the phase III clinical trial (CONTACT-03, NCT04338269), patients will receive 1200mg atezolizumab administered by intravenous (IV) infusion once every three weeks plus 60mg cabozantinib administered orally once daily.¹

Key Innovation

Immune checkpoint inhibitors (ICIs) such as atezolizumab have successfully been developed for multiple types of human tumours. However, only a subgroup of patients with cancer would benefit from immune checkpoint blockade. Some patients experience primary resistance to initial immunotherapy, and a majority eventually develop acquired resistance to ICIs.³ However, the combination of ICIs and anti-angiogenic agents (such as cabozantinib) could be a promising therapeutic strategy for overcoming the low efficacy of ICIs.⁴ Moreover, through their direct anti-cancer effect by inhibiting tumour growth and metastasis, anti-angiogenic drugs reprogram the tumour milieu from an immunosuppressive to an immune permissive microenvironment.⁵ This combination of an ICI with an anti-angiogenic drug has shown an improved anti-cancer efficacy and prolonged survival in patients in previous clinical trials.⁶

If licensed, atezolizumab in combination with cabozantinib will offer an additional treatment option for adult patients with previously treated advanced RCC.

Regulatory & Development Status

Atezolizumab, as a monotherapy and in combination, has Marketing Authorisation in the EU/UK for the following indications:²

- Urothelial carcinoma
- Small cell lung cancer
- Early-stage non-small cell lung cancer
- Metastatic non-small cell lung cancer
- Triple-negative breast cancer
- Hepatocellular carcinoma

Atezolizumab in combination with cabozantinib is currently in phase III/II clinical trials for the treatment of a number of conditions, some of which include: ⁷

- Prostate cancer
- Non-small cell lung cancer
- Advanced hepatocellular carcinoma
- Oesophageal cancer
- Neoplasms of the endocrine system

Patient Group

Disease Area and Clinical Need

RCC (also called kidney cancer or renal cell adenocarcinoma) is a disease in which malignant (cancer) cells are found in the lining of tubules (very small tubes) in the kidney.⁸ The cells can grow into surrounding tissues or organs and may spread to other areas of the body, known as advanced RCC.⁹ RCC usually affects people in their 60s and 70s and is rare in people under 50.¹⁰ Risk factors for RCC include obesity, smoking, high blood pressure, family history/genetics and long-term kidney dialysis. Many patients remain symptomless until later in the disease course, but patients may experience lower back pain, lump or swelling on the side, blood in urine, fatigue, loss of appetite, high blood pressure, night sweats, swollen glands, bone pain, coughing up blood and swelling of the testicles in males.^{10,11}

The age-standardised incidence rate of malignant neoplasm of kidney (ICD10 C64) is 23.7 in males and 12.7 in females per 100,000 population of newly diagnosed cases of cancer in England (data from 2017).¹² Incidence rates for kidney cancer are projected to rise by 26% in the UK between 2014 and 2035, to 32 cases per 100,000 people.¹³ Kidney cancer has a 79.3% 1-year and 63.8% 5-year age standardised survival rate.^{14,15} In England, in 2021-21, there were 20,380 finished consultant episodes (FCE) and 17,908 admissions for malignant neoplasm of kidney, except renal pelvis (ICD-10 code C64) which resulted in 9,984 day-cases and 38,608 FCE bed days.¹⁶

Recommended Treatment Options

NICE recommends the following treatment options for previously treated advanced RCC:¹⁷⁻²²

- Lenvatinib with everolimus
- Cabozantinib
- Everolimus
- Nivolumab
- Axitinib
- Sunitinib

Clinical Trial Information

Trial

CONTACT-03; [NCT04338269](#); A Phase III, Multicenter, Randomized, Open-Label Study to Evaluate the Efficacy and Safety of Atezolizumab Given in Combination With Cabozantinib Versus Cabozantinib Alone in Patients With Inoperable, Locally Advanced, or Metastatic Renal Cell Carcinoma Who

	<p>Experienced Radiographic Tumor Progression During or After Immune Checkpoint Inhibitor Treatment Phase III - Active, not recruiting Location(s): 7 EU countries, UK, USA, Canada and other countries Primary completion date: September 2022</p>
Trial Design	Randomised, parallel-assignment, open-label
Population	N=523; aged 18 years and older; subjects with histologically confirmed locally advanced or metastatic clear cell or non-clear cell RCC; radiographic disease progression to prior ICI therapy
Intervention(s)	<ul style="list-style-type: none"> Atezolizumab 1200mg administered at a fixed dose on day 1 of each 21-day cycle by IV infusion every 3 weeks Cabozantinib 60mg (three 20-mg tablets) administered orally once daily
Comparator(s)	Cabozantinib 60 mg (three 20-mg tablets) administered orally once daily.
Outcome(s)	<p>Primary outcome:</p> <ul style="list-style-type: none"> Progression-Free Survival (PFS), as assessed by Independent Review Facility (IRF) [Time frame: Randomisation up to approximately 27 months] Overall survival (OS) [Time frame: Randomisation up to approximately 52 months] <p>See trial record for full list of other outcomes.</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Atezolizumab is already marketed in the UK; a 1200mg/20ml vial costs £3,807.69.²³
 Cabozantinib is already marketed in the UK; a pack of 30 x 20mg tablets costs £5,143.²⁴

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Tivozanib for treating advanced renal cell carcinoma. (TA512). March 2018.
- NICE technology appraisal. Lenvatinib with everolimus for previously treated advanced renal cell carcinoma. (TA498). January 2018.
- NICE technology appraisal. Cabozantinib for previously treated advanced renal cell carcinoma. (TA463). August 2017.
- NICE technology appraisal. Everolimus for advanced renal cell carcinoma after previous treatment. (TA432). February 2017.
- NICE technology appraisal. Nivolumab for previously treated advanced renal cell carcinoma. (TA417). November 2016.
- NICE technology appraisal. Axitinib for treating advanced renal cell carcinoma after failure of prior systemic treatment. (TA333). February 2015.

- NICE technology appraisal. Bevacizumab (first-line), sorafenib (first- and second-line), sunitinib (second-line) and temsirolimus (first-line) for the treatment of advanced and/or metastatic renal cell carcinoma. (TA178). August 2009.

NHS England (Policy/Commissioning) Guidance

- NHS England. Specialised kidney, bladder and prostate cancer services (adults); Service specification. 170114S. February 2019
- NHS England. 2013/14 NHS Standard Contract for Cancer: Specialised kidney, bladder and prostate cancer services (adult). B14/S/a

Other Guidance

- The European Association of Urology (EAU). Renal Cell Cancer (RCC) Guidelines (2021).²⁵
- European Society for Medical Oncology (ESMO). Renal Cell Carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (2019).²⁶

Additional Information

References

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