

## Health Technology Briefing February 2022

### Atezolizumab adjuvant therapy for treating renal cell carcinoma in people at high risk of developing metastasis following nephrectomy

Company/Developer

Roche Products Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 12887

NICE ID: 10492

UKPS ID: 656131

#### Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

#### Summary

Atezolizumab adjuvant therapy is in clinical development for renal cell carcinoma (RCC), which is also called kidney cancer and affects the lining of tubes in the kidney. In many cases of renal cell carcinoma there are no obvious symptoms at first and kidney cancer is found during tests for another reason. For patients at increased risk of cancer returning and spreading (high-risk RCC), there is a  $\geq 40\%$  risk of recurrence after surgery (nephrectomy). Adjuvant treatment for RCC, which is used to prevent cancer returning, has been an area of interest for clinicians to improve disease-free survival and overall survival in patients at high risk of recurrence.

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 and thereby slow down progression of the disease. Atezolizumab is given intravenously and is designed to be used after surgery to remove all or part of the affected kidney, to reduce the risk of the cancer recurring or spreading to other parts of the body. If licensed, atezolizumab would offer an adjuvant treatment option for patients with RCC at high risk of developing metastasis following nephrectomy.

This briefing reflects the evidence available at the time of writing 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. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

## Proposed Indication

Adjuvant treatment in adult patients with RCC at high risk of developing metastasis following nephrectomy.<sup>1</sup>

## Technology

### Description

Atezolizumab (MPDL3280A; anti-PDL1; Tecentriq) is a humanised engineered immunoglobulin G1 monoclonal antibody that selectively targets PD-L1 to block its interaction with PD-1 and the co-stimulatory molecule B7.1, 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.<sup>2,3</sup>

Atezolizumab is in clinical development for adjuvant treatment in RCC at high risk of developing metastasis following nephrectomy. In the phase III clinical trial (IMmotion010, NCT03024996), patients receive 1200mg atezolizumab intravenously every 3 weeks for 16 treatment cycles (of 21 days) or up to 1 year (whichever occurs first).<sup>1</sup>

### Key Innovation

High-risk RCC is associated with a  $\geq 40\%$  risk of recurrence after surgery. Adjuvant treatment for RCC has been an area of interest for clinicians to improve disease-free survival and overall survival (OS) in patients at high risk of recurrence. Systemic therapies, including cytokines and vascular endothelial growth factor (VEGF), tyrosine kinase inhibitors (TKIs) with efficacy in metastatic RCC (mRCC), have been evaluated in the adjuvant setting of RCC. However, none of these therapies demonstrated an improvement in OS among patients with high-risk RCC who had undergone nephrectomy. Immune checkpoint inhibitors, such as atezolizumab, have shown significant antitumour activity with prolonged and durable responses in metastatic RCC, which led to an interest in evaluating these agents in the adjuvant setting.<sup>4</sup>

If licensed, atezolizumab will offer an adjuvant treatment option for patients with RCC at high-risk of recurrence or metastasis after nephrectomy.

### Regulatory & Development Status

Atezolizumab is licensed in the EU/UK for treating the following indications:<sup>5</sup>

- Urothelial carcinoma
- Non-small cell lung cancer
- Small cell lung cancer
- Hepatocellular carcinoma
- Triple-negative breast cancer

Atezolizumab is in phase II/III clinical development for a large number of indications, including:<sup>6</sup>

- Squamous cell carcinoma of head and neck
- Gastrointestinal Cancer
- Gynaecological Cancer
- Haematological cancer

- Genitourinary Cancer
- Neuroendocrine Cancer

## 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.<sup>7</sup> The cells can grow into surrounding tissues or organs and may spread to other areas of the body.<sup>8</sup> RCC usually affects people in their 60s and 70s and is rare in people under 50. 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 disease course, but patients may experience pain, swelling and/or 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.<sup>9,10</sup>

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).<sup>11</sup> 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 by 2035.<sup>12</sup> Kidney cancer has a 79.3% 1-year and 63.8% 5-year age standardised survival rate.<sup>13</sup> 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.<sup>14</sup>

### Recommended Treatment Options

Partial or radical nephrectomy is recommended as the preferred treatment option for RCC. Patients may also undergo cryotherapy or radiofrequency ablation – where the cancerous cells are destroyed by freezing or heating; embolisation – a procedure to cut off the blood supply to the cancer; and /or radiotherapy – using high-energy radiation to target cancer cells and relieve symptoms.<sup>9</sup>

Advanced or metastatic RCC patients may be eligible to receive biological therapies such as pembrolizumab, avelumab, nivolumab, bevacizumab, or small molecule inhibitor/s, such as sorafenib, sunitinib, temsirolimus, cabozantinib, tivozanib, lenvatinib, everolimus or axitinib.<sup>15</sup>

## Clinical Trial Information

<p>Trial</p>	<p>IMmotion010; <a href="#">NCT03024996</a>. <a href="#">2018-000367-83</a>. A Phase III, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study of Atezolizumab (Anti-PD-L1 Antibody) as Adjuvant Therapy in Patients With Renal Cell Carcinoma at High Risk of Developing Metastasis Following Nephrectomy Phase III - ongoing Locations: 11 EU countries, UK, USA, Canada and other countries Primary completion date: May 2022</p>
<p>Trial Design</p>	<p>Randomised, parallel assignment, double -blind, placebo-controlled</p>
<p>Population</p>	<p>N= 778; 18 Years and older; Subjects with pathologically confirmed RCC with a component of either clear cell histology or sarcomatoid histology that has not</p>

	been previously treated in the adjuvant or neoadjuvant setting and classified as being at high risk of RCC recurrence, and with radical or partial nephrectomy.
Intervention(s)	Atezolizumab (IV) 1200mg every 3 weeks
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: Investigator-assessed Disease-Free Survival (DFS) [ Time Frame: From Baseline up to first occurrence of event by investigator assessment (up to approximately 88 months)]  See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

### Estimated Cost

Atezolizumab is already marketed in the UK for a number of cancer types; a 1200mg vial costs £3,807.69.<sup>16</sup>

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal in development. Nivolumab for neoadjuvant and adjuvant treatment of localised renal cell carcinoma [ID4047]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Pembrolizumab for adjuvant treatment of renal cell carcinoma [ID3810]. Expected July 2022.
- NICE clinical guideline. Suspected cancer: recognition and referral [NG12]. June 2015.
- NICE cancer service guideline. Improving outcomes in urological cancers [CSG2]. September 2002

#### 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).<sup>17</sup>
- ESMO. Renal Cell Carcinoma: ESMO Clinical Practice Guidelines. 2019 – Ann Oncol (2019); 30: 706-720.<sup>18</sup>

### Additional Information

## References

- 1 Clinicaltrials.gov. *A Study of Atezolizumab as Adjuvant Therapy in Participants With Renal Cell Carcinoma (RCC) at High Risk of Developing Metastasis Following Nephrectomy (IMmotion010)*. Trial ID: NCT03024996. 2017. Status: Active, not recruiting. Available from: <https://clinicaltrials.gov/ct2/show/NCT03024996> [Accessed 4th January 2022].
- 2 McDermott DF HM, Atkins MB, Motzer RJ, Rini BI, Escudier B, Fong L, Joseph RW, Pal SK, Reeves JA, Sznol M, Hainsworth J, Rathmell WK, Stadler WM, Hutson T, Gore ME, Ravaud A, Bracarda S, Suárez C, Danielli R, Gruenwald V, Choueiri TK, Nickles D, Jhunjunwala S, Piault-Louis E, Thobhani A, Qiu J, Chen DS, Hegde PS, Schiff C, Fine GD, Powles T. Clinical activity and molecular correlates of response to atezolizumab alone or in combination with bevacizumab versus sunitinib in renal cell carcinoma. *Nat Med* 2018;24(6):749-57 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6721896/>.
- 3 Electronic Medicines Compendium. *Tecentriq 1,200 mg concentrate for solution for infusion SmPC*. 2021. Available from: [https://www.medicines.org.uk/emc/product/8442/smpc#PHARMACOLOGICAL\\_PROPS](https://www.medicines.org.uk/emc/product/8442/smpc#PHARMACOLOGICAL_PROPS) [Accessed 28th January 2022].
- 4 Gul A., Rini B.I. Adjuvant therapy in renal cell carcinoma. *Cancer*. 2019;125:2935-44. Available from: <https://doi.org/10.1002/cncr.32144>.
- 5 European Medicines Agency. *Tecentriq (atezolizumab) Medicines Overview*. Available from: <https://www.ema.europa.eu/en/medicines/human/EPAR/tecentriq> [Accessed 5th January 2022].
- 6 Clinicaltrials.gov. *Atezolizumab phase II/III clinical trials* 2021. Available from: [https://clinicaltrials.gov/ct2/results?term=atezolizumab&age\\_v=&gndr=&type=&rslt=&phase=1&phase=2&Search=Apply](https://clinicaltrials.gov/ct2/results?term=atezolizumab&age_v=&gndr=&type=&rslt=&phase=1&phase=2&Search=Apply) [Accessed 5th January 2022].
- 7 National Cancer Institute. *Renal Cell Cancer Treatment (PDQ®)—Patient Version*. 2021. Available from: <https://www.cancer.gov/types/kidney/patient/kidney-treatment-pdq> [Accessed 18th February 2022].
- 8 Cancer Research UK. *About Kidney Cancer*. 2021. Available from: <https://www.cancerresearchuk.org/about-cancer/kidney-cancer/about> [Accessed 28th January 2022].
- 9 National Health Service. *Condition overview: Kidney cancer*. 2021. Available from: <https://www.nhs.uk/conditions/kidney-cancer/> [Accessed 4th January 2022].
- 10 National Health Service. *Kidney Cancer: Symptoms*. 2021. Available from: <https://www.nhs.uk/conditions/kidney-cancer/symptoms/> [Accessed 28th January 2022].
- 11 Office for National Statistics. *Cancer diagnoses and age-standardised incidence rates for all types of cancer by age and sex including breast, prostate, lung and colorectal cancer*. . 2017. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland> [Accessed 5th January 2022].
- 12 Cancer Research UK. *Selected Cancers, Number of Projected and Observed Cases and European Age-Standardised Incidence Rates per 100,000 people by Cancer Type and Sex*. 2021. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer#heading-Zero> [Accessed 5th January 2022].
- 13 Office for National Statistics. *Cancer Survival in England: adults diagnosed between 2013 and 2017 and followed up to 2018*. 2018. Available from: <https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsa>

- [nddiseases/bulletins/cancersurvivalinengland/stageatdiagnosisandchildhoodpatientsfollowe  
dupto2018](#) [Accessed 5th January 2022].
- 14 NHS Digital. *Hospital Episode Statistics (HES)*. 2021. Available from:  
[https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-  
patient-care-activity/2020-21](https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21) [Accessed 5th January 2022].
- 15 National Institute for Clinical Excellence. *Renal Cell Carcinoma publications* 2021. Available  
from: <https://www.nice.org.uk/search?q=renal%20cell%20carcinoma> [Accessed 5th January  
2022].
- 16 National Institute for Clinical Excellence. *Atezolizumab for untreated PD-L1-positive  
advanced urothelial cancer when cisplatin is unsuitable*. Last Update Date: 27 October 2021.  
Available from: [https://www.nice.org.uk/guidance/ta739/resources/atezolizumab-for-  
untreated-pdl1positive-advanced-urothelial-cancer-when-cisplatin-is-unsuitable-pdf-  
82611262903237](https://www.nice.org.uk/guidance/ta739/resources/atezolizumab-for-untreated-pdl1positive-advanced-urothelial-cancer-when-cisplatin-is-unsuitable-pdf-82611262903237) [Accessed 4th January 2022].
- 17 European Association of Urology. *Renal Cell Cancer (RCC) Guidelines* Available from:  
<https://uroweb.org/guideline/renal-cell-carcinoma/?type=summary-of-changes> [Accessed  
5th January 2022].
- 18 European Society For Medical Oncology. *Renal Cell Carcinoma: ESMO Clinical Practice  
Guidelines*. . Available from: [https://www.esmo.org/guidelines/genitourinary-cancers/renal-  
cell-carcinoma](https://www.esmo.org/guidelines/genitourinary-cancers/renal-cell-carcinoma) [Accessed 5th January 2022].

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