Health Technology Briefing
August 2023

Nivolumab adjuvant therapy for renal cell carcinoma

Company/Developer	Bristol-Myers Squibb Pharmaceuticals Ltd

☐New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 36970	NICE TSID: Not Available	UKPS ID: 670817

Licensing and Market Availability Plans

Currently in phase 3 clinical development.

Summary

Nivolumab is in clinical development as adjuvant therapy for adult patients with localised renal cell carcinoma (RCC) who underwent surgical removal of partial or entire of a kidney. RCC (the most common type of kidney cancer in adults) is a disease that affects the lining of tiny tubes within the kidney which filter waste from the blood, making urine. Localised RCC means the cancer is either completely inside the kidney or has grown into surrounding tissues but has not spread to another part of the body. The main treatment for localised RCC is surgery to remove part or the whole kidney. After surgery, the disease may relapse and spread to other parts of the body. The aim of adjuvant treatment for localised RCC is to reduce the number of people whose disease relapse after surgery, and this remains an unmet need.

Nivolumab is a monoclonal antibody, a type of protein that has been designed to attach to a receptor called PD-1 found on cells of the immune system called T cells. By attaching to PD-1, nivolumab prevents cancer cells from switching off the activity of the T cells, thereby increasing the ability of the immune system to kill cancer cells. Nivolumab is administered by intravenous infusion. If licensed, nivolumab could provide an adjuvant treatment option for patients with localised renal cell carcinoma who underwent surgical removal of partial or entire of a kidney .

Proposed Indication

Adjuvant therapy for adult patients (aged 18 years and older) with localised renal cell carcinoma (RCC) who underwent radical or partial nephrectomy and at high risk of relapse.[1]

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.

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Technology

Description

Nivolumab (Opdivo, BMS-936558) is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb), which binds to the programmed death-1 (PD-1) receptor and blocks its interaction with PD-L1 and PD-L2. Engagement of PD-1 with the ligands PD-L1 and PD-L2, which are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, results in inhibition of T-cell proliferation and cytokine secretion. Nivolumab potentiates T-cell responses, including anti-tumour responses through blockade of PD-1 binding to PD-L1 and PD-L2.[2]

Nivolumab is currently in clinical development as adjuvant therapy for adult patients with localised RCC who underwent partial or entire removal of a kidney and at high risk of relapse. In the phase III clinical trial (CheckMate 914, NCT03138512), patients received nivolumab 240mg intravenously (IV) every 2 weeks for 12 doses, as a monotherapy, or plus ipilimumab (1 mg/kg) IV every 6 weeks for four doses for an expected treatment period of 24 weeks.[1,3]

Key Innovation

Surgery is standard treatment for non-metastatic RCC. Unfortunately, patients with stage II or III RCC have high risk of relapse with 5-year disease-free survival rates of approximately 51%–56%; prevention of recurrence is an unmet need. In a previous study (CheckMate 214; NCT02231749), first-line nivolumab demonstrated significant overall survival improvements in patients with advanced/metastatic RCC, with a manageable safety profile. These findings indicate a potential for improved clinical outcomes in the early-stage adjuvant RCC setting.[4]

If licensed, nivolumab would offer an adjuvant treatment option for adult patients with localised RCC who have undergone partial or radical nephrectomy.

Regulatory & Development Status

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

- Melanoma
- Non-small cell lung cancer (NSCLC)
- Malignant pleural mesothelioma (MPM)
- Renal cell carcinoma (RCC)
- Classical Hodgkin lymphoma (cHL)
- Squamous cell cancer of the head and neck (SCCHN)
- Urothelial carcinoma
- Mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) colorectal cancer (CRC)
- Oesophageal squamous cell carcinoma (OSCC)
- Gastric, gastro-oesophageal junction (GEJ) or oesophageal adenocarcinoma

Nivolumab is currently in phase III clinical development for:[5]

- Squamous cell carcinoma or Head and Neck
- Melanoma
- Non-small cell Lung cancer
- Gastric cancer
- Mesothelioma
- And others

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Patient Group

Disease Area and Clinical Need

Renal cell carcinoma (RCC) (the most common type of kidney cancer in adults) is a disease in which malignant (cancer) cells are found in the lining of tubules (very small tubes) in the kidney.[6] The cells can grow into surrounding tissues or organs and may spread to other areas of the body.[7] Stage I, II, and III RCCs are referred to as localised RCCs, meaning the cancer is either completely inside the kidney or has grown into surrounding tissues but has not spread to another part of the body.[8,9] Risk factors for RCC include obesity, smoking, high blood pressure, family history/genetics and long-term kidney dialysis.[10] Many patients remain symptomless until later in 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.[11]

There are around 13,000 new kidney cancer cases in the UK every year, that is 36 every day (2016-2018).[12] 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).[13] Kidney cancer incidence rates are projected to rise by 15% in the UK between 2023-2025 and 2038-2040.[12] Kidney cancer has a 79.3% 1-year and 63.8% 5-year age standardised survival rate.[12] In England, in 2021-22, there were 26,315 finished consultant episodes (FCE) and 23,664 admissions for malignant neoplasm of kidney, except renal pelvis (ICD-10 code C64) which resulted in 14,550 day-cases and 47,072 FCE bed days.[14]

Recommended Treatment Options

NICE recommends Pembrolizumab for adjuvant treatment of renal cell carcinoma.[15]

Clinical Trial Information

Trial	**CheckMate 914; NCT03138512; 2016-004502-34;** A Phase 3 Randomized, Double-Blind Study of Nivolumab Monotherapy or Nivolumab Combined With Ipilimumab vs Placebo in Participants With Localized Renal Cell Carcinoma Who Underwent Radical or Partial Nephrectomy and Who Are at High Risk of Relapse **Phase III** – Active, not recruiting **Location(s):** UK, 10 EU countries, USA, Canada, and other countries **Primary completion date**: July 2024
Trial Design	Randomised, parallel assignment, quadruple blinded, placebo controlled
Population	N=1641; aged 18 years and older; patients with kidney tumour that has been completely resected, with no evidence of residual disease or distant metastases after nephrectomy
Intervention(s)	Nivolumab 240mg IV Ipilimumab (1 mg/kg) IV[3]
Comparator(s)	Matched placebos
Outcome(s)	Primary outcome measure: Disease-free survival (DFS) as assessed by BICR (Part A and Part B) [Time frame: Up to 10 years]

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	See trial record for full list of other outcomes
Results (efficacy)	With a median follow-up of 37·0 months (IQR 31·3–43·7), median disease-free survival was not reached in the nivolumab plus ipilimumab group and was 50·7 months (95% CI 48·1 to not estimable) in the placebo group (hazard ratio 0·92, 95% CI 0·71–1·19; p=0·53). The number of events required for the planned overall survival interim analysis was not reached at the time of the data cut-off, and only 61 events occurred (33 in the nivolumab plus ipilimumab group and 28 in the placebo group).[3] Results from arm A of the trial. Monotherapy results to follow.
Results (safety)	155 (38%) of 404 patients who received nivolumab plus ipilimumab and 42 (10%) of 407 patients who received placebo had grade 3–5 adverse events. All-cause adverse events of any grade led to discontinuation of nivolumab plus ipilimumab in 129 (32%) of 404 treated patients and of placebo in nine (2%) of 407 treated patients. Four deaths were attributed to treatment with nivolumab plus ipilimumab and no deaths were attributed to treatment with placebo.[3] Results from arm A of the trial. Monotherapy results to follow.

Estimated Cost

Nivolumab is already marketed in the UK as follows:[16]

- 100mg/10ml concentrate for solution for infusion (1 vial) costs £1,097.00
- 120mg/12ml concentrate for solution for infusion (1 vial) costs £1,317.00
- 240mg/24ml concentrate for solution for infusion (1 vial) costs £2,633.00
- 40mg/4ml concentrate for solution for infusion (1 vial) costs £439.00

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Pembrolizumab for adjuvant treatment of renal cell carcinoma [TA830]. October 2022.
- NICE interventional procedure guidance. Irreversible electroporation for treating renal cancer (IPG443). February 2013.
- NICE interventional procedure guidance. Laparoscopic cryotherapy for renal cancer (IPG405). August 2011.
- NICE interventional procedure guidance. Percutaneous cryotherapy for renal cancer (IPG402). July 2011.
- NICE interventional procedure guidance. Percutaneous radiofrequency ablation for renal cancer (IPG353). July 2010.
- NICE interventional procedure guidance. Laparoscopic partial nephrectomy (IPG151). January 2006.
- NICE interventional procedure. Laparoscopic nephrectomy (including nephroureterectomy (IPG136). August 2005

NHS England (Policy/Commissioning) Guidance

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- 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
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All ages). Service specification. B01/S/a

Other Guidance

- The European Association of Urology (EAU). Renal Cell Cancer (RCC) Guidelines (2023).[17]
- European Society for Medical Oncology (ESMO). Renal Cell Carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up (2019).[18]

Additional Information

References

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