Health Technology Briefing
November 2021

Nivolumab for adjuvant and neoadjuvant treatment of localised renal cell carcinoma

Company/Developer	Bristol Myers Squibb

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 13426	NICE ID: 9412	UKPS ID: 641474

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Nivolumab is in clinical development for the adjuvant and neoadjuvant treatment of adults with localised renal cell carcinoma (RCC) who are undergoing surgical removal of a kidney. RCC is a common form of kidney cancer caused by the growth of a tumour in the cells lining the inside of small vessels in the kidney, known as nephrons. Localised RCC occurs when the tumour has not spread beyond the kidney to other areas of the body. RCC often does not present symptoms at early stages. The current standard treatment for localised RCC is for patients to undergo partial or full surgical removal of a kidney; and the aim of adjuvant treatment (treatment following a surgical procedure) is to reduce the number of people whose disease relapses. Neoadjuvant treatment is given before a surgical procedure and aims to shrink the tumour as much as possible before removal and further therapy. There are currently no medicinal products recommended for adjuvant and neoadjuvant treatment of localised RCC.

Nivolumab is a type of protein (monoclonal antibody) administered by intravenous (IV) infusion to increase the ability of the immune system to kill cancer cells. Nivolumab is currently in use to treat later stage RCC, where the cancer has spread to other areas of the body. Nivolumab could also offer beneficial treatment when used before and immediately following the removal of the kidney. If licensed, nivolumab could provide a pharmacological treatment option for adjuvant and neoadjuvant treatment of localised RCC.

Proposed Indication

Adjuvant and neoadjuvant treatment of adults undergoing nephrectomy for localised RCC.[1,2]

Technology

Description

Nivolumab (Opdivo) 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. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. Engagement of PD-1 with 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 ligands.[3]

Nivolumab is currently in phase III clinical development for the adjuvant and neoadjuvant treatment of adults with localised RCC undergoing nephrectomy. In the phase III clinical trial (PROSPER RCC, NCT03055013), patients were administered nivolumab 480mg via IV every 4 weeks with 1 dose prior to surgery followed by 9 adjuvant doses.[1,2]

Key Innovation

There is no standard adjuvant systemic therapy for localised RCC.[4,5] Nivolumab has already been shown to improve overall survival (OS) in metastatic RCC and is well tolerated.[2] Approximately 40% of patients undergoing nephrectomy will have a recurrence of disease due to microscopic spread of the cancer prior to surgery. The addition of a therapy shown to be effective in a metastatic setting has the potential to eliminate microscopic disease and increase treatment outcomes.[6]

Regulatory & Development Status

Nivolumab has a Marketing Authorisation in the UK for the following RCC indications:[3]

- As a monotherapy for the treatment of advanced RCC after prior therapy in adults
- In combination with ipilimumab for the first-line treatment of adults with intermediate/poor-risk advanced RCC
- In combination with cabozantinib for the first-line treatment of adults with advanced RCC

Additionally, nivolumab as a monotherapy or in combination with various other medicinal products has a Marketing Authorisation in the UK for the following indications:[3]

- Melanoma
- Non-small cell lung cancer (NSCLC)
- Malignant pleural mesothelioma (MPM)
- Classical Hodgkin lymphoma (cHL)
- Squamous cell cancer of the head and neck (SCCHN)
- Urothelial carcinoma
- Colorectal cancer (CRC)
- Oesophageal squamous cell carcinoma (OSCC)
- Oesophageal or gastro-oesophageal junction cancer (OC or GEJC)

Nivolumab as a monotherapy and in addition to various other medicinal products is being developed for numerous indications in phase II and phase III clinical trials.[7]

Patient Group

Disease Area and Clinical Need

RCC is a form of kidney cancer which accounts for around 80% of all kidney cancers.[5] Tumours form from the cells lining the tubules inside nephrons. RCC can be split in to two histological forms: clear cell and non-clear cell.[8,9] RCC is often asymptomatic or may present with haematuria and a lump or mass in the kidney area.[10] Localised RCC refers to a tumour that has not spread beyond the kidney. This may be any stage of tumour size up to T2 RCC.[11] Known risk factors for RCC can include obesity, smoking, kidney disease and genetic disorders.[12]

In 2016-18, there were an average of 13,322 cases of kidney cancer each year in the UK.[13] It can therefore be estimated that on average there are 10,657 cases of RCC diagnosed yearly in the UK. The incidence rate of kidney cancer increases with age and is highest in people over 85 years of age.[14] Statistics from 2013-2014 suggest that around 56% of kidney cancer patients will undergo a nephrectomy as part of their treatment.[15] In England in 2020-21 there were 17,908 hospital admissions for malignant neoplasm of kidney, except renal pelvis (ICD-10 C64).[16] Approximately, 63% of patients diagnosed with kidney cancer in England will survive for five years following diagnosis.[17]

Recommended Treatment Options

The main treatment recommended for localised RCC is a partial or total nephrectomy procedure. Patients may also receive radiofrequency ablation and cryoablation procedures.[14] There are not currently any recommended pharmacological treatments for adjuvant, neoadjuvant or perioperative therapy.[4,5]

Clinical Trial Information

Trial	PROSPER RCC, NCT03055013; NCI-2016-00326, EA8143; A Phase 3 Randomised Study Comparing PERioperative Nivolumab vs. Observation in Patients With Renal Cell Carcinoma Undergoing Nephrectomy (PROSPER RCC) Phase III – Active, not recruiting Locations: USA, Canada, Israel Primary completion date: November 2023
Trial Design	Randomised, parallel assignment, single masking
Population	N=766; adults aged 18 years and older; Subjects with renal cell carcinoma for which radical or partial nephrectomy is planned
Intervention(s)	• Nephrectomy 7-28 days following end of initial nivolumab treatment • Nivolumab (IV) on day 1 every 14 days for 2 cycles prior to nephrectomy. Following nephrectomy, patients receive nivolumab on day 1 every 14 days 6 cycles and then on day 1 every 28 days for 6 cycles
Comparator(s)	Nephrectomy
Outcome(s)	Primary outcome measure: Event-free survival (EFS) [Time Frame: Time from randomization to disease recurrence or death from any cause, assessed up to 10 years]

	See trial record for a full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Nivolumab is already marketed in the UK for various indications; a 100mg/10ml vial costs £1097.00, a 240mg/24ml vial costs £2633.00 and a 40mg/4ml vial costs £439.00.[18]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Pembrolizumab for adjuvant treatment of renal cell carcinoma (GID-TA10693). Expected publication date: TBC.
- NICE Interventional procedures guidance. Laprascopic partial nephrectomy (IPG151). January 2006.
- NICE Interventional procedures guidance. Laprascopic nephrectomy (including nephroureterectomy) (IPG136). August 2005

NHS England (Policy/Commissioning) Guidance

- 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 Ex-Vivo Partial Nephrectomy Service (Adult). A06/S(HSS)b.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). Ref B15/S/a.

Other Guidance

- Escudier B, Porta C, Schmidinger M, Rioux-Leclerq N, Bex A et al. Renal cell carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2019.[5]

Additional Information

References

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