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HEALTH TECHNOLOGY BRIEFING
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Retifanlimab for squamous carcinoma of the anal canal – after platinum based chemotherapy

NIHRIO ID	26651	**NICE ID**	10299
Developer/Company	Incyte Corp	**UKPS ID**	Not available

Licensing and market availability plans	Currently in phase II clinical trial.

SUMMARY

Retifanlimab is in clinical development for the treatment of adult patients with squamous carcinoma of the anal canal (SCAC) who have progressed on or are intolerant of platinum-based chemotherapy. Squamous cell cancers (SCCs) are the most common type of anal cancer. SCCs make up around 90% of all anal cancers and are also called epidermoid cancers. This type of anal cancer starts in squamous cells, which make up the lining of the anal canal and anal margin. Locally advanced stage occurs when the cancer has grown outside the organ it started in but has not yet spread to distant parts of the body. While in metastatic stage, the cancer has spread to distant organs or tissues. Current treatment options induce significant acute toxicities, with high rates of dermatitis and gastrointestinal adverse effects.

Retifanlimab is an intravenous drug. It works by binding to protein called PD-1 and blocks its interaction with programmed cell death ligands 1 and 2 (PD-L1 and PD-L2), thereby increasing the immune system's ability to kill the cancer cells. If licensed, retifanlimab will provide a treatment option for patients with SCAC who have progressed on or are intolerant of platinum-based chemotherapy.

PROPOSED INDICATION

Treatment of adult patients with squamous carcinoma of the anal canal (SCAC) who have progressed on or are intolerant of platinum-based chemotherapy.[1,a]

TECHNOLOGY

DESCRIPTION

Retifanlimab (MGA012, INCMGA00012) is a PD-1 inhibitor. It is a humanised, hinge-stabilised immunoglobulin G4 (IgG4) monoclonal antibody that blocks the interaction of PD-1 with PD-L1 and PD-L2, interrupts PD-1 signalling and enhances antigen-induced interferon-γ release.[2] Certain tumours overexpress PD-L1, which allows the tumour cells to become tolerant to an immune response. PD-1 inhibitors prevent this tolerance and lead to an immune response and destruction of tumour cells.[3]

Retifanlimab is in clinical development for the treatment of SCAC who have progressed on or are intolerant of platinum-based chemotherapy. In the phase II clinical trial (POD1UM-202; NCT03597295), patients received intravenous infusion retifanlimab (25 mg/ml) once every 28 days.[1,4]

INNOVATION AND/OR ADVANTAES

Current treatment options for anal cancer are limited to chemotherapy, radiotherapy or surgical interventions.[5] Retifanlimab is a biological therapy and biologicals are not currently used for anal cancer. Biological therapies are often better tolerated by patients than systemic treatments.[6] Retifanlimab has demonstrated acceptable tolerability in a phase 1 study in patients with solid tumours. Retifanlimab at different regimens/doses investigated is biologically active and can lead to an increase in circulating T cell activation.[7]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Retifanlimab does not currently have Marketing Authorisation in the EU/UK for any indication.

Retifanlimab is in phase II clinical development for selected solid tumours including; metastatic non-small cell lung cancer (NSCLC), metastatic advanced urothelial cancer, metastatic urothelial cancer, unresectable melanoma, metastatic melanoma, metastatic merkel cell carcinoma, locally advanced renal cell carcinoma, metastatic clear-cell renal cell carcinoma, endometrial cancer.[8,a]

Retifanlimab is in phase III clinical development for NSCLC, metastatic squamous NSCLC, and metastatic non-squamous NSCLC.[8]

[a] Information provided by Incyte Corp

PATIENT GROUP

DISEASE BACKGROUND

Squamous cell cancers or carcinomas (SCCs) are the most common type of anal cancer.[9] Ninety percent of anal cancers are SCCs.[10] The anus is a canal that connects the lower part of the large intestine (rectum) to the outside of the body. It allows the faeces to pass from the large intestine during a bowel movement. Faeces are formed in the longest part of the large intestine (colon), stored in the rectum, and pass through the anus. SCC of the anus forms from the lining of the anal canal.[11] Locally advanced stage includes occurs when the cancer has grown outside the organ it started in but has not yet spread to distant parts of the body. While in the metastatic stage, cancer has spread to distant organs or tissues.[12] Most often, anal cancer first spreads to lungs, liver, brain or bones but it can spread anywhere.[13] The prognosis for patients with the metastatic disease is generally poor.[14]

The most well-known risk factor is the human papillomavirus (HPV), particularly HPV type 16, which is present in approximately 80% of patients diagnosed with anal cancer. Other risk factors are smoking, increased number of sexual partners, sexually transmitted infections, a history of vaginal or cervical malignancy, other conditions associated with lowered immunity, for example, transplant recipients and those with anal inflammatory conditions.[14]

The most common symptoms of anal cancer include; bleeding from the anus, pain in the anal area, straining during a bowel movement, anal itching, change in bowel habits, change in the diameter of stool, abnormal discharge and swollen lymph node in the anal or groin areas.[11]

CLINICAL NEED AND BURDEN OF DISEASE

In the UK in 2015-17, there were around 1500 new anal cancer cases. Anal cancer accounts for less than 1% of new cancer cases. In the UK, incidence rates for anal cancer are highest in people aged 90 or over and this cancer is more common in females as compared to males. Over the last decade, anal cancer incidence rates have increased by around two-fifths (41%) in the UK. Rates in males have increased by around a seventh (15%), and rates in females have increased by around three-fifths (59%) (2015-17). Anal cancer incidence rates are likely to fall in future decades, according to projections accounting for the expected impact of HPV vaccination.[15]

In 2017, there were 1,226 registrations of newly diagnosed cases of malignant neoplasm of anus and anal canal (ICD-10 code: C21) and the direct age-standardised rate per 100,000 population of newly diagnosed cases was 3.0 among females and 1.7 among males in England.[16]

In England, in 2018-19 there were 4,424 finished consultant episodes for malignant neoplasm of anus and anal canal (ICD-10 code C21), and 4,048 admissions resulting in 10,845 bed days and 2,896 day cases.[17]

In the UK in 2015-17, there were around 400 anal cancer deaths ever year.[15] The age-standardised 1-year and 5-year survival for persons diagnosed with anal cancer in England in 2017 was 85% and 59%, while 1- year survival for stage IV was 53%.[18]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Treatment options for anal cancer depend on the location of the cancer, how big it is and whether it has spread to anywhere else in the body.[19] A team of specialists composing of; surgeon, oncologist, nurse, pathologist, pharmacist, radiologist and a dietician is normally employed throughout the treatment.[20] A key goal of treatment is saving the anal sphincter muscles for having bowel control and to improve overall quality of life.[21]

The treatment of anal cancer depends on the staging of the tumour and is based on radiation therapy, chemotherapy and surgery. Local and locally advanced anal tumours are managed with a combination of chemotherapy and radiotherapy, whereas chemotherapy alone is generally used to treat metastatic disease.[22]

CURRENT TREATMENT OPTIONS

According to the European Society for Medical Oncology (ESMO), current treatment options for anal cancer include:[5]

- For stage II-III;
  - standard-dose radiotherapy, infused fluorouracil (FU) and mitomycin C
- For stage IV
  - 5-FU and cisplatin carboplatin/taxol, or possibly irinotecan/cetuximab

PLACE OF TECHNOLOGY

If licensed, retifanlimab will provide a treatment option for adult patients with SCAC who have progressed on or are intolerant of platinum-based chemotherapy.[1,b]

CLINICAL TRIAL INFORMATION

Trial	**POD1UM-202**; NCT03597295, EudraCT2018-002070-51; A Phase 2 study of INCMGA00012 in participants with squamous carcinoma of the anal canal who have progressed following platinum-based chemotherapy (POD1UM-202) **Phase II**- Ongoing **Location (s)**: EU (Including UK) and US
Trial design	Single group assignment, open label
Population	n= (81); locally advanced or metastatic SCAC; at least 1 prior line of platinum-based chemotherapy and received no more than 2 prior systemic treatments
Intervention(s)	Retifanlimab

[b] Information provided by Incyte Corp

	• Retifanlimab administered at the recommended Phase 2 dose (25 mg/ml) by intravenous infusion once every 28 days
Comparator(s)	No comparator
Outcome(s)	Overall response rate [Time frame: up to approximately 2 years] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

ESTIMATED COST

The cost of retifanlimab is not known yet.

RELEVANT GUIDANCE

NICE GUIDANCE

- No relevant guidance identified

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. 2013. Standard Contract for Cancer: Anal (Adult). A08/S/g

OTHER GUIDANCE

- National Comprehensive Cancer Network (NCCN): Clinical Practice Guidelines in Oncology. Anal Carcinoma, Version 2. 2018.[23]
- Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus- Anal Cancer. 2017.[24]
- European Society for Medical Oncology. Anal cancer: ESMO-ESSO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2014.[5]
- Cancer Care Ontario. Management of squamous cell cancer of the anal canal. 2013.[25]

ADDITIONAL INFORMATION

Incyte Corp, did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision-making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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