NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
July 2024

Retifanlimab with carboplatin with paclitaxel for treating locally advanced or metastatic squamous cell anal carcinoma

Company/Developer	Incyte Biosciences Distribution B.V.

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30214	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase lll clinical development.

Summary

Retifanlimab is in clinical development as a combination therapy, with carboplatin and paclitaxel, for treating inoperable locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC). SCAC is a rare cancer that starts in the squamous cells in the anal canal. Squamous cells make up the lining of the anal canal which is the opening at the end of the bowel. A locally recurrent cancer is a case of cancer that has remerged in the same part of the body, or very close to the original site, following previous treatment. Metastatic cancers are cancers that have spread to other parts of the body. Symptoms of SCAC can include bleeding from the bottom, bowel incontinence, and small lumps around and inside the bottom. There are currently limited options for treating recurrent or metastatic SCAC, which means there remains an unmet need for people with the condition.

Retifanlimab is a monoclonal antibody (type of protein) that binds to specific other proteins in the body, called T cells; this helps to prevent cancer cells from suppressing the body's own immune response. Retifanlimab is administered intravenously and is in development to be used in combination with carboplatin and paclitaxel. If licensed, retifanlimab with carboplatin and paclitaxel would provide another option for the treatment of recurrent and metastatic SCAC.

Proposed Indication

Treatment of inoperable, locally recurrent or metastatic squamous cell carcinoma of the anal canal (SCAC) not previously treated with systemic chemotherapy.[1]

Technology

Description

Retifanlimab (retifanlimab-dlwr, Zynyz) is a monoclonal antibody which acts as an immune checkpoint inhibitor. It works by binding to the protein PD-1, expressed on the surface of certain immune cells called T cells, which helps to prevent cancer cells from suppressing the immune response. This allows the immune system to target cancerous cells, leading to cell death.[2]

Retifanlimab with carboplatin and paclitaxel is in clinical development for treating adults with inoperable, locally recurrent or metastatic SCAC that has not previously been treated with systemic chemotherapy. In the phase III clinical trial (POD1UM-303/InterAACT 2, NCT04472429) participants are given 500 mg retifanlimab intravenously on day 1 of a 28 day cycle, along with 80 mg/m^2 intravenous carboplatin (day 1) and paclitaxel (days 1, 8 and 15).[1,3]

Key Innovation

There are currently no clinical guidelines or treatment options recommended by the National Institute for Health and Care Excellence (NICE) for SCAC, though the National Health Service (NHS) states that current treatment options for anal cancer include chemotherapy, radiotherapy or surgical interventions.[4,5] Retifanlimab is a biological therapy, which are not currently used for SCAC.[4] Biological therapies are often better tolerated by patients than systemic treatments.[6] The results of a recent phase II clinical trial suggest that retifanlimab may show efficacy and an acceptable safety profile in adults with previously treated advanced or metastatic SCAC, including patients with well-controlled HIV infection.[7]If licenced, retifanlimab with carboplatin-paclitaxel will offer an additional treatment option to adults with SCAC.

Regulatory & Development Status

Retifanlimab does not currently have Marketing Authorisation in the UK for any indication.[8]In the EU, retifanlimab is authorised for the treatment of Merkel cell carcinoma and anal cancer.[9]

Retifanlimab is in phase II/III clinical development as a monotherapy for:[10]

- advanced or metastatic endometrial cancer
- locally advanced renal cell carcinoma
- metastatic Merkel cell carcinoma
- unresectable or metastatic melanoma
- metastatic non-small cell lung cancer
- locally advanced or metastatic urothelial cancer.

Retifanlimab is in phase II/III clinical development as a combination therapy for:[10]

- metastatic squamous and non-squamous non-small cell lung cancer
- oesophageal adenocarcinoma
- PD-L1-positive recurrent or metastatic squamous cell head and neck cancer

Retifanlimab has the following regulatory designations/awards:

- an orphan drug in the EU in 2024 for treating recurrent or metastatic Merkel cell carcinoma.[8]
- an orphan drug in the EU in 2020 for treating anal cancer.[9]

Patient Group

Disease Area and Clinical Need

Anal cancer is a rare cancer that forms in anus, the opening at the end of the bowel. Squamous cell cancers start in squamous cells that make up the lining of the anal canal; most anal cancers are squamous cell cancers.[11] Locally recurrent cancer is a cancer that has returned following treatment in the same location or very close to where it was prior to treatment.[12] Metastatic cancer occurs when the cancer spreads to other areas of the body.[13] The risk of developing anal cancer increases with age, and it is more common in women than in men. The main risk factor for anal cancer is the human papilloma virus (HPV) infection, which is linked to around 90% of anal cancers in the UK.[11] Symptoms of anal cancer can include: bleeding from the bottom; itching and pain around the anus; small lumps around and inside the bottom; a discharge of mucus from your bottom; bowel incontinence; and needing to poo often with looser, runnier poos. Anal cancer may have no symptoms at all, or they might be hard to spot.[14]

Anal cancer is not amongst the 20 most common cancers in the UK, accounting for less than 1% of all new cancer cases between 2017 and 2019. Between 2017 and 2019, the age standardised incidence rate of anal cancer in England was 1.8 and 3.1 per 100,000 amongst males and females, respectively.[15] In England (2022-23) there were 5282 finished consultant episodes (FCEs) and 4757 admissions for malignant neoplasm of anus and anal canal (ICD-10 code C21), which resulted in 3588 day cases and 11,880 FCE bed days.[16] In England (2017), there were 1226 patients diagnosed with malignant neoplasm of anus and anal canal (ICD-10 code C21) and 360 deaths registered.[17] For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates were 80.2% and 52.0%, respectively.[18]

Recommended Treatment Options

There is currently no treatment option recommended by NICE for treating SCAC. The NHS notes that treatment for anal cancer depends on the size of the cancer, where it is, if it has spread, and the person's general health. The main treatment for anal cancer is a combination of radiotherapy and chemotherapy (chemoradiotherapy). Surgery is also a treatment option if chemoradiation does not get rid of the cancer or it comes back or the person is unable to have radiotherapy.[5]

Clinical Trial Information

Trial	**POD1UM-303/InterAACT 2, NCT04472429;** Carboplatin-paclitaxel With Retifanlimab or Placebo in Participants With Locally Advanced or Metastatic Squamous Cell Anal Carcinoma (POD1UM-303/InterAACT 2). **Phase III** - active, not recruiting **Location(s)**: seven EU countries, UK, USA and five other countries **Estimated completion date**: October 2024
Trial Design	Randomised, parallel-assignment, placebo-controlled, double blind
Population	N=308; adults aged 18 years or older with histologically or cytologically verified, inoperable locally recurrent or metastatic SCAC and no prior systemic therapy other than either chemotherapy administered concomitantly with radiotherapy

	as a radiosensitising agent or prior neoadjuvant or adjuvant therapy if completed ≥ 6 months before study entry.
Intervention(s)	• Retifanlimab 500 mg via IV infusion on day 1 of each 28-day cycle for up to 13 cycles[3] • Carboplatin (area-under-the-curve 5 on day 1) via IV infusion • Paclitaxel 80 mg/m^2 on days 1, 8, and 15 via IV infusion[3]
Comparator(s)	Carboplatin and paclitaxel and placebo as an IV
Outcome(s)	Primary outcome measures: Progression Free Survival (PFS) [Time frame: up to 4.5 years] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of retifanlimab is not yet known.
Carboplatin 150mg/15ml concentrate for solution for infusion vials can be purchased for hospitals from a number of sources starting at £56.92 per unit.[19] Paclitaxel 100mg/16.7ml concentrate for solution for infusion vials can be purchased for hospitals from a number of sources starting at £200.35.[20]

Relevant Guidance

NICE Guidance

- No relevant guidance identified.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.
- 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. 2023.[21]
- Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus- Anal Cancer. 2017.[22]
- European Society for Medical Oncology. Anal cancer: ESMO-ESSO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2014.[4]
- Cancer Care Ontario. Management of squamous cell cancer of the anal canal. 2013.[23]

Additional Information

Incyte Biosciences Distribution B.V. 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.

References

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