Health Technology Briefing
January 2022

Vedolizumab for treating active pouchitis

Company/Developer	Takeda UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33497	NICE ID: 10720	UKPS ID: 661313

Licensing and Market Availability Plans

Completed phase IV clinical trials

Summary

Vedolizumab is in clinical development for the treatment of active pouchitis in patients who have undergone recent ileal pouch anastomosis (IPAA). Pouchitis is an inflammation of the pouch, an area of the gut created by joining two ends of the intestines during surgery. The pouch is created following IPAA surgery in order to reconnect the small intestine to the anus. Active pouchitis occurs when a patient has increased bowel movements and a characteristic appearance of cells under a microscope. Patients who do not respond to current recommended treatments have limited therapeutic options.

Vedolizumab is a human monoclonal antibody, which is a manufactured version of an immune protein created by the body to fight infection. It is given as an injection into a vein. Vedolizumab blocks the binding of immune cells to cells in the gut known as endothelial cells, therefore stopping the action of the immune cell in the gut and potentially decreasing inflammation. Vedolizumab has already demonstrated positive treatment outcomes in pouchitis patients in single case studies and clinical trials. If approved vedolizumab would offer this patient group a new treatment approach.

Proposed Indication

Treatment of adult patients with active pouchitis who have undergone IPAA for ulcerative colitis[1]

Technology

Description

Vedolizumab is a humanised monoclonal antibody that binds specifically to the $\alpha_4\beta_7$ integrin, which is preferentially expressed on gut homing T helper lymphocytes. By binding to $\alpha_4\beta_7$ integrin on certain lymphocytes, vedolizumab inhibits adhesion of these cells to mucosal adhesin cell adhesion molecule-1 (MAdCAM-1), but not to vascular cell adhesion molecule-1 (VCAM-1). MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T lymphocytes to tissues within the gastrointestinal tract. The α4β7 integrin is expressed on a discrete subset of memory T helper lymphocytes which preferentially migrate into the gastrointestinal (GI) tract and cause inflammation that is characteristic of ulcerative colitis, which is a chronic inflammatory immunologically mediated condition of the GI tract. Vedolizumab reduces gastrointestinal inflammation in UC.[2]

Vedolizumab was in phase IV clinical development for the treatment of adults with active pouchitis who have undergone IPAA for ulcerative colitis. In a phase IV clinical trial (EARNEST, NCT02790138), participants received vedolizumab 300mg via intravenous (IV) infusion once at day 1 on weeks 2, 6, 14, 22 and 30.[1]

Key Innovation

The main treatments currently used in pouchitis are antibiotics and anti-TNF therapies such as infliximab and adalimumab.[3] However patients may become refractory to these therapies and antibiotic resistance may become a problem. Vedolizumab has previously been used off-label in pouchitis treatment and shown beneficial treatment outcomes.[4] Furthermore, vedolizumab demonstrated good safety and efficacy in the EARNEST clinical trial.[5] If approved, vedolizumab would offer patients with pouchitis a novel treatment approach.

Regulatory & Development Status

Vedolizumab has a Marketing Authorisation in the UK for the following indications:[2]

- Treatment of adults with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist
- Treatment of adults with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist

Vedolizumab as a monotherapy is also being developed for acute graft versus host disease (aGVHD) in a phase III clinical trial.[6]

Patient Group

Disease Area and Clinical Need

Pouchitis is a non-specific inflammation of the ileal reservoir characterised by increased stool frequency and liquidity, increased urgency, tenesmus and abdominal cramping. It is the most common complication

that can follow a protocolectomy with IPAA procedure that is often carried out in ulcerative colitis patients. Active pouchitis refers to a stage of pouchitis where there patient currently has increased bowel frequency with endoscopic appearances and histology consistent with pouchitis. Active pouchitis may also be acute or chronic depending on the disease duration.[3]

Pouchitis occurs in up to 50% of patients in the 10 years following an IPAA procedure.[3] In England in 2020-21, there were 30 admissions and 34 finished consultant episodes (FCEs) for panprotocolectomy and anastomosis of ileum to anus and creation of pouch (OPCS-4 H04.2).[7]

Recommended Treatment Options

The current recommendation for treatment of pouchitis is to give a combination of ciprofloxacin and metronidazole in the first line. If the first line treatment fails and pouchitis becomes chronic, patients may then receive further combinations of antibiotics including ciprofloxacin, metronidazole, tinidazole and rifaximin. Other potential treatment options can include oral budesonide and oral beclomethasone. Finally, patients can also be offered anti-TNF biologic therapies such as infliximab and adalimumab for chronic refractory pouchitis.[8]

Clinical Trial Information

Trial	**EARNEST, NCT02790138, 2015-003472-78;** A randomized, Double-Blind, Placebo-Controlled Phase 4 Study to Evaluate the Efficacy and Safety of Entyvio (Vedolizumab IV) in the Treatment of Chronic Pouchitis (EARNEST) **Phase IV**: Completed **Locations**: 6 EU countries, UK, USA and Canada **Study completion date:** February 2021
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=102; adults aged 18 to 80 years with chronic or recurrent pouchitis, a history of IPAA for ulcerative colitis
Intervention(s)	Vedolizumab (IV)
Comparator(s)	Ciprofloxacin (oral tablet), placebo (IV)
Outcome(s)	Primary outcome: Percentage of patients with chronic or recurrent pouchitis achieving clinically relevant remission at week 14 (Time frame: Week 14) See trial record for full list of other outcomes
Results (efficacy)	Clinical remission rates at week 14 were 31.4% (16/51) with vedolizumab, compared to 9.8% (5/51) with placebo (95% CI 4.9-37.5, p=0.013).[5]
Results (safety)	Adverse events were reported in 47 (92.2%) and 44 (86.3%) of patients treated with vedolizumab and placebo respectively. Treatment related adverse events were reported in 12 (23.5%) and 11 (21.6%) of patients treated with vedolizumab and placebo respectively. Serious adverse events were reported in 3 (5.9%) and 4 (7.8%) of patients treated with vedolizumab and placebo respectively.[5]

Estimated Cost

Vedolizumab is already marketed in the UK for Crohn's disease and ulcerative colitis; a 10mg/0.68ml solution for injection pre-filled pen/syringe costs £512.50. A 300mg powder for concentrate for solution for infusion vial costs £2050.00.[9]

Relevant Guidance

NICE Guidance

No relevant guidance identified

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified

Other Guidance

- Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. 2019.[8]
- Magro F, Gionchetti P, Eliakim R, Ardizzone S, Armuzzi A et al. Third European Evidence-based Consensus on Diagnosis and Management of Ulcerative Colitis. Part 1: Definitions, Diagonsis, Extra-intestinal Manifestations, Pregnancy, Cancer Surveillance, Surgery and Ileo-anal Pouch Disorders. 2017.[3]
- NICE. Evidence summary: Pouchitis: Rifaximin (ESUOM30). 2014.[10]

Additional Information

References

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9 National Institute for Health and Care Excellence. *BNF: Medicinal forms: Vedolizumab.* 2021. Available from: https://bnf.nice.org.uk/medicinal-forms/vedolizumab.html [Accessed 24 November 2021].

10 National Institute for Health and Care Excellence. *Evidence summary: Pouchitis: Rifaximin (ESUOM30)*. Last Update Date: Available from: https://www.nice.org.uk/advice/esuom30/chapter/Key-points-from-the-evidence [Accessed 4 January 2022].

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