NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
February 2022

Benralizumab for treating eosinophilic oesophagitis in people aged 12-65 years

Company/Developer	AstraZeneca UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 29739	NICE ID: 10567	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Benralizumab is currently in clinical development for treating eosinophilic oesophagitis (EoE). EoE is a condition in which the oesophagus (gullet) becomes inflamed as a result of an allergic reaction. The inflammation is caused by a type of white blood cell called eosinophils. The oesophagus transmits food from the mouth to the stomach, so the inflammation makes swallowing difficult as the oesophagus becomes narrower than usual.

Benralizumab, administered subcutaneously (SC), is a type of protein designed to attach to receptors (targets) called interleukin-5 (IL-5) receptors on the surface of eosinophils. By attaching to IL-5 receptors, benralizumab activates the immune system (the body's natural defences) to kill the eosinophils in the blood and lungs which helps to reduce inflammation. Benralizumab also inhibits eosinophil development. This double function induces almost complete fast and maintained depletion of eosinophils that is much greater than that induced by other proteins targeting the IL-5 pathway. If licensed, benralizumab will offer an additional treatment option for patients with EoE who currently have few effective therapies available.

Proposed Indication

Treatment of patients aged 12-65 years with eosinophilic oesophagitis (EoE).[1]

Technology

Description

Benralizumab (Fasenra, MEDI-563) is a humanised, afucosylated, anti–interleukin-5Rα (IL-5Rα) monoclonal antibody that selectively depletes eosinophils and basophils through enhanced antibody-dependent cell-mediated cytotoxicity.[2]

Benralizumab is currently in clinical development for EoE. In a phase III clinical trial (NCT04543409) benralizumab will be administered subcutaneously (SC), at a dosage of 1 mL fill volume.[1]

Key Innovation

Benralizumab blocks the binding of interleukin 5 (IL-5) to its receptor and results in inhibition of eosinophil differentiation and maturation in bone marrow. In addition, this medicinal product is able to bind through its afucosylated Fc domain to the RIIIa region of the Fcy receptor on natural killer (NK) cells, macrophages, and neutrophils, thus strongly inducing antibody-dependent, cell-mediated cytotoxicity in both circulating and tissue-resident eosinophils. This double function of benralizumab induces almost complete fast and maintained depletion of eosinophils that is much greater than that induced by other monoclonal antibodies targeting the IL-5 pathway.[3] Therefore, if licensed, benralizumab will offer an additional treatment option for patients with EoE who currently have few effective therapies available.

Regulatory & Development Status

In the EU and UK, benralizumab is licensed to treat eosinophilic asthma.[4,5]

Benralizumab is in phase III/II clinical development for:[6]

- Gastritis
- Bullous Pemphigoid
- Chronic Spontaneous Urticaria
- Non-cystic Fibrosis Bronchiectasis
- Hypereosinophilic Syndrome
- Nasal Polyps

Benralizumab has the following regulatory designations:[7]

- An orphan drug in the USA in 2019 for EoE

Patient Group

Disease Area and Clinical Need

EoE is a condition in which the oesophagus (gullet) becomes inflamed as a result of an allergic reaction. The inflammation is caused by a type of white blood cell called eosinophils. The oesophagus transmits food from the mouth to the stomach, so the inflammation makes swallowing difficult as the oesophagus becomes narrower than usual.[8] The symptoms of EoE can vary from one person to another, and depend on age. In adults, symptoms normally include difficulty swallowing (dysphagia), food getting stuck in the oesophagus after swallowing (impaction), chest pain that is often centrally located and does not respond to antacids, and backflow of undigested food (regurgitation). In children, symptoms can include: difficulty

eating, vomiting, abdominal pain, dysphagia, impaction, no response to gastroesophageal reflux disease medication and failure to thrive (poor growth, malnutrition and weight loss).[9] EoE is caused by the presence of a large number of eosinophils in the oesophagus. The production and accumulation of eosinophils may be caused by many factors such as immune hypersensitivity responses to particular foods (e.g., milk, wheat, nuts, soya, fish, and eggs) or environmental proteins (allergens) in some affected individuals. Some individuals with this condition have been found to have an unusually high expression of a particular gene called eotaxin-3. This gene codes for a protein that is important in controlling the accumulation of eosinophils. EoE can run in families but the risk for additional family members is <5% unless they are twins with the EoE patient. Several genes have been identified to contribute to EoE including *CAPN14* (calpain 14) and *TSLP* (Thymic Stromal Lymphopoietin). A fundamental step in the development of EoE is loss of oesophageal barrier function which is mediated by loss of anti-proteases such as SPINK7 (Serine Peptidase Inhibitor Kazal Type 7) and desmosomal proteins such as desmoglein-1 and dysregulated expression of the CAPN14 gene product .[10,11]

A large meta-analysis, which included studies from North America, Europe and Australia, estimated EoE incidence and prevalence rates of 3.7 cases/100,000 persons/year and 22.7 cases/100,000 persons, respectively.[12] EoE is diagnosed in 2–6.5% of patients undergoing esophagogastroduodenoscopy (EGD) for any indication and this increases to 12–22% if dysphagia is the indication. While EoE can affect patients of all age groups, it has bimodal peak with most cases in either paediatric age group or the third decade of life. EoE is more common in Caucasian males and has a strong association with concomitant atopic conditions such as asthma, eczema, rhinitis, and food allergies.[13] In 2020-21, in England, there were 13,052 hospital admissions of which primary diagnosis was oesophagitis (ICD10 K20).[14] The population likely to be eligible to receive benralizumab could not be estimated from available published sources.

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends budesonide as an orodispersible tablet as an option for inducing remission of eosinophilic oesophagitis in adults.[15]

Clinical Trial Information

Trial	**MESSINA**; NCT04543409, EudraCT 2019-002871-32; A Multicenter, Randomized, Double-blind, Parallel-group, Placebo Controlled Study to Investigate the Use of Benralizumab for Eosinophilic Esophagitis **Phase III:** Recruiting **Location(s):** Six EU countries, UK, USA, Canada, Russia, Japan and Israel **Primary completion date:** September 2022
Trial Design	Randomised, parallel assignment, triple-blinded
Population	N=170; subjects with documented previous diagnosis of EoE by endoscopy; aged 12 to 65 years old
Intervention(s)	Benralizumab SC
Comparator(s)	Matched placebo
Outcome(s)	• Proportion of patients with a histologic response at week 24, defined as a peak esophageal intraepithelial eosinophil count ≤ 6 eos/hpf. [time frame: week 24]

	• Changes from baseline in Dysphagia Symptom Questionnaire [time frame: week 24] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Benralizumab is already marketed in the UK for treatment of eosinophilic asthma; a 30mg/1ml pre-filled disposable injection pen or syringe costs £1,955.00.[5]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Budesonide orodispersible tablet for inducing remission of eosinophilic oesophagitis (TA708). June 2021.

NHS England (Policy/Commissioning) Guidance

No relevant guidance identified.

Other Guidance

- American Gastroenterological Association. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. 2020.[16]
- Lucendo A. *et al.* Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. 2017.[17]

Additional Information

AstraZeneca UK Ltd 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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