Health Technology Briefing
December 2022

Guselkumab for treating ulcerative colitis

Company/Developer	Janssen-Cilag Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 28191	NICE ID: 10713	UKPS ID: 656226

Licensing and Market Availability Plans

Currently in phase II/III clinical development.

Summary

Guselkumab is in clinical development for the treatment of moderately to severely active ulcerative colitis (UC). UC is a long-term condition where parts of the large bowel become inflamed, causing urgent bloody diarrhoea and abdominal pain. The symptoms of UC often follow a pattern where individuals with the condition have periods of no symptoms or mild symptoms (remission) followed by periods where their symptoms are particularly troublesome (flare-ups or relapses). There are therapeutic options available for UC, however these are not effective in more than one third of patients and can be associated with adverse effects that limit their use.

Guselkumab is a monoclonal antibody (a type of protein) which is designed to attach to interleukin 23 (IL-23) and block its activity. IL-23 is a messenger substance that controls the growth and maturation of some types of T cells. These T cells, which are part of the body's immune system (the body's natural defences), are involved in causing inflammation. By blocking the action of interleukin 23, guselkumab reduces inflammation and other symptoms of the disease. Guselkumab is administered as a subcutaneous injection (under the skin). If licenced, guselkumab will provide an additional treatment option for adult patients with moderately to severely active ulcerative colitis who do not respond to currently available treatments.

Proposed Indication

Moderately to severely active ulcerative colitis (UC).[1]

Technology

Description

Guselkumab (Tremfya) is a human IgG1λ monoclonal antibody (mAb) that binds selectively to the interleukin 23 (IL-23) protein with high specificity and affinity. IL-23, a regulatory cytokine, affects the differentiation, expansion, and survival of T cell subsets, (e.g., Th17 cells and Tc17 cells) and innate immune cell subsets, which represent sources of effector cytokines, including IL-17A, IL-17F and IL-22 that drive inflammatory disease. In humans, selective blockade of IL-23 was shown to normalise production of these cytokines.[2]

Guselkumab is currently in clinical development for the treatment of moderately to severely active UC. In the phase II/III clinical trial (QUASAR, NCT04033445) patients are given guselkumab as an intravenous (IV) or subcutaneous (SC) injection.[1]

Key Innovation

Treatment of UC aims to control symptoms and to suppress intestinal inflammation. Despite considerable advances, a proportion of patients do not respond to currently available drugs. The interleukin IL-23 axis plays a significant role in the pathogenesis of UC and has thus become an important target for drug development.[3] Preliminary data on anti-IL-23 agents also show promising results in terms of efficacy and safety.[4]

Guselkumab was the first approved fully human monoclonal antibody that selectively binds to the p19 subunit of interleukin IL-23 and inhibits its interaction with the IL-23 receptor.[5]

UC is a new indication being investigated for guselkumab.[2] If licensed, guselkumab, will provide an additional treatment option for adult patients with moderately to severely active ulcerative colitis who do not respond to currently available medicinal products.

Regulatory & Development Status

Guselkumab is currently licensed in the UK for the following indications:[2]

- Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.
- Alone or in combination with methotrexate (MTX) for the treatment of active psoriatic arthritis in adult patients who have had an inadequate response or who have been intolerant to a prior disease-modifying antirheumatic drug (DMARD) therapy

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

- Pityriasis rubra pilaris
- Psoriatic arthritis
- Crohn's disease
- Giant cell arteritis
- Scalp psoriasis
- Generalised pustular psoriasis
- Erythrodermic psoriasis
- Systemic sclerosis

Patient Group

Disease Area and Clinical Need

UC is one of two major types of inflammatory bowel disease (IBD), the other condition being Crohn's disease.[7] UC is the most common type of IBD. It is a long-term condition where the colon and rectum become inflamed and small ulcers can develop on the colon's lining, which can bleed and produce pus. Some people may go for weeks or months with very mild symptoms, or none at all, known as remission, followed by periods where the symptoms are particularly troublesome, known as flare-ups or relapses. Symptoms of UC include recurring diarrhoea, which may contain blood, mucus or pus, stomach pain, needing to frequently empty bowels, fatigue, loss of appetite and weight loss.[8,9] The exact cause of UC is unknown, although it is thought to be the result of a problem with the immune system. Many experts believe UC is the result of an autoimmune condition whereby the immune system mistakes bacteria in the colon which aids digestion, for a harmful infection. This causes the immune system to attack healthy tissue and leads to the colon and rectum becoming inflamed.[10] It is also believed that inherited genes are a factor in the development of UC, and certain environmental factors such as viral and bacterial infection, air pollution, medication and diet may be potential triggers.[7,10]

At least 1 in every 227 people in the UK is diagnosed with UC.[7] Around 146,000 people in England have UC, of whom about 52% have moderate to severe disease. It can develop at any age, but peak incidence is between the ages of 15 and 25 years, with a second, smaller peak between 55 and 65 years.[11] In England (2021-22), there were 132,930 finished consultant episodes (FCEs) and 119,889 admissions for UC (ICD-10 code K51) which resulted in 82,597 FCE bed days and 107,914 day cases.[12]

Recommended Treatment Options

Initial management depends on clinical severity, extent of disease and the person's preference, and may include corticosteroids, or topical or oral aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine). If the disease does not adequately respond to oral corticosteroids (beclometasone, budesonide, hydrocortisone or prednisolone) then an immunosuppressant (such as mercaptopurine or azathioprine) may be considered.[11]

The National Institute for Health and Care Excellence (NICE) recommends the following options for treating moderately to severely active UC in adults where conventional therapy or a biological agent cannot be tolerated, or the disease has responded inadequately or lost response to treatment:[13]

- Tofactinib
- Filgotinib
- Ozanimod
- Vedolizumab
- Ustekinumab
- Infliximab, adalimumab and golimumab

Clinical Trial Information

Trial	**QUASAR**, NCT04033445, 2018-004002-25; A Phase 2b/3, Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Protocol to Evaluate the Efficacy and Safety of Guselkumab in Participants With Moderately to Severely Active Ulcerative Colitis **Phase II/III** – Active, not recruiting

	Locations: 16 EU countries, UK, USA, Canada and other countries **Primary completion date:** September 2023
Trial Design	Randomised, parallel assignment, double-blind
Population	N=1064 (actual); documented diagnosis of moderately to severely active UC; aged 18 years and older
Intervention(s)	Guselkumab IV or SC
Comparator(s)	Matching placebo
Outcome(s)	**Primary outcome measures:** - Induction study 1: clinical response at week 12 [Time frame: week 12] - Induction study 2: clinical remission at week 12 [Time frame: week 12] - Maintenance study: clinical remission at week 44 [Time frame: week 44] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Guselkumab is already marketed in the UK for the treatment of plaque psoriasis and psoriatic arthritis; one 100mg/1ml solution for injection pre-filled pen costs £2,250.[14]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Etrasimod for treating moderately to severely active ulcerative colitis (GID-TA10991). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Mirikizumab for treating moderately to severely active ulcerative colitis (GID-TA10872). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Etrolizumab for treating moderately to severely active ulcerative colitis (GID-TA10717). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Upadacitinib for treating moderately to severely active ulcerative colitis (GID-TA10866). Expected January 2023.
- NICE technology appraisal. Ozanimod for treating moderately to severely active ulcerative colitis (TA828). October 2022.
- NICE technology appraisal. Filgotinib for treating moderately to severely active ulcerative colitis (TA792). June 2022.
- NICE technology appraisal. Ustekinumab for treating moderately to severely active ulcerative colitis (TA633). June 2020.
- NICE technology appraisal. Tofacitinib for moderately to severely active ulcerative colitis (TA547). November 2018.
- NICE technology appraisal. Vedolizumab for treating moderately to severely active ulcerative colitis (TA342). June 2015.
- NICE technology appraisal. Infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy (TA329). February 2015.
- NICE guideline. Ulcerative colitis: management (NG130). May 2019.

- NICE quality standard. Inflammatory bowel disease (QS81). February 2015.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Colorectal: Complex Inflammatory Bowel Disease (Adult). A08/S/c.

Other Guidance

- European Crohn´s and Colitis Organisation (ECCO). ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. 2021.[15]
- British Society of Gastroenterology (BSG). BSG consensus guidelines on the management of inflammatory bowel disease in adults. 2019.[16]
- American College of Gastroenterology (ACG). ACG Clinical Guideline: Ulcerative Colitis in Adults. 2019.[17]

Additional Information

References

1 Clinicaltrials.gov. *A Study of Guselkumab in Participants With Moderately to Severely Active Ulcerative Colitis (QUASAR)*. *Trial ID: NCT04033445*. Available from: https://clinicaltrials.gov/ct2/show/NCT04033445 [Accessed 4 November 2022].

2 Electronic Medicines Compendium. *Tremfya 100 mg solution for injection in pre-filled pen.* 2022. Available from: https://www.medicines.org.uk/emc/medicine/34321 [Accessed 2 November 2022].

3 Hanžel J, D'Haens GR. Anti-interleukin-23 agents for the treatment of ulcerative colitis. *Expert Opinion on Biological Therapy*. 2020 2020/04/02;20(4):399-406. Available from: https://doi.org/10.1080/14712598.2020.1697227.

4 Noviello D, Mager R, Roda G, Borroni RG, Fiorino G, Vetrano S. The IL23-IL17 Immune Axis in the Treatment of Ulcerative Colitis: Successes, Defeats, and Ongoing Challenges. *Frontiers in immunology*. 2021;12:611256-. Available from: https://doi.org/10.3389/fimmu.2021.611256.

5 BioSpace. *TREMFYA® (guselkumab) Induces Clinical and Endoscopic Improvements in Patients with Moderately to Severely Active Crohn's Disease based on Interim Results from Phase 2 Study*. 2020. Available from: https://www.biospace.com/article/releases/tremfya-guselkumab-induces-clinical-and-endoscopic-improvements-in-patients-with-moderately-to-severely-active-crohn-s-disease-based-on-interim-results-from-phase-2-study/ [Accessed 4 November 2022].

6 Clinicaltrials.gov. *Search of: Guselkumab | Recruiting, Not yet recruiting, Active, not recruiting, Completed, Enrolling by invitation Studies | Phase 2, 3.* 2022. Available from: https://clinicaltrials.gov/ct2/results?cond=&term=guselkumab&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= [Accessed 4 November 2022].

7 Crohn's and Colitis UK. *Ulcerative Colitis.* 2021. Available from: https://crohnsandcolitis.org.uk/info-support/information-about-crohns-and-colitis/all-

information-about-crohns-and-colitis/understanding-crohns-and-colitis/ulcerative-colitis [Accessed 17 November 2022].

8 National Health Service. *Overview: Ulcerative Colitis.* 2019. Available from: https://www.nhs.uk/conditions/ulcerative-colitis/ [Accessed 17 November 2022].

9 National Institute for Health and Care Excellence. *Ulcerative colitis: management.* 2019. Available from: https://www.nice.org.uk/guidance/ng130/resources/ulcerative-colitis-management-pdf-66141712632517 [Accessed 24 November 2022].

10 National Health Service. *Causes: Ulcerative Colitis.* 2019. Available from: https://www.nhs.uk/conditions/ulcerative-colitis/causes/ [Accessed 17 November 2022].

11 National Institute for Health and Care Excellence. *Tofacitinib for moderately to severely active ulcerative colitis* (*TA547)*. Last Update Date: Available from: https://www.nice.org.uk/guidance/ta547/documents/final-scope [Accessed 17 November 2022].

12 NHS Digital. *Hospital Admitted Patient Care Activity, 2021-22.* 2022. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2021-22 [Accessed 11 October 2022].

13 National Institute for Health and Care Excellence. *Search of: moderately to severely active ulcerative colitis.* 2022. Available from: https://www.nice.org.uk/search?q=moderately+to+severely+active+ulcerative+colitis [Accessed 17 November 2022].

14 National Institute for Health and Care Excellence. *Guselkumab: Medicinal Forms.* Available from: https://bnf.nice.org.uk/drugs/guselkumab/medicinal-forms/ [Accessed 15 November 2022].

15 Raine T, Bonovas S, Burisch J, Kucharzik T, Adamina M, Annese V, et al. ECCO Guidelines on Therapeutics in Ulcerative Colitis: Medical Treatment. *Journal of Crohn's and Colitis*. 2021;16(1):2-17. Available from: https://doi.org/10.1093/ecco-jcc/jjab178.

16 Lamb CA, Kennedy NA, Raine T, Hendy PA, Smith PJ, Limdi JK, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*. 2019;68(Suppl 3):s1-s106. Available from: https://doi.org/10.1136/gutjnl-2019-318484.

17 Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *Official journal of the American College of Gastroenterology | ACG*. 2019;114(3):384-413. Available from: https://doi.org/10.14309/ajg.0000000000000152.

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