Health Technology Briefing
September 2024

Inebilizumab for immunoglobulin G4-related disease

Company/Developer	Amgen Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30519	NICE ID: Not Available	UKPS ID: 674920

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Inebilizumab is in development for the treatment of immunoglobulin G4-related disease (IgG4-RD). Immunoglobulin G4 is a type of antibody, which are proteins essential to the immune system as they can bind to unwanted substances within the body and eliminate them. In IgG4-RD these antibodies do not function correctly, which leads to inflammation of organs. Prolonged inflammation of an organ can damage and/or reduce that organ's ability to perform its function. Although this may not be noticed immediately, the disease can damage one or more organs even whilst the individual is feeling healthy. Symptoms depend on the organs affected, but commonly include abdominal pain, weight loss, headaches, dysfunction of the cranial nerves, bulging of one or both eyes and painless jaundice (a yellow tint to the skin).

Inebilizumab is a monoclonal antibody that specifically binds to a receptor on the surface of B-cells, another type of cell involved in the body's immune response. Once bound, inebilizumab can destroy B-cells. When the amount of active B-cells in the body is reduced, the scale of the body's immune response, which includes inflammation, decreases. Inebilizumab is administered intravenously via an infusion. If licensed, inebilizumab would offer another option in the treatment of IgG4-RD.

Proposed Indication

Treatment of adults with immunoglobulin G4-related disease (IgG4-RD).[1]

Technology

Description

Inebilizumab (Uplizna, MEDI551, MedImmune) is a monoclonal antibody that specifically binds to CD19, a cell surface antigen present on pre-B and mature B-cell lymphocytes, including plasmablasts and some plasma cells.[2-4] Following cell surface binding to B lymphocytes, inebilizumab supports antibody-dependent cellular cytolysis and antibody-dependent cellular phagocytosis.[4]

Inebilizumab is currently in clinical development for the treatment of IgG4-RD. In the phase III clinical trial MITIGATE; NCT04540497, participants were given inebilizumab via an intravenous (IV) infusion.[1]

Key Innovation

Although most patients with IgG4-RD respond to glucocorticosteroids, around 40% of patients fail to achieve complete remission or experience relapse within 1 year of treatment, suggesting that there is an unmet need for more treatment options with different mechanisms of action.[5] In clinical trials, inebilizumab achieved rapid and durable peripheral CD19+ B-cell depletion with a 6 month gap between dosages, as well as demonstrating an acceptable safety profile. CD19+ B-cell depletion could improve the outcomes of IgG4-RD patients by reducing the level of plasmablasts, which are strongly correlated with disease activity.[6] If licenced, inebilizumab will provide an additional treatment option for patients with IgG4-RD.

Regulatory & Development Status

Inebilizumab does not currently have marketing authorisation in the UK for any indication. Inebilizumab has market authorisation in the EU as a monotherapy for the treatment of adult patients with neuromyelitis optica spectrum disorders (NMOSD) who are anti-aquaporin-4 immunoglobulin G seropositive.[4]

Inebilizumab is also in phase II and phase III clinical development for paediatric NMOSD, adults with myasthenia gravis and NMDAR encephalitis.[7]

Patient Group

Disease Area and Clinical Need

IgG4-RD is a rare inflammatory disease that can cause irritation and scarring in many different sites in the body. This can commonly include lumps appearing around the lymph nodes, in glands in the head and neck, as well as in the chest, liver, pancreas and kidneys.[8] The disease symptoms most commonly manifest in middle-aged to older adults, with males more likely to develop the disease than females. Many patients with IgG4-RD have no symptoms of the disease for months or sometimes years before they are diagnosed since the disease can damage one or more organs even whilst the individual is feeling healthy.[9] When symptoms do present, they depend largely on which organ or organs have been damaged and to what extent, but common symptoms include fatigue, weight loss, headaches, dysfunction of the cranial nerves, bulging of one or both eyes, large vessel vasculitis, shortness of breath, blockage of urine flow from the kidney, enlarged kidneys, and painless jaundice.[9] The causes and risk factors for IgG4-RD are still poorly understood and the subject of ongoing research, however it has been suggested that tobacco use,

environmental exposure to occupational antigens (such as solvents) and antecedent malignancy may increase the risk of developing IgG4-RD.[10]

The incidence of IgG4-RD is difficult to accurately state due to a relative lack of epidemiology data, although prevalence or identification appear to be increasing. In a nationwide survey conducted in the Ishikawa prefecture in Japan, the incidence of IgG4-RD was reported to be 0.28–1.08/100,000.[11] The mortality rate for IgG4-RD patients has been estimated at 3.42 per 100 person-years.[12] The population likely to be eligible to receive Inebilizumab in the UK could not be estimated from available published sources.

Recommended Treatment Options

There are currently no approved pharmacological treatment options for IgG4-RD recommended by NICE.[13] The first-line treatment for IgG4-RD provided by the NHS is glucocorticosteroids to suppress the body's immune response, with rituximab being used in cases where patients cannot have other treatments, have side effects arising from other treatments or when other treatments no longer work well enough.[14]

Clinical Trial Information

Trial	NCT04540497; A Phase 3, Randomized, Double-blind, Multicenter, Placebo Controlled Study of Inebilizumab Efficacy and Safety in IgG4-Related Disease **Phase III** – active, not recruiting **Location(s)**: 9 EU countries, UK, USA and 10 other countries **Estimated completion date**: April 2024
Trial Design	Randomized, quadruple-blind, parallel assignment, placebo controlled
Population	N=135 (actual); adults aged 18 years or older with a clinical diagnosis of IgG4-RD, experiencing (or recently experienced) an IgG4-RD flare that requires initiation or continuation of glucocorticoid treatment, IgG4-RD affecting at least two organs/sites at any time
Intervention(s)	300mg inebilizumab administered as an IV infusion.
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measures: time to disease flare, in days from dosing. See trial record for full list of other outcomes.
Results (efficacy)	87% reduction in IgG4RD flares compared to placebo ($p < 0.0001$)[15]
Results (safety)	-

Estimated Cost

The cost of inebilizumab is not currently known.

Relevant Guidance

NICE Guidance

There is currently no NICE guidance for IgG4-RD.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Rituximab for immunoglobulin G4 – related disease (IgG4 – RD). December 2016.

Other Guidance

- Löhr J, Beuers U, Vujasinovic M, Alvaro D, Brøndum Frøkjær J, Buttgereit F, et al. European Guideline on IgG4-related digestive disease - UEG and SGF evidence-based recommendations. 2020.[16]
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Additional Information

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