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Fasenra recommended for approval in the EU by CHMP for the treatment of eosinophilic granulomatosis with polyangiitis

New indication supported by the MANDARA trial which showed nearly 60% of patients achieved remission and 41% of patients fully stopped taking oral corticosteroids

AstraZeneca's *Fasenra* (benralizumab) has been recommended for approval in the European Union (EU) as an add-on treatment for adult patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA). EGPA is a rare, immune-mediated vasculitis that can result in damage to multiple organs, and without treatment, can be fatal.[1,2]

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency based its positive opinion on results from the MANDARA Phase III trial published in *The New England Journal of Medicine*,[3] which compared the efficacy and safety of *Fasenra* to the only approved EGPA treatment, mepolizumab, in patients with relapsing or refractory EGPA.[3-5] MANDARA was the first head-to-head non-inferiority trial of biologics in patients with EGPA.[4,6] Patients were randomised to receive either a single 30 mg subcutaneous injection of *Fasenra*, or three separate 100 mg subcutaneous injections of mepolizumab every four weeks.[3,4]

In the trial, nearly 60% of *Fasenra*-treated patients achieved remission which was comparable to mepolizumab-treated patients.[3] Data also showed 41% of *Fasenra*-treated patients fully tapered off oral corticosteroids (OCS) (vs. 26% in the comparator arm (difference: 16%; 95% CI: 1,31)).[3]

Bernhard Hellmich, Chair of the Department of Internal Medicine, Rheumatology, and Immunology at the Medius Klinik Kirchheim, Teaching Hospital of the University of Tübingen, Co-Director of the Vasculitis Center Tübingen-Kirchhei, and MANDARA Principal Investigator said: "People living with EGPA in Europe often face debilitating symptoms and suffer serious and long-lasting side effects from treatment with long-term oral corticosteroids. With its unique mechanism of action that leads to near complete depletion of eosinophils, *Fasenra* represents a much-needed potential treatment option for EGPA patients to help them achieve remission and taper off steroid therapy."

Ruud Dobber, Executive Vice President, BioPharmaceuticals Business Unit, AstraZeneca said: "With today's recommendation, the EGPA community in Europe is one step closer to accessing a new and convenient treatment option to alleviate some of the impact of this debilitating disease. With over 15 years of clinical data, *Fasenra* is a well-established, leading treatment for severe eosinophilic asthma, and now has the potential to transform care for patients with EGPA. Today's news demonstrates the potential of *Fasenra* to help patients suffering from eosinophilic diseases beyond severe asthma."

The safety and tolerability profile for *Fasenra* in the MANDARA trial was consistent with the known profile of the medicine.[3]

Approximately half of patients with EGPA have adult-onset severe eosinophilic asthma (SEA) and often have sinus and nasal symptoms.[2,7,8] If approved, *Fasenra* would be only the second biologic approved to treat this disease.[3,4]

Fasenra was recently approved in the US for the treatment of EGPA[9] and is also approved as an add-on maintenance treatment for severe eosinophilic asthma (SEA) in more than 80 countries including the US, Japan, EU and China.[10-13] It is also approved in children and adolescents ages six and above in the US and Japan.[12]

Notes

Eosinophilic granulomatosis with polyangiitis
EGPA, formerly known as Churg-Strauss Syndrome, is a rare, immune-mediated inflammatory disease that is caused by inflammation of small to medium-sized blood vessels.[1,2] It is estimated that 118,000 people throughout the world live with EGPA.[14] EGPA can result in damage to multiple organs, including lungs, upper airway, skin, heart, gastrointestinal tract and nerves.[2] The most common symptoms and signs include extreme fatigue, weight loss, muscle and joint pain, rashes, nerve pain, sinus and nasal symptoms, and shortness of breath.[2,16] Without treatment, the disease may be fatal.[2,15] Almost half (47%) of patients do not achieve remission with current treatments.[16]

There are limited treatment options for EGPA. Patients are often treated with chronic high-dose OCS and experience recurrent relapses when attempting to taper off OCS.[15,17]

MANDARA
MANDARA was a Phase III, randomised, double-blinded, active-controlled trial, which compared the efficacy and safety of *Fasenra* to mepolizumab in adult patients with relapsing or refractory EGPA.[4] In the trial, 140 patients were randomised 1:1 to receive either a single 30 mg subcutaneous injection of *Fasenra* or three separate 100 mg subcutaneous injections of the active comparator every four weeks.[3]

The primary endpoint was the proportion of patients who were in remission at both weeks 36 and 48.[4] Remission is defined as Birmingham Vasculitis Activity Score (BVAS)=0 and OCS dose less than or equal to 4 mg/day.[4] A

secondary endpoint was the proportion of patients who were able to fully taper off OCS at weeks 48 through 52.[3] The primary statistical analysis was to demonstrate non-inferiority of *Fasenra* versus mepolizumab based on the primary endpoint.[3]

Fasenra

Fasenra (benralizumab) is currently approved in more than 80 countries, including the US, EU, Japan, and China.[10-13] *Fasenra* has been prescribed to over 130,000 patients globally.[18]

Fasenra is in development for other diseases including chronic obstructive pulmonary disease, chronic rhinosinusitis with nasal polyps and hypereosinophilic syndrome.[19-21]

Fasenra was developed by AstraZeneca and is in-licensed from BioWa, Inc., a wholly owned subsidiary of Kyowa Kirin Co., Ltd., Japan.

AstraZeneca in Respiratory & Immunology
Respiratory & Immunology, part of AstraZeneca BioPharmaceuticals, is a key disease area and growth driver to the Company.

AstraZeneca is an established leader in respiratory care with a 50-year heritage and a growing portfolio of medicines in immune-mediated diseases. The Company is committed to addressing the vast unmet needs of these chronic, often debilitating, diseases with a pipeline and portfolio of inhaled medicines, biologics and new modalities aimed at previously unreachable biologic targets. Our ambition is to deliver life-changing medicines that help eliminate COPD as a leading cause of death, eliminate asthma attacks and achieve clinical remission in immune-mediated diseases.

AstraZeneca

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