

## Update on MESSINA Phase III trial

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### Update on the MESSINA Phase III trial for *Fasenra* in eosinophilic esophagitis

***MESSINA did not meet one of the two dual-primary endpoints, demonstrating a statistically significant improvement in histological disease remission with *Fasenra*, but not in dysphagia symptoms, compared to placebo***

Eosinophilic esophagitis (EoE) is a rare, progressive, chronic inflammatory disease of the esophagus currently believed to be characterised by the abnormal presence of eosinophils, a type of white blood cell, in the inner lining of the esophagus.<sup>1-3</sup> Patients experience difficulty with swallowing (dysphagia), pain, food getting stuck and anxiety.<sup>4,5</sup>

High-level results from the MESSINA Phase III trial showed that AstraZeneca's *Fasenra* (benralizumab) did not meet one of the two dual-primary endpoints. *Fasenra* demonstrated a statistically significant improvement in histological disease remission, but not a change in dysphagia symptoms, compared to placebo, in patients with EoE aged 12 years or older.

Mene Pangalos, Executive Vice President, BioPharmaceuticals R&D, AstraZeneca said: "The results from the MESSINA Phase III trial in eosinophilic esophagitis confirm that *Fasenra* achieved near complete depletion of tissue eosinophils, consistent with its mechanism of action, however this did not translate into an improvement in dysphagia symptoms. We will continue to analyse the complete data set to share with the scientific community."

In the trial, histological disease remission was measured as the proportion of patients with less than or equal to six eosinophils per high power field at Week 24. Burden of dysphagia was assessed using the patient-reported Dysphagia Symptom Questionnaire (DSQ) and measured as a mean change from baseline at Week 24. The trial included 210 patients, who received either *Fasenra* or placebo at four-week intervals.

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

Results from MESSINA will be presented at an upcoming medical meeting.

*Fasenra* is currently approved as an add-on maintenance treatment for severe eosinophilic asthma in the US, EU, Japan and other countries,<sup>6</sup> and is approved for self-administration in the US,<sup>6</sup> EU<sup>7</sup> and other countries.

### Notes

#### **MESSINA**

MESSINA is a randomised, placebo-controlled, double-blind, parallel-group, multicentre, global Phase III trial designed to investigate the efficacy and safety of *Fasenra* compared to placebo in patients aged 12 to 65 years of age with symptomatic and histologically active EoE.<sup>8,9</sup>

The dual-primary endpoints analysed at Week 24 were the proportion of patients with a histologic response, defined as a peak esophageal eosinophil count less than or equal to 6 eosinophils per high power field, and mean changes from baseline in Dysphagia Symptom

Questionnaire (DSQ).<sup>8</sup> The peak eosinophil count is obtained when a biopsy of the tissue of the esophagus is examined under a microscope. The histologic response endpoint used in the trial is consistent with histologic remission.<sup>10</sup> The DSQ captures the presence and severity of dysphagia symptoms in the past day in a 4-item patient-reported questionnaire and the score is calculated over 14-day periods, ranging from 0 to 84, with a lower score indicating less severe dysphagia.<sup>8</sup>

The trial period consists of a 24-week double-blind, placebo-controlled treatment period followed by a 28-week open-label treatment period.<sup>8</sup> Eligible patients were randomised in a 1:1 ratio to receive either 30 mg of *Fasenra* or placebo at 4-week intervals for the double-blind period. Patients who complete the double-blind period on *Fasenra* continue into the open-label treatment period with all patients receiving *Fasenra* 30 mg at 4-week intervals until Week 52, with a further open-label extension offered to eligible patients thereafter.<sup>9</sup>

In the trial, patients were allowed to remain on background medications for EoE, including proton pump inhibitors, topical corticosteroids, and EoE-driven diet elimination, provided that they were stable prior to entry and during the first 52 weeks of treatment, unless changes were clinically indicated.<sup>8,9</sup>

### ***Fasenra***

*Fasenra* (benralizumab) is a monoclonal antibody that binds directly to IL-5 receptor alpha on eosinophils and attracts natural killer cells to induce rapid and near-complete depletion of blood and tissue eosinophils in most patients via apoptosis (programmed cell death).<sup>11</sup>

*Fasenra* is currently approved as an add-on maintenance treatment for severe eosinophilic asthma in the US, EU, Japan and other countries,<sup>6</sup> and is approved for self-administration in the US,<sup>6</sup> EU<sup>7</sup> and other countries. *Fasenra* has been studied in almost 4,000 patients in global clinical trials.<sup>12-16</sup>

*Fasenra* is in development for other eosinophilic diseases including bullous pemphigoid, chronic obstructive pulmonary disease, chronic rhinosinusitis with nasal polyps, chronic spontaneous urticaria, eosinophilic esophagitis, eosinophilic gastritis/eosinophilic gastroenteritis, eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome and non-cystic fibrosis bronchiectasis.

*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 and Immunology**

Respiratory & Immunology, part of BioPharmaceuticals, is one of AstraZeneca's main disease areas and is a key growth driver for the Company.

AstraZeneca is an established leader in respiratory care with a 50-year heritage. The Company aims to transform the treatment of asthma and COPD by focusing on earlier biology-led treatment, eliminating preventable asthma attacks, and removing COPD as a top-three leading cause of death. The Company's early respiratory research is focused on emerging science involving immune mechanisms, lung damage and abnormal cell-repair processes in disease and neuronal dysfunction.

With common pathways and underlying disease drivers across respiratory and immunology, AstraZeneca is following the science from chronic lung diseases to immunology-driven disease areas. The Company's growing presence in immunology is focused on five mid- to late-stage franchises with multi-disease potential, in areas including rheumatology (including systemic lupus erythematosus), dermatology, gastroenterology, and systemic eosinophilic-driven diseases. AstraZeneca's ambition in Respiratory & Immunology is to achieve disease modification and durable remission for millions of patients worldwide.

## AstraZeneca

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## Contacts

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