RNS Number : 6617E
AstraZeneca PLC
18 September 2024

18 September 2024

Fasenra approved in the US for 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 approved in the US for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).[1] EGPA is a rare, immune-mediated vasculitis that can result in damage to multiple organs, and without treatment, can be fatal.[2,3]

The approval by the US Food and Drug Administration (FDA) was based on positive results from the MANDARA Phase III trial published in *The New England Journal of Medicine*,[4] which compared the efficacy and safety of *Fasenra* to the only approved EGPA treatment, mepolizumab, in patients with relapsing or refractory EGPA.[4-6] MANDARA was the first head-to-head non-inferiority trial of biologics in patients with EGPA.[5,7] 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.[4,5]

In the trial, nearly 60% of *Fasenra*-treated patients achieved remission which was comparable to mepolizumab-treated patients.[4] Data also showed 41% of *Fasenra*-treated patients fully tapered off oral corticosteroids (OCS) (vs. 26% in the mepolizumab arm (difference: 16%; 95% CI: 1,31)).[4]

Dr. Michael Wechsler, Professor of Medicine and Director of The Asthma Institute at National Jewish Health, and International Coordinating Investigator of the MANDARA trial said: "This approval is great news for patients with EGPA in the US who continue to suffer from debilitating symptoms. Patients often rely on long-term oral corticosteroids, which can cause serious and lasting side effects. Benralizumab is a much-needed treatment option, with data showing that not only is remission an achievable goal for EGPA patients, but benralizumab can also help patients taper off steroid therapy."

Joyce Kullman, Executive Director, Vasculitis Foundation said: "This disease has a devastating impact on patients and the quality of their life, and they need more treatment options. The approval of another treatment in EGPA is welcome news to the approximately 15,000 patients living in the US with this difficult-to-treat rare disease."

Ruud Dobber, Executive Vice President, BioPharmaceuticals Business Unit, AstraZeneca said: "*Fasenra* is already well established for the treatment of severe eosinophilic asthma, and with this approval, physicians in the US will now be able to offer an important new, convenient single monthly subcutaneous injection to their 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.[4]

Approximately half of patients with EGPA have adult-onset severe eosinophilic asthma (SEA) and often have sinus and nasal symptoms.[3,8,9] *Fasenra* is only the second biologic approved to treat this disease.[4,5]

Fasenra is currently approved as an add-on maintenance treatment for 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. The FDA granted Orphan Drug Designation for *Fasenra* for EGPA in 2018.[14]

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.[2,3] It is estimated that 118,000 people throughout the world live with EGPA and approximately 15,000 patients living in the US have EGPA.[15,16] EGPA can result in damage to multiple organs, including lungs, upper airway, skin, heart, gastrointestinal tract and nerves.[3] 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.[3,17] Without treatment, the disease may be fatal.[3,17] Almost half (47%) of patients do not achieve remission with current treatments.[18]

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.[17,19]

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.[5] In the trial, 140 patients were randomised 1:1 to receive either a single 30mg subcutaneous injection of *Fasenra* or three separate 100mg subcutaneous injections of the active comparator every four weeks.[4]

The primary endpoint was the proportion of patients who were in remission at both weeks 36 and 48.[5] Remission is defined as Birmingham Vasculitis Activity Score (BVAS)=0 and OCS dose less than or equal to 4 mg/day.[5] A secondary endpoint was the proportion of patients who were able to fully taper off OCS at weeks 48 through 52.[5] The primary statistical analysis was to demonstrate non-inferiority of *Fasenra* versus mepolizumab based on the primary endpoint.[4]

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.[20]

Fasenra is in development for other diseases including chronic obstructive pulmonary disease, chronic rhinosinusitis with nasal polyps and hypereosinophilic syndrome.[21-23]

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

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca

Contacts

For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

References

1. *Fasenra* (benralizumab) US prescribing information; September 2024.
2. Furuta S, *et al*. Update on eosinophilic granulomatosis with polyangiitis. *Allergol Int*. 2019;68:430-436.
3. American Partnership for Eosinophilic Disorders. Eosinophilic Granulomatosis with Polyangiitis (EGPA). Available at: https://apfed.org/about-ead/eosinophilic-granulomatosis-with-polyangiitis/. [Last accessed: September 2024].
4. Wechsler ME, *et al*. Benralizumab versus Mepolizumab for Eosinophilic Granulomatosis with Polyangiitis. *N Engl J Med*. 2024;390(10):911-921.
5. Clinicaltrials.gov. Efficacy and Safety of Benralizumab in EGPA Compared to Mepolizumab. (MANDARA). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT04157348. [Last accessed: September 2024].
6. Mepolizumab US prescribing information. Available from: https://www.fda.gov/files/drugs/published/125526-Mepolizumab-Clinical-PREA.pdf [Last accessed: September 2024].
7. AstraZeneca plc. MANDARA Phase III data published in New England Journal of Medicine show remission is an achievable goal in eosinophilic granulomatosis with polyangiitis (EGPA) with Fasenra. Available at: https://www.astrazeneca.com/media-centre/medical-releases/mandara-phase-iii-data-published-new-england-journal-medicine-show-remission-achievable-goal-eosinophilic-granulomatosis-polyangiitis-egpa-fasenra.html. [Last accessed: September 2024].
8. Cottin V, *et al*. Respiratory manifestations of eosinophilic granulomatosis with polyangiitis (Churg-Strauss). *Eur Respir J*. 2016;48:1429-1441.
9. Heaney L *et al*. Eosinophilic and Noneosinophilic Asthma: An Expert Consensus Framework to Characterize Phenotypes in a Global Real-Life Severe Asthma Cohort. *Chest*. 2021 Sep;160(3):814-830.
10. AstraZeneca news release. Available at: https://www.astrazeneca.com/media-centre/press-releases/2019/fasenra-approved-in-the-us-for-self-administration-in-a-new-pre-filled-auto-injector-the-fasenra-pen-04102019.html#. [Last accessed: September 2024].
11. AstraZeneca news release. Available at: https://www.astrazeneca.com/media-centre/press-

releases/2019/fasenra-receives-positive-eu-chmp-opinion-for-self-administration-and-the-new-fasenra-pen-a-pre-filled-single-use-auto-injector-01072019.html#. [Last accessed: September 2024].
12. AstraZeneca Annual Report 2023. Available at: https://www.astrazeneca.com/content/dam/az/Investor_Relations/annual-report-2023/pdf/AstraZeneca_AR_2023.pdf. [Last accessed: September 2024].
13. AstraZeneca news release. Fasenra met the primary endpoint in the MANDARA Phase III trial in eosinophilic granulomatosis with polyangiitis (EGPA). Available at: https://www.astrazeneca.com/media-centre/press-releases/2023/fasenra-phase-iii-egpa-trial-met-primary-endpoint.html#:~:text=Positive%20high%2Dlevel%20results%20from,EGPA)%20who%20were%20receiving%20oral. [Last accessed: September 2024].
14. AstraZeneca news release. Available at: https://www.astrazeneca.com/media-centre/press-releases/2018/us-fda-grants-fasenra-orphan-drug-designation-for-eosinophilic-granulomatosis-with-polyangiitis-26112018.html. [Last accessed: September 2024].
15. IQVIA data on file. 2024.
16. AstraZeneca Data on file. 2024. REF- 244520.
17. Baldini C, et al. Clinical Manifestations and Treatment of Churg-Strauss Syndrome. *Rheum Dis Clin N Am*. 2010;36:527-543.
18. Wechsler ME, *et al*. Mepolizumab or Placebo for Eosinophilic Granulomatosis with Polyangiitis. *N Engl J Med*. 2017:376;1921-1932.
19. Bell CF, *et al*. Burden of illness and costs associated with eosinophilic granulomatosis with polyangiitis: evidence from a managed care database in the United States. *J Manag Care Spec Pharm*. 2021;27(9):1249-1259.
20. AstraZeneca data on file. 2024. REF-235794.
21. Clinicaltrials.gov. Efficacy and Safety of Benralizumab in Moderate to Very Severe Chronic Obstructive Pulmonary Disease (COPD) With a History of Frequent Exacerbations (RESOLUTE). Available from: https://clinicaltrials.gov/ct2/show/NCT04053634 [Last accessed: September 2024].
22. Clinicaltrials.gov. Efficacy and Safety Study of Benralizumab in Patient With Eosinophilic Chronic Rhinosinusitis With Nasal Polyps (ORCHID). Available at: https://clinicaltrials.gov/ct2/show/NCT04157335 [Last accessed: September 2024].
23. Clinicaltrials.gov. A Phase 3 Study to Evaluate the Efficacy and Safety of Benralizumab in Patients With Hypereosinophilic Syndrome (HES) (NATRON). Available from: https://clinicaltrials.gov/ct2/show/NCT04191304 [Last accessed: September 2024].

Adrian Kemp
Company Secretary
AstraZeneca PLC

END

REASFLSIAELSEFU