Depemokimab in eosinophilic asthma – a new era in biological therapy?

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The management of severe eosinophilic asthma has experienced a paradigm shift with the advent of biological therapies targeting interleukin 5 (IL-5) and its receptor (IL-5R). The recent publication by Jackson *et al.*[1] introduces depemokimab, an ultra-long-acting anti-IL-5 monoclonal antibody, as a promising addition to this therapeutic landscape.

Anti-IL-5 therapies that have been available for some time include mepolizumab, reslizumab and benralizumab. Depemokimab has set itself apart from the currently available biologicals by offering a more convenient twice-yearly dosing schedule. The Study of Well-Being in Asthma: Investigating Future Treatments (SWIFT)-1 and SWIFT-2 trials showed that in comparison with placebo, depemokimab significantly reduced the annual rate of severe asthma exacerbations in patients with an eosinophilic phenotype by 54%, although the absolute risk reduction was small, possibly owing to a milder asthma severity population.[1] These findings are comparable to results observed in studies of earlier biological agents, where exacerbation rates were reduced by 17 - 59% depending on the cohort.[2] Notably, the study included patients with a blood eosinophil count ≥300 cells/μL during the preceding year or ≥150 cells/μL at screening. The researchers noted a rapid and sustained fall in blood eosinophil count from baseline in the treatment groups, 83% in SWIFT-1 and 82% in SWIFT-2.[1]

The most significant advantage of depemokimab is its potential to reduce the treatment burden for patients. Adherence to available biological agents poses a challenge to patients, requiring monthly or fortnightly subcutaneous administration. The 6-monthly dosing of depemokimab could significantly improve patient adherence, particularly in individuals with limited access to healthcare facilities. Research has shown that reducing the pill burden and dosing frequency in patients with chronic medical conditions achieves improved adherence and overall quality of life.[3,4]

Patients in low- to middle-income countries face substantial economic challenges. In theory, the twice-yearly administration of depemokinab could offer significant advantages to patients by reducing the frequency of their scheduled and unscheduled healthcare visits. However, the exorbitant costs of biologicals continue to overshadow any logistic benefit offered from reduced dosing schedules. Public health facilities in South Africa struggle to provide even basic asthma care, let alone expensive biological therapies.[5]

Although depemokimab demonstrated significant efficacy in reducing exacerbations, there were no significant difference in patient-reported outcomes, such as St George's Respiratory Questionnaire (SGRQ) scores. This disconnect between objective clinical outcomes and subjective quality-of-life measures is not unique to depemokimab. Similar patterns have been observed with other anti-IL-5 therapies, suggesting that exacerbation control may not fully capture the multifaceted nature of asthma's impact on patients' daily lives.[2]

In both SWIFT trials, depemokimab showed an encouraging safety profile. The frequency of adverse events was similar in the placebo and control arms. The investigators reported that no deaths or serious adverse events were attributed to the drug. Of note, there were five patients who required discontinuation of the drug because of liver enzyme derangements, although these discontinuations were not deemed to be drug related. Across SWIFT-1 and SWIFT-2, ~12% and 5%, respectively, developed binding antibodies, with only two patients developing neutralising antibodies, highlighting the importance of ongoing immunogenicity assessments.[1]

Further studies looking at the long-term safety, real-world efficacy and cost-effectiveness of depemokimab are warranted. Studies comparing depemokimab with existing biologicals would also assist physicians in making informed choices when prescribing biological therapy. Additionally, understanding the role of biomarkers such as exhaled nitric oxide, which was not assessed in the SWIFT trials, may help refine patient selection and optimise treatment outcomes.[6]

The arrival of depemokimab marks an exciting development in the biological treatment of eosinophilic asthma. While the drug's ability to reduce exacerbations is promising, its ultimate success will depend on balancing clinical efficacy with improvements in patient-reported outcomes and ensuring safety over prolonged use. As we celebrate medical advancements like depemokimab, we must ensure that innovation is paired with strong patient advocacy and equitable accessibility.

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