Health Technology Briefing
August 2023

Tezepelumab for treating severe chronic rhinosinusitis with nasal polyps

Company/Developer	AstraZeneca UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33226	NICE TSID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Tezepelumab is in clinical development for the treatment of severe chronic rhinosinusitis with nasal polyps. Chronic rhinosinusitis is a condition in which the lining of the sinuses (air-filled spaces behind the nose, eyes, and cheeks) becomes inflamed for more than 12 weeks. People with the condition may have nasal polyps which are growths inside the nasal passages and sinuses. This is called chronic rhinosinusitis with nasal polyps (CRSwNP), for which the cause is not completely understood, however it is more common in people with other conditions including asthma. Symptoms include nasal blockage, loss of smell, continuous runny nose, and lower airway problems. Oral or intranasal steroid treatments are usually the first approach but if these are ineffective, then sinus surgery may be needed. However, these options are not a permanent solution because polyps tend to recur and are associated with risks.

Tezepelumab is an antibody (a type of protein) which is administered via subcutaneous (under the skin) injection, in a pre-filled syringe. It blocks the activity of a protein called thymic stromal lymphopoietin (TSLP) that has been shown to have increased expression in patients with CRSwNP. It plays a role in allergic and immune disorders as it has an important role in the inflammation pathway. Preventing TSLP from attaching to cells thereby reduces airway inflammation, which may then result in the reduction of the size of the polyps or eliminate them. If licensed, tezepelumab would offer a novel treatment option for CRSwNP.

Proposed Indication

For the treatment of severe, chronic rhinosinusitis with nasal polyps (CRSwNP) in patients aged 18 years and older.[1]

Technology

Description

Tezepelumab (Tezspire) is a monoclonal antibody (IgG2λ) directed against thymic stromal lymphopoietin (TSLP), preventing its interaction with the heterodimeric TSLP receptor.[2] TSLP is a key epithelial cytokine that sits at the top of multiple inflammatory cascades and is critical in the initiation and persistence of allergic, eosinophilic and other types of airway inflammation.[3] Blocking TSLP with tezepelumab reduces a broad spectrum of biomarkers and cytokines associated with airway inflammation (e.g. blood eosinophils, airway submucosal eosinophils, IgE, FeNO, IL-5, and IL-13).[2]

Tezepelumab is in clinical development for the treatment of severe CRSwNP. In the phase III clinical trial (WAYPOINT; NCT04851964) tezepelumab is administered via subcutaneous (SC) injection using an accessorised pre-filled syringe.[1]

Key Innovation

It is estimated that around a third of patients with nasal polyps may have uncontrolled disease with the current therapeutics options.[4] Current options include steroid treatment, although are associated with concerns of side effects. Surgery may be offered to remove the polyps, although in 3 out of 4 patients, the polyps' returns after an average of 4 years.[5] Patients with CRSwNP can relapse after steroid treatment or sinus surgery, hence may need several surgeries. In addition, there are risks with long-term corticosteroid use and major complications have been reported with sinus surgeries. Therefore, biologics therapy could be considered as an innovative treatment option for such patients. In phase II and III clinical trials, biologics therapy has shown promising activity in CRSwNP, thus may fulfil unmet needs in the treatment of CRSwNP.[4]

More recent work in CRSwNP has shown increased expression and/or activity of TSLP in nasal polyp tissue compared to healthy sinus tissue.[6] Tezepelumab is a potential first-in-class treatment that targets TSLP. In a phase III trial (NAVIGATOR; NCT03347279), it had shown reduced nasal symptoms in patients with uncontrolled asthma and comorbid nasal polyps.[7] Therefore, if licensed tezepelumab would offer a novel treatment option for CRSwNP.

Regulatory & Development Status

Tezepelumab is licensed in the UK as an add-on maintenance treatment in patients aged 12 years and older with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids plus another medicinal product for maintenance treatment.[2]

Tezepelumab is currently in phase II and III trials for the treatment of asthma, chronic obstructive pulmonary disease, and eosinophilic esophagitis.[8]

Patient Group

Disease Area and Clinical Need

Chronic rhinosinusitis (CRS) is characterised by chronic inflammation within the paranasal sinuses, lasting for more than twelve weeks. CRS has been clinically divided into two subgroups: CRS without nasal polyps (CRSsNP) and with nasal polyps (CRSwNP).[9] Nasal polyps are inflammatory outgrowths of sinonasal tissue. In CRSwNP, nasal polyps are benign and typically develop bilaterally in the sinonasal cavity. Patients with CRSwNP represent approximately 25-30% of patients with CRS, however, they have more severe disease so have significant morbidity and decreased quality of life.[10] Symptoms experienced by patients with nasal polyps include nasal blockage, loss of smell, rhinorrhoea (continuously runny nose), and symptoms derived from lower airway involvement.[11] CRSwNP is often associated with co-morbidities such as asthma, and aspirin/non-steroidal anti-inflammatory drug exacerbated respiratory disease (AERD).[12] The cause of CRSwNP is unknown, but multiple factors including allergies and fungal infection, are known to be contributory factors.[13]

The average age of onset for CRSwNP is 42 years and the typical age of diagnosis ranges from 40–60 years. Men are more likely to be affected than women, but no specific genetic or environmental factors have been linked to the development of the disorder.[10] Sinusitis is common, affecting around 15% of the UK population.[13] Chronic rhinosinusitis affects 10.9% of the UK adult population.[14] In England 2021-22, there were 2,468 finished consultant episodes (FCE) and 2,443 admissions for nasal polyps (ICD-10 code J33.9). This resulted in 482 FCE bed days and 1,928 day cases.[15] The specific population likely to be eligible to receive tezepelumab could not be estimated from available published sources.

Recommended Treatment Options

There are currently no National Institute for Health and Care Excellence (NICE) recommended biological therapies for CRSwNP.[16] Steroid nose drops or spray to shrink the nasal polyps and/or control symptoms can be used. Stronger steroids in drop form or as a tablet can be used to relieve symptoms but effects are short-lived. If medicines are ineffective then surgery may be required to remove the polyps.[5] In the UK, mometasone furoate, administered as a nasal spray, is indicated for the treatment of nasal polyps in adults.[17]

Clinical Trial Information

Trial	**WAYPOINT**; NCT04851964, **EudraCT** 2020-003062-39; A Multicentre, Randomised, Double-Blind, Parallel-Group, Placebo-Controlled Phase 3 Efficacy and Safety Study of Tezepelumab in Participants With Severe Chronic Rhinosinusitis With Nasal Polyposis (WAYPOINT) **Phase III** – recruiting **Location(s):** 5 EU countries, UK, USA, and other countries **Primary completion date:** August 2024
Trial Design	Randomised, quadruple-masked, double-blind, parallel assignment
Population	N=400 (estimated); patients aged 18 years and older with severe CRSwNP.
Intervention(s)	Tezepelumab administered via SC injection
Comparator(s)	Placebo
Outcome(s)	Primary outcome measures:

	• Nasal Polyp Score [time frame: Baseline to Week 52] • Participant Reported Nasal Congestion [time frame: Baseline to Week 52] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The NHS indicative price for one pre-filled syringe of tezepelumab (210 mg/1.91 ml) is £1,265.00.[18]

Relevant Guidance

NICE Guidance

- NICE technology appraisal awaiting development. Benralizumab for previously treated severe nasal polyps (GID- TA10818). Expected publication date to be confirmed.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All Ages). B09/S/b.

Other Guidance

- International Forum of Allergy & Rhinology. International consensus statement on allergy and rhinology: rhinosinusitis 2021. 2021.[19]
- Fokkens WJ, Lund VJ, Hopkins C et al. European Position Paper on Rhinosinusitis and Nasal Polyps. 2020.[20]
- NHS Tayside Department of ENT. Nasal polyps management. 2017.[21]
- British Society for Allergy and Clinical Immunology (BSACI). BSACI guidelines for the management of rhinosinusitis and nasal polyposis. 2008.[22]

Additional Information

AstraZeneca UK Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

1 ClinicalTrials.gov. *Efficacy and Safety of Tezepelumab in Participants With Severe Chronic Rhinosinusitis With Nasal Polyposis (WAYPOINT)*. *Trial ID: NCT04851964*. 2021. Status: Recruiting. Available from: https://classic.clinicaltrials.gov/ct2/show/NCT04851964 [Accessed 3 July 2023].

2 Electronic Medicines Compendium (eMC). *Tezspire 210 mg solution for injection in pre-filled syringe*. 2022. Available from: https://www.medicines.org.uk/emc/product/14064 [Accessed 3 July 2023].

3 AstraZeneca. *Tezspire approved for self-administration in the EU in a new pre-filled pen*. Press release 13 January 2023. Available from: https://www.astrazeneca.com/media-centre/press-releases/2023/tezspire-approved-for-self-administration-in-the-eu-in-a-new-pre-filled-pen.html [Accessed 7 July 2023].

4 Bachert C, Zhang N, Cavaliere C, Weiping W, Gevaert E, Krysko O. Biologics for chronic rhinosinusitis with nasal polyps. *Journal of Allergy and Clinical Immunology*. 2020;145(3):725-39. Available from: https://doi.org/10.1016/j.jaci.2020.01.020.

5 Ear Nose and Throat UK. *ENT Conditions and Procedures - Nasal polyps*. 2021. Available from: https://www.entuk.org/patients/conditions/41/nasal_polyps/ [Accessed 3 July 2023].

6 Morse JC, Miller C, Senior B. Management of Chronic Rhinosinusitis with Nasal Polyposis in the Era of Biologics. *J Asthma Allergy*. 2021;14:873-82. Available from: https://doi.org/10.2147/jaa.S258438.

7 AstraZeneca. *New tezepelumab data show 86% reduction in exacerbations in patients with severe asthma and comorbid nasal polyps*. Press release 5 September 2021. Available from: https://www.astrazeneca.com/media-centre/medical-releases/new-tezepelumab-data-show-86-reduction-in-exacerbations-in-patients-with-severe-asthma-and-comorbid-nasal-polyps.html [Accessed 14 July 2023].

8 ClinicalTrials.gov. *10 Studies found for: tezepelumab | Recruiting, Not yet recruiting, Active, not recruiting, Enrolling by invitation, Unknown status Studies | Phase 2, 3*. Available from: https://classic.clinicaltrials.gov/ct2/results?term=tezepelumab&Search=Apply&recrs=b&recrs=a&recrs=f&recrs=d&recrs=m&age_v=&gndr=&type=&rslt=&phase=1&phase=2 [Accessed 3 July 2023].

9 Bachert C, Zhang N, Hellings PW, Bousquet J. Endotype-driven care pathways in patients with chronic rhinosinusitis. *Journal of Allergy and Clinical Immunology*. 2018;141(5):1543-51. Available from: https://doi.org/10.1016/j.jaci.2018.03.004.

10 Stevens WW, Schleimer RP, Kern RC. Chronic Rhinosinusitis with Nasal Polyps. *The Journal of Allergy and Clinical Immunology: In Practice*. 2016;4(4):565-72. Available from: https://doi.org/10.1016/j.jaip.2016.04.012.

11 Bachert C, Sousa AR, Lund VJ, Scadding GK, Gevaert P, Nasser S, et al. Reduced need for surgery in severe nasal polyposis with mepolizumab: Randomized trial. *Journal of Allergy and Clinical Immunology*. 2017;140(4):1024-31.e14. Available from: https://doi.org/10.1016/j.jaci.2017.05.044.

12 Khan A, Huynh TMT, Vandeplas G, Joish VN, Mannent LP, Tomassen P, et al. The GALEN rhinosinusitis cohort: chronic rhinosinusitis with nasal polyps affects health-related quality of life. *Rhinology*. 2019;57(5):343-51. Available from: https://doi.org/10.4193/Rhin19.158.

13 National Institute for Health and Care Excellence (NICE). *Proposed Health Technology Appraisal: Dupilumab for treating chronic rhinosinusitis with nasal polyps - Draft scope (pre-referral)*. 2019. Available from: https://www.nice.org.uk/guidance/ta648/documents/draft-scope-pre-referral [Accessed 7 July 2023].

14 Dickson E, Hopkins C. Chronic rhinosinusitis. *InnovAiT*. 2020;13(4):199-206. Available from: https://doi.org/10.1177/1755738019837295.

15 NHS Digital. *Hospital Admitted Patient Care Activity, 2021-22: Diagnosis*. 2023. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2021-22 [Accessed 7 July 2023].

16 National Institute for Health and Care Excellence (NICE). *Search for: chronic rhinosinusitis with nasal polyps*. Available from: https://www.nice.org.uk/search?q=%20chronic%20rhinosinusitis%20with%20nasal%20polyps [Accessed 14 July 2023].

17 British National Formulary. *Mometasone furoate*. Available from: https://bnf.nice.org.uk/drugs/mometasone-furoate/ [Accessed 3 July 2023].

18 British National Formulary. *Tezepelumab - Medicinal forms*. Available from: https://bnf.nice.org.uk/drugs/tezepelumab/medicinal-forms/ [Accessed 23 June 2023].

19 Orlandi RR, Kingdom TT, Smith TL, Bleier B, DeConde A, Luong AU, et al. International consensus statement on allergy and rhinology: rhinosinusitis 2021. *International Forum of Allergy & Rhinology*. 2021;11(3):213-739. Available from: https://doi.org/10.1002/alr.22741.

20 Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. *Rhinology*. 2020;58(Suppl S29):1-464. Available from: https://doi.org/10.4193/Rhin20.600.

21 NHS Tayside Department of ENT. *Nasal polyps management*. Last Update Date: August 2021. Available from: https://www.nhstaysideadtc.scot.nhs.uk/approved/guidance/Nasal%20polyps%20management%20algorithm.pdf [Accessed 23 June 2023].

22 Scadding GK, Durham SR, Mirakian R, Jones NS, Drake-Lee AB, Ryan D, et al. BSACI guidelines for the management of rhinosinusitis and nasal polyposis. *Clinical & Experimental Allergy*. 2008;38(2):260-75. Available from: https://doi.org/10.1111/j.1365-2222.2007.02889.x.

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