Report Tezspire® - tezepelumab

Product & Mechanism of action

Substance: Tezepelumab

Brand Name: Tezspire

Originator/licensee: AstraZeneca AB

Classification: NCE

ATC code: R03DX11

Orphan Status:
Eu: No
Us: No

Mechanism of action:
Tezepelumab is a human monoclonal antibody (IgG2 lambda) directed against TSLP. Blocking TSLP with tezepelumab reduces a broad spectrum of biomarkers and cytokines associated with airway inflammation, but the mechanism of action of tezepelumab in asthma has not been definitively established [1].

Authorized indications Licensing status

Authorized Indication:
EMA: tezspire is indicated as an add-on maintenance treatment in adults and adolescents ≥12 years with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids plus another medicinal product for maintenance treatment [1].
FDA: tezspire is a thymic stromal lymphopoietin (TSLP) blocker, human monoclonal antibody (IgG2λ), indicated for the add-on maintenance treatment of adult and pediatric patients aged ≥12 years with severe asthma [2].

Route of administration: IV

Licensing status
EU CHMP P.O. date: 21/07/2022
FDA M.A. date: 17/12/2021

EU Speed Approval Pathway: No
FDA Speed Approval Pathway: No

ABBREVIATIONS:
AE: Adverse Event
CHMP: Committee for Medicinal Products for Human Use
CI: Confidence Interval
IV: intravenous
M.A.: Marketing Authorization
P: P-value
PBO: placebo
P.O.: Positive Opinion
Pts: patients
Q4W: every 4 weeks
SAE: Serious Adverse Event
TSLP: thymic stromal lymphopoietin
URTI: Upper respiratory tract infection
Yrs: years

Essential therapeutic features

Summary of clinical EFFICACY:
NAVIGATOR (NCT03347279) is a phase III, multicenter, randomized, double-blind, placebo-controlled trial to evaluate the efficacy and safety of tezepelumab in pts aged 12 to 80 yrs (N=1061) diagnosed with asthma for at least 12 months. The primary end-point was the annualized rate of asthma exacerbations over a period of 52 weeks; this end-point was also assessed in pts with a baseline blood eosinophil count of less than 300 cells per microliter. Pts were randomly assigned in a 1:1 ratio to receive tezepelumab (N=528) at a dose of 210 mg or PBO (N=531) Q4W for 52 weeks.
Pts with severe, uncontrolled asthma who received tezepelumab had fewer exacerbations and better lung function, asthma control, and health-related quality of life than those who received placebo. The annualized rate of asthma exacerbations is summarized in the following table [3]:

	tezepelumab	**PBO**	**Rate Ratio**
Annualized rate of asthma exacerbations	0.93 (95% CI, 0.80-1.07)	2.10 (95% CI, 1.84-2.39)	0.44; 95% CI, 0.37-0.53; P<0.001
// in pts with a blood eosinophil count< 300 cells per microliter	1.02 (95% CI, 0.84-1.23)	1.73 (95% CI, 1.46-2.05)	0.59; 95% CI, 0.46-0.75; P<0.001

Summary of clinical SAFETY:
The frequencies and types of AEs did not differ meaningfully between the two groups:

AE	**Any AEs***	**Any SAEs**	**Any AE leading to discontinuation of treatment**	**Any AE resulting in death**
tezepelumab	407 (77%)	52 (10%)	11 (2%)	0 (0%)
PBO	429 (81%)	73 (18%)	19 (4%)	2 (0.4%)**

*The most common AEs (that occurred in ≥3% of pts) in tezepelumab and PBO were nasopharyngitis (21% vs 22%), URTI (11% vs 16%), headache (8% vs 9%), asthma (5% vs 11%) which was more frequently observed in the placebo group than in the tezepelumab group).
**One from heart failure and one of unknown cause [3].

Ongoing studies:
- ***For the same indication:*** Yes
- ***For other indications:*** Yes

Discontinued studies (for the same indication): No

References:

[1]. Tezspire: Pending EC decision | European Medicines Agency (europa.eu)
[2].https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761224s000lbl.pdf
[2]. Tezepelumab in Adults and Adolescents with Severe, Uncontrolled Asthma | NEJM
[3]. Asma. Al via la Campagna di comunicazione sull'Asma Grave con "Le storie che tolgono il fiato" - Quotidiano Sanità (quotidianosanita.it)
[4]. GINA_pocket_asma_grave_ita_2019.pdf (ginasma.it)
[5]. Technology name [formulation]* for indication [– first/second/third line]* (nihr.ac.uk)
[6]. Tezepelumab - Amgen/AstraZeneca - AdisInsight (springer.com)
[7]. Home - ClinicalTrials.gov

NHS impact

Cost of therapy:
Price is not available yet.

Epidemiology:
In Italy 300,000 pts are affected by severe asthma and they represent the 10% of pts with bronchial asthma [4].

POSSIBLE PLACE IN THERAPY
In pts with severe asthma inadequately controlled despite inhaled corticosteroids plus medicinal product for maintenance treatment, biological therapies may be prescribed: Anti-IgE (omalizumab), Anti-IL5/anti-IL5R (mepolizumab, reslizumab, benralizumab), Anti-IL4R (dupilumab) [5-6].

OTHER INDICATIONS IN DEVELOPMENT:
Rhinosinusitis [7].

SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: No

OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:
Mepolizumab,
Depemokimab [8].

*Service reorganization: No
*Possible off label use: Yes

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