Medical Release

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New data presented at ATS 2024 show the potential of tezepelumab to play a role in the future treatment of chronic obstructive pulmonary disease

Late-breaking results from the Phase IIa COURSE trial provide insight into tezepelumab's impact on COPD exacerbations in patients with a broad range of eosinophil levels

The Phase IIa COURSE trial was a proof-of-concept study in people with moderate to very severe chronic obstructive pulmonary disease (COPD) with a broad range of blood eosinophil counts (BEC) and irrespective of emphysema, chronic bronchitis or smoking status.[1] The primary results showed that treatment with AstraZeneca and Amgen's *Tezspire* (tezepelumab) led to a 17% numerical reduction in the annual rate of moderate or severe COPD exacerbations compared to placebo at week 52, which was not statistically significant (90% CI (Confidence Interval): -6, 36], p [1-sided]=0.1042).[1] The results are being presented at the American Thoracic Society (ATS) International Conference.

Importantly, in patients with BEC ≥150 cells/µL, tezepelumab led to a nominally significant reduction of 37% in the rate of moderate or severe exacerbations compared to placebo.[1] Studies suggest that approximately 65% of bio-eligible patients with COPD have a BEC greater than or equal to 150 cells/µL.[2] In patients with BEC ≥300 cells/µL tezepelumab led to a numerical reduction of 46% in the rate of moderate or severe exacerbations.[1] (Table 1.)

Dr Dave Singh, Professor of Respiratory Pharmacology at the University of Manchester and lead investigator on the trial, said: "I believe that biologics will play a critical role in the future care of COPD and trials such as the tezepelumab COURSE trial are central to understanding and shaping the treatment landscape. The tezepelumab COURSE results are particularly important as they show activity in COPD across a broad patient population including those with baseline blood eosinophil counts greater than 150 cells/µL."

Sharon Barr, Executive Vice President, BioPharmaceuticals R&D, AstraZeneca, said: "These proof-of-concept results from the COURSE trial are encouraging as they signal the potential efficacy of tezepelumab in a broad range of people with COPD irrespective of emphysema, chronic bronchitis and smoking status. As a result of these promising data, we are actively in Phase III planning for tezepelumab in COPD."

A subgroup analysis of the COURSE trial also showed treatment with tezepelumab resulted in numerical improvements in lung function as measured by forced expiratory volume (FEV1) (improvement of 63mL and 146mL in BEC ≥150 and ≥300 cells/µL respectively, compared to placebo) and in quality of life as measured by the St. George's Respiratory Questionnaire (SGRQ) score (reduction of 4.2 points and 9.5 points in BEC ≥150 and ≥300 cells/µL respectively).[1] The safety and tolerability profile for tezepelumab was consistent with its approved severe asthma indication; the most frequently reported (>10%) adverse events for tezepelumab were worsening of COPD (12.1%) and incidents of COVID-19 infections (14.5%) (this trial commenced in July 2019).[1] (Table 2.)

COURSE Phase IIa analysis:

Table 1: Tezepelumab impact on COPD exacerbations versus placebo over 52 weeks[1]

	Reduction in exacerbations compared to placebo	**Annualised rate of exacerbations**
Moderate or severe exacerbations		
Overall population (n=333)	17% (90% CI: -6, 36)	1.75 in tezepelumab group versus 2.11 in placebo group
BEC less than 150 cells/µL (n=137)	-19% (95% CI: -90, 25)	2.04 in tezepelumab group versus 1.71 in placebo group
BEC greater than or equal to 150 cells/µL (n=196)	37% (95% CI: 7, 57)	1.52 in tezepelumab group versus 2.40 in placebo group
BEC greater than or equal to 300 cells/µL (n=56)	46% (95% CI: -15, 75)	1.20 in tezepelumab group versus 2.24 in placebo group
Severe exacerbations		
Overall population (n=333)	48% (95% CI: -11, 76)	0.13 in tezepelumab group versus 0.25 in placebo group

Table 2: Tezepelumab impact on quality of life and lung function versus placebo over 52 weeks[1]

	Lung function as measured by pre-bronchodilator forced expiratory volume (FEV1, µL)			**Quality of life improvement as measured by St. George's Respiratory Questionnaire (SGRQ) score**		
	Tezepelumab (n)/LS Mean	**Placebo (n)/LS Mean**	**LS mean difference (95% CI)**	**Tezepelumab (n)/LS Mean**	**Placebo (n)/LS Mean**	**LS mean difference (95% CI)**
BEC less than 150 cells/µL	73/-0.002	63/-0.053	0.051 (-0.012,0.114)	69/-1.91	60/-0.30	-1.62 (-6.69, 3.45)
BEC greater than or equal to 150 cells/µL	90/0.049	103/-0.014	0.063 (0.009, 0.116)	88/-7.08	96/-2.85	-4.23 (-8.51, 0.06)
BEC counts greater than or equal to	24/0.160	31/0.013	0.146 (0.044, 0.248)	22/-10.22	27/-0.68	-9.53 (-18.11, -0.96)

300 cells/µL						

Notes

COURSE Phase IIa trial

COURSE was a Phase IIa multicentre, randomised, double-blind, placebo-controlled, parallel group trial designed to evaluate the safety and efficacy of tezepelumab in adults with moderate to very severe chronic obstructive pulmonary disease (COPD) receiving triple inhaled maintenance therapy, and having had two or more documented COPD exacerbations in the 12 months prior to Visit 1. A total of 337 patients were randomised globally, with patients stratified by region and prior number of exacerbations (two vs. three or more). Patients received tezepelumab 420 mg, or placebo, administered via subcutaneous injection at the trial site every four weeks over a 52-week treatment period. The trial included a post-treatment follow-up period of 12 weeks.[1,3]

COPD

COPD refers to a group of lung diseases, including chronic bronchitis and emphysema, that cause airflow blockage and breathing-related problems.[4] COPD is a major public health threat and a leading cause of death.[5,6] It affects an estimated 391 million people around the world with global costs connected to the disease expected to rise to US $4.8 trillion by 2030.[6,7]

COPD is a highly complex disease with multiple pathways and disease drivers.[8] A single COPD exacerbation can increase the risk of hospitalisation and is associated with an increased risk of death.[9-11] Baseline blood eosinophil counts are a key factor in how physicians select optimal treatments for COPD.[4]

Tezepelumab

Tezepelumab is being developed by AstraZeneca in collaboration with Amgen as a first-in-class human monoclonal antibody that inhibits the action of TSLP, 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 associated with severe asthma, including airway hyperresponsiveness.[12,13] TSLP is released by airway epithelium in response to smoke, particles, virus, and other stimuli and may be a key driver of symptoms and severe exacerbations experienced by COPD patients.[13,14] Tezepelumab acts at the top of the inflammation cascade and research indicates that targeting TSLP released by the airway epithelium may be a potential approach to treating diseases of the lower airways in the future.[12,15]

Tezepelumab is approved in the US and the EU for the add-on maintenance treatment of adult and paediatric patients aged 12 years and older with severe asthma.[16-19] In addition to COPD, tezepelumab is also being investigated in Phase III trials, WAYPOINT for chronic rhinosinusitis with nasal polyps (CRSwNP) and CROSSING for eosinophilic esophagitis (EoE,) with results expected later this year. In October 2021, tezepelumab was granted Orphan Drug Designation by the FDA for the treatment of EoE.[20]

Amgen collaboration

In 2020, Amgen and AstraZeneca updated a 2012 collaboration agreement for *Tezspire*. Both companies will continue to share costs and profits equally after payment by AstraZeneca of a mid single-digit inventor royalty to Amgen. AstraZeneca continues to lead development and Amgen continues to lead manufacturing. All aspects of the collaboration are under the oversight of joint governing bodies. Under the amended agreement, Amgen and AstraZeneca will jointly commercialise *Tezspire* in North America. Amgen will record product sales in the US, with AZ recording its share of US profits as Collaboration Revenue. Outside of the US, AstraZeneca will record product sales, with Amgen recording profit share as Other/Collaboration revenue.

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 operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

Contacts

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