SUPPLEMENTARY MATERIAL

Table.

Acronym	Title	Identifier	Phase	Design/Duration	Key inclusion criteria	Dose	Primary endpoint	Countries and sites	Population (n)	Results/variables	Main conclusions	Results in CRSwNP	ACQ-6	Systemic corticosteroids	Other comments
Not available	Effects of an Anti-TSLP Antibody on Allergen-Induced Asthmatic Responses. Randomized, Double-blind, Placebo-controlled, Parallel Design, Multiple Dose Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of AMG 157 in Subjects with Mild Atopic Asthma	Not available	1b	multi-center, randomized, double-blind, placebo-controlled, parallel design, multiple dose study in which a single cohort of subjects with mild atopic asthma (n=30) will be enrolled to receive AMG 157 or placebo. 12 weeks.	Positive skin prick test to common aeroallergens and Will not have an exposure that causes an asthmatic reaction	700 mg AMG 157 or matching placebo on Days 1, 29, and 57. Each subject will be followed for approximately 112 days post-dosing with investigational product.	The primary end point was the late asthmatic response, as measured 3 to 7 hours after the allergen challenge. The primary outcome measures that were used to evaluate the late response were the maximum percentage decrease in FEV1 and the area under the curve (AUC) of the time-adjusted percent decrease in FEV1	1 country (canada 5 sites)	31 non-smoker patients 18-60 years old	Treatment with AMG 157, as compared with placebo, partially attenuated both the late response and the early response at days 42 and 84 in each of the four measures in the allergen. The maximum percentage decrease in the FEV1 during the late response was 34.0% smaller in the AMG-157 group than in the placebo group on day 42 (P=0.09) and 45.9% smaller (a decrease of 11.7% vs. 21.6%) on day 84 (P=0.02).	treatment for 12 weeks with AMG 157 reduced the fraction of exhaled nitric oxide and blood and sputum eosinophils in patients with allergic asthma. This treatment also attenuated allergen-induced changes in these inflammatory measures, as well as the early and late asthmatic responses, and increased the methacholine PC20	Not available	Not available	Not available	Instead of Tezepelumab it was named AMG157
PATHWAY	Tezepelumab in adults with uncontrolled asthma (Corren et al; Emson et al, 2021)	NCT02054130	2	Randomized, placebo controlled, double-blind, multiple dose, evaluate efficacy and safety. 52 weeks.	Severe uncontrolled asthma, history of exacerbations the year prior entry	70 mg or 210 mg SC Q4W or 280 mg SC or placebo Q2W	Annualized Rate of Asthma Exacerbations (AAER) at Week 52	12 countries (108 sites)	550 non-smoker patients 18-75 years old	Reduction of AAER: 62% (low dose), 71% (medium dose), 66% (high dose)	Teze reduced clinically significant asthma exacerbations by 62-71%, independent of baseline Eosinophil counts	CRSNP+: reduction in AAER 75% CRSNP-:73%	Medium dose: -0.29 High dose:-0.31	Non-evaluated	
NAVIGATOR	NAVIGATOR: a phase 3 multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the efficacy and safety of tezepelumab in adults and adolescents with severe, uncontrolled asthma; (Menzies-Gow 2020; Menzies-Gow 2021)	NCT03347279	3	multicenter, randomized, double-blind, placebo-controlled to evaluate safety and efficacy. 52 weeks	asthma remained uncontrolled despite medium or high dose of inhaled glucocorticoids for at leat 12 months and at least one additional controller medication, with or without oral glucocorticoids, for at least 3 months before of the informed consent.	210 mg sc Q4W	Effect on asthma exacerbations at week 52	18 countries (297 sites)	1061 nonsmoker-patients 18-80 years old	lower annualized rate of asthma exacerbations in the group of sc tezepelumab 210 mg/4weeks (0.93) compared with placebo (2.10	Lower annualized rate of asthma exacerbations independent of baseline Eos counts, reduction in ACQ-6 scores, improvement in AQLQ(S)+12 score and	supporting the benefits of tezepelumab in a broad population irrespective of NP status	210 mg sc Q4W: -0.33		Higher effects if ≥300 Eos; FeNO≥25 ppb and positive sensitization to perennial allergens

											reduction in ASD (-0.12)				
SOURCE	multicentre, randomised, double-blind, placebo-controlled study (Weschler et al, 2020; Weschler t al 2022)	NCT03406078	3	multicentre, randomised, double-blind, placebo-controlled study to evaluate efficacy and safety. 48 weeks.	asthma remained uncontrolled despite receiving medium (high dose 3 months before inclusion) or high-dose inhaled corticosteroids and had at least one asthma exacerbation in the 12 months before screening	210 mg sc Q4W	categorised percentage reduction from baseline in daily oral corticosteroid dose at week 48 without the loss of asthma control.	7 countries (60 sites)	150 adult patients 18-80 years old	patients with a 100% reduction from baseline in daily oral corticosteroid dose at week 48: 54% (Teze) vs 46% (placebo); reduction of ≥50% daily oral corticosteroid dose at eek 48:74% (Teze) vs 70% (placebo); daily oral corticosteroid dose≤5mg:72%; significant differences in terms of ACQ-6 and AQLQ(S)+12 scores	not observed a significant improvement in oral corticosteroi d dose reduction with tezepelumab versus placebo in the overall population of this oral corticosteroi d-sparing study, although an improvement was observed in participants with baseline blood eosinophil counts of at least 150 cells per µL.		Significant reduction in ACQ-6 and AQLQ(S)+12 scores	Assessed their reduction. After grouping by baseline eosinophil count, those patients with >150eosinophils/ µL showed greater reductions in oral corticosteroid use.	included an oral corticosteroi d optimisation phase of up to 8 weeks. no significant differences between groups in the percentage reduction in daily oral corticosteroi d dose (OCS
UPSTREAM	The effect of tezepelumab on airway hyperresponsiveness to mannitol in asthma (Sverrild A, et al 2021)	NCT02698501	2	Single study centre (Denmark), double-blind, placebo-controlled randomised trial. 52 weeks.	adult patients with asthma and airway hyperresponsiveness (AHR) to mannitol	700 mg iv Q4W for 12 weeks	change in AHR from baseline to week 12 [change in PD15 (expressed as doubling doses (DD)) to inhaled mannitol from baseline to week 12, supported by the number of subjects who achieved a negative mannitol test (PD15 >635 mg) at week 12]	University Hospital Bispebjerg (Denmark)	40 nonsmoking adults (18–75 years of age) with uncontrolled asthma (ACQ-6 score >1) and AHR to inhaled mannitol baseline (provoking dose of mannitol causing a 15% reduction in FEV1 (PD15) ⩽315 mg) despite any stable doses of ICS. Additional treatment controllers were allowed but OCS, immunosuppresiv e drugs and biologicals (4 months prior to inclusion).	AHR to mannitol improved although not significantly from baseline to week 12 in patients treated with tezepelumab (change in PD15 of 1.9) compared with the placebo group (change in PD15 of 1.0)	a 12 week treatment period with tezepelumab reduced the proportion of patients with AHR compared with placebo, although not statistically significant.		Non significant reduction in ACQ-6 (-1.0 vs 0.5 with placebo). AQLQ improved both in the tezepelumab group and ith placebo (1.0 and 0.7, respectively).	despite any stable doses of ICS. Additional treatment controllers were allowed but OCS, immunosuppresiv e drugs and biologicals (4 months prior to inclusion)	
CASCADE	CASCADE: a phase 2, randomized, double-blind, placebo-controlled, parallelgroup trial to evaluate the effect of tezepelumab on airway inflammation in patients with uncontrolled asthma. Effect of tezepelumab on airway inflammatory cells, remodelling, and hyperresponsiveness in patients with moderate-tosevere uncontrolled asthma (CASCADE): a double-blind, randomised, placebo-controlled, phase 2 trial. (Emson et al. 2020; Diver et al 2021.)	NCT03688074	2	randomized, double-blind, placebo-controlled, parallelgroup trial to evaluate the effect of tezepelumab on airway inflammation, cells, remodelling and	adult patients with moderate-to-severe asthma whose received subcutaneous (sc) 210 mg tezepelumab or placebo (sc) every 4 weeks for 28 weeks who underwent	210 mg or placebo (sc) Q4W for 28 weeks	was the change in the number of airway submucosal inflammatory cells in bronchoscopi c biopsy samples from	5 countries (17 sites)	116 adult patients (18-75 years of age) Patients must have been receiving medium-dose or high-dose inhaled corticosteroids plus at least one	significant reduction from baseline to the end of treatment in airway submucosal eosinophils versus placebo in the active group. Reduction in AHR	tezepelumab achieved a significant reduction of eosinophils in the submucosa versus placebo, across blood		Non significant reduction in ACQ-6 in Tezelepumab group (1.10) vs placebo (0.66). AQLQ not assessed	with or without maintenance oral corticosteroids, for 3 months or longer at screening	extended to 52 weeks in the case of COVID-19-related disruption. AHR as exploratory endpoint

				hyperresponsiveness . 28 weeks.	bronchoscopy with transbronchial biopsy		baseline to week 28.		additional asthma controller medication	to mannitol was significantly greater in the tezepelumab (difference of 138.8 mg of mmanitoldose compared with placebo)	eosinophil count subclasses, despite low mean submucosal eosinophil counts at baseline				
PATHHOME	Functionality and performance of an accessorized pre-filled syringe and an autoinjector for at-home administration of tezepelumab in patients with severe, uncontrolled asthma (Alpizar et al)	NCT03968978	3	open-label, parallel-group, randomised trial,	6 subcutaneous doses of tezepelumab via pre-filled siringe (APFS) or an autoinjector (AI), being the first dose administered by a HCP. First, second, third (weeks 0, 4 and 8) and final doses were administered in the clinic (week 20) (Alpizar S et al 2021). The fourth and 5th doses; week 12 and 16, were administered at home. The study comprised a 2-week screening period, a 24-week treatment period and a 12-week follow-up period	210 mg sc	to evaluate the success of administration of tezepelumab 210 mg (sc) with an APFS or AI in the clinic and at home by HCP and patients or caregivers.		216 non-smoker patients (12-80 years old)	A 91.7% of HCPs, patients or caregivers successfully administered tezepelumab via APFS. Similarly tezepelumab was successfully administered by 92.4% via autoinjector. At weeks 12 and 16, at-home administration of tezepelumab was succesful in 95.4% of the patients/caregivers in the APFS group. With regards the AI device, 97.1% of the patients or caregivers administered it successfully at home.	exposure to tezepelumab after at-home self administration using an APFS or AI is sufficient to obtain the clinical benefit		Clinically meaningful improvements in ACQ-6 score were observed after 24 weeks in 81.1% and 76.2% of the patients in the APFS and AI groups, respectively.	Non-evaluated	
DESTINATION	DESTINATION: a phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group trial to evaluate the long-term safety and tolerability of tezepelumab in adults and adolescents with severe, uncontrolled asthma.. DESTINATION study investigators. Long-term safety and efficacy of tezepelumab in people with severe, uncontrolled asthma (DESTINATION): a randomised, placebo-controlled extension study. Menzies-Gow et al, 2020; Menzies-Gow et al; 2023	NCT03706079	3	Patients who completed either the NAVIGATOR or SOURCE studies were elegible and the aim was to assess the long term (1 year) tolerability and safety of tezepelumab compared with placebo. Therefore, out of 1061 previously randomized patients of the NAVIGATOR study, 570 entered extended follow-up (DESTINATION study) and out of 150 randomized from the SOURCE study, 109 completed the extended follow-up (DESTINATION study).	severe uncontrolled asthma who are receiving medium or high-dose of inhaled corticosteroids plus at least one additional controller medication with or wothout oral corticosteroids.	210 mg every 4 weeks (Q4W)	exposure-adjusted incidence of adverse events and serious adverse events.	18 countries (182 sites)	18 countries (182 sites) in adolescents (12-17 years old) and adults (18-80 years old). out of 1061 previously randomized patients of the NAVIGATOR study, 570 entered extended follow-up (DESTINATION study) and out of 150 randomized from the SOURCE study, 109 completed the extended follow-up (DESTINATION study).	AAER tezepelumab reduced them over 104 weeks compared with placebo, both in patients initially participating in NAVIGATOR study (0.42; 95% CI 0.35 to 0.51) and in SOURCE study (0.61; 95% CI 0.38 to 0.96). In patients from NAVIGATOR study, asthma exacerbation rate over 104 weeks in the randomised tezepelumab group was 0.82 (95% CI 0.71–0.95) compared with 1.93 (1.70–2.20) in the	In participants initially from NAVIGATOR, the annualised asthma exacerbation rate was consistently lower in the randomised tezepelumab group than in the randomised placebo group, irrespective of baseline inflammatory biomarkers and other clinical characteristics over 104 weeks. In		ACQ-6, St George's Respiratory Questionnaire score (SGRQ)	With or without oral corticosteroids	the first long-term extensión study of a biologic treament for severe asthma to include a placebo arm

				104 weeks.						randomised placebo group (rate ratio 0.42, 95% CI 0.35–0.51). Similarly, in patients from SOURCE, the AAER over 104 weeks in the randomised tezepelumab group was 1.07 (0.76–1.51) compared with 1.76 (1.27–2.45) in the randomised placebo group (rate ratio 0.61, 0.38–0.96).	general, reductions in exacerbations were seen independently of baseline clinical characteristics and biomarkers, however, there were greater reductions in patients with high levels of type 2 inflammatory biomarkers or with nasal polyps.				
SUNRISE (not closed)	Tezepelumab Efficacy and Safety in Reducing Oral Corticosteroid Use in Adults With Oral Corticosteroid Dependent Asthma (SUNRISE): Link: https://clinicaltrials.gov/ct2/show/NCT05398263	NCT05398263	3	Randomised, Double-Blind, Parallel-Group, Placebo-Controlled 28-week Phase 3 Efficacy and Safety Study of Tezepelumab in Reducing Oral Corticosteroid Use in Adults With Oral Corticosteroid Dependent Asthma. 28 weeks.	Participant must be 18 to 80 years of age, with documented physician-diagnosed asthma for at least 12 months prior to Visit 1, and a physician-prescribed medium- or high-dose ICS for at least 12 months prior to Visit 1. Moreover, participants must have received physician prescribed LABA and high dose ICS for at least 3 months prior to Visit 1. Additional maintenance asthma controller medications are allowed. Interestingly, participants must have received OCS for the treatment of asthma for at least 6 months prior to Visit 1 and on a stable dose of between ≥7.5 to ≤ 30 mg (prednisone or prednisolone) daily or daily equivalent for at least 1 month prior to Visit 1. Morning pre-bronchodilator (BD) FEV1 must be < 80% predicted normal at Visit 1 or Visit 2	Not specified	Categorised percent reduction from baseline in the daily maintenance OCS dose at Week 28 whilst maintaining asthma control. [Time Frame: Baseline to Week 28] Categorized percent reduction from baseline at Week 28. Percent change from baseline is defined as {final dose-baseline dose)/baseline dose}*100%, and the categories of percent change from baseline in daily OCS dose are defined as: ≥90% to ≤100% reduction, ≥75% to <90% reduction,	207 participants (82 sites)	18 to 80 years of age,	Not available	Not available	Not available	Not available	As secondary variable: Proportion of subjects with 100% reduction from baseline in daily OCS dose at Week 28. Proportion of subjects with ≥50% reduction from baseline in daily OCS dose at Week 28.	Expected to complete: june 2025

							≥50% to <75% reduction, >0% to <50% reduction, and, no change or any increase.								
PASSAGE	Effectiveness and Safety Study of Tezepelumab in Adults & Adolescent Participants With Severe Asthma in the United States (PASSAGE): Link: https://www.clinicaltrials.gov/ct2/show/NCT05329194	NCT05329194	4	Multicenter, Single-arm, Open-label, Post-Authorization, Phase 4 Effectiveness and Safety Study of Tezepelumab (210 mg of Tezepelumab every 4 weeks during 48 weeks) in Adult and Adolescent Participants With Severe Asthma Including Several Under-Studied Populations in the United States. 56 weeks	a real-world population of adults and adolescent participants with asthma requiring medium-dose to high-dose inhaled corticosteroids (ICS), with additional controller(s) for at least 12 months with documented history of at least 2 asthma exacerbations during the year prior to enrolment. The total duration of the study for each participant will be approximately 56 weeks	210 mg Q4W sc		400 participants expected	≥12 years old	Not available	Not available	Not available	Not availabe	Not available	Expected to complete: july 2025
DIRECTION	Study to Evaluate Tezepelumab in Adults With Severe Uncontrolled Asthma	NCT03927157	3	A Regional, Multicentre, Randomized, Double-Blind, Placebo Controlled, Parallel Group., 52 week period.	adults with severe, uncontrolled asthma on medium to high-dose ICS and at least one additional asthma controller medication with or without OCS. Inclusion Criteria: Age. 18-80 Documented physician-diagnosed asthma for at least 12 months Participants who have received a physician-prescribed asthma controller medication with medium or high dose ICS for at least 6 months. Documented treatment with a total daily dose of either medium or high dose ICS (≥ 500 µg fluticasone propionate dry powder formulation equivalent total daily dose) for at least 3 months.	210 mg Q4W (SC)	Annualized asthma exacerbation rate (AERR) [Time Frame: Randomization to Week 52] The annualized exacerbation rate is based on exacerbations reported by the investigator in the eCRF over 52 weeks.	396 participants expected in 71 centers (China and outside China)	18-80 years old	Not available	Not available	Not available	Not available	With or without	Expected to complete: august 2024

					At least one additional maintenance asthma controller medication is required according to standard practice of care and must be documented for at least 3 months. Morning pre-BD FEV1 <80% predicted normal Evidence of asthma as documented by either: Documented historical reversibility of FEV1 ≥12% and ≥200 mL in the previous 12 months OR Post-BD (albuterol/salbutamol) reversibility of FEV1 ≥12% and ≥200 mL during screening. Documented history of at least 2 asthma exacerbation events within 12 months, and at least one of the exacerbations should occur during the treatment of medium-to-high dose ICS. ACQ-6 score ≥1.5 at screening and on day of randomization									
WAYFINDER	to evaluate efficacy and safety of Tezepelumab in reducing oral corticosteroid use in adult patients with severe asthma who are receiving oral corticosteroids with or without additional asthma controller medications.	NCT05274815	3b	A Multicentre, Single-arm, Phase 3b Efficacy and Safety Study of Tezepelumab 210 mg Administered Subcutaneously to Reduce Oral Corticosteroid Use in Adult Participants With Severe Asthma on High-dose Inhaled Corticosteroid Plus Long-acting β2 Agonist and Long-term Oral Corticosteroid Therapy	Documented long-term OCS therapy for asthma, equivalent to a daily dose of at least 5 mg and up to 40 mg of prednisone/prednisolone for at least 3 continuous months directly preceding Visit 1. Participant should be on a stable maintenance OCS dose for at least 4 weeks prior to Visit 1.	210 mg sc	Proportion of participants who discontinued OCS without loss of asthma control (week 28 and 52) Proportion of participants who reduced daily prescribed maintenance OCS dose to ≤ 5 mg/day without loss of asthma control (week 28 and 52)	89 locations	18-80 years old	Not available	Not available	Not available	ACQ-6, St George's Respiratory Questionnaire score (SGRQ) and AQLQ Will be asssessed at week 28 and 52	Categorised percent reduction from baseline in the daily maintenance OCS dose at week 28 and 52	Expected to complete: July 12 2024