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VALIANT: a phase 2 trial of the efficacy and safety of verekitug, a thymic stromal lymphopoietin (TSLP) receptor antagonist, for severe asthma

Michael E. Wechsler,[1] Ian Pavord,[2] Grazyna Pulka,[3] Shahrukh Kureishy,[4] Dimo Dimov,[5] Ahmed A. Arif,[6] Todor A. Popov,[7] Dinesh Saralaya,[8] James Lee,[9]* Sumathi Sivapalasingam,[9] Ashish Kalra,[9] Arkadeep Sinha,[9] Fang Xie,[9] Rui Zhang,[9] Aaron Deykin[9]

[1]National Jewish Health, Denver, CO, USA; [2]University of Oxford, Oxford, UK; [3]Centrum Medyczne ALL-MED-Badania Kliniczne, Kraków, Poland; [4]Metroplex Pulmonary and Sleep Center, McKinney, TX, USA; [5]Trakia University, Medical Faculty, Stara Zagora, Bulgaria; [6]AA Medical Research Center, Flint, MI, USA; [7]Medical Center Excelsior, Sofia, Bulgaria; [8]NIHR CRDC Bradford & West Yorkshire, Bradford UK; [9]Upstream Bio, Inc., Waltham, MA, USA
*At the time of the study

Conflict of interest disclosure
Presenter: Michael E. Wechsler

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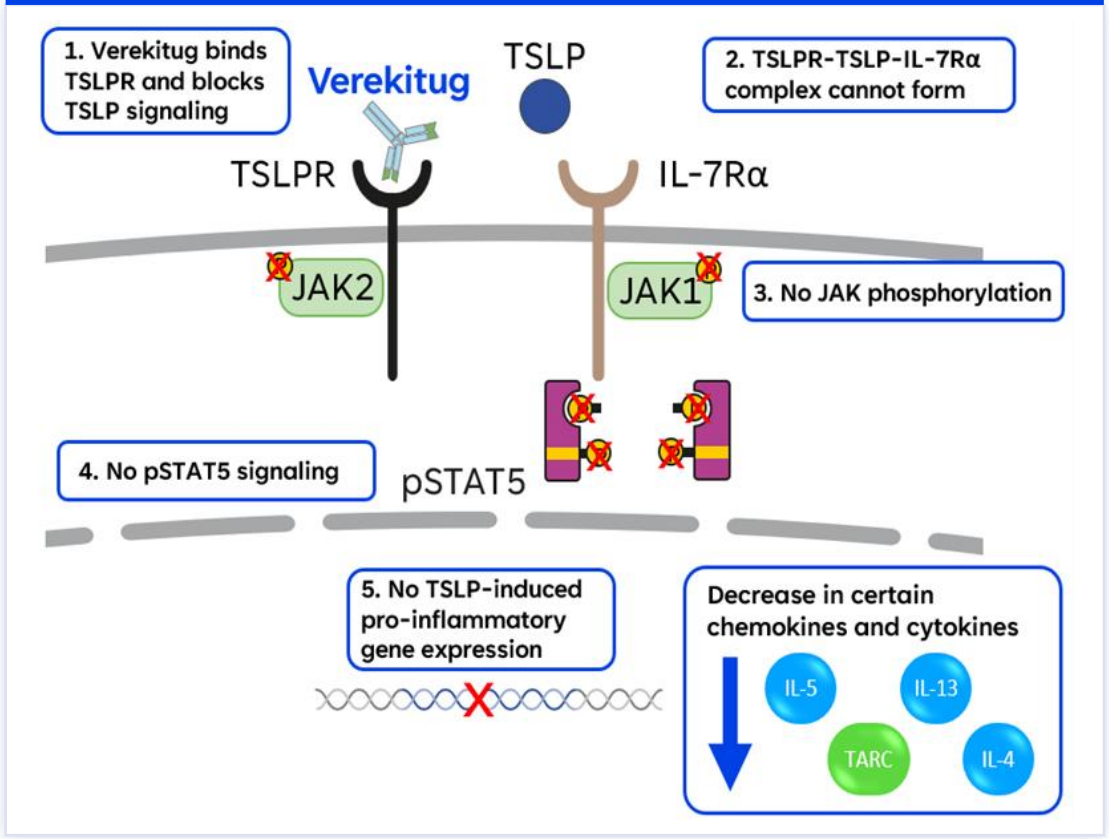
Introduction

- Verekitug is a novel, unmodified, fully human monoclonal antibody antagonist to the receptor for TSLP, and the only known TSLP receptor antagonist antibody in clinical development[1–6]
- Low circulating verekitug concentrations are sufficient to saturate TSLP receptors and abrogate TSLP signaling, thus enabling extended dosing intervals[2–4]
- The phase 2 VIBRANT trial demonstrated statistically significant and durable reductions in nasal polyp score and symptom burden in patients with CRSwNP[5]
- We report results of VALIANT, a phase 2, randomized, placebo-controlled, dose-ranging trial evaluating the efficacy and safety of verekitug in adults with uncontrolled, severe asthma

Verekitug mechanism of action[1,3,7]



CRSwNP, chronic rhinosinusitis with nasal polyps; IL, interleukin; JAK, Janus kinase; pSTAT5; phosphorylated signal transducer and activator of transcription 5; TARC, thymus and activation-regulated cytokine; TSLP, thymic stromal lymphopoietin; TSLPR, TSLP receptor.

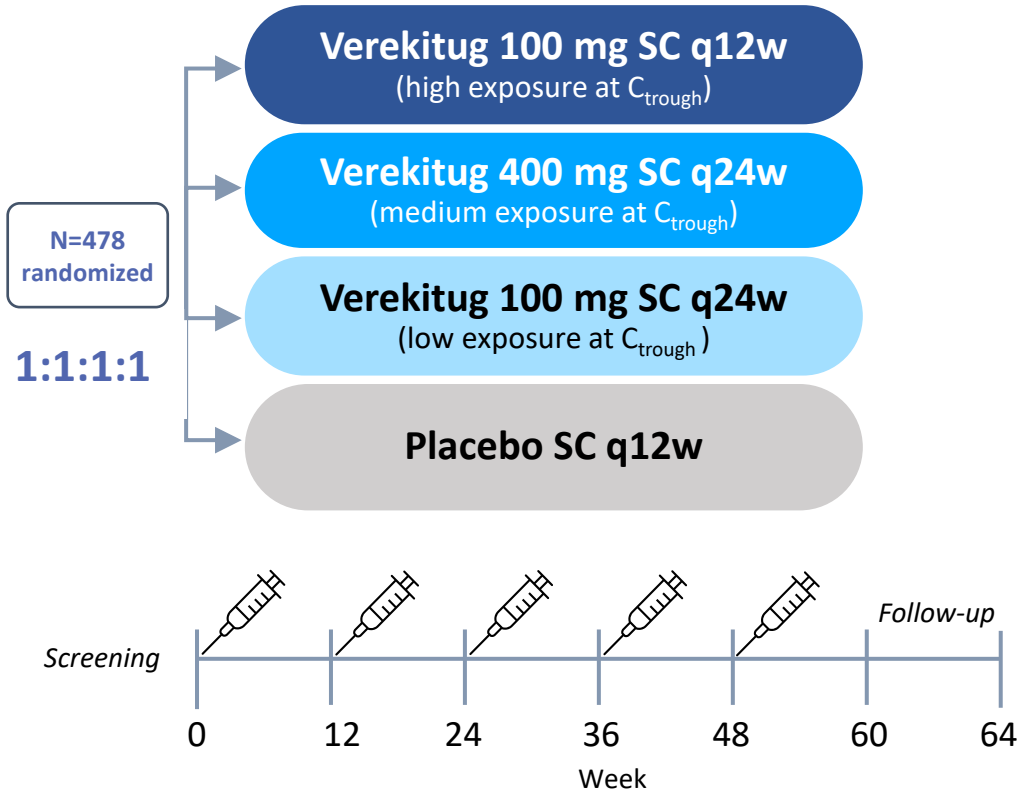
1. Numazaki M, et al. *J Pharmacol Exp Ther*. 2022;380:26–33. 2. Kalra A, et al. Presented at the EAACI Congress 2025, June 13–16; Glasgow, Scotland. 3. Chowdhury F, et al. Presented at the ERS 2025 Congress; September 27–October 1; Amsterdam, the Netherlands. 4. Singh D, et al. *Clin Pharmacol Ther*. 2026;119:782–790. 5. Han J, et al. *J Allergy Clin Immunol*. 2026;157:AB432. 6. Deykin A, et al. *Am J Respir Crit Care Med*. 2023;207:A3013. 7. Verstraete K, et al. *Nat Commun*. 2017;8:14937.

Study design

Multicenter, randomized, placebo-controlled phase 2 trial with up to 60-week treatment period (NCT06196879)

Key inclusion criteria

- Aged 18–80 years
- Physician-diagnosed asthma for at least 12 months
- Pre-BD FEV_1 ≥ 30% and ≤ 80% predicted with evidence of BD reversibility
- Treatment with medium/high-dose ICS ≥ 3 months
- Documented history of asthma exacerbation(s) in past 12 months as defined by any of
  - ≥ 2 events req. SCS
  - ≥ 1 event req. inpatient care ≥ 24 hours
  - ≥ 1 event req. SCS + FeNO ≥ 50 ppb
- ACQ-6 ≥ 1.5



Variable treatment period design:

Min 24 weeks, max 60 weeks

Primary endpoint

- Annualized asthma exacerbation rate (AAER) from baseline up to week 60
- 90% power to detect ≥ 50% reduction vs PBO

Key secondary endpoints

(study not powered for secondary endpoints)

- Change from baseline to week 60; including a prespecified change to week 24 analysis
  - Pre-BD FEV_1
  - FeNO
  - ACQ-6

ACQ-6, Asthma Control Questionnaire; BD, bronchodilator; FeNO, fractional exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; ppb, parts per billion; q×w, every × weeks; SC, subcutaneous; SCS, systemic corticosteroids.

Baseline characteristics generally balanced across arms

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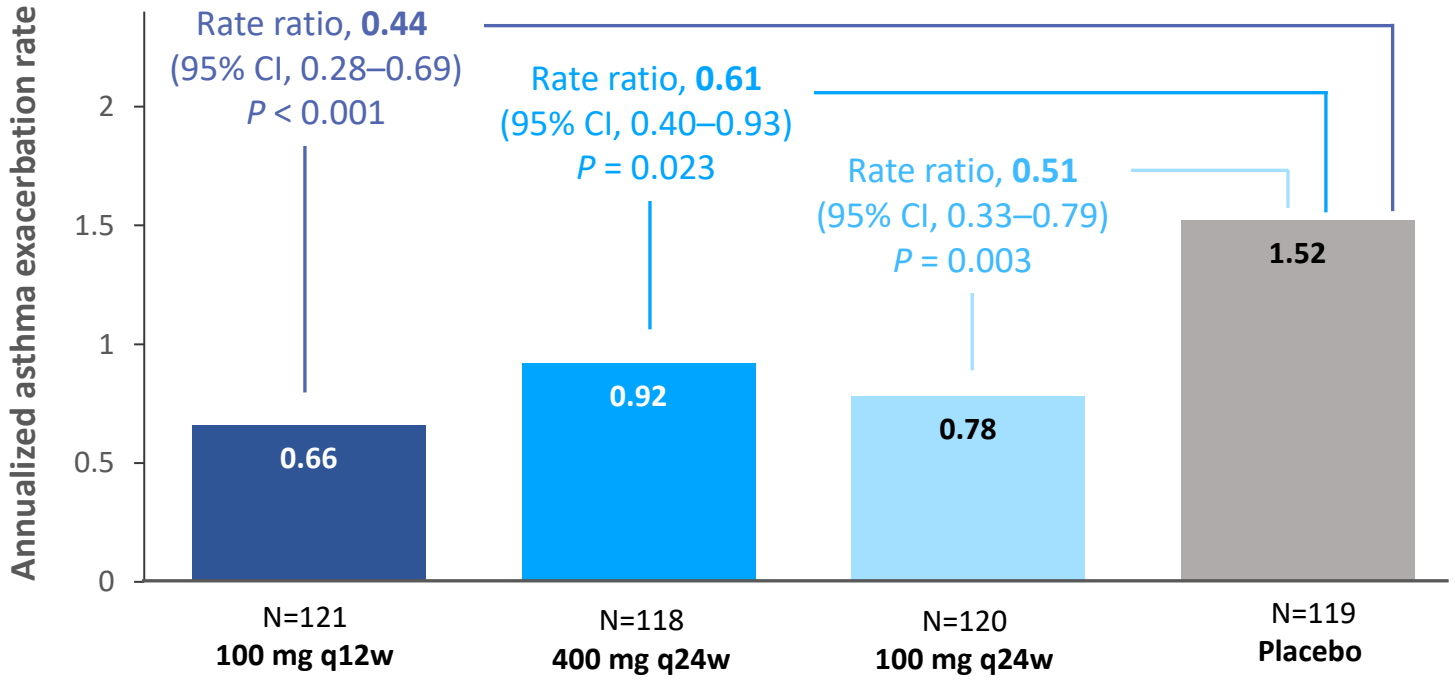
		Verekitug 100 mg q12w N=121	Verekitug 400 mg q24w N=118	Verekitug 100 mg q24w N=120	Placebo N=119
Age, mean (SD), years		54.6 (12.2)	53.8 (11.7)	51.7 (15.4)	54.0 (13.1)
Race, n (%)	White	91 (75.2)	90 (76.3)	90 (75.0)	93 (78.2)
	Black/African American	13 (10.7)	12 (10.2)	15 (12.5)	8 (6.7)
	Other	17 (14.1)	16 (13.6)	15 (12.5)	18 (15.1)
Region, n (%)	North America	32 (26.4)	29 (24.6)	33 (27.5)	38 (31.9)
	Western Europe	17 (14.0)	13 (11.0)	15 (12.5)	19 (16.0)
	Central/Eastern Europe	35 (28.9)	38 (32.2)	41 (34.2)	33 (27.7)
	Rest of the world[a]	37 (30.6)	38 (32.2)	31 (25.8)	29 (24.4)
Dose of inhaled glucocorticoids, n (%)	Medium	63 (52.1)	62 (52.5)	59 (49.2)	61 (51.3)
	High[b]	58 (47.9)	56 (47.5)	61 (50.8)	58 (48.7)
Historical asthma exacerbations, n (%)	≥2 ER visits + SCS ≥3 days	99 (81.8)	96 (81.4)	96 (80.0)	100 (84.0)
	≥1 hospitalization	14 (11.6)	16 (13.6)	20 (16.7)	11 (9.2)
Asthma duration, mean (SD), years		27.2 (17.0)	22.0 (17.0)	24.2 (15.3)	26.8 (17.6)
Prebronchodilator FEV_1, mean (SD), mL		1802 (620)	1831 (590)	1878 (623)	1873 (644)
Baseline FeNO, mean (SD), ppb		41.9 (44.8)	39.3 (46.5)	32.7 (28.8)	37.9 (37.2)
Baseline ACQ-6 score, mean (SD)		2.72 (0.66)	2.54 (0.57)	2.67 (0.67)	2.65 (0.67)
Blood eosinophil count, cells/µL	Median (min–max)	290 (30–1850)	270 (30–3090)	260 (30–2720)	250 (30-2090)

[a]Includes Latin America, Asia-Pacific, and South Africa. [b]Medium-dose ICS without oral corticosteroid; high-dose ICS and/or oral corticosteroids.
ACQ-6, Asthma Control Questionnaire; ER, emergency room; FeNO, fractionated exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; ppb, parts per billion; q×w, every × weeks; SCS, systemic corticosteroids; SD, standard deviation.

Primary endpoint: asthma exacerbations were significantly reduced with verekitug



Median follow-up (IQR), weeks	**37.1** (28.1–51.6)	**36.6** (28.1–51.1)	**36.4** (28.9–49.1)	**36.6** (28.3–51.1)

AAER, rate ratios, 95% CIs, and *P* values are from a negative binomial regression model with number of asthma exacerbations as the dependent variable and fixed effects for study treatment, region, and baseline steroid use as randomized, and baseline eosinophil level as randomized. AAER, annual asthma exacerbation rate; IQR, interquartile range; q×w, every × weeks.

Verekitug led to meaningful improvements in secondary endpoints at week 24 that were generally sustained to week 60

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	Endpoint	Verekitug 100 mg q12w N=121	Verekitug 400 mg q24w N=118	Verekitug 100 mg q24w N=120
Change from baseline to week 24	**Pre-BD FEV_1** LSM difference vs placebo (95% CI), mL Nominal *P* value	N=108 **99** (9–189) 0.0317	N=108 **157** (67–248) 0.0007	N=105 **47** (−44 to 137) 0.3102
	ACQ-6 LSM difference vs placebo (95% CI) Nominal *P* value	N=114 **−0.21** (−0.43 to 0.01) 0.0651	N=111 **−0.34** (−0.57 to −0.12) 0.0027	N=112 **−0.23** (−0.45 to −0.01) 0.0447
	FeNO LSM difference vs placebo (95% CI), ppb Nominal *P* value	N=113 **−13.7** (−18.6 to −8.8) < 0.0001	N=109 **−12.2** (−17.2 to −7.3) < 0.0001	N=111 **−7.5** (−12.4 to −2.6) 0.0028
Change from baseline to week 60	**Pre-BD FEV_1** LSM difference vs placebo (95% CI), mL Nominal *P* value	N=19 **150** (−45 to 346) 0.1309	N=18 **140** (−59 to 339) 0.1674	N=17 **85** (−116 to 287) 0.4057
	ACQ-6 LSM difference vs placebo (95% CI) Nominal *P* value	N=19 **0.06** (−0.42 to 0.55) 0.8000	N=19 **−0.21** (−0.70 to 0.28) 0.3928	N=17 **−0.24** (−0.74 to 0.26) 0.3541
	FeNO LSM difference vs placebo (95% CI), ppb Nominal *P* value	N=19 **−20.4** (−31.5 to −9.4) 0.0003	N=18 **−26.3** (−37.6 to −15.0) < 0.0001	N=17 **−17.0** (−28.4 to −5.6) 0.0036

Verekitug improvements were observed as early as week 2 across secondary outcomes

ACQ-6, Asthma Control Questionnaire; BD, bronchodilator; FeNO, fractionated exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; LSM, least squares mean; ppb, parts per billion; q×w, every × weeks.

Subgroup analysis demonstrated an 87% AAER reduction among high BECs and robust FEV_1 improvement across most subgroups (100 mg q12w vs placebo)

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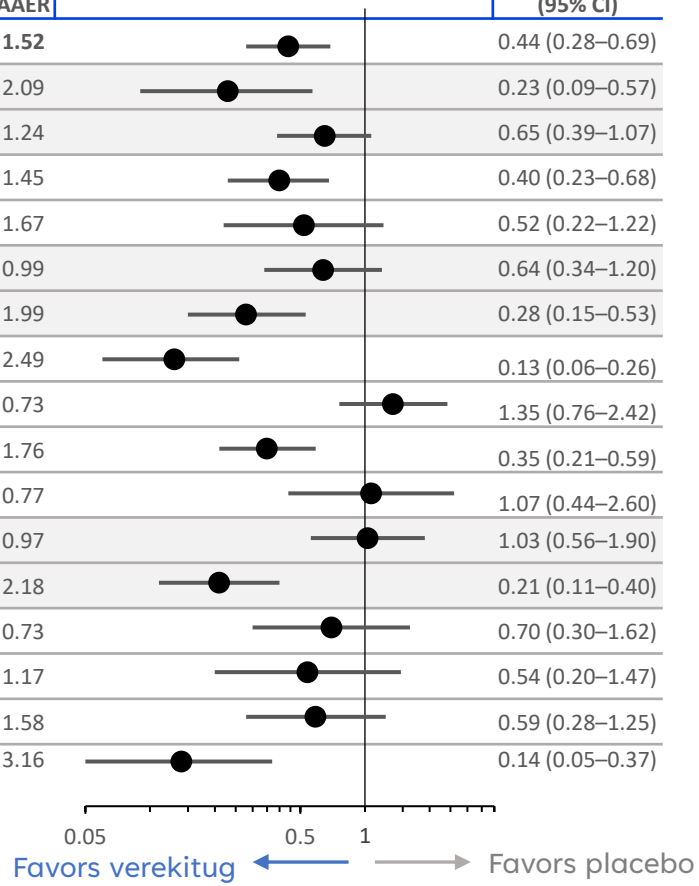
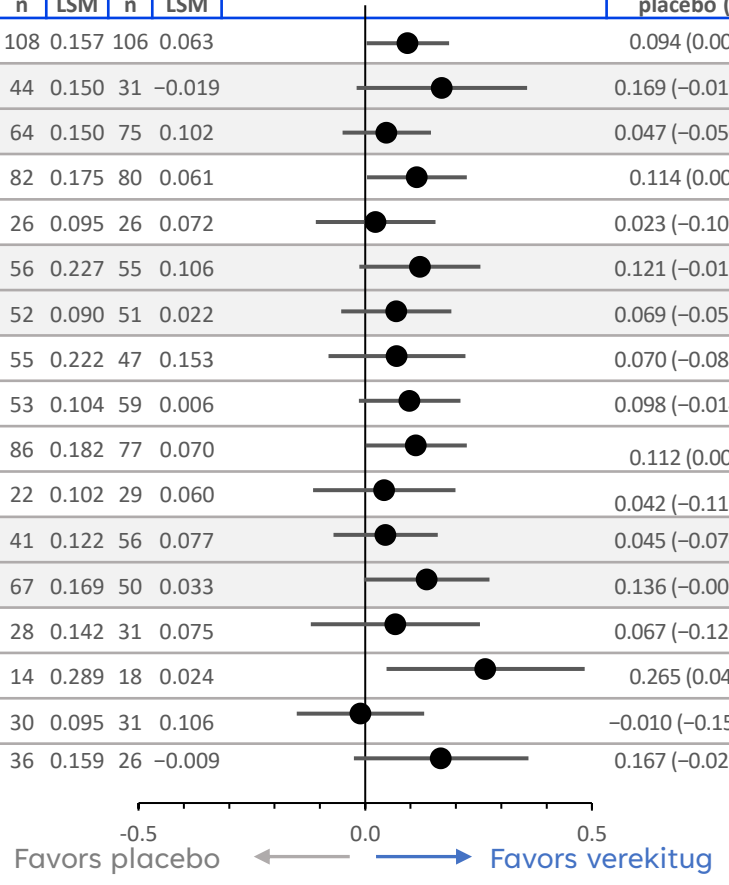
AAER by subgroup

Subgroups		Verekitug n	Verekitug AAER	Placebo n	Placebo AAER	Rate ratio (95% CI)
Overall		**121**	**0.66**	**119**	**1.52**	0.44 (0.28–0.69)
Sex	Male	48	0.47	38	2.09	0.23 (0.09–0.57)
	Female	73	0.80	81	1.24	0.65 (0.39–1.07)
Age, years	< 65	91	0.58	91	1.45	0.40 (0.23–0.68)
	≥ 65	30	0.87	28	1.67	0.52 (0.22–1.22)
Steroid use and dose[a]	Medium ICS	63	0.63	61	0.99	0.64 (0.34–1.20)
	High ICS or OCS	58	0.55	58	1.99	0.28 (0.15–0.53)
Blood eosinophil level, cells/µL	≥ 300	59	0.31	51	2.49	0.13 (0.06–0.26)
	< 300	62	0.98	68	0.73	1.35 (0.76–2.42)
	≥ 150	97	0.62	84	1.76	0.35 (0.21–0.59)
	< 150	24	0.82	35	0.77	1.07 (0.44–2.60)
FeNO at baseline, ppb	< 25	48	0.99	63	0.97	1.03 (0.56–1.90)
	≥ 25	73	0.45	56	2.18	0.21 (0.11–0.40)
Region	North America	32	0.51	38	0.73	0.70 (0.30–1.62)
	Western Europe	17	0.63	19	1.17	0.54 (0.20–1.47)
	C/E Europe	35	0.93	33	1.58	0.59 (0.28–1.25)
	APAC/LATAM/ S. Africa	37	0.44	29	3.16	0.14 (0.05–0.37)



FEV_1 at week 24 by subgroup

Subgroups		Verekitug n	Verekitug LSM	Placebo n	Placebo LSM	LSM difference vs placebo (95% CI)
Overall		108	0.157	106	0.063	0.094 (0.003–0.185)
Sex	Male	44	0.150	31	−0.019	0.169 (−0.019 to 0.357)
	Female	64	0.150	75	0.102	0.047 (−0.050 to 0.145)
Age, years	< 65	82	0.175	80	0.061	0.114 (0.004–0.224)
	≥ 65	26	0.095	26	0.072	0.023 (−0.109 to 0.155)
Steroid use and dose[a]	Medium ICS	56	0.227	55	0.106	0.121 (−0.013 to 0.254)
	High ICS or OCS	52	0.090	51	0.022	0.069 (−0.053 to 0.190)
Blood eosinophil level, cells/µL	≥ 300	55	0.222	47	0.153	0.070 (−0.081 to 0.221)
	< 300	53	0.104	59	0.006	0.098 (−0.014 to 0.210)
	≥ 150	86	0.182	77	0.070	0.112 (0.001–0.224)
	< 150	22	0.102	29	0.060	0.042 (−0.115 to 0.199)
FeNO at baseline, ppb	< 25	41	0.122	56	0.077	0.045 (−0.070 to 0.160)
	≥ 25	67	0.169	50	0.033	0.136 (−0.003 to 0.274)
Region	North America	28	0.142	31	0.075	0.067 (−0.120 to 0.253)
	Western Europe	14	0.289	18	0.024	0.265 (0.047–0.484)
	C/E Europe	30	0.095	31	0.106	−0.010 (−0.151 to 0.130)
	APAC/LATAM/ S. Africa	36	0.159	26	−0.009	0.167 (−0.025 to 0.360)



[a]Medium-dose ICS without oral corticosteroid vs high-dose ICS and/or oral corticosteroids. AAER, annual asthma exacerbation rate; APAC, Asia-Pacific; BEC, blood eosinophil count; C/E, central/eastern; FeNO, fractionated exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second; ICS, inhaled corticosteroid; LATAM, Latin America; LSM, least squares mean; OCS, oral corticosteroids; ppb, parts per billion; q×w, every × weeks.

Verekitug was well tolerated, with a similar safety profile to placebo

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	Verekitug 100 mg q12w N=121	Verekitug 400 mg q24w N=118	Verekitug 100 mg q24w N=119	Placebo N=119
Any TEAE	75 (62.0)	69 (58.5)	74 (62.2)	78 (65.5)
TEAE related to study treatment[a]	10 (8.3)	4 (3.4)	9 (7.6)	8 (6.7)
Any serious TEAEs	5 (4.1)	8 (6.8)	6 (5.0)	10 (8.4)
Any serious TEAEs related to study treatment[a]	0	1 (0.8)	0	0
TEAEs with outcome of death	0	0	0	0
Grade ≥ 3 TEAEs	8 (6.6)	13 (11.0)	10 (8.4)	10 (8.4)
TEAEs leading to study drug discontinuation/interruption	4 (3.3)	1 (0.8)	4 (3.4)	2 (1.7)
TEAEs of special interest[b]	2 (1.7)	0	1 (0.8)	2 (1.7)
Most common TEAEs (≥ 5% in any group)[c]				
Nasopharyngitis	13 (10.7)	9 (7.6)	9 (7.6)	12 (10.1)
Urinary tract infections	7 (5.8)	7 (5.9)	6 (5.0)	6 (5.0)
Headache	8 (6.6)	3 (2.5)	8 (6.7)	6 (5.0)
Bronchitis	9 (7.4)	8 (6.8)	2 (1.7)	3 (2.5)
Upper respiratory tract infection	3 (2.5)	5 (4.2)	6 (5.0)	7 (5.9)
Influenza	4 (3.3)	3 (2.5)	5 (4.2)	8 (6.7)
Asthma	3 (2.5)	3 (2.5)	6 (5.0)	7 (5.9)
Back pain	6 (5.0)	3 (2.5)	2 (1.7)	4 (3.4)

Most common TEAEs

- Nasopharyngitis
- Urinary tract infections
- Headache
- Bronchitis

Injections site reactions

- Similar across active groups and placebo
- Mild severity
- No grade 3 or greater

Antidrug antibodies were detected in 50%–60% of participants and had no impact on safety findings, pharmacodynamics, or efficacy

[a]Adverse events assessed by the investigator as related to study treatment or adverse events with missing relationship to study treatment. [b]Adverse events associated with the drug class. [c]Adverse events were coded according to the preferred terms of the Medical Dictionary for Regulatory Activities, version 28.0. q×w, every × weeks; TEAE, treatment-emergent adverse event.

Conclusions

- Verekitug every 12 or 24 weeks led to statistically significant, clinically meaningful reductions in asthma exacerbations
- Verekitug improved secondary outcomes of FEV_1, ACQ-6, and FeNO, with improvements observed as early as week 2 in all regimens
- AAER reductions were up to 87% and up to 65% among participants with BECs ≥ 300 cells/µL and ≥ 150 cells/µL, respectively
  - While improvements in FEV_1 were observed in participants with lower BECs, no reductions in AAER were observed in this subgroup
- Verekitug was well tolerated, with a safety profile comparable to placebo, and no new safety concerns identified
- A phase 3 trial is planned to confirm the efficacy and safety of verekitug

Verekitug, administered at extended dosing intervals of every 12 or 24 weeks, has the potential to improve outcomes in patients with severe asthma

AAER, annual asthma exacerbation rate; ACQ-6, Asthma Control Questionnaire; BEC, blood eosinophil count; FeNO, fractionated exhaled nitric oxide; FEV_1, forced expiratory volume in 1 second.

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