Poster L60

Efficacy and safety of verekitug, an anti-TSLP receptor antibody, in chronic rhinosinusitis with nasal polyps: results of the phase 2 VIBRANT trial

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KEY FINDINGS

Verekitug, a novel, high-affinity, fully human monoclonal antibody targeting the thymic stromal lymphopoietin receptor (TSLPR), when dosed every 12 weeks in participants with inadequately controlled chronic rhinosinusitis with nasal polyps (CRSwNP), led to significant improvements in nasal polyp size, sinonasal symptoms, and need for nasal polyp surgery or systemic corticosteroids at week 24

Verekitug was well tolerated with no serious adverse events

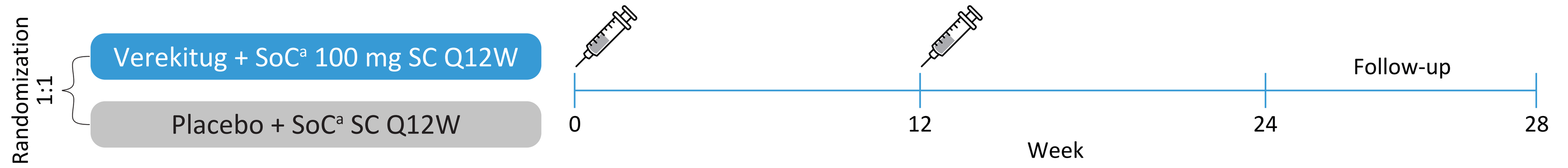
RATIONALE

- CRSwNP, a disorder characterized by sinonasal inflammation, loss of smell, and polyp formation, is associated with a reduced quality of life[1–3]
- The thymic stromal lymphopoietin (TSLP) signaling pathway functions to initiate a type 2 inflammatory response, and has emerged as a key driver of immune activation underlying CRSwNP morbidity[2]
- Verekitug (previously UPB-101 and ASP7266) is an investigational, novel, highly potent, fully human monoclonal antibody targeting the TSLPR[4]
  - Preclinically, verekitug demonstrated superior potency at suppressing TSLP-driven responses relative to tezepelumab, an anti-TSLP antibody[4]
  - In a phase 1 study in participants with asthma, verekitug led to sustained reductions in blood eosinophil levels and fractional exhaled nitric oxide up to 24 weeks[5]
- Here, we present data from a phase 2 trial assessing the safety and efficacy of verekitug in participants with severe, inadequately controlled CRSwNP[6]

METHODS

- VIBRANT (NCT06164704) is a double-blind, randomized phase 2 trial assessing the efficacy and safety of standard of care with either 100 mg subcutaneous verekitug or matching placebo every 12 weeks for 24 weeks (**Figure 1**)[6]

Figure 1. Study design



Key inclusion criteria
Aged 18–85 years
History of NP surgery or NP exacerbation requiring SCS in the past 24 months
Endoscopic NPS ≥ 5
NCS ≥ 2 over 14 days
CRSwNP symptoms for ≥ 8 weeks
Stable SoC treatment for CRSwNP for ≥ 30 days

Endpoints	
Primary endpoint	Change from baseline in endoscopic NPS at week 24
Key secondary endpoints	• Change from baseline at week 24 in: – Nasal congestion score – Total symptom score – Difficulty with sense of smell – Lund-Mackay score • Proportion requiring NP surgery or SCS by week 24
Safety	Treatment-emergent adverse events

[a]Inhaled corticosteroid.
CRSwNP, chronic rhinosinusitis with nasal polyps; NCS, nasal congestion score; NP, nasal polyp; NPS, nasal polyp score; Q12W, every 12 weeks; SC, subcutaneous; SCS, systemic corticosteroids; SoC, standard of care.

- In addition to the primary analysis, efficacy endpoints were analyzed using a worst-observation-carried-forward (WOCF) approach to account for use of rescue nasal polyp surgery or systemic corticosteroids, or escalation of maintenance/background treatment for CRSwNP

RESULTS

Baseline participant characteristics

- Eighty-one participants were randomized (verekitug, n=41; placebo, n=40); baseline participant characteristics were generally balanced between the treatment groups (**Table 1**)

Table 1. Baseline participant characteristics and demographics

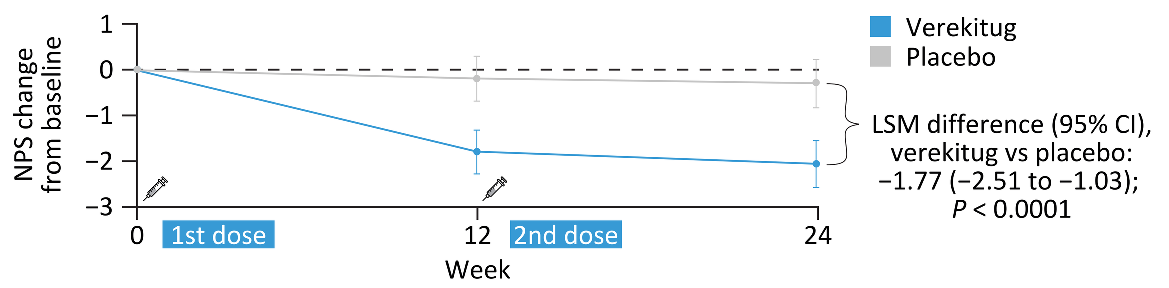
	Verekitug (n=41)	Placebo (n=40)	Total (N=81)
Median age (range), years	50.0 (19–75)	50.0 (21–76)	50.0 (19–76)
Male assigned at birth, n (%)	26 (63.4)	26 (65.0)	52 (64.2)
Blood eosinophil count, mean (SD), cells/μL	404 (260.4)	496 (378.1)[a]	449 (324.4)[b]
History of CRSwNP surgery, n (%)	26 (63.4)	26 (65.0)	52 (64.2)
History of SCS use, n (%)	18 (43.9)	16 (40.0)	34 (42.0)
History of comorbid asthma and/or NSAID-ERD, n (%)	24 (58.5)	23 (57.5)	47 (58.0)
Nasal polyp score, mean (SD)	5.90 (1.62)	6.13 (1.30)	6.01 (1.47)
Nasal congestion score, mean (SD)	2.60 (0.43)	2.67 (0.44)	–
Total symptom score, mean (SD)	17.52 (4.40)	18.23 (5.11)	–
Difficulty with sense of smell, mean (SD)	2.85 (0.33)	2.75 (0.57)	–
Lund-Mackay score, mean (SD)	17.13 (4.84)[a]	16.86 (4.92)[c]	–

[a]n=39. [b]n=80. [c]n=36.
CRSwNP, chronic rhinosinusitis with nasal polyps; NSAID-ERD, nonsteroidal anti-inflammatory drug–exacerbated respiratory disease; SCS, systemic corticosteroids; SD, standard deviation.

Primary endpoint

- Verekitug led to significant and clinically meaningful improvements in nasal polyp score (NPS) at week 12, and continued through week 24 (**Figure 2**)

Figure 2. Primary endpoint: change from baseline in NPS at 24 weeks



	Primary analysis (treatment policy)		WOCF analysis	
	Verekitug (n=41)	Placebo (n=40)	Verekitug (n=41)	Placebo (n=40)
CFB[a] at week 24 (SE)	−2.05 (0.26)[b]	−0.28 (0.27)[c]	−1.97 (0.26)[b]	−0.02 (0.26)[d]
Difference[a] (95% CI), verekitug vs placebo	−1.77 (−2.51 to −1.03); $P < 0.0001$		−1.95 (−2.66 to −1.24); $P < 0.0001$	

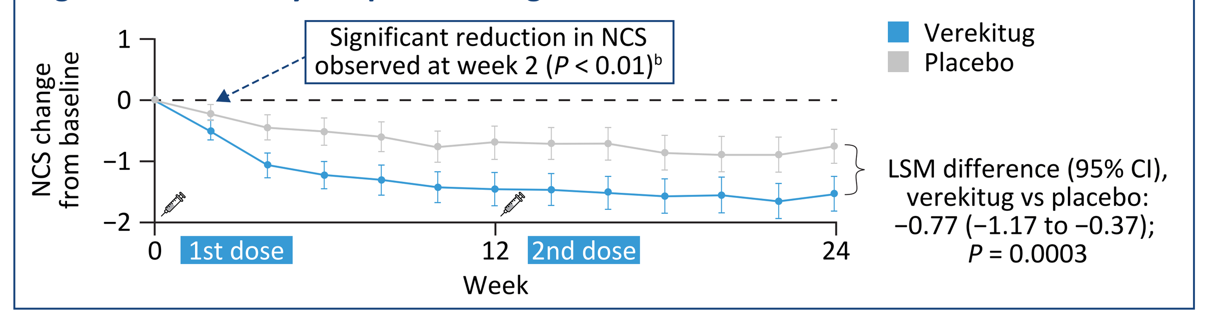
[a]All CFB are LSM. [b]n=39. [c]n=35. [d]n=37.
CI; confidence interval; CFB, change from baseline; LSM, least squares mean; NPS, nasal polyp score; SE, standard error; WOCF, worst observation carried forward.

RESULTS

Secondary endpoints

- Verekitug led to significant improvements in nasal congestion score (NCS) as early as week 2 and continued through week 24 (**Figure 3**)
- Verekitug reduced the need for surgery or systemic corticosteroids (SCS) by 76% compared with placebo (**Table 2**)
- Significant improvements were observed in all other secondary endpoints at week 24 (**Table 2**)

Figure 3. Secondary endpoint: change from baseline in NCS[a] at 24 weeks



[a]NCS was calculated as the 14-day average of the daily scores. [b]Nominal *P* value.
CI; confidence interval; LSM, least squares mean; NCS, nasal congestion score.

Table 2. Key secondary endpoints

	Primary analysis (treatment policy)		WOCF analysis	
	Verekitug (n=41)	Placebo (n=40)	Verekitug (n=41)	Placebo (n=40)
Nasal congestion score				
CFB[a] at week 24 (SE)	−1.53 (0.14)[b]	−0.76 (0.14)[c]	−1.48 (0.15)[b]	−0.52 (0.15)[d]
Difference[a] (95% CI), verekitug vs placebo	−0.77 (−1.17 to −0.37); $P = 0.0003$		−0.96 (−1.37 to −0.55); $P < 0.0001$	
Total symptom score				
CFB[a] at week 24 (SE)	−10.18 (0.97)[b]	−5.49 (0.98)[c]	−9.88 (1.02)[b]	−3.54 (1.02)[d]
Difference[a] (95% CI), verekitug vs placebo	−4.69 (−7.41 to −1.96); $P = 0.0010$		−6.34 (−9.19 to −3.49); $P < 0.0001$	
Difficulty with sense of smell				
CFB[a] at week 24 (SE)	−1.47 (0.15)[b]	−0.62 (0.16)[c]	−1.46 (0.14)[b]	−0.37 (0.15)[d]
Difference[a] (95% CI), verekitug vs placebo	−0.85 (−1.29 to −0.42); $P = 0.0002$		−1.08 (−1.49 to −0.68); $P < 0.0001$	
Lund-Mackay score				
CFB[a] at week 24 (SE)	−9.45 (0.75)[b]	−1.38 (0.78)[e]	−9.56 (0.71)[b]	−1.35 (0.74)[e]
Difference[a] (95% CI), verekitug vs placebo	−8.07 (−10.23 to −5.92); $P < 0.0001$		−8.22 (−10.26 to −6.18); $P < 0.0001$	
Proportion of participants requiring NP surgery and/or SCS at week 24				
Participants, n (%)	3 (7.3)[f]	10 (25.0)[g]	–	–
Odds ratio (95% CI)	0.24 (0.06–0.94); $P = 0.03$		–	

[a]All CFB are LSM. [b]n=36. [c]n=35. [d]n=38. [e]n=33. [f]All 3 participants required SCS, but not NP surgery. [g]Nine participants required SCS and 1 required NP surgery.
CFB, change from baseline; CI, confidence interval; LSM, least squares mean; NP, nasal polyp; SCS, systemic corticosteroids; SE, standard error; WOCF, worst observation carried forward.

Safety outcomes

- In general, treatment-emergent adverse events (TEAEs) and treatment-related TEAEs occurred more frequently with placebo than with verekitug (**Table 3**)

Table 3. Treatment-emergent adverse events

TEAEs,[a] n (%)	Verekitug (n=41)	Placebo (n=40)
All	27 (67.5)	26 (65.0)
Related to study treatment	1 (2.5)[b]	3 (7.5)
Serious	0	0
Grade ≥ 3	2 (5.0)	5 (12.5)
Leading to study drug discontinuation	0	1 (2.5)

[a]No injection site reactions were reported as adverse events in the verekitug group. [b]Dry mouth.
TEAE, treatment-emergent adverse event.

CONCLUSIONS

- Verekitug, dosed every 12 weeks, met the primary endpoint of NPS reduction by treatment policy analysis (−1.77 , $P < 0.0001$) and by WOCF analyses (−1.95) to account for rescue treatment with SCS or nasal polyp surgery
- The study met all key secondary endpoints, including NCS reduction (−0.77, $P = 0.0003$) and risk reduction for surgery/steroids (76%, $P = 0.03$)
- Verekitug was generally well tolerated, with no serious TEAEs observed
- Efficacy of verekitug is being investigated in ongoing trials in severe asthma (NCT06196879, NCT06966479) and chronic obstructive pulmonary disease (NCT06981078)[7–9]

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