Sustained Improvement in Clinical Efficacy, Asthma Control, and Quality of Life in Patients With Severe, Oral Corticosteroid (OCS)-Dependent Asthma Treated With Dupilumab: LIBERTY ASTHMA TRAVERSE Study

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Background

Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for interleukin-4/interleukin-13, key and central drivers of type 2 inflammation. In phase 3 LIBERTY ASTHMA VENTURE (NCT02528214), add-on dupilumab 300mg every 2 weeks (q2w) vs placebo significantly reduced OCS use from baseline in patients aged ≥12 years with OCS-dependent asthma and improved clinical outcomes. The single-arm, open-label extension LIBERTY ASTHMA TRAVERSE study (NCT02134028) evaluated the long-term safety, tolerability, and efficacy of add-on dupilumab in patients enrolled from previous dupilumab studies. Safety was consistent with the known dupilumab safety profile. In this study, we assessed dupilumab efficacy, asthma control, and quality of life in TRAVERSE patients with OCS-dependent asthma and different baseline disease severity, as measured by their OCS dose at the start of VENTURE.

Methods

Patients with OCS-dependent asthma received add-on dupilumab 300mg q2w or placebo for 24 weeks during VENTURE, followed by add-on dupilumab 300mg q2w for up to 96 weeks in TRAVERSE. Patients were analyzed by this as dupilumab/dupilumab (DPL/DPL) and placebo/dupilumab

(PBO/DPL) groups, respectively, and stratified by OCS dose at VENTURE study baseline (≤10 or >10 mg/day).

Results

The analyses included 187 patients (≤10 mg/day— PBO/DPL: n=61, DPL/DPL: n=60; >10 mg/day— PBO/DPL: n=36, DPL/DPL: n=30). The unadjusted AER continued to decline during TRAVERSE (range: 0.284–0.599; **Table**) along with continued reductions in OCS use. Pre-bronchodilator FEV_1 greatly improved from VENTURE study baseline at TRAVERSE Week 48 in both the DPL/DPL and PBO/DPL groups irrespective of baseline OCS dose (range at TRAVERSE Week 48: 1.83–1.92 L). Dupilumab also maintained the improvement in asthma control and quality of life seen in VENTURE during TRAVERSE, irrespective of baseline OCS use (**Table**). Mean 5-item Asthma Control Questionnaire (ACQ-5) scores at TRAVERSE Week 0 ranged from 1.38 to 2.07; at Week 24 from 1.29 to 1.61; and at Week 48 from 1.24 to 1.59. Mean Asthma Quality of Life Questionnaire (AQLQ) scores at TRAVERSE Week 0 ranged from 4.86 to 5.45; at Week 24 from 5.12 to 5.41; and at Week 48 from 5.11 to 5.51.

Conclusions

During the open-label TRAVERSE study, the improvement in FEV_1 observed during dupilumab treatment in VENTURE was sustained; dupilumab maintained the improvement in AER and improved asthma control and asthma-related quality of life.

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Table. OCS use, AER, pre-bronchodilator FEV_1, ACQ-5 and AQLQ scores at various time points in VENTURE and TRAVERSE.

	VENTURE baseline OCS dose ≤10 mg/day		VENTURE baseline OCS dose >10 mg/day	
	PBO/DPL n=61	DPL/DPL n=60	PBO/DPL n=36	DPL/DPL n=30
OCS use (mg/day)				
VENTURE				
Baseline, mean (SD)	8.07 (2.06)	7.42 (2.16)	17.57 (5.69)	18.08 (5.40)
TRAVERSE				
Week 0, mean (SD)	4.80 (4.50)	1.60 (2.85)	9.10 (9.18)	6.17 (7.95)
Week 48, mean (SD)	4.35 (3.98)	1.06 (1.87)	6.06 (6.49)	4.58 (4.72)
Unadjusted annualized rate of exacerbations (AER)				
VENTURE	1.587	0.463	1.492	1.070
TRAVERSE	0.311	0.294	0.284	0.599
Pre-bronchodilator FEV_1 (L)				
VENTURE				
Baseline, mean (SD)	1.62 (0.66)	1.50 (0.48)	1.63 (0.57)	1.58 (0.55)
TRAVERSE				
Week 0, mean (SD)	1.63 (0.68)	1.82 (0.60)	1.59 (0.62)	1.82 (0.63)
Week 48, mean (SD)	1.92 (0.80)	1.83 (0.66)	1.91 (0.75)	1.87 (0.70)
ACQ-5 scores (range 0–6, lower score = better asthma control)				
VENTURE				
Baseline, mean (SD)	2.54 (1.14)	2.39 (1.18)	2.69 (1.06)	2.53 (1.05)
TRAVERSE				
Week 0, mean (SD)	2.07 (1.14)	1.38 (1.19)	1.91 (1.28)	1.74 (1.25)
Week 24, mean (SD)	1.61 (1.13)	1.29 (1.14)	1.38 (1.13)	1.41 (0.96)
Week 48, mean (SD)	1.53 (0.98)	1.42 (1.15)	1.24 (1.00)	1.59 (1.24)
AQLQ scores (range 1–7, higher score = better quality of life)				
VENTURE				
Baseline, mean (SD)	4.43 (1.11)	4.41 (1.08)	4.19 (1.17)	4.26 (1.26)
TRAVERSE				
Week 0, mean (SD)	4.86 (0.97)	5.45 (1.20)	4.90 (1.23)	5.01 (1.24)
Week 24, mean (SD)	5.28 (1.02)	5.41 (1.15)	5.39 (1.23)	5.12 (1.13)
Week 48, mean (SD)	5.28 (0.97)	5.36 (1.10)	5.51 (1.16)	5.11 (1.30)

SD, standard deviation.