Evaluation of Antibody Properties and Clinically Relevant Immunogenicity, Anaphylaxis, and Hypersensitivity Reactions in Two Phase III Trials of Tralokinumab in Severe, Uncontrolled Asthma

Drug Safety

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Electronic Supplementary Material 8

Independent evaluation of anaphylaxis and hypersensitivity reactions

AE identified as possible anaphylaxis	Number of events			Presence of the following, consistent with Sampson criteria					AE considered by external evaluator as	
	Tralo Q2W	Tralo Q4W	Placebo	Shock	Respiratory component	Dermatology component	Cardiovascular component	Gastrointestinal component	Anaphylaxis	Non-anaphylactic hypersensitivity
STRATOS 1										
Angioedema	1	0	0	No	No	No	No	No	No	Undetermined
Asthma	1	0	0	No	No	No	No	No	No	No
Blood pressure decreased	0	0	1	No	No	No	No	No	No	No
Circulatory collapse	1	0	0	Undetermined	No	No	No	No	No	No
Cough	1	0	1	No	No	No	No	No	No	No
Dizziness	0	0	2	No	No	No	No	No	No	No
Drug hypersensitivity	0	3	0	No	No	No	No	No	No	No
Dyspnea	1	0	0	No	No	No	No	No	No	No
Erythema	1	0	0	No	No	No	No	No	No	No
Injection site reaction	1	0	0	No	No	No	No	No	No	No
Injection site urticaria	1	0	0	No	No	No	No	No	No	No
Lip swelling	0	1	0	No	No	No	No	No	No	No
Pharyngeal edema	1	0	0	No	No	No	No	No	No	Undetermined*
Pruritus	1	0	0	No	No	No	No	No	No	No

Rash	0	0	1	No	No	No	No	No	No	No
Somnolence	0	2	0	No	No	No	No	No	No	No
Swollen tongue	1	0	0	No	No	No	No	No	No	Undetermined*
Syncope	1	2	2	No	No	No	No	No	No	No
Throat irritation	1	0	0	No	No	No	No	No	No	No
Vomiting	0	0	2	No	No	No	No	No	No	No
Wheezing	1	0	1	No	No	No	No	No	No	No
STRATOS 2										
Blood pressure decreased	1	–	0	No	No	No	Yes	No	No	No
Eyelid edema	1	–	1	No	No	No (*n* = 1, placebo); Yes (*n* = 1, tralo Q2W)	No	No	No	No (*n* = 1, placebo); Undetermined (*n* = 1, tralo Q2W)
Hypotension	0	–	1	No	No	No	Yes	No	No	No
Pruritus	2	–	1	No	No	Yes	No	No	No	Undetermined
Rash	4	–	0	No	No	No (*n* = 1); Yes (*n* = 3)	No	No	No	No (*n* = 1); Undetermined (*n* = 3)
Rash generalized	0	–	1	No	No	Yes	No	No	No	No
Rash macular	0	–	1	No	No	Yes	No	No	No	Undetermined
Urticaria	2	–	3	No	No (*n* = 4: *n* = 2, placebo; *n* = 2, Q2W); Yes (*n* = 1, placebo)	Yes	No	No	No (*n* = 4; *n* = 2, placebo; *n* = 2, tralo Q2W); Yes (*n* = 1, placebo)	Undetermined (*n* = 3; *n* = 2, placebo; *n* = 1, tralo Q2W); Yes (*n* = 1, tralo Q2W); [a](*n* = 1, placebo)

Wheezing	0	–	1	No	Yes	Yes	No	No	Yes	[a]

AE, adverse event; *Q2W*, every 2 weeks; *Q4W*, every 4 weeks; *tralo*, tralokinumab

[a]No anaphylactic hypersensitivity judgment made by external evaluator, due to lack of narrative information available

– indicates Q4W treatment arm not used in STRATOS 2 trial

***Case narrative for subject who discontinued treatment due to pharyngeal oedema and swollen tongue, reported as serious AEs**

This subject's current medical conditions included asthma triggered by allergens and iodine, allergic rhinitis, chronic sinusitis, and eczema. The subject was randomized to receive tralokinumab with a dosing regimen of Q2W (total expected doses 26). On the day of first dose (of one dose received) of tralokinumab, the subject developed serious adverse events of swollen tongue and pharyngeal oedema. At the time of discharge, two hours after receiving the investigational product, no complications had been reported. However, 5 minutes after discharge, the subject experienced slight symptoms of tingling on the tongue and in the throat. After 10 more minutes, the subject had difficulty swallowing water, following which the subject took diphenhydramine 25 mg daily orally. At 30 minutes from discharge, the subject had difficulty forming words due to swelling of the tongue. The subject did not seek any medical help, but decided to self-medicate with cetirizine 10 mg daily orally for swollen tongue. The symptoms dissipated gradually on the same day but did not resolve completely. However, the subject's condition improved by next morning and had recovered from the events two days after receiving the dose.

Both the events were considered by the Investigator to be important medical events of moderate intensity, related to the investigational product. As a result of the events, the investigational product was permanently discontinued on the first day of administration, which was also the last dose prior to discontinuation.