

Infections in Children Aged 6 Months to 5 Years Treated With Dupilumab in a Placebo-Controlled Clinical Trial of Moderate-to-Severe Atopic Dermatitis

Pediatric Drugs

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SUPPORTING INFORMATION

- 1. Table S1. Exposure-Adjusted Numbers of Patients With ≥ 2 Treatment-Emergent Infections During the Study Treatment Period**
- 2. Table S2. Treatment-Emergent Recurrent Infections (≥ 2 events, by MedDRA PT, under SOC 'Infections and Infestations') by Incidence Rate: Number of Patients per 100 PY**
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Table S1. Exposure-Adjusted Numbers of Patients With ≥ 2 Treatment-Emergent Infections During the Study Treatment Period

	Patients with ≥2 events, nP/PY (nP/100 PY)		RR vs placebo (95%CI), P value
	Placebo + TCS (n = 78)	Dupilumab 200/300 mg q4w + TCS (n = 83)	
Total infections (SOC)	20/19.4 (103.1)	7/23.7 (29.5)	0.29 (0.12-0.68) 0.004
Infections leading to treatment discontinuation (SOC)	0/24.0	0/25.8	NE (NE-NE) NE
Serious or severe infections	0/24.0	0/25.8	NE (NE-NE) NE
Adjudicated skin infections (excluding herpes infections)	10/21.7 (46.0)	1/25.5 (3.9)	0.09 (0.01-0.67) 0.019
Non-skin infections ¹	14/20.6 (67.9)	5/24.4 (20.5)	0.30 (0.11-0.84) 0.021
Herpes viral infections (HLT)	0/24.0	0/25.8	NE (NE-NE) NE
Bacterial infections (HLGT)	5/22.8 (21.9)	0/25.8	NE (NE-NE) NE
Viral infections (HLGT)	1/23.7 (4.2)	0/25.8	NE (NE-NE) NE
Fungal infections (HLGT)	0/24.0	0/25.8	NE (NE-NE) NE
Helminthic infections (HLGT)	0/24.0	0/25.8	NE (NE-NE) NE
Skin structures and soft tissue infections (HLT) ²	3/23.3 (12.9)	0/25.8	NE (NE-NE) NE

1. Includes all adverse events in the SOC 'Total infections' except adjudicated non-herpetic skin infections and the HLT 'Herpes viral infections'

2. Only includes infections that fall within HLGT category of 'pathogens unspecified'

Abbreviations: CI, confidence interval; HLGT, MedDRA High Level Group Term; HLT, MedDRA High Level Term; MedDRA, Medical Dictionary for Regulatory Activities; NE, not estimated; nP/100 PY, number of patients per 100 patient-years; PT, MedDRA Preferred Term; q4w, every 4 weeks; RR, rate ratio; SOC, MedDRA System Organ Class; TCS, topical corticosteroids.

Table S2. Treatment-Emergent Recurrent Infections (≥ 2 events, by MedDRA PT, under SOC ‘Infections and Infestations’) by Incidence Rate: Number of Patients per 100 PY

Preferred Term (PT)	Patients with ≥2 events, nP/PY (nP/100 PY)	
	Placebo + TCS (n = 78)	Dupilumab 200/300 mg q4w + TCS (n = 83)
Nasopharyngitis	1/23.8 (4.2)	1/25.5 (3.9)
Upper respiratory tract infection	1/23.7 (4.2)	0/25.8
Molluscum contagiosum	0/24.0	0/25.8
Conjunctivitis	0/24.0	0/25.8
Gastroenteritis viral	0/24.0	0/25.8
Impetigo	1/23.8 (4.2)	0/25.8
Herpes virus infection	0/24.0	0/25.8
Varicella	0/24.0	0/25.8
Bronchitis	0/24.0	0/25.8
COVID-19	0/24.0	0/25.8
Cellulitis	0/24.0	0/25.8
Coronavirus infection	0/24.0	0/25.8
Croup infectious	0/24.0	0/25.8
Dermatitis infected	0/24.0	0/25.8
Keratitis viral	0/24.0	0/25.8
Oral herpes	0/24.0	0/25.8
Otitis media	0/24.0	0/25.8
Otitis media acute	1/23.7 (4.2)	0/25.8
Paronychia	1/23.8 (4.2)	0/25.8
Pustule	0/24.0	0/25.8
Skin infection	1/23.7 (4.2)	0/25.8
Respiratory tract infection viral	0/24.0	0/25.8
Staphylococcal skin infection	1/23.7 (4.2)	0/25.8
Ear infection	0/24.0	0/25.8
Skin bacterial infection	2/23.5 (8.5)	0/25.8
Viral upper respiratory tract infection	0/24.0	0/25.8
Abscess limb	0/24.0	0/25.8
Cellulitis staphylococcal	0/24.0	0/25.8
Eczema herpeticum	0/24.0	0/25.8
Furuncle	1/23.8 (4.2)	0/25.8

Gastroenteritis	0/24.0	0/25.8
Genital candidiasis	0/24.0	0/25.8
Herpes simplex	0/24.0	0/25.8
Pharyngitis	0/24.0	0/25.8
Respiratory syncytial virus infection	0/24.0	0/25.8
Staphylococcal abscess	0/24.0	0/25.8
Staphylococcal bacteremia	0/24.0	0/25.8
Staphylococcal infection	0/24.0	0/25.8
Superinfection	0/24.0	0/25.8

Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; nP/100 PY, number of patients per 100 patient-years; PT, MedDRA Preferred Term; q4w, every 4 weeks; SOC, MedDRA System Organ Class; TCS, topical corticosteroids.

Table S3. Number of Patients With Concomitant Systemic Anti-Infectives

Preferred Term	Placebo + TCS (N = 78) nP/PY (nP/100 PY)	Dupilumab 200/300 mg q4w + TCS (N = 83) nP/PY (nP/100 PY)
Systemic Anti-Infectives	32/15.8 (203.0)	21/20.0 (104.7)
Cefalexin (antibacterial)	11/21.3 (51.6)	6/24.0 (25.0)
Clindamycin (antibacterial)	8/21.6 (37.0)	5/24.2 (20.6)
Acyclovir (antiviral)	4/23.4 (16.2)	4/24.8 (16.1)
Amoxicillin (antibacterial)	5/23.0 (21.7)	3/25.2 (11.9)
Sulfamethoxazole; Trimethoprim (antibacterial)	5/22.8 (21.9)	3/25.0 (12.0)
Cefdinir (antibacterial)	5/22.8 (22.0)	2/25.3 (7.9)
Amoxicillin trihydrate; clavulanate potassium (antibacterial)	0/24.0	1/25.5 (3.9)
Azithromycin (antibacterial)	0/24.0	1/25.5 (3.9)
Cefadroxil (antibacterial)	1/23.7 (4.2)	1/25.5 (3.9)
Ceftriaxone (antibacterial)	0/24.0	1/25.5 (3.9)
Inosine pranobex (antiviral)	1/23.9 (4.2)	1/25.6 (3.9)
Linezolid (antibacterial)	2/23.6 (8.5)	1/25.7 (3.9)
Vancomycin (antibacterial)	1/23.9 (4.2)	1/25.5 (3.9)
Flucloxacillin (antibacterial)	3/23.7 (12.7)	0/25.8
Amoxicillin; Clavulanic acid (antibacterial)	2/23.5 (8.5)	0/25.8
Clarithromycin (antibacterial)	2/23.5 (8.5)	0/25.8
Valacyclovir (antiviral)	2/23.4 (8.6)	0/25.8
Cefazolin (antibacterial)	1/23.7 (4.2)	0/25.8
Ciprofloxacin (antibacterial)	1/23.9 (4.2)	0/25.8
Doxycycline (antibacterial)	1/23.9 (4.2)	0/25.8
Erythromycin (antibacterial)	1/23.7 (4.2)	0/25.8
Fluconazole (antifungal)	1/23.7 (4.2)	0/25.8
Immunoglobulin human normal	1/23.7 (4.2)	0/25.8
Roxithromycin (antibacterial)	1/23.7 (4.2)	0/25.8

Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; nP/100 PY, number of patients per 100 patient-years; q4w, every 4 weeks; TCS, topical corticosteroids.