

Supplementary materials for the article:
**Dupilumab suppresses type 2 inflammatory biomarkers across multiple atopic, allergic
diseases**

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This appendix has been provided by the authors to give readers additional information about their
work.

APPENDICES

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APPENDIX S1 Baseline demographics and history of atopic disease in patients with atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps and eosinophilic esophagitis

Type 2 disease	Atopic dermatitis		Asthma		Chronic rhinosinusitis with nasal polyps		Atopic dermatitis		Eosinophilic esophagitis	
Study name	CHRONOS		QUEST		SINUS-52		SOLO-1 and SOLO-2		EoE PoC	
Study duration	52 weeks		52 weeks		52 weeks		16 weeks		12 weeks	
Treatment group	Placebo	Dupilumab 300 mg	Placebo 2mL q2w + ICS/LABA,	Dupilumab 300 mg q2w + ICS/LABA,	Placebo q2w + INCS,	Dupilumab 300 mg q2w + INCS,	Placebo qw,	Dupilumab 300 mg q2w,	Placebo qw,	Dupilumab 300 mg qw,
	qw + TCS, n = 315	q2w + TCS, n = 106	n = 321	n = 633	n = 153	n = 150	n = 460	n = 457	n = 24	n = 23
Baseline demographics										
Age, mean (SD), years	36.6 (13.0)	39.6 (14.0)	48.2 (14.7)	47.7 (15.6)	51.7 (12.7)	51.9 (11.9)	38.4 (14.0)	38.3 (14.4)	36.1 (12.8)	33.1 (8.7)
Male, n (%)	193 (61.3)	62 (58.5)	103 (32.1)	239 (37.8)	95 (62.1)	97 (64.7)	250 (54.3)	267 (58.4)	10 (41.7)	13 (56.5)

Female, n (%)	122 (38.7)	44 (41.5)	218 (67.9)	394 (62.2)	58 (37.9)	53 (35.3)	210 (45.7)	190 (41.6)	14 (58.3)	10 (43.5)
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Current history of comorbid type 2 immune diseases,^a n (%)

Allergies (other than food allergy)	201 (63.8)	68 (61.8)							9 (37.5)	14 (60.9)
Allergic conjunctivitis (kerato-conjunctivitis)	68 (21.6)	31 (28.2)	49 (15.3)	89 (14.1)	10 (6.5)	6 (4.0)			3 (12.5)	3 (13.0)
Allergic rhinitis	134 (42.5)	53 (48.2)	225 (70.1)	438 (69.2)	74 (48.4)	72 (48.0)	224 (48.7)	224 (49.0)	14 (58.3)	16 (69.6)
Asthma	130 (41.3)	45 (40.9)			91 (59.5)	85 (56.7)	205 (44.6)	226 (49.5)	8 (33.3)	8 (34.8)
Atopic dermatitis	310 (98.4)	108 (98.2)	38 (11.8)	62 (9.8)	10 (6.5)	4 (2.7)	–	–	4 (16.7)	3 (13.0)
Chronic rhinosinusitis	26 (8.3)	7 (6.4)	63 (19.6)	113 (17.9)	–	–			8 (33.3)	2 (8.7)
Eosinophilic esophagitis	0	1 (0.9)	2 (0.6)	0	0	1 (0.7)			–	–
Food allergy	96 (30.5)	39 (35.5)	36 (11.2)	47 (7.4)	16 (10.5)	8 (5.3)	174 (37.8)	177 (38.7)	16 (66.7)	14 (60.9)

Hives	34 (10.8)	14 (12.7)	15 (4.7)	30 (4.7)	6 (3.9)	3 (2.0)			5 (20.8)	6 (26.1)
Nasal polyps	7 (2.2)	2 (1.8)	40 (12.5)	81 (12.8)	–	–	18 (3.9)	19 (4.2)	2 (8.3)	1 (4.3)

Note: SOLO: full analysis set; CHRONOS and EoE PoC: safety analysis set; QUEST and SINUS-52: randomized population. Grey cells indicate that data were not collected or available for these patients.

Abbreviations: EoE, eosinophilic esophagitis; ICS, inhaled corticosteroids; INCS, intranasal corticosteroids; LABA, long-acting β_2 -agonist; n, number; PoC, proof of concept; qw, weekly; q2w, every 2 weeks; SD, standard deviation; TCS, topical corticosteroids.

^aFor asthma, this refers to a medical history.

APPENDIX S2 Mean biomarkers at baseline and end of treatment for patients with atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyps, and eosinophilic esophagitis

Type 2 disease	Atopic dermatitis		Asthma		Chronic rhinosinusitis with nasal polyps		Atopic dermatitis		Eosinophilic esophagitis	
Study name	CHRONOS		QUEST		SINUS-52		SOLO-1 and SOLO-2		EoE PoC	
Study duration	52 weeks		52 weeks		52 weeks		16 weeks		12 weeks	
Treatment group	Placebo qw + TCS	Dupilumab 300 mg q2w + TCS	Placebo 2mL q2w + ICS/LABA	Dupilumab 300 mg q2w + ICS/LABA	Placebo q2w + INCS	Dupilumab 300 mg q2w + INCS	Placebo qw	Dupilumab 300 mg q2w	Placebo qw	Dupilumab 300 mg qw
Serum TARC (pg/mL)										
n	313	110	319	622	149	147	454	464	24	22
Mean (SE) at baseline	7291.72 (738.03)	9678.78 (1828.09)	398.00 (19.27)	364.66 (11.84)	370.20 (21.03)	372.27 (20.94)	5933.28 (487.89)	6864.12 (703.81)	350.83 (43.43)	275.54 (27.82)
n	120	84	248	479	127	139	194	361	19	22
Mean (SE) at end of treatment	1960.14 (377.87)	479.11 (43.13)	520.36 (143.08)	234.72 (7.95)	332.49 (20.13)	219.43 (10.77)	3239.13 (738.27)	572.33 (38.71)	322.63 (43.09)	203.38 (22.29)

n	119	84	246	473	126	137	193	360	19	21
Mean change (SE) from baseline at end of treatment	-2450.77 (592.10)	-10341.70 (2315.52)	137.66 (137.49)	-122.78 (10.02)	-15.09 (11.67)	-158.53 (14.93)	-1043.61 (446.81)	-5370.36 (700.55)	-10.11 (24.98)	-71.23 (17.90)
n	119	84	246	473	126	137	193	360	19	21
Mean % change (SE) from baseline at end of treatment	-29.14 (11.50)	-78.37 (3.97)	25.90 (9.43)	-22.74 (2.31)	1.28 (2.99)	-36.16 (1.91)	10.22 (9.49)	-69.80 (1.71)	0.14 (6.70)	-21.06 (5.73)

Plasma eotaxin-3 (pg/mL)

n		318	625	150	146
Mean (SE) at baseline		50.90 (3.25)	69.53 (19.26)	90.84 (9.08)	70.61 (3.74)
n		246	473	127	139
Mean (SE) at end of treatment		50.46 (2.89)	29.81 (1.73)	82.62 (8.13)	30.40 (1.28)
n		243	469	127	136

Mean change (SE) from baseline at end of treatment			0.28 (2.76)	-48.00 (24.33)	1.40 (4.75)	-39.95 (3.60)				
n			243	469	127	136				
Mean % change (SE) from baseline at end of treatment			57.13 (20.38)	-20.95 (5.39)	14.88 (5.42)	-39.10 (7.01)				

Serum total IgE (IU/mL)										
n	312	110	318	626	150	148	456	465	24	23
Mean (SE) at baseline	5082.55 (249.43)	5653.27 (423.00)	448.47 (44.67)	415.05 (28.03)	228.59 (21.94)	211.79 (21.16)	6999.88 (481.27)	6715.38 (485.50)	478.46 (198.56)	204.17 (66.31)
n	117	83	251	482	128	140	196	366	19	23
Mean (SE) at end of treatment	4203.74 (390.15)	2132.49 (331.55)	432.44 (49.46)	135.61 (14.64)	292.03 (46.24)	54.64 (5.78)	5676.28 (649.71)	3444.88 (295.04)	423.05 (169.52)	137.09 (40.04)
n	116	83	248	478	128	139	196	366	19	23

Mean change (SE) from baseline at end of treatment	-118.83 (219.48)	-3797.40 (399.55)	-4.03 (20.45)	-294.80 (23.76)	64.09 (32.08)	-156.92 (17.93)	366.67 (243.19)	-3027.83 (277.28)	-74.84 (76.03)	-67.09 (27.11)
n	116	83	248	478	128	139	196	366	19	23
Mean % change (SE) from baseline at end of treatment	68.42 (52.90)	-66.25 (3.17)	9.89 (4.33)	-58.43 (7.24)	20.82 (5.72)	-67.28 (1.63)	22.74 (4.25)	-41.90 (2.71)	4.9 (5.1)	-25.3 (2.8)

Serum periostin (ng/mL)

n		319	629	150	147		24	22
Mean (SE) at baseline		80.94 (2.28)	78.42 (1.51)	113.00 (4.03)	109.70 (4.06)		62.16 (6.20)	61.18 (3.90)
n		253	490	120	128		18	23
Mean (SE) at end of treatment		75.52 (2.36)	59.82 (1.13)	108.11 (5.06)	66.06 (2.31)		73.18 (7.19)	52.67 (3.04)
n		251	488	120	127		18	22

Mean change (SE) from baseline at end of treatment			-5.05 (1.76)	-18.90 (1.40)	-4.73 (3.52)	-45.42 (3.91)			9.91 (5.20)	-8.25 (3.23)
n			251	488	120	127			18	22
Mean % change (SE) from baseline at end of treatment			-2.37 (1.88)	-17.80 (1.11)	0.15 (3.66)	-33.93 (2.64)			32.85 (19.31)	-8.22 (6.95)

Blood eosinophils (Giga/L)

n	314	110	320	632	150	148	454	465	24	23
Mean (SE) at baseline	0.55 (0.03)	0.58 (0.06)	0.39 (0.02)	0.35 (0.02)	0.45 (0.03)	0.45 (0.03)	0.62 (0.03)	0.60 (0.03)	0.43 (0.06)	0.31 (0.04)
n	120	83	245	476	129	140	195	360	21	22
Mean (SE) at end of treatment	0.34 (0.02)	0.40 (0.04)	0.35 (0.02)	0.33 (0.02)	0.44 (0.04)	0.37 (0.03)	0.45 (0.04)	0.57 (0.04)	0.43 (0.07)	0.17 (0.02)
n	119	83	245	476	129	139	194	360	21	22

Mean change (SE) from baseline at end of treatment	-0.17 (0.03)	-0.20 (0.05)	-0.05 (0.02)	-0.01 (0.02)	0 (0.03)	-0.08 (0.04)	-0.07 (0.03)	0 (0.03)	0 (0.08)	-0.14 (0.03)
n	119	83	242	469	128	139	190	346	20	21
Mean % change (SE) from baseline at end of treatment	-10.02 (6.69)	-19.92 (7.07)	33.60 (13.26)	43.76 (13.93)	12.88 (8.85)	24.12 (18.25)	-1.49 (7.14)	12.89 (5.91)	-8.06 (11.94)	-43.71 (6.11)

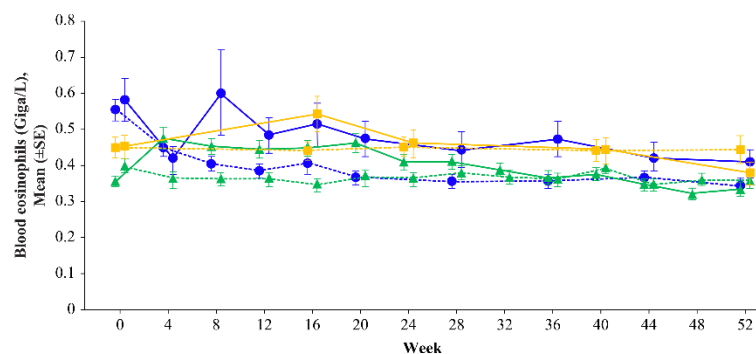
Note: Grey cells indicate that data were not collected or available for these patients.

Abbreviations: EoE, eosinophilic esophagitis; IU, international units; ICS, inhaled corticosteroids; IgE, immunoglobulin E; INCS, intranasal corticosteroids; LABA, long-acting β_2 -agonist; n, number; PoC, proof of concept; qw, weekly; q2w, every 2 weeks; SE, standard error; TARC, thymus and activation-regulated chemokine; TCS, topical corticosteroids.

APPENDIX S3 The effect of dupilumab on mean (\pm SE) concentrations of blood eosinophils (Giga/L). AD, atopic dermatitis; CRSwNP, chronic rhinosinusitis with nasal polyps; EoE, eosinophilic esophagitis; PoC, proof of concept; qw, weekly; q2w, every 2 weeks; SE, standard error.

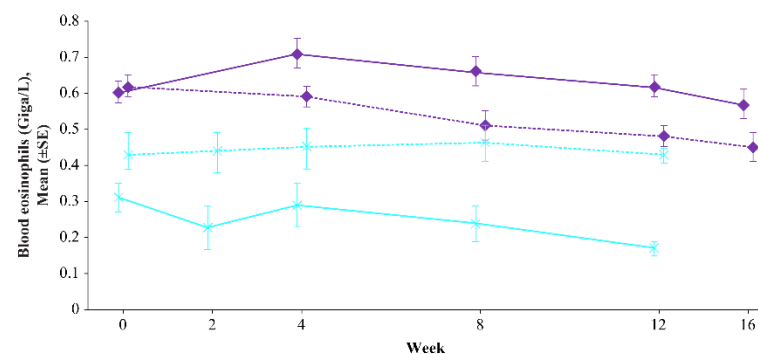
AD patients from CHRONOS Asthma patients from QUEST CRSwNP patients from SINUS-52 AD patients from SOLO-1 and SOLO-2 EoE patients from EoE PoC
 ●---● Placebo qw ●---● Dupilumab 300 mg q2w ▲---▲ Placebo q2w ▲---▲ Dupilumab 300 mg q2w ■---■ Placebo q2w ■---■ Dupilumab 300 mg q2w ◆---◆ Placebo qw ◆---◆ Dupilumab 300 mg q2w ✕---✕ Placebo qw ✕---✕ Dupilumab 300 mg qw

(A) 52-week studies in AD, asthma, and CRSwNP



Number of patients	0	4	8	12	16	20	24	28	32	36	40	44	48	52
AD, placebo qw	314	269	240	207	187	172		151		135		125		120
AD, dupilumab 300 mg q2w	110	98	97	90	91	90		86		84		83		83
Asthma, placebo q2w	320	307	305	302	300	291	289	294	294	290	290	281	277	245
Asthma, dupilumab 300 mg q2w	632	616	587	595	596	581	577	576	560	568	561	552	537	476
CRSwNP, placebo q2w	150				143		137				131			129
CRSwNP, dupilumab 300 mg q2w	148				141		142				140			140

(B) 12- to 16-week studies in EoE and AD



Number of patients	0	2	4	8	12	16
AD, placebo qw	454		324	235	208	195
AD, dupilumab 300 mg q2w	465		412	392	382	360
EoE, placebo qw	24	23	21	20	21	
EoE, dupilumab 300 mg qw	23	23	23	21	22	