A Case Series of Live Attenuated Vaccine Administration in Dupilumab-Treated Children With Atopic Dermatitis

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BACKGROUND

- In patients with atopic dermatitis (AD), it is unknown whether suppression of the dysregulated type 2 immune cytokines interleukin-4 and interleukin-13 with dupilumab impacts the risk of vaccine-related viral infections following live attenuated vaccination
- Current U.S. regulatory labelling recommends completing age-appropriate vaccinations according to immunization guidelines prior to starting dupilumab and avoidance of live vaccines in patients on dupilumab treatment
- The LIBERTY AD PRESCHOOL (NCT03346434, part B) study protocol prohibited administration of live attenuated vaccines within 4 weeks before the baseline visit and during treatment
- The LIBERTY AD PED open-label extension study (OLE; NCT02612454) protocol specified that dupilumab be discontinued 12 weeks prior to live attenuated vaccine administration and could be re-initiated 4 weeks after administration

OBJECTIVE

- **To describe the clinical course of children with severe AD administered a live attenuated vaccine during the LIBERTY AD PRESCHOOL or LIBERTY AD PED-OLE study**

METHODS

- This case series describes 9 patients with severe AD at parent study baseline (Investigator's Global Assessment [IGA] = 4) who were administered a live attenuated vaccine during either:
  - LIBERTY AD PRESCHOOL (part B; n = 1): received a live attenuated vaccine with a gap of ≤ 12 weeks between dupilumab administration and vaccination
  - LIBERTY AD PED-OLE study (n = 8): 4 with a gap of ≤ 12 weeks and 4 with a gap of > 12 weeks between vaccination and the most recent prior dose of dupilumab
- The LIBERTY AD PED-OLE study (200 mg dupilumab every 4 weeks [q4w] if baseline weight was 5 to < 15 kg, 300 mg q4w if 15 to < 30 kg, or 200 mg every 2 weeks if 30 to < 60 kg) included patients who had previously participated in either:
  - LIBERTY AD PRESCHOOL (part A; 3 or 6 mg/kg dupilumab single dose)
  - LIBERTY AD PRESCHOOL (part B; 200 mg dupilumab q4w if baseline weight was 5 to < 15 kg, or 300 mg q4w if 15 to < 30 kg)

RESULTS

Table 1. Demographics and clinical characteristics at parent trial baseline.

	≤ 12 weeks between dupilumab and live vaccination					> 12 weeks between dupilumab and live vaccination			
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9
Study site	Poland	USA	USA	USA	USA	UK	UK	USA	USA
Age, months	56	36	22	43	22	19	20	8	30
Sex	M	M	F	M	M	M	M	M	M
Race	White	Black or African American	Black or African American	White	White	White	White	White	White
Weight, kg	15.1	13.7	11.7	16.7	9.1	10	11.6	7.8	13.1
Age at first AD diagnosis, months	5	0	6	3	0	2	0	3	3
Duration of AD at trial enrollment, months	51	36	16	40	22	17	20	5	27
Medical history	Asthma Other allergies[a] Hypermetropia	Asthma Food allergy Allergic rhinitis Milk allergy Other allergies[a]	Allergic conjunctivitis (keratoconjunctivitis) Asthma Allergic rhinitis Aspirin sensitivity Food allergy Seasonal allergy Milk allergy Other allergies[a]	Food allergy Hives Other allergies[a]	Allergic rhinitis Asthma Seborrheic dermatitis Impetigo	Allergic rhinitis Asthma Food allergy Hives Seasonal allergy Milk allergy Drug hypersensitivity Wheezing Other allergies[a]	Asthma Food allergy Hives Milk allergy	Food allergy Milk allergy Other allergies[a] Prior non-steroid systemic immunosuppressant therapy	Allergic rhinitis Food allergy Seasonal allergy
IGA (range 0–4)	4	4	4	4	4	4	4	4	4
BSA (%)	59.5	56	82	43	60	41	35	66.5	57
EASI (range 0–72)	44.9	31.5	26.2	30.3	37.2	23.2	21.2	38.5	49.8
Peak pruritus NRS (range 0–10)	5.2	9	10	9	9	9	8	8	10

[a]Other allergies include allergies to medications, animals, plants, mold, dusts, and other allergens. BSA, body surface area; EASI, Eczema Area and Severity Index; NRS, Numerical Rating Scale.

Table 2. Vaccines administered during dupilumab trial when live attenuated vaccination was received.

	≤ 12 weeks between dupilumab and live vaccination					> 12 weeks between dupilumab and live vaccination			
	Patient 1[a]	Patient 2[b]	Patient 3[b]	Patient 4[b]	Patient 5[b]	Patient 6[b]	Patient 7[b]	Patient 8[b]	Patient 9[b]
	Vaccines administered[c]								
	Diphtheria, pertussis MMR	DTaP MMR IPV Varicella	DTaP MMR IPV Varicella	DTaP MMR IPV Varicella	DTaP/IPV MMR	DTaP/IPV MMR	Diphtheria, tetanus, IPV MMR	Hep A MMR Pneumococcal Varicella	DTaP MMR IPV Varicella

[a]Data taken from LIBERTY AD PRESCHOOL study. [b]Data taken from LIBERTY AD PED-OLE study. [c]Non-live vaccines are indicated in blue and live attenuated vaccines are indicated in red. All non-live vaccines were administered ≤ 4 weeks following live vaccination. DTaP, diphtheria, tetanus, and pertussis; DTaP/IPV, diphtheria, tetanus, pertussis, and inactivated polio virus; Hep, hepatitis; IPV, inactivated polio virus; MMR, measles, mumps, and rubella.

Table 3. Clinical course of live attenuated vaccination and dupilumab administration.

	≤ 12 weeks between dupilumab and live vaccination					> 12 weeks between dupilumab and live vaccination			
	Patient 1[a]	Patient 2[b]	Patient 3[b]	Patient 4[b]	Patient 5[b]	Patient 6[b]	Patient 7[b]	Patient 8[b]	Patient 9[b]
Dupilumab dose	300 mg q4w	6 mg/kg qw → 200 or 300 mg q4w	3 mg/kg qw → 200 or 300 mg q4w	3 mg/kg qw → 200 or 300 mg q4w	3 mg/kg qw → 200 or 300 mg q4w	6 mg/kg qw → 200 or 300 mg q4w	3 mg/kg qw	6 mg/kg qw → 200 or 300 mg q4w	3 mg/kg qw → 200 or 300 mg q4w
Duration of treatment up to date of live vaccination, days	85	750	840	443	758	617	358	189	485
Live vaccine name (order)	MMR (1)	MMR (1) Varicella (2)	MMR (1) Varicella (2)	MMR (1) Varicella (2)	MMR (1)	MMR (1)	MMR (1)	MMR (1) Varicella (2)	MMR (1) Varicella (2)
Interval between live vaccine administration and most recent prior dose of dupilumab, days	28	7	12	50	7	85	192	91	91
Interval between live vaccination and next dose of dupilumab post-vaccination, days	30[b]	2	18	43	37	N/A	N/A	31	33

[a]Data taken from LIBERTY AD PRESCHOOL study. [b]Data taken from LIBERTY AD PED-OLE study. N/A, not applicable; qw, every week.

Table 4. Safety outcomes of live attenuated vaccination and dupilumab administration.

	≤ 12 weeks between dupilumab and live vaccination					> 12 weeks between dupilumab and live vaccination			
	Patient 1[a]	Patient 2[b]	Patient 3[b]	Patient 4[b]	Patient 5[b]	Patient 6[b]	Patient 7[b]	Patient 8[b]	Patient 9[b]
	≤ 4 weeks following live vaccination								
AEs, SAEs, TEII[c]	None reported								
	> 4 weeks following live vaccination								
AEs, SAEs	None reported								
TEII[c]	None	Nasopharyngitis	COVID-19[d]	None	None	None	Croup infectious[e] *Molluscum contagiosum*	None	Hand, foot, and mouth disease Hordeolum

[a]Data taken from LIBERTY AD PRESCHOOL study. [b]Data taken from LIBERTY AD PED-OLE study. [c]Dictionary-derived term. [d]Moderate severity; duration 27 April–2 May 2021; recovered/resolved. [e]Mild severity; duration 9–10 September 2020; recovered/revised. AE, adverse event; SAE, serious adverse event; TEII, treatment-emergent infections and infestations.

CONCLUSIONS

- **In this limited retrospective case series of children with severe AD who also received the live attenuated MMR vaccine, with or without live attenuated varicella vaccine, no vaccine-related viral infections or SAEs were observed either in the immediate 4-week period following vaccination or beyond 4 weeks post-vaccination**
- **Additional research is needed to assess the safety of live attenuated vaccines in patients on dupilumab treatment, and to investigate whether dupilumab treatment impacts vaccine efficacy**

*This author has been included to serve as a presenter.

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