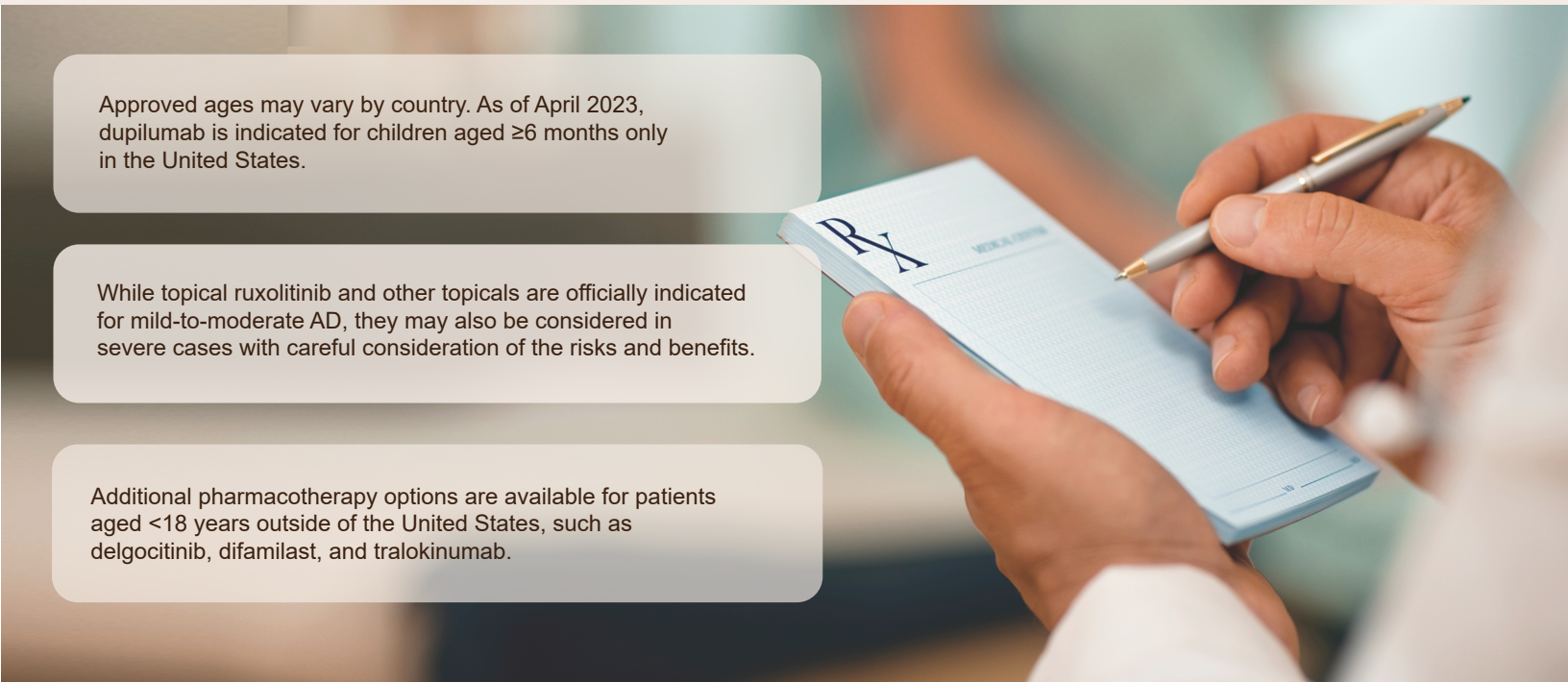
Pearls for Managing AD in Pediatric Patients

FDA-Approved Management Options for AD in Children

Mild AD Patches of dry skin, some itching, minimal impact on QOL or sleep	**Moderate AD** Dry skin, frequent itching, excoriation, skin redness, significant impact on QOL and sleep	**Severe AD** Large areas of dry skin, constant itching, redness, excoriation that strongly impedes daily routine and sleep
Basic maintenance treatment ▪ Skin care involving regular use of emollients and moisturizers, as well as bathing in warm water using non-soap cleansers or mild soaps ▪ Avoidance of irritants (eg, soaps, wool), temperature extremes, and proven allergens	**Basic maintenance treatment** ▪ All elements of basic maintenance treatment for mild disease, **PLUS** – Maintenance TCS – **OR** maintenance TCI – **OR** crisaborole 2%* – **OR** ruxolitinib 1.5%† – **AND/OR** dilute bleach baths and other antiseptic measures, especially in patients with recurrent skin infections	**Basic maintenance treatment** ▪ Chosen elements of basic maintenance treatment for moderate disease, **PLUS** – A referral to an AD specialist – Phototherapy – Dupilumab‡ – Abrocitinib or upadacitinib§ – Systemic immunosuppressant therapy – Other options if AD remains uncontrolled Wet wrap therapy • Hospitalization
Acute treatment ▪ Low- to medium-potency TCS applied to inflamed skin ▪ **OR** TCI ▪ **OR** crisaborole 2%* ▪ **OR** ruxolitinib 1.5%†	**Acute treatment** ▪ A medium- to high-potency TCS applied to inflamed skin, low-potency TCS for other sensitive areas ▪ **OR** TCI ▪ **OR** crisaborole 2%* ▪ **OR** ruxolitinib 1.5%†	**Acute treatment** ▪ A medium- to high-potency TCS applied to inflamed skin, low-potency TCS for other sensitive areas ▪ If unresolved after 7 days, consider the following: – Potential nonadherence – Infection – Misdiagnosis – Contact allergy treatment – **Referral** to an AD specialist
Advancing from mild to moderate AD: When symptoms persist despite appropriate use of TCS, antiseptic measures, and irritant avoidance **Advancing from moderate to severe AD:** When symptoms persist despite an aggressive course of TCS/TCI/crisaborole/ruxolitinib prescription therapy, especially when there is a large negative impact on daily routine, sleep, or psychosocial health		

Approvals current as of April 2023.
*Indicated for patients aged ≥3 months with mild-to-moderate AD. †Indicated for short-term and noncontinuous chronic treatment of mild-to-moderate AD in nonimmunocompromised patients aged ≥12 years whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. ‡Indicated for patients aged ≥6 months with moderate-to-severe AD. §Indicated for adults and pediatric patients aged ≥12 years with refractory, moderate-to-severe AD. Adapted for educational purposes only from Eichenfield LF, et al. *Paediatr Drugs*. 2022;24:293-305.



Dupilumab in Children Aged 6 Months to ≤6 Years With Uncontrolled AD

Liberty AD PRESCHOOL: A Randomized, Double-Blinded, Placebo-Controlled Phase 3 Trial

Patient Population

- Aged 6 months to 6 years at screening
- Moderate-to-severe AD (IGA 3 or 4), diagnosed according to AAD consensus criteria
- Inadequate response to TCS (defined as a course of TCS for 27 days within the past 6 months) before screening

N=162

R

- Dupilumab + low-potency TCS (n=83)
- Placebo + low-potency TCS (n=79)

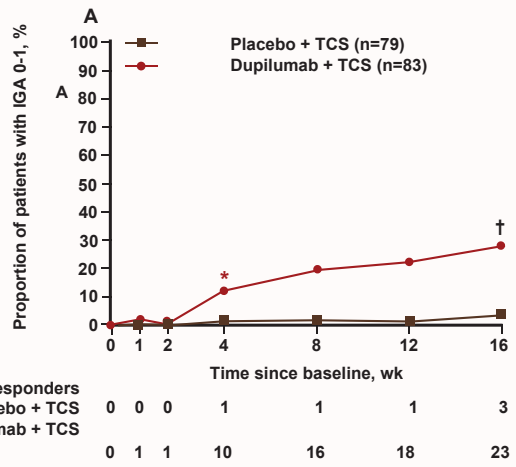
Primary Efficacy Endpoint

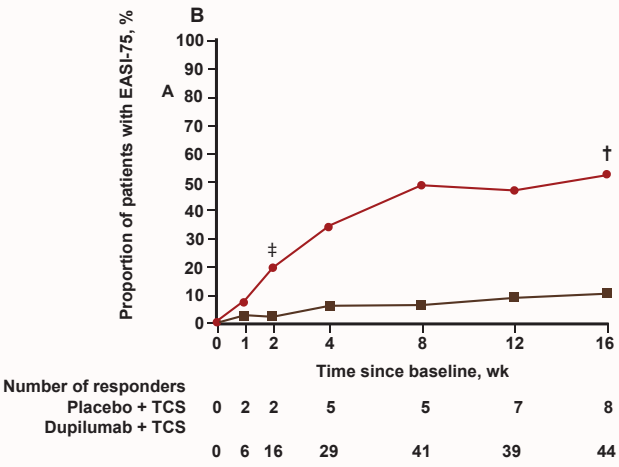
- Proportion of patients with IGA 0 or 1

Key Secondary Endpoints

- % change from baseline to week 16 in EASI
- Weekly mean of daily worst scratch and itch NRS score

Primary and Key Secondary Endpoints





A) Proportion of patients with an IGA score of 0-1 through to week 16 (primary endpoint). B) Proportion of patients with EASI-75 through to week 16 (key secondary endpoint, identified as a coprimary endpoint for EU or EU Reference Market Countries). Values after first rescue treatment use were set to missing. Patients with missing values at week 16 because of rescue treatment, withdrawn consent, AEs, and lack of efficacy (as deemed by the investigator) were considered as nonresponders. Patients with missing values because of other reasons, including COVID-19, were imputed by multiple imputation. Reproduced for educational purposes only from Paller AS, et al. *Lancet.* 2022;400:908-919. *Nominal $p < .012$. †$p < .0001$. ‡Nominal $p < .0022$.

Dupilumab significantly improved AD signs

and symptoms vs placebo in children aged 6 months to 6 years.

Dupilumab was well tolerated

and showed an acceptable safety profile, similar to results in older children and adults.

Adverse Events

Treatment-emergent AEs that occurred in at least 3% of patients in the dupilumab group and at a higher rate than in the placebo group were molluscum contagiosum, viral gastroenteritis, rhinorrhea, and dental caries

- **Transient increase in mean eosinophil count was observed, without clinical relevance, consistent with previous trials**
- **All cases of conjunctivitis were mild and resolved**
- **Observed rates of viral gastroenteritis and dental caries were higher with dupilumab; however, the numbers of affected patients were too few to draw conclusions**

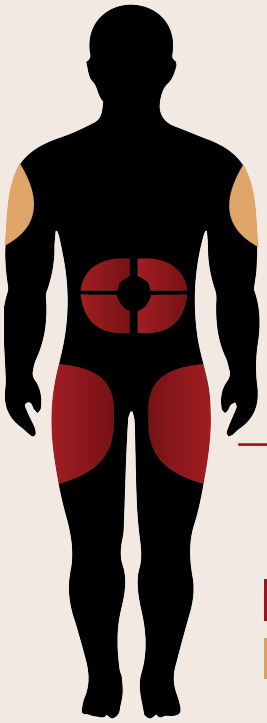
Recommendations for Vaccination in Pediatric Patients With AD Treated With Dupilumab

- **Consider completing all age-appropriate vaccinations as recommended by guidelines before initiating treatment with dupilumab**
- **Inactivated vaccines**
  - Dupilumab does not appear to affect the development of protective antibody titers to inactivated vaccines
  - Dupilumab treatment does not need to be interrupted for administration of inactivated vaccines
  - For patients receiving dupilumab treatment, seasonal inactivated influenza vaccination should continue as recommended

- **Live attenuated vaccines**
  - Avoid use of live attenuated vaccines in patients treated with dupilumab
  - When live attenuated vaccinations are required, they should be given ≥4 weeks before initiation of dupilumab treatment, if possible
- **During dupilumab treatment, measurement of specific antibody levels can be considered to ensure serologic protection after vaccination on dupilumab treatment**
- **There is no evidence to suggest that immunization during dupilumab treatment causes an exacerbation of AD**

Mitigation and Management of Dupilumab-Related AEs

- **Injection site reactions**
  - Dupilumab administration may be associated with injection site reactions
  - Select a different site each time dupilumab is injected



- **Conjunctivitis**
  - Monitor for conjunctival infection regularly
    - Encourage patients and caregivers to report any eye discomfort
    - Evaluate for conjunctival erythema at follow-up visits
    - Counsel and closely monitor patients with a history of eye discomfort
  - Diagnose and adequately treat all patients with ocular symptoms; refer patients to an ophthalmologist for further assessment and comanagement if necessary
  - Employ topical treatments for dupilumab-associated conjunctivitis
    - Artificial tears
    - Fluorometholone 0.1% eye drops
    - Cyclosporine-containing eye drops (multiple formulations available)
    - Tacrolimus 0.03% eye ointment (off label)

Abbreviations:

AAD: American Academy of Dermatology
AD: atopic dermatitis
AE: adverse event
EASI: Eczema Area and Severity Index
EU: European Union
FDA: US Food and Drug Administration
IGA: Investigator Global Assessment
NRS: Numerical Rating Scale
R: randomized
QOL: quality of life
TCI: topical calcineurin inhibitor
TCS: topical corticosteroid

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