Pharmaceutical Treatments for Atopic Dermatitis

Surveillance Report

Washington P&T Committee Meeting

June 21, 2023

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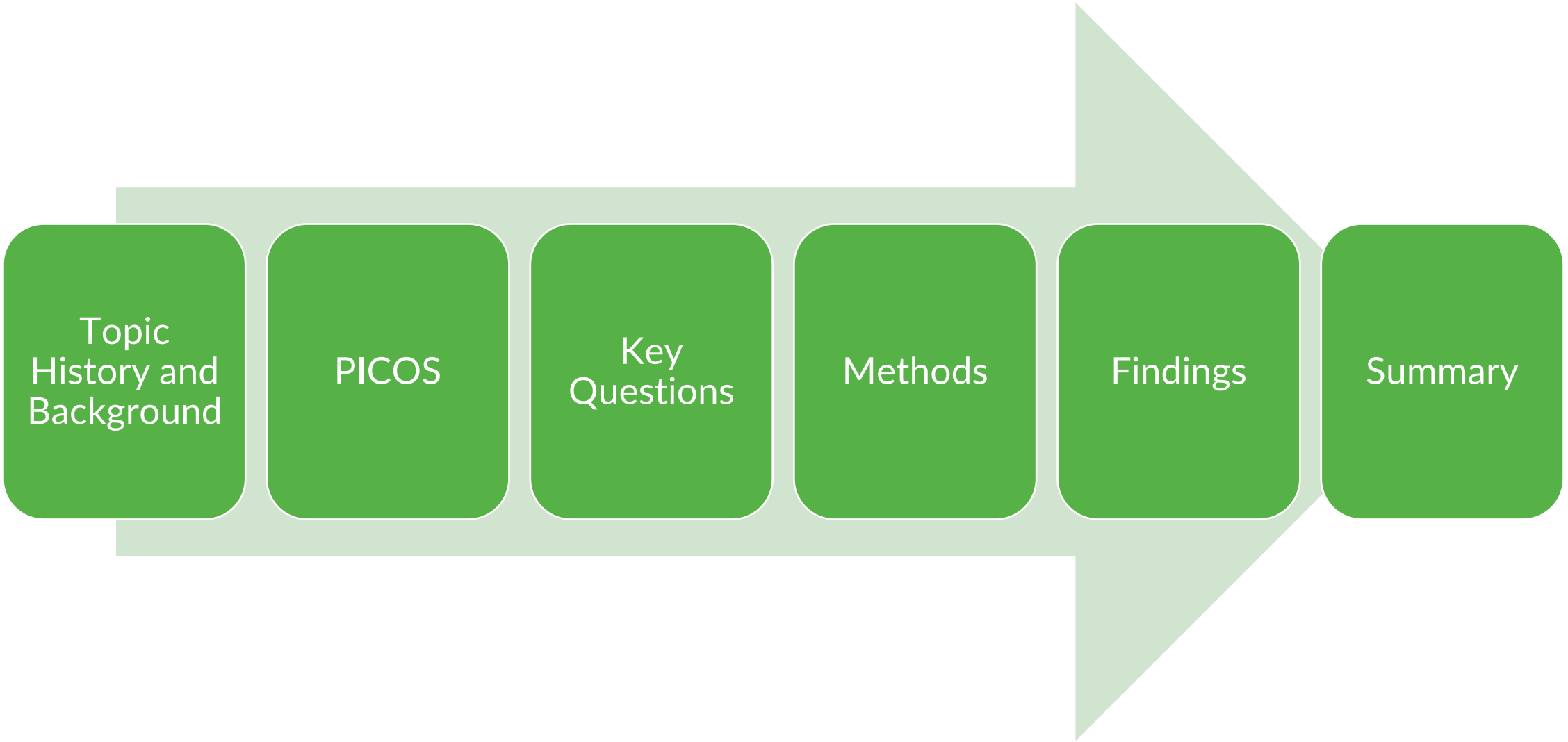
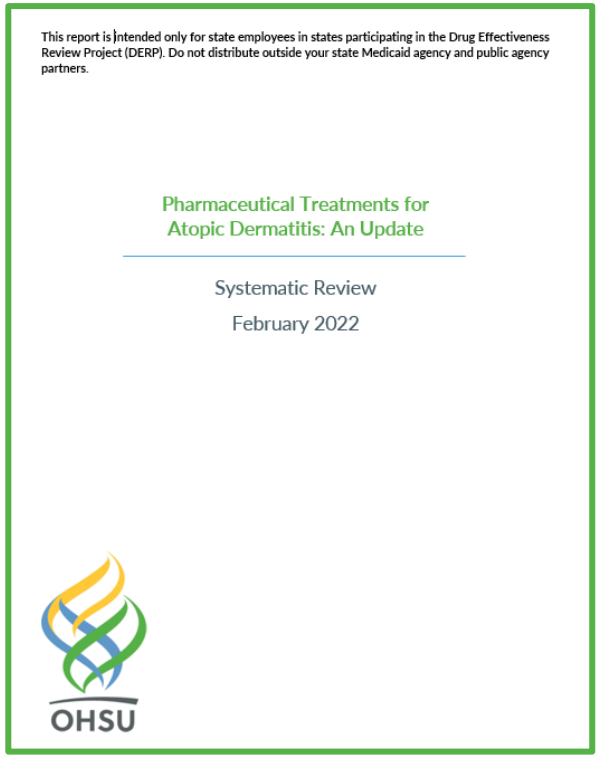
OHSU

Overview


Topic History and Background
PICOS
Key Questions
Methods
Findings
Summary

Topic History

Research Product Type	Date Presented	Search Dates
Systematic Review Update	February 2022	1/1/2017 to 8/25/2021
Surveillance Report	January 2019	September 2017 to November 2018
Systematic Review	November 2017	Database inception to September 2017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Pharmaceutical Treatments for Atopic Dermatitis: An Update

Systematic Review

February 2022

OHSU

Abbreviations

- AE: adverse event
- BSA: body surface area
- DLQI: Dermatology Life Quality Index
- EASI: Eczema Area and Severity Index
- FDA: US Food and Drug Administration
- IGA: Investigator's Global Assessment
- IL: interleukin
- JAK: Janus kinase
- POEM: Patient-Oriented Eczema Measure
- PP-NRS: Peak Pruritus Numerical Rating Scale
- QoL: quality of life
- RCT: randomized controlled trial
- SAE: serious adverse event
- SCORAD: scoring atopic dermatitis
- TCS: topical corticosteroids

Background

- Atopic dermatitis is an inflammatory skin disease causing intense itching and recurrent eczematous lesions that relapse and remit
  - Negatively affects self-esteem, limits social interactions
- Caused by environmental, genetic, and immunological components
- Affects roughly 7% of adults and 10% of children in the US
- First-line treatments include counseling to avoid triggers, and using moisturizers, TCS, and phototherapy
- Newer therapies include oral and injected systemic agents with anti-inflammatory properties

PICOS

- Population
  - Adults and children (all ages, including infants) with moderate-to-severe atopic dermatitis (eczema)

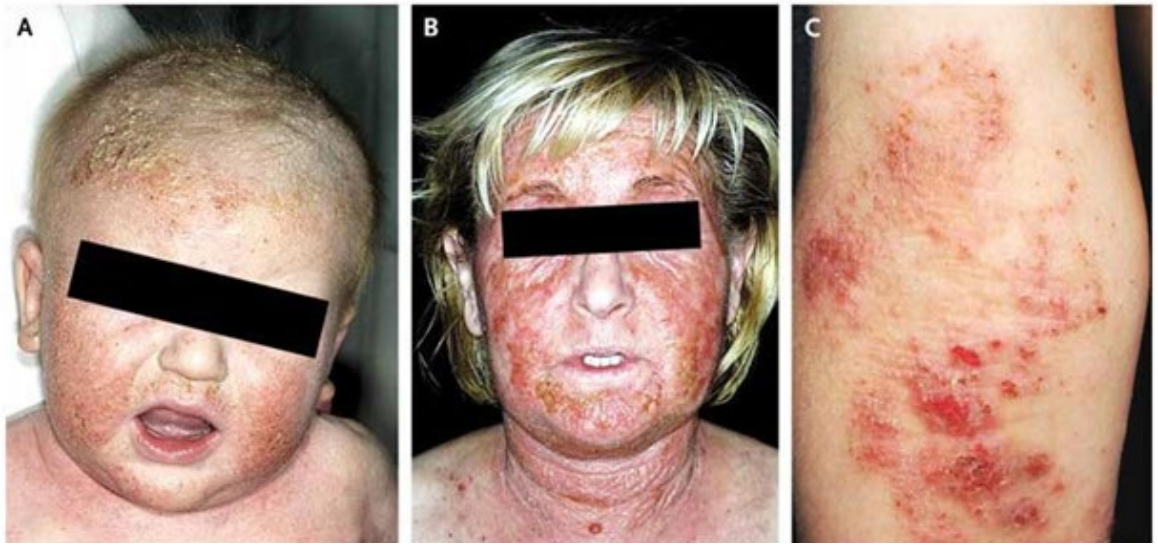


Image Source. New England Journal of Medicine

PICOS

- Interventions

Generic Name	Brand Name	Drug Class	Administration Route	FDA-Approval Date for Indication
FDA-approved therapies				
Abrocitinib	**Cibinqo**	JAK inhibitor	Oral	January 2022
Crisaborole	Eucrisa	Phosphodiesterase 4 inhibitor	Topical (ointment)	December 2016
Dupilumab	**Dupixent**	IL-4 receptor alpha antagonist	Injection	March 2017
Pimecrolimus	Elidel	Calcineurin inhibitor immunosuppressant	Topical (cream)	December 2001
Ruxolitinib	Opzelura	JAK inhibitor	Topical (cream)	September 2021
Tacrolimus	**Protopic**	Calcineurin inhibitor immunosuppressant	Topical (ointment)	December 2000
Tralokinumab	**Adbry**	IL-13 agonist	Injection	December 2021
Upadacitinib	**Rinvoq**	JAK inhibitor	Oral	January 2022

Note. ***Bold*** *is for indication of moderate-to-severe atopic dermatitis; all others listed are indicated for mild-to-moderate atopic dermatitis.*
Abbreviations. FDA: US Food and Drug Administration; IL: interleukin; JAK: Janus kinase.

PICOS

- Interventions (cont.)

Generic Name	Brand Name	Drug Class	Administration Route	FDA-Approval Date for Indication
Key pipeline therapies				
Baricitinib	Olumiant	JAK inhibitor	Oral	Not applicable
Lebrikizumab	Not applicable	IL-13 antagonist	Injection	Not applicable
Nemolizumab	Not applicable	IL-13 antagonist	Injection	Not applicable
Other therapies used off-label				
Azathioprine	Imuran	Immunosuppressant	Oral	Not applicable
Cyclosporine	Neoral	Immunosuppressant	Oral	Not applicable
Mycophenolate	Myfortic	Immunosuppressant	Oral	Not applicable
Omalizumab	Xolair	Monoclonal antibody	Injection	Not applicable

Abbreviations. FDA: US Food and Drug Administration; IL: interleukin; JAK: Janus kinase.

PICOS

- Comparators
  - Another included intervention (head-to-head)
  - TCS
  - Standards of care or placebo (for pipeline therapies only)

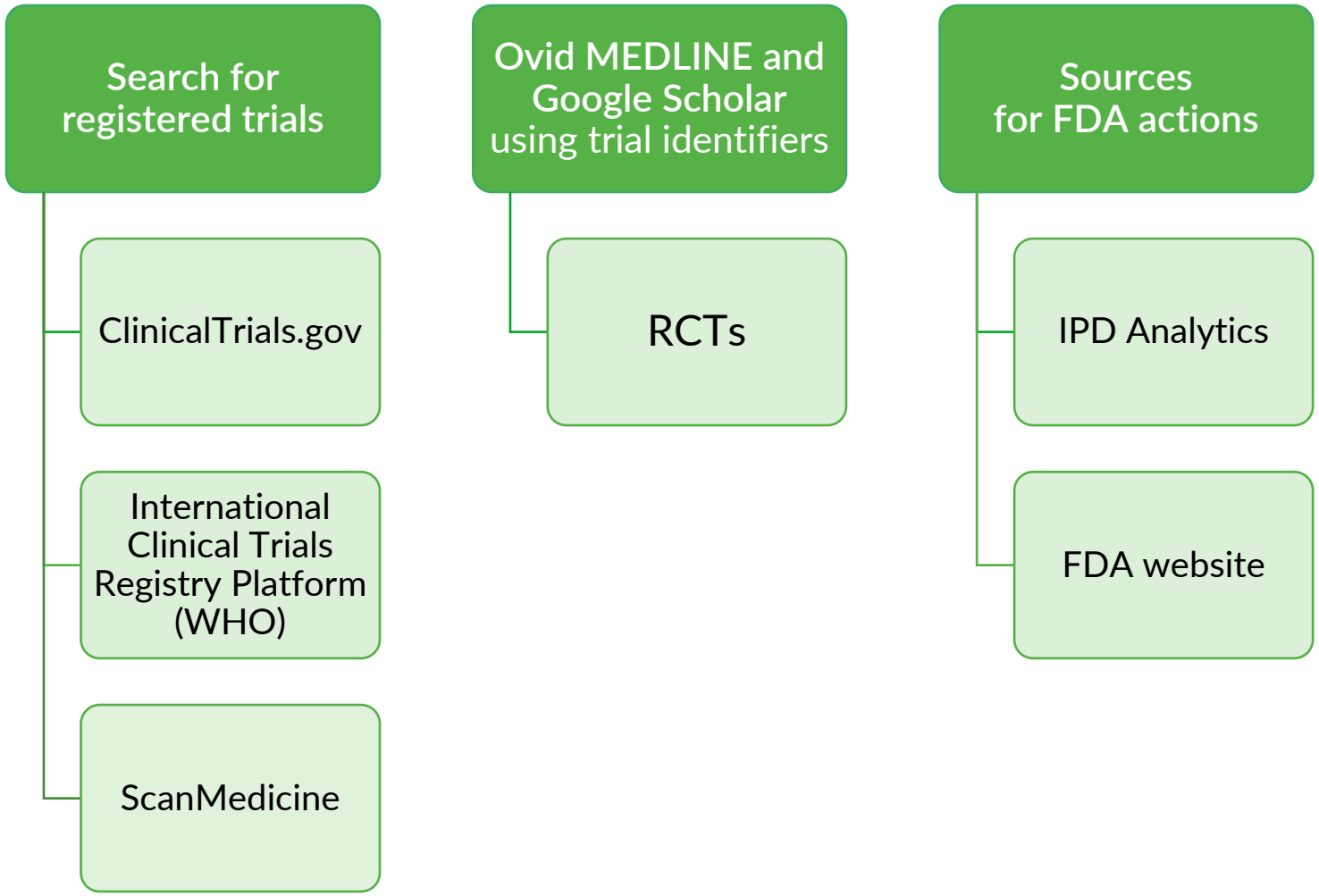
Image Source. Lampe & Company

- Outcomes:
  - Response to treatment (e.g., IGA)
  - Disease symptoms (e.g., EASI scores, PP-NRS, SCORAD, POEM, percentage of BSA affected)
  - QoL (e.g., DLQI)
  - AEs
  - SAEs
- Study Designs:
  - RCTs

Key Questions

1. Comparative effectiveness of included interventions for atopic dermatitis
2. Effectiveness of pipeline therapies for atopic dermatitis
3. Comparative harms of included interventions for atopic dermatitis
4. Harms of pipeline therapies for atopic dermatitis
5. Ongoing studies for all included interventions

Methods



- All searches covered August 1, 2021 through January 6, 2023

Findings

Findings: New Published Studies

- We identified 6 new RCTs for 5 of the 8 FDA-approved drugs for atopic dermatitis
  - 1 new head-to-head trial of abrocitinib versus dupilumab
  - 5 new placebo-controlled trials for:
    - Abrocitinib
    - Crisaborole
    - Dupilumab
    - Tralokinumab
    - Upadacitinib
- No new eligible published RCTs were identified for pimecrolimus, ruxolitinib, or tacrolimus

Findings: New Published Studies (cont.)

Author, Year Trial Number/Name Location	Population Sample Size	Treatment Groups Study Duration	Eligible Published Outcomes
Head-to-head trial (abrocitinib vs. dupilumab)			
Reich et al., 2022 NCT04345367 JADE DARE 15 countries including the US	Individuals ≥ 18 years with moderate-to-severe atopic dermatitis and inadequate response to topical treatments N = 727	• Abrocitinib, 200 mg daily + placebo injection every other week • Dupilumab, 300 mg injection every other week (with 600 mg loading dose) + daily oral placebo 26 weeks	• Disease symptoms • QoL • AEs, SAEs
Abrocitinib (Cibinqo)			
Blauvelt et. el., 2022 NCT03627767 JADE REGIMEN 21 countries including the US	Individuals ≥ 12 years with moderate-to-severe atopic dermatitis and inadequate response to topical treatments N = 798	• Abrocitinib 200 mg daily • Abrocitinib 100 mg daily • Placebo 12 week open-label induction period followed by 40- to 52-week randomized period	• Response • Disease symptoms • QoL • AEs, SAEs • Withdrawals due to AEs
Crisaborole (Eucrisa)			
Fujita et al., 2021 NCT03954158 Japan	Individuals ≥ 2 years in Japan with mild-to-moderate atopic dermatitis N = 727	• Crisaborole, 2%, ointment • Placebo 2 weeks	• Response • Disease symptoms • QoL • AEs, SAEs

Abbreviations. AE: adverse event; QoL: quality of life; SAE: serious adverse event.

Findings: New Published Studies (cont.)

Author, Year Trial Number/Name Location	Population Sample Size	Treatment Groups Study Duration	Eligible Published Outcomes
Dupilumab (Dupixent)			
Zhao et al., 2022 NCT03912259 China	Individuals ≥ 18 years in China with moderate-to-severe atopic dermatitis and inadequate response to topical treatments N = 165	• Dupilumab, 300 mg injection every other week (with 600 mg loading dose) • Placebo 16 week treatment and 12 week follow up periods	• Response • Disease symptoms • QoL • AEs, SAEs
Tralokinumab (Adbry)			
Gutermuth et al., 2022 NCT03761537 ECZTRA 7 7 countries	Individuals ≥ 18 years with severe atopic dermatitis and inadequate response to topical treatments N = 277	• Tralokinumab, 300 mg injection every 2 weeks (with 600 mg loading dose) • Placebo 26 weeks	• Disease symptoms • QoL • AEs, SAEs
Upadacitinib (Rinvoq)			
Katoh et al., 2022 NCT03661138 Rising Up Japan	Individuals ≥ 18 years in Japan with moderate-to-severe atopic dermatitis and inadequate response to topical treatments N = 272	• Upadacitinib, 15 mg daily + TCS • Upadacitinib, 30 mg daily + TCS • Placebo + TCS 16 weeks intervention, up to 112 weeks open label	Interim results (112 weeks) • Response • Disease symptoms • AEs, SAEs

Abbreviations. AE: adverse event; QoL: quality of life; SAE: serious adverse event; TCS: topical corticosteroid.

Findings: Ongoing Studies for FDA-Approved Therapies

We identified 15 ongoing studies that would be eligible, if published:

- 3 head-to-head RCTs
  - **Crisaborole** versus **tacrolimus** in youth, 2 to 15 years
    - Sample size: 92 (actual)
    - Completed and with results
  - **Dupilumab** versus **cyclosporine** versus TCS in youth, 2 to 18 years
    - Sample size: 318 (estimated)
    - Completion date: January 2024 (estimated)
  - **Upadacitinib** versus **dupilumab** in adolescents and adults, 12 to 64 years
    - Sample size: 880 (estimated)
    - Completion date: May 2025 (estimated)

Findings: Ongoing Studies for FDA-Approved Therapies (cont.)

- 1 RCT of **abrocitinib** versus placebo in adults
  - Sample size: 46 (actual); completed in November 2021
- 4 RCTs of **crisaborole** versus placebo (1 also with TCS)
  - Sample size range 31 (estimated) to 494 (actual); 3 completed, 1 with results
- 1 RCT of **dupilumab** versus placebo in adults
  - Sample size: 30 (estimated); completion date: August 2022 (estimated)
- 2 RCTs of **ruxolitinib** versus placebo; 1 study in children, 1 study ages 12 to 70 years
  - Sample sizes: 75 and 315 (estimated); completion dates: September 2022, March 2023
- 2 RCTs of **tacrolimus** versus TCS in youth
  - Sample sizes: 30 and 200 (estimated); completion dates: May 2022, 1 not reported
- 2 RCTs of **tralokinumab** versus placebo (1 also with TCS)
  - Sample sizes: 106 and 301 (actual); both completed with results

Findings: Ongoing Studies for Key Pipeline Therapies

We identified 11 ongoing studies that would be eligible, if published:

- 3 RCTs of **baricitinib** versus placebo in individuals 2 years and older
  - Sample size range: 463 (actual) to 1,645 (actual)
  - Completion date range: November 2019 (actual) to April 2022 (estimated)
  - 2 with results on ClinicalTrials.gov
- 6 RCTs of **lebrikizumab** versus placebo in individuals 6 months and older
  - Sample size range: 228 (actual) to 445 (actual)
  - Completion date range: June 2021 (actual) to July 2024 (estimated)
  - 3 with results on ClinicalTrials.gov
- 2 RCTs of **nemolizumab** versus placebo in individuals 12 years and older
  - Sample sizes: 750 for both trials
  - Completion dates: August 2022 (actual) to December 2022 (estimated)

New FDA Actions

Drugs, Formulations, Indications, Serious Harms, or Warnings

New FDA Actions: Drugs and Formulations

- No new FDA-approved drugs were identified since the searches in the most recent systematic review
  - 17 additional pipeline therapies were identified in IPD analytics for atopic dermatitis (in addition to 3 key pipeline drugs in the prior report)
- 2 new formulations were identified for the FDA-approved therapies
  - Dupilumab (Dupixent): new dose of 100 mg in 0.67 mL solution
  - Upadacitinib (Rinvoq): new dose of 45 mg extended-release tablet

New FDA Actions: Indications, Harms, and Warnings

- On June 7, 2022, the FDA approved an expanded **indication** for dupilumab (Dupixent) for atopic dermatitis in children 6 months to 5 years of age

- One **new boxed warning** was listed on FDA labels for JAK inhibitors indicating higher rates for all-cause mortality, including sudden cardiovascular death

Image Source. clker.com

Summary

New Clinical Evidence and
FDA Actions Since the Most Recent Systematic Review

New Clinical Evidence and FDA Actions

- 6 new RCTs for FDA-approved drugs
  - 1 head-to-head study (abrocitinib versus dupilumab)
  - 5 placebo-controlled trials (1 each for abrocitinib, crisaborole, dupilumab, tralokinumab, and upadacitinib)
- 25 ongoing studies
  - 15 ongoing studies for FDA-approved drugs
    - 3 head-to-head studies
    - 4 with TCS
    - 8 with placebo only
  - 11 ongoing studies for the 3 key pipeline drugs
    - All with placebo only

New Clinical Evidence and FDA Actions (cont.)

- No new FDA-approved drugs
  - 3 key pipeline drugs and 17 other pipeline drugs have not been approved by the FDA
- 2 new formulations
  - 2 new doses
- 1 new indication for atopic dermatitis
  - Dupilumab for pediatric patients ages 6 months to 5 years
- 1 new serious boxed warning for all JAK inhibitors (abrocitinib, ruxolitinib, upadacitinib)
  - Increased risk for all-cause mortality (based on study in persons with a different inflammatory condition taking drug via oral route)

Questions?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