A compilation of key content from select presentations at the 2021 South Beach Symposium Part I: Medical Dermatology Summit and the Masters of Pediatric Dermatology

David E. Cohen, M.D., M.P.H.
Charles and Dorothea Harris Professor and Vice Chairman for Clinical Affairs
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Mark Lebwohl, MD
Dean for Clinical Therapeutics
Icahn School of Medicine at Mount Sinai
Chairman Emeritus
Kimberly and Eric J. Waldman Department of Dermatology
Psoriasis Pathogenesis

IL-23/T17–mediated effects on immune cell populations and keratinocyte biology in psoriatic skin

IL-36Ra = IL36RN (gene)

Dr. David Cohen
IL-12/IL-23 Inhibitors

- **Ustekinumab**
  - Approved by FDA for treatment of psoriasis in 2009
  - Most recently approved by FDA for pediatric psoriasis in 2020

Dr. Mark Lebwohl
IL-23 Inhibitors

- **Guselkumab**
  - Approved by FDA for treatment of plaque psoriasis in 2017
  - Currently in phase 3 trials for pediatric patients aged 6 years and older

- **Tildrakizumab**
  - Approved by FDA for treatment of plaque psoriasis in 2018
  - Currently in phase 2/3 trials for pediatric patients aged 12 years and older

Macrophage


Dr. Mark Lebwohl
IL-23 Inhibitors

- **Risankizumab**
  - Approved by FDA for treatment of plaque psoriasis in 2019
  - Currently in phase 3 trials for pediatric patients aged 6 years and older

- **Mirikizumab**
  - Recently completed phase 3 studies in adult patients with moderate-to-severe plaque psoriasis with favorable results
IL-17A Inhibitors

- **Ixekizumab**
  - Approved by FDA for treatment of plaque psoriasis in 2016
  - Most recently approved by FDA for pediatric psoriasis in 2020

- **Secukinumab**
  - Approved by FDA for treatment of plaque psoriasis in 2016
  - Currently in phase 3 trials studying safety and efficacy in pediatric patients aged 6 years and older

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Dr. Mark Lebwohl
IL-17 Inhibitors

- **Brodalumab**
  - Approved by FDA for treatment of psoriasis in 2017
  - Currently in phase 3 trials studying safety and efficacy in pediatric patients aged 12 years and older
Tapinarof

• **Tapinarof**
  - Topical, small molecular TAMA that directly binds to and activates AhR transcription factor
  - AhR activation via tapinarof *in vitro* and animal models leads to:
    - Reduction of Th17 cytokine expression
    - Reduction of Th2 cytokine expression
    - Decreased oxidative stress
    - Increased skin barrier proteins
  - Recently completed phase 3 clinical trials with positive results reported

AhR pathway

1. Ligand crosses cell membrane and binds to cytoplasmic AhR
2. Nuclear translocation of activated AhR complex
3. Heterodimerization with ARNT
4. Activated AhR-ARNT complex binds DNA and modulates gene expression

AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; TAMA, therapeutic aryl hydrocarbon receptor modulating agent; Th, T helper cell.


Dr. Leon Kircik
Roflumilast

- **Roflumilast (ARQ-151)**
  - Topical cream, a potent, selective PDE-4 inhibitor
  - Demonstrates ~25 to >300-fold higher potency than currently available PDE-4 inhibitors
  - Recently hit primary endpoints in pair of Phase 3 clinical trials, and seeking FDA approval for late 2021

**ARQ-151, Roflumilast Cream, Improved Chronic Plaque Psoriasis in Phase 2b Study**

Mark G. Lebwohl¹, Kim A. Papp², Linda Stein Gold³, Melinda J. Gooderham⁴, Leon H. Kirick⁵, Zoe D. Draelos⁶, Steven E. Kempers⁷, Mathew Zirwas⁸, Kathleen Smith⁹, David W. Osborne⁹, Marie-Louise Trotman¹⁰, Lynn Navale⁹, Charlotte Merritt⁹, David R. Berk⁹, Howard Welgus⁹

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Dr. Leon Kirick
Pediatric Psoriasis: Treatment Landscape

• Only 6 FDA medications approved for pediatric patients

• Biologics:
  - Etanercept: ≥ 6 years
  - Ustekinumab: ≥12 years
  - Ixekizumab: ≥ 6 years

• Topicals:
  - Calcipotriene Foam 0.005%: ≥ 4 years scalp and body
  - Calcipotriene 0.005% and betamethasone 0.064% foam:
    ≥ 12 years: mild to severe plaque psoriasis
  - Calcipotriene 0.005% and betamethasone 0.064% suspension:
    scalp and body: ≥ 12 years

Dr. Adelaide Hebert
Pediatric Psoriasis: Therapeutic Outlook

**BIOLOGICS:**
- Secukinumab: IL 23 inhibitor: 6 to 17 years of age
- Brodalumab: anti IL 17: 6 to 17 years of age
- Tildrakizumab: IL 23 inhibitor: 12 to 17 years of age

**TOPICALS:**
- Halobetasol 0.01%/ tazarotene 0.045% lotion
- Roflumilast: PDE 4 inhibitor: 2 to adulthood
  - used systemically in COPD in adults
Treating Psoriasis in Pediatric Patients

- **Younger** children
  - Consider strep throat
  - Coal tar topical
  - Topical steroids
  - Topical calcineurin inhibitors (inverse psoriasis)
  - Phototherapy

- **Older** children
  - Topical steroids/other topicals
  - Phototherapy / laser
  - Methotrexate
  - Cyclosporin
  - Topical/oral retinoids
  - Biologics

Dr. Adelaide Hebert
Network meta-analysis: Quality of life with novel treatments of moderate to severe plaque psoriasis

- Phase 2 and 3 clinical trials all anchored on placebo
- Interventions studied:
  - Anti-TNF agents: adalimumab, etanercept, infliximab, certolizumab pegol
  - Anti-IL agents: ustekinumab, secukinumab, ixekizumab, brodalumab, risankizumab, guselkumab, tildrakizumab
  - Anti-PDE4: apremilast
  - Fumaric acid esters: dimethyl fumarate

Quality of Life Across Therapeutic Agents

Estimated median DLQI 0/1 response rates at Weeks 12–16

*Weight-based

Warren R, et al. EADV 2019, P1716 Sponsored by AbbVie