

# Treatment updates for children and teens with AA

Cathryn Sibbald, MD MSc FRCPC DABD

University of Toronto, SickKids Hospital

July 2024

# Disclosures

- I have received honoraria for speaking from the following:
  - Abbvie
  - Leo
  - Novartis
  - Pfizer
  - Sanofi/Regeneron
  - UCB
  
- I have received consultancy fees from the following:
  - Sanofi/Regeneron
  - Pfizer

# Alopecia areata in children and teens

- Disease differences
- Treatment considerations
  - Often more data/ indications for adults
  - Family unit decision
  - Consideration of pain/ fear (needles, bloodwork)
  - Vaccine considerations
  - Pregnancy considerations

---

# The Alopecia Areata Consensus of Experts (ACE) study: Results of an international expert opinion on treatments for alopecia areata



Nekma Meah, MBChB, MRCP (UK),<sup>a</sup> Dmitri Wall, MBBCh, BAO, MRCP,<sup>a</sup>  
Katherine York, MBBCh, FCDerm (SA),<sup>b</sup> Bevin Bhojrul, MBBS, MRCP (UK),<sup>a</sup> Laita Bokhari, MPhil Med,<sup>a</sup>  
Daniel Asz Sigall, MD,<sup>c</sup> Wilma F. Bergfeld, MD,<sup>d</sup> Regina C. Betz, MD,<sup>e</sup> Ulrike Blume-Peytavi, MD,<sup>f</sup>  
Valerie Callender, MD,<sup>g</sup> Vijaya Chitreddy, FACD,<sup>a</sup> Andrea Combalia, MD,<sup>h</sup> George Cotsarelis, MD,<sup>i</sup>  
Brittany Craiglow, MD,<sup>j</sup> Jeff Donovan, MD, PhD,<sup>k</sup> Samantha Eisman, MBChB, MRCP, FACD,<sup>a</sup>  
Paul Farrant, MBBS, BSc, MRCP,<sup>l</sup> Jack Green, FACD,<sup>m</sup> Ramon Grimalt, MD, PhD,<sup>n</sup>  
Matthew Harries, PhD, FRCP,<sup>o</sup> Maria Hordinsky, MD, FAAD,<sup>p</sup> Alan D. Irvine, MD, DSc,<sup>q</sup>  
Satoshi Itami, MD, PhD,<sup>r</sup> Victoria Jolliffe, MA(Cantab), FRCP, FRCS(Ed), MRCGP, SFHEA,<sup>s</sup>  
Brett King, MD, PhD,<sup>t</sup> Won-Soo Lee, MD, PhD,<sup>u</sup> Amy McMichael, MD,<sup>v</sup> Andrew Messenger, MD, FRCP,<sup>w</sup>  
Paradi Mirmirani, MD,<sup>x</sup> Elise Olsen, MD,<sup>y</sup> Seth J. Orlow, MD, PhD,<sup>z,aa</sup> Bianca Maria Piraccini, MD, PhD,<sup>bb</sup>  
Adriana Rakowska, MD,<sup>cc</sup> Pascal Reygagne, MD,<sup>dd</sup> Janet L. Roberts, MD,<sup>ee</sup> Lidia Rudnicka, MD, PhD,<sup>cc</sup>  
Jerry Shapiro, MD, FAAD,<sup>z</sup> Pooja Sharma, MBBS, FACD,<sup>a</sup> Antonella Tosti, MD,<sup>ff</sup> Annika Vogt, MD,<sup>gg</sup>  
Martin Wade, FACD,<sup>hh</sup> Leona Yip, MBChB, PhD, FACD,<sup>ii</sup> Abraham Zlotogorski, MD,<sup>jj</sup> and  
Rodney Sinclair, MBBS, MD, FACD<sup>a</sup>

(2020)

# Consensus for 1<sup>st</sup> line Tx: Steroids!

Age	SALT 0-30		SALT 31-50		SALT >50	
	Acute	Chronic	Acute	Chronic	Acute	Chronic
0-6	TOPICAL					
7-12						
13-18	Topical OR <b>ILK</b>	<b>ILK</b>	Topical OR <b>ORAL</b>		Topical +/- <b>ORAL</b>	Topical



- ✓ 2.5-5mg/ml
- ✓ 0.1mL , 1cm apart, dermis/SC
- ✓ Areas with active disease
- ✓ Max 10-20mg/session (adult)



- ✓ Prednisolone preferred
- ✓ Daily administration
- ✓ 0.4-0.6mg/k/d taper over 12wks
- ✓ (adults: >12wks)

# Antihistamines

- Lower immune cell activity
  - **Olopatadine, desloratadine, fexofenadine**
- May prevent immune cell migration
  - ↓ CXCL10, ↓ IL15
- affect IFN gamma, perifollicular mast cells
  - **Esp Fexofenadine**
- Japan “C1” evidence (11 studies)
  - **Fexofenadine** (n=133) better vs DPCP alone
  - No effect: ebastine (n=26)

## For seasonal allergies:

Dosing  
(Per label, OTC)

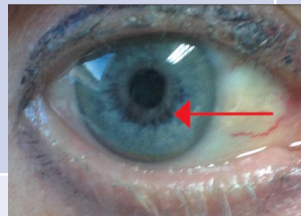
Age 2-12y:  
30mg every 12 hrs

Age 12y+:  
60mg every 12 hrs



# Non-Corticosteroid options, 2<sup>nd</sup> line

TOPICAL	PHOTOTHERAPY	SYSTEMIC
<ul style="list-style-type: none"> <li>✓ <b>Contact Immunotherapy</b> DPCP: 50-70% (1/wk x1y)</li> <li>✓ <b>Minoxidil (25-80%)</b> Adjunct to accelerate growth rate</li> <li>✓ <b>Calcineurin Inhibitors</b> Adjunct for scalp/eyebrow/beard</li> <li>✓ <b>Prostaglandin inhibitors</b> For eyelash AA (risk: iris discolouration)</li> </ul>	<p>Excimer laser</p>	<ul style="list-style-type: none"> <li>✓ <b>Methotrexate</b> Age 13y+ 0.4mg/kg/day (15-20mg/wk)</li> <li>✓ <b>Cyclosporine</b> Adults, 3-5mg/kg/d</li> <li>✓ <b>Janus Kinase inhibitors</b> Age 13y+, check varicella</li> </ul>
<p>No consensus: Anthralin: 25-75%, 0.5-1% x30min/d</p>		<p>No consensus: Azathioprine, dapsone, SSZ, statins, apremilast, etc</p>



# Minoxidil: likely works by >1 mechanism

- Converted to active drug in hair follicle
- Causes dilation of blood vessels
- Prolongs growth phase of hair
- May increase growth factors
- Evidence for both topical + oral forms in children!







REVIEW

# Evaluation of the Safety and Effectiveness of Oral Minoxidil in Children: A Systematic Review

Kimberly N. Williams · Christlene T. Y. Olukoga · Antonella Tosti

- 41 studies, 442 pediatric patients
- low-dose oral minoxidil may represent a safe option for the treatment of hair disorders in children.

# Methotrexate

✓ **Appropriate for tx of severe AA in age 13 +**

Dose: 0.4mg/kg/week (adults: 15-20mg weekly)

Children: 38.5-70% regrowth

Studies	Estimate (95% C.I.)	Ev/Trt
Phan	0.700 (0.376, 0.900)	7/10
Landis	0.571 (0.316, 0.794)	8/14
Chong	0.429 (0.206, 0.684)	6/14
Lucas	0.385 (0.170, 0.656)	5/13
Batalla	0.667 (0.154, 0.957)	2/3
Royer	0.429 (0.206, 0.684)	6/14
<b>Overall (<math>I^2 = 0\%</math>, <math>P = 0.645</math>)</b>	<b>0.497 (0.378, 0.617)</b>	<b>34/68</b>

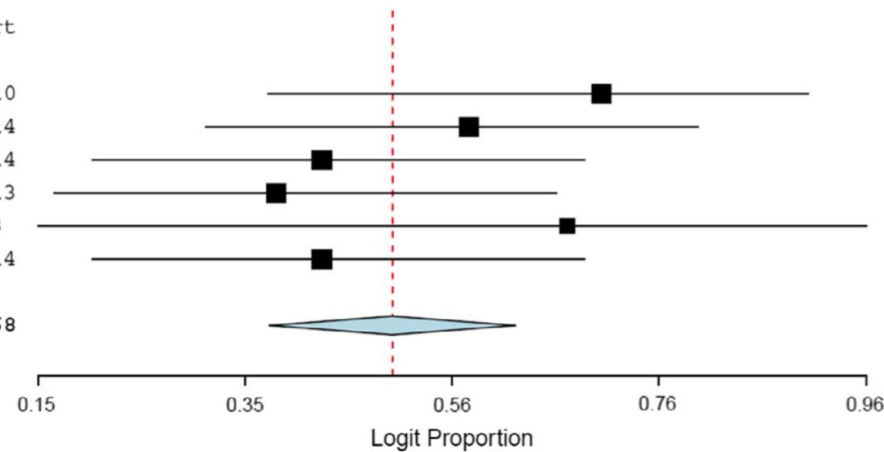
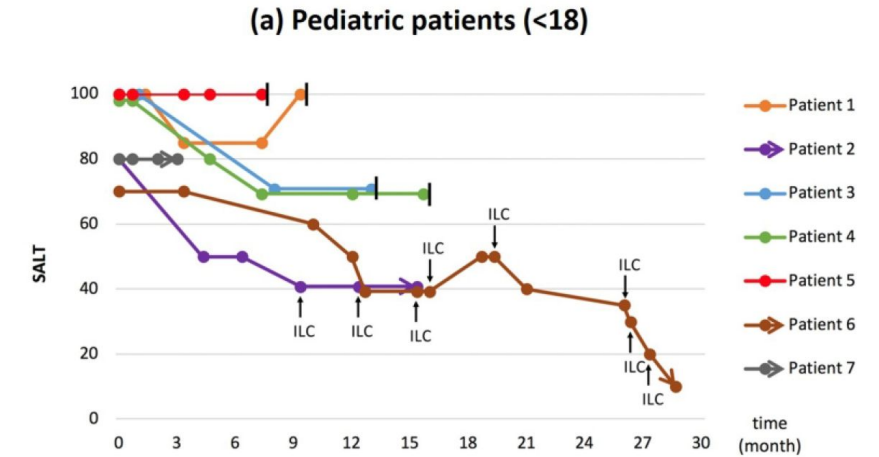


Figure 1 Forest plot showing pooled proportion of good or complete response to methotrexate in paediatric alopecia areata



**Minimal information on duration of tx or risk of relapse**

# Ritlecitinib (JAK3/TEC): ALLEGRO, Phase IIb/III Study

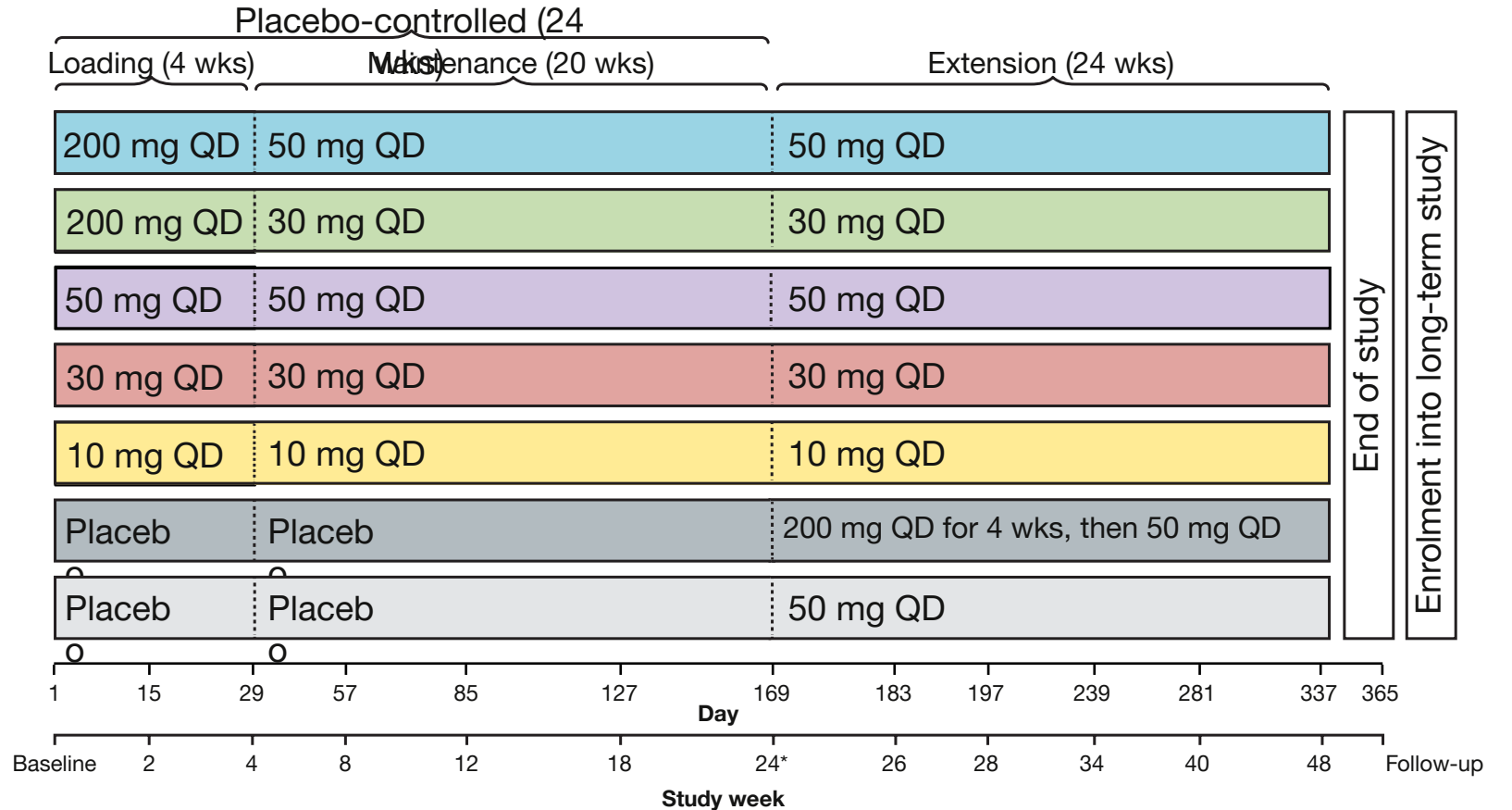
Patients (N=718)<sup>1</sup>

Males or females  $\geq 12$  years with  $\geq 50\%$  AA, including AT + AU

No evidence of terminal hair regrowth over 6 months

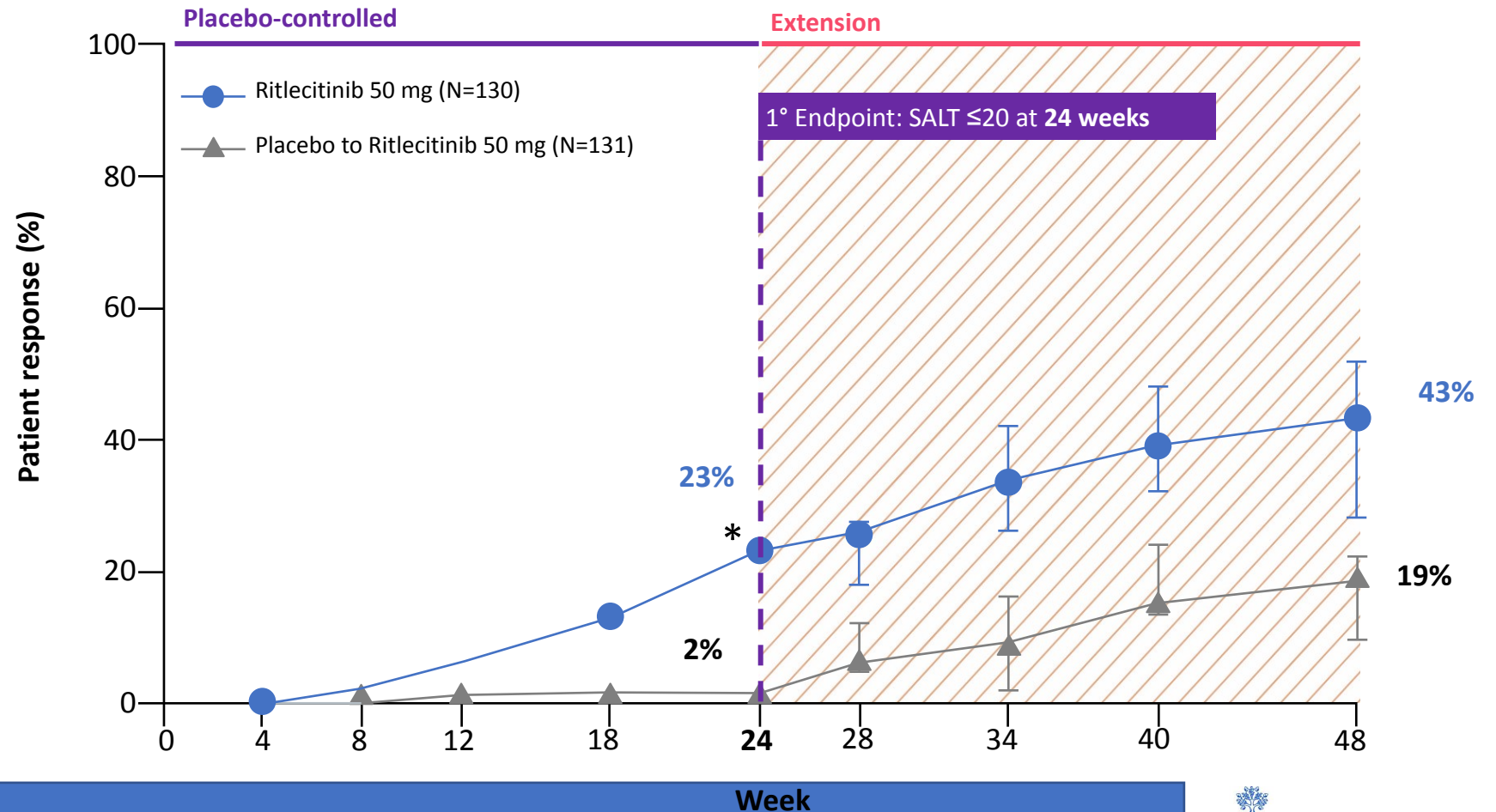
Current episode  $\leq 10$  years

No other known cause of alopecia



# Ritlecitinib (JAK3/TEC): ALLEGRO, Phase IIb/III Study

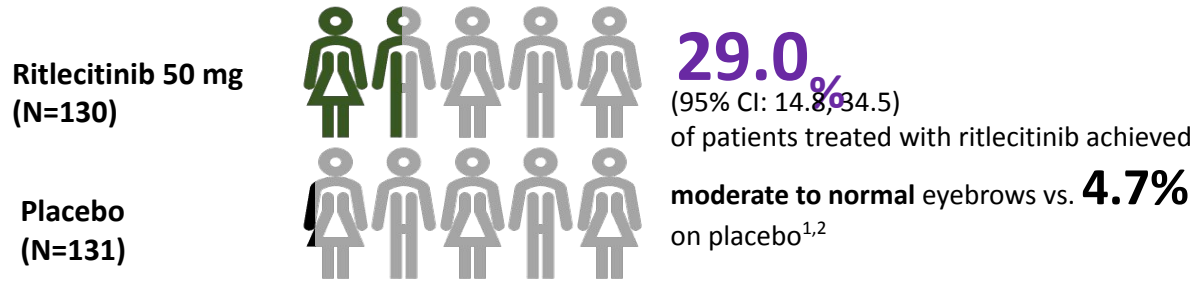
Study participants included both **adults and adolescents** (12 years and older)



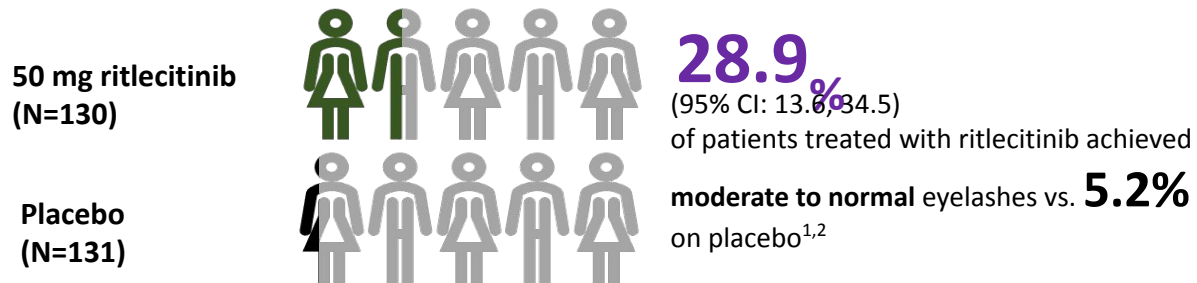
# Ritlecitinib: Regrowth of eyebrows and eyelashes

Week

24  
Eyebrows

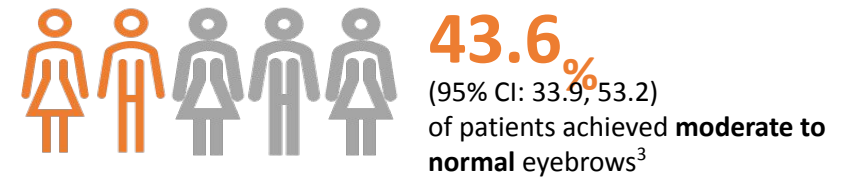


Eyelashes

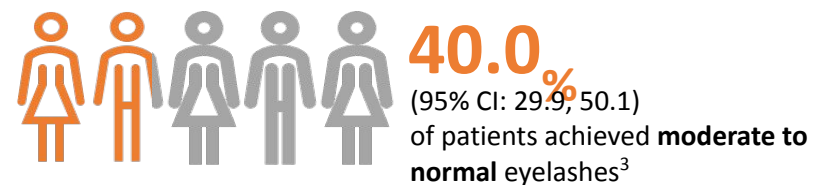


Week

48  
Eyebrows

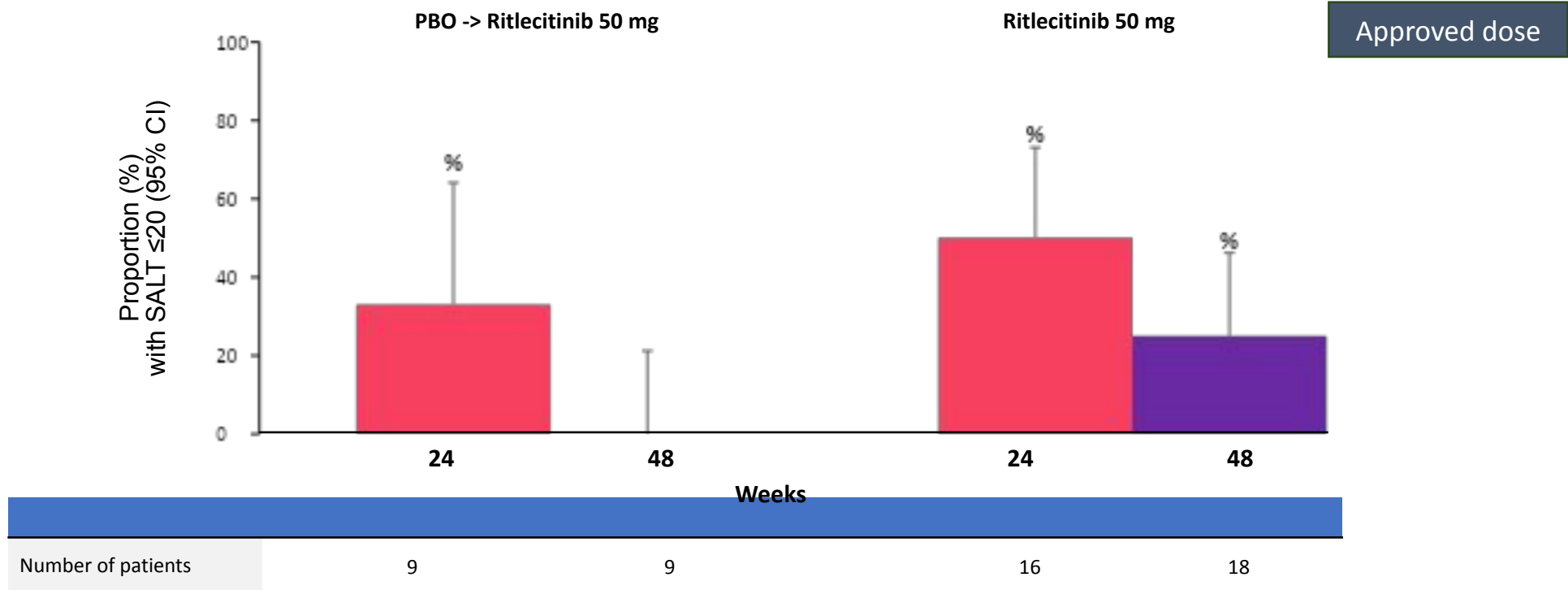


Eyelashes



# Ritlecitinib results in Adolescent patients

Proportion of Adolescents With Response Based on SALT Score  $\leq 20$  at Weeks 24 and 48



**Indication:** Treatment of adults and adolescents 12 years and older with severe AA

Prior to treatment initiation

**Screen** patient for tuberculosis and viral hepatitis



Patient **monitoring:**

- Liver enzymes
- Lymphocytes
- Platelets
- Malignancies
- Immunization



Consider **drug-drug interactions:**

- Sumatriptan
- Midazolam
- Rifampin
- Medicines containing caffeine



Consider **reproductive health** including pregnancy and lactation



Warnings:

- Serious infections
- Cancers (skin)

Stop if no response after 36 weeks

Chance of losing regrowth if stopped

# Other JAK inhibitors: none approved for alopecia areata in <18yrs

## Tofacitinib (JAK1, 3)

-approved for juvenile arthritis in age 2yrs + (USA)

## Upadacitinib (JAK1)

-approved for atopic dermatitis in age 12+ (USA, Canada)  
-approved for juvenile arthritis in age 2+ (USA)

## Baricitinib (JAK1, 2)

-approved for alopecia areata in adults (USA, Canada)  
-approved for atopic dermatitis in age 4yrs+ (Europe)

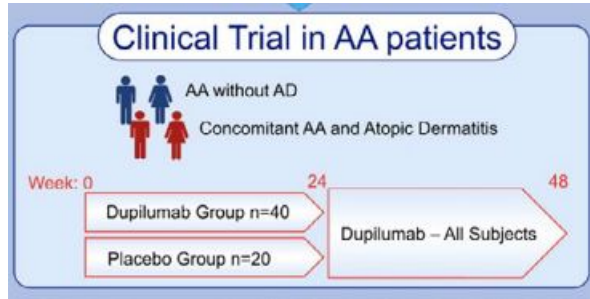
## Abrocitinib (JAK1)

-approved for atopic dermatitis in age 12+ (USA, Canada)



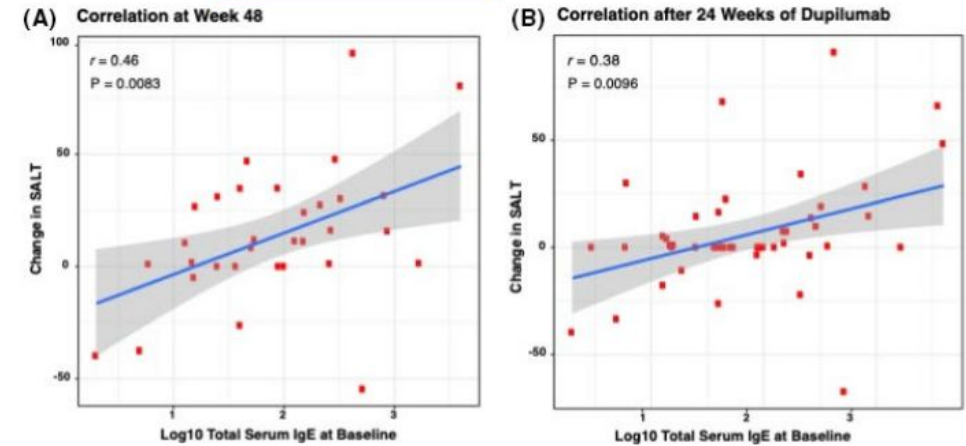
# Dupilumab: The Evidence

## Those with **history of atopy +/- or high IgE**

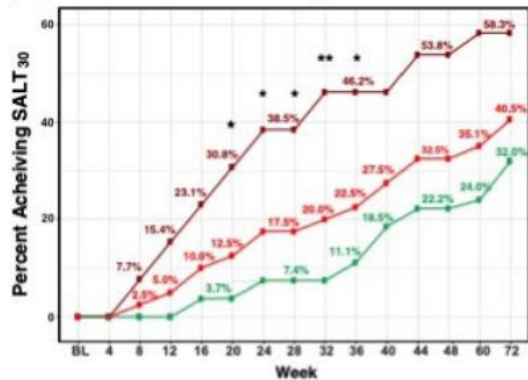


Dupilumab dosing:  
**300mg weekly**

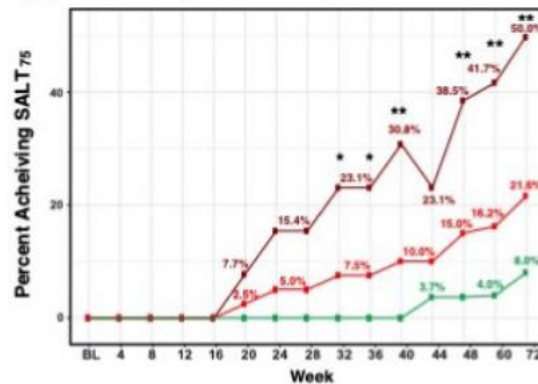
SALT30 in 90%  
(vs 31% w/ no atopy bkgd)



(D) SALT<sub>30</sub> Responders in Drug Arm



(F) SALT<sub>75</sub> Responders in Drug Arm



High IgE at Baseline and Background Atopy Predict Dupilumab Response

History of AD: 38%  
Active AD: 12%  
Family Hx: 45%

# Take Away

- Many options
- Shared decision
- Many others being studied....

Study Title	Study Status	Conditions
Methotrexate Versus Triamcinilone Acetonide in Treatment of Recalcitrant Alopecia Areata	NOT_YET_RECRUITING	Alopecia Areata
Topical Pentoxifylline; Metformin Versus Betamethasone in the Treatment of Alopecia Areata.	NOT_YET_RECRUITING	Alopecia Areata
Dupilumab in the Treatment of Pediatric Alopecia Areata	RECRUITING	Alopecia Areata
A Study to Evaluate the Safety and Effectiveness of Upadacitinib Tablets in Adult and Adolescent Participants With Severe Alopecia Areata	RECRUITING	Alopecia Areata
Topical Simvastatin Versus Topical Steroid in Treatment of Alopecia Areata	NOT_YET_RECRUITING	Alopecia Areata
Topical Cetirizine in Treatment of Localized Alopecia Areata	NOT_YET_RECRUITING	Alopecia Areata
Evaluation of Serum Levels of Interlukin-15 and Interlukin-21 in Patients With Alopecia Areata	NOT_YET_RECRUITING	Alopecia Areata
Polymorphism of Janus Kinase 1 and 2 (JAK 1&2) in Patients With Alopecia Areata	RECRUITING	Alopecia Areata
Combined Microneedling With Either 1% Lactic Acid Solution or Vitamin D3 or Triamcinolone Acetonide in The Treatment of Alopecia Areata	RECRUITING	Alopecia Areata
Role of Minoxidil in Alopecia Areata Transepidermal Drug Delivery of Minoxidil Via Either Fractional Carbon Dioxide Laser or Microneedling Ver	NOT_YET_RECRUITING	Alopecia Areata
Study Evaluating Efficacy of Topical Squaric Acid Dibutyl Ester in Children and Adolescents With Alopecia Areata	RECRUITING	Alopecia Areata
Litfulo Capsules Special Investigation	RECRUITING	Alopecia Areata
Systemic Treatments for Alopecia Areata Registry	RECRUITING	Alopecia Areata Alopecia T
Determinants of Chronic Inflammatory Skin Disease Trajectories	RECRUITING	Atopic Dermatitis Psoriasis
Evaluate the Efficacy and Safety of Ruxolitinib on Hair Regrowth in Patients With Autoimmune Polyendocrinopathy Candidiasis Ectodermal Dy	RECRUITING	Autoimmune Polyendocrin
A Study of Baricitinib (LY3009104) in Children From 6 Years to Less Than 18 Years of Age With Alopecia Areata	RECRUITING	Areata Alopecia Alopecia f
Tofacitinib for Immune Skin Conditions in Down Syndrome	RECRUITING	Down Syndrome Alopecia
A Longitudinal Observational Study of Patients Undergoing Therapy for IMISC	RECRUITING	Atopic Dermatitis Alopecia
Prevention of Alopecia in Patients With Localised Breast Cancer	RECRUITING	Chemotherapy-induced Al
A Study of Oral Minoxidil to Treat Hair Loss in Children, Teens, and Young Adults Who Are Cancer Survivors	RECRUITING	Survivors of Childhood Ca
Measure of Acceptance of chRonic Visible sKin conditionS	RECRUITING	Acceptance of Visible Chrn