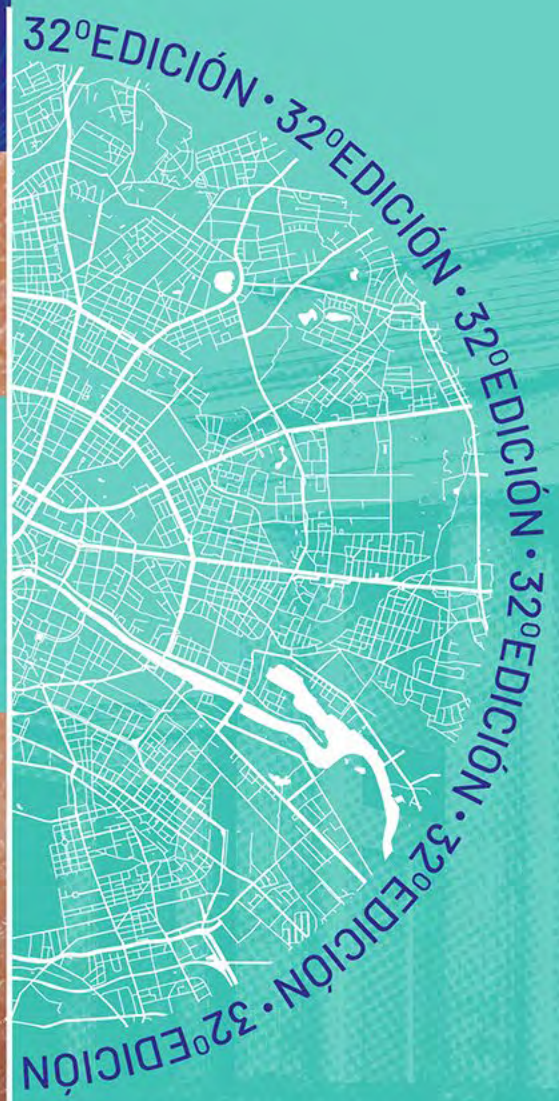
# AEDV 2023 Highlights

Con el patrocinio de:

ucb




# BERLÍN

11-14 OCTUBRE

Iniciativa científica de:

AEDV 1909

ACADEMIA ESPAÑOLA DE DERMATOLOGÍA Y VENEREOLOGÍA

AEDV2023 Highlights

# Dermatología Pediátrica Parte II

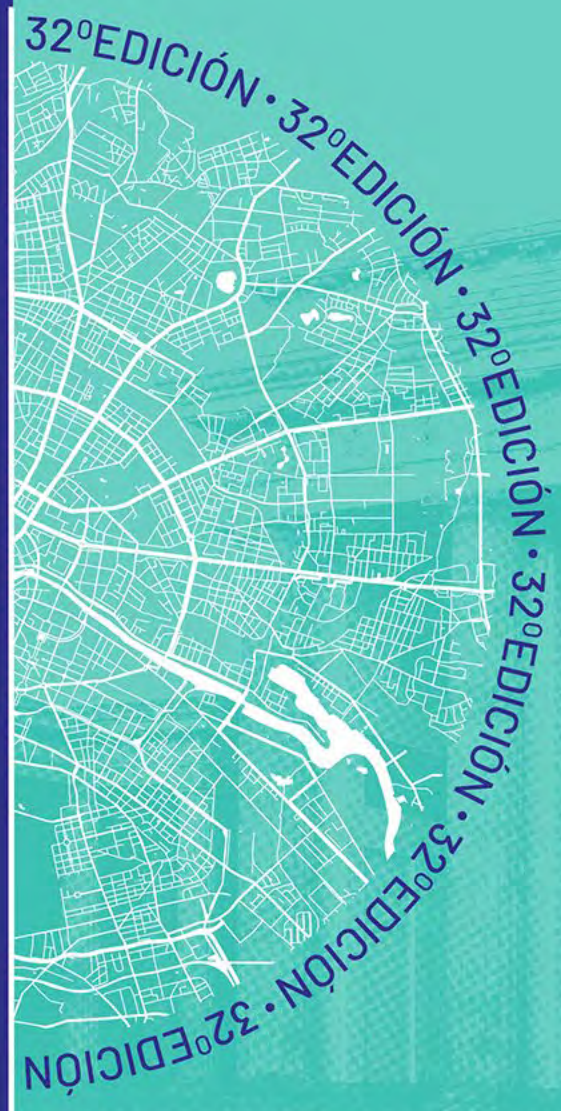

**Miguel Mansilla Polo**

**Hospital Universitario y Politécnico La Fe**

**@mig_yec**

## Conflicto de intereses

## UCB ha financiado esta ponencia




BERLIN

11-14 OCTUBRE

U.PORTO
ICBAS INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
SCHOOL OF MEDICINE AND BIOMEDICAL SCIENCES

santo antónio
CENTRO HOSPITALAR UNIVERSITÁRIO DE SANTO ANTÓNIO

# Biologics in children

## Focus on psoriasis

**Tiago Torres, MD, PhD**

*Department of Dermatology - Centro Hospitalar Universitário de Santo António*
*Unit for Multidisciplinary Research in Biomedicine – ICBAS/University of Porto*

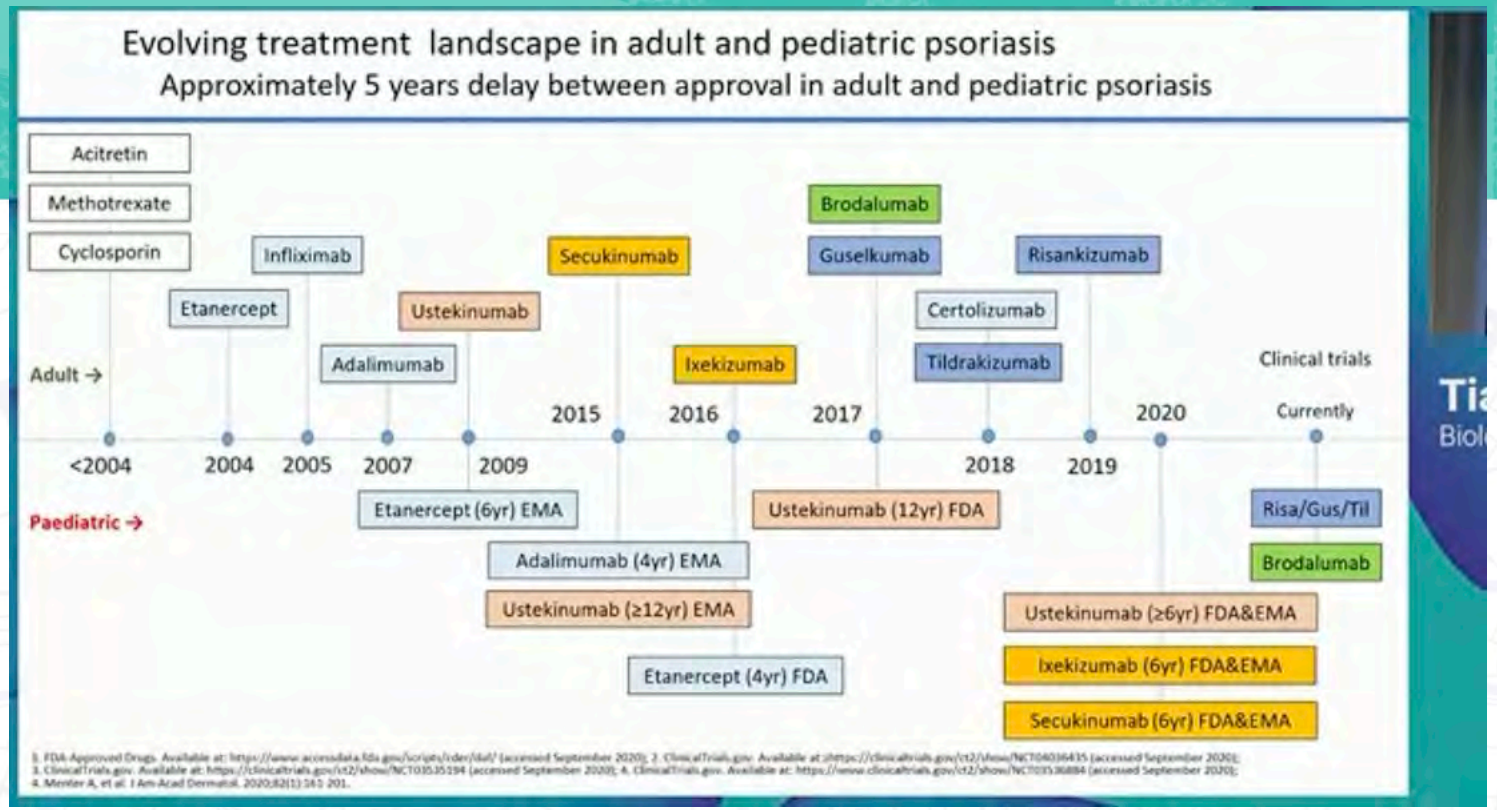
# Why to use highly effective drugs in pediatric psoriasis?

- Early and appropriate treatment of psoriasis is critical in the paediatric population
  - Children with psoriasis are likely to experience:
    - Social discrimination and stigmatization
    - Impairment in emotional, social and school functioning
    - Higher risk of depression and anxiety and to believe that psoriasis had caused their depression
    - Undertreatment of moderate-to-severe psoriasis: low use of systemic therapy, particularly biologics

- Psoriasis at a young age is likely to negatively influence children's social-emotional and personality development and future, resulting in an inability to achieve 'full-life potential' (also termed cumulative life course impairment)

**Psoriasis' cumulative life course impairment**


Image from: Ofidani E, et al. Curr Probl Dermatol 2013;44:17-32.




**Mejores resultados en PASI y EEAA que tradicionales**

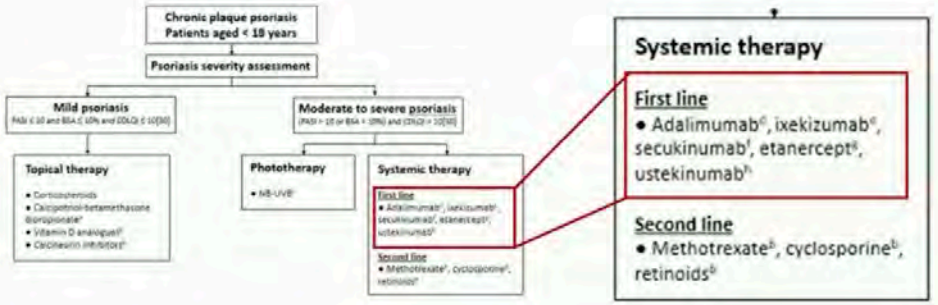
**No new safety signals have been observed and safety profile was consistent with that observed in long-term studies in adults with psoriasis and children with other diseases**

**Biologic agents have a shown a favorable safety profile In children**

# Should we consider biologics as first-line therapy for pediatric psoriasis?

- Biologic therapy vs conventional systemic therapy
  - Robust evidence (RCT, long-term efficacy and safety data and RWE)
  - On-label therapy
  - Higher efficacy
  - Fewer treatment-related toxic effects
  - Less monitoring

- Recommendations/guidelines proposing biologics should be considered as first-line treatment for children with severe plaque psoriasis





Guideline
DOI: 10.1111/ddg.13936
JDDG

S2k guidelines for the treatment of psoriasis in children and adolescents – Short version part 2

Lisa Eisert[1], Matthias Augustin[2], Sabine Bach[3], Martin Dittmann[4], Renate Eiler[5], Regina Fölster-Holst[6], Sascha Gerdes[7], Henning Hamm[8], Peter Höger[9], Gerd Horneff[10], Ralph von Kiedrowski[11], Sandra Philipp[12], Marc Pleimes[13], Martin Schlaeger[14], Volker Schuster[15], Petra Staubach[16], Tobias Weberschock[17,18], Ricardo Niklas Werner[1], Alexander Nast[19], Michael Sticherling[19]


ORIGINAL RESEARCH

Update on the Management of Pediatric Psoriasis: An Italian Consensus

Ketty Peris · Anna Belloni Fortina · Luca Bianchi · Gabriella Fabbrocini · Paolo Gisondi · Anna Balato · Federico Bardazzi · Nicoletta Bernardini · Domenico Bonamonte · Maria Rita Bongiorno · Cinzia Buligan · Francesco Cusano · Maria Beatrice De Felici Del Giudice · May El Hachem · Maria Concetta Fargnoli · Giulio Gualdi · Claudio Guarneri · Katharina Hansel · Giovanna Malara · Carlo Mazzatenta · Giuseppe Micali · Alessandra Narcisi · Iria Neri · Teresa Oranges · Michele Panzone · Aurora Parodi · Lucia Restano · Oriana Simonetti · Marina Venturini · Vito Di Lernia

Peris K, et al. Dermatol Ther. 2022; Lansang P, et al. J Am Acad Dermatol 2019; Eisert L, et al. J Dtsch Dermatol Ges. 2019

Etanercept, Adalimumab
Ustekinumab <<<

**Secukinumab**

**Ixekizumab**

| Biologic therapy | Clinical trial | | | Status |
|---|---|---|---|---|
| Brodalumab | NCT04305327 | Efficacy and Safety of Brodalumab in Adolescents From 12 to 17 Years of Age With Moderate-to-severe Plaque Psoriasis | Phase 3 | Early terminated due to difficulty recruiting participants |
| Guselkumab | NCT03451851 | A Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Subcutaneously Administered Guselkumab for the Treatment of Chronic Plaque Psoriasis in Pediatric Participants | Phase 3 | Recruting |
| Risankizumab | NCT04435600 | A Study of Subcutaneous Risankizumab Injection for Pediatric Participants With Moderate to Severe Plaque Psoriasis to Assess Change in Disease Symptoms | Phase 3 | Recruting |
| Tildrakizumab | NCT03997786 | A Study of Tildrakizumab in Pediatric Subjects With Chronic Plaque Psoriasis | Phase 3 | Recruting |
| **Non-biologic therapy** | | | | |
| Apremilast | NCT03701763 | Efficacy and Safety Study of Apremilast (CC-10004) in Pediatric Subjects From 6 Through 17 Years of Age With Moderate to Severe Plaque Psoriasis | Phase 3 | Completed |
| Deucravacitinib | NCT04772079 | A Study to Evaluate the Drug Levels, Efficacy and Safety of Deucravacitinib in Pediatric Participants With Moderate to Severe Plaque Psoriasis | Phase 3 | Recruting |

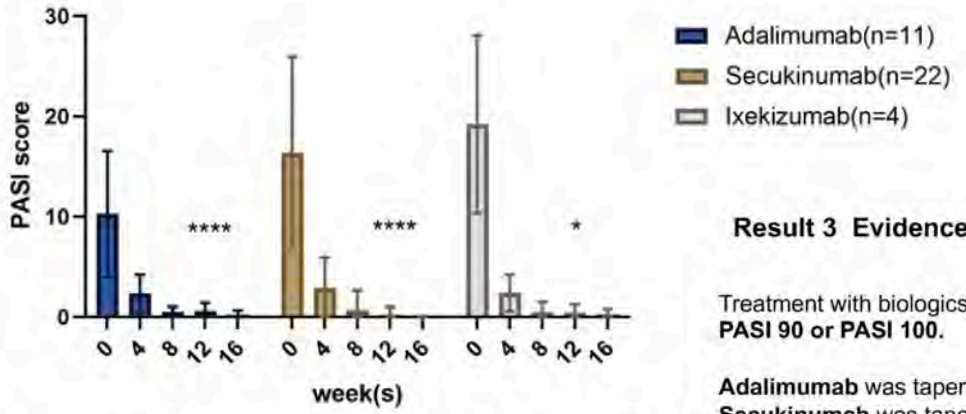
**Dado la potencial necesidad de tratamiento a largo plazo y basado en datos de eficacia y seguridad actual, se propone que la terapia biológica debería ser considerada a día de hoy como tto de 1ªL en psoriasis pediátrica moderada-severa**

浙大二院 THE SECOND AFFILIATED HOSPITAL ZHEJIANG UNIVERSITY SCHOOL OF MEDICINE

# Biologics for psoriasis patients under 18 years of age: Real-world evidence from the Chinese Psoriasis Real World Evidence Research Group

Yu-Xin Zheng, Xiao-Yong Man
Dermatology, Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China.

**Efectividad y seguridad ADA, SECU, IXE**




scores of children with psoriasis treated with three differer

umab, secukinumab, and ixekizumab administration

## Result 3 Evidence on extending the dose interval

Treatment with biologics was initiated according to the registered standard dose and **was tapered after a certain period when the patients reached PASI 90 or PASI 100.**

**Adalimumab** was tapered from a standard dose of 40 mg Q2W to 40 mg Q4W.
**Secukinumab** was tapered from the standard dose 75mg/150mg/300 mg Q4W to 75mg/150mg/300 mg Q8W.
**Ixekizumab** dose was tapered from 80 mg Q4W to 80 mg Q8W.

In each group, 7 of 8 (87.5%) adalimumab patients, 10 of 10 (100%) secukinumab patients, and 1 of 3 (33.3%) ixekizumab patients could successfully prolong their dosing interval maintaining PASI 90 or above and the absolute PASI score < 3 for at least 6 months.

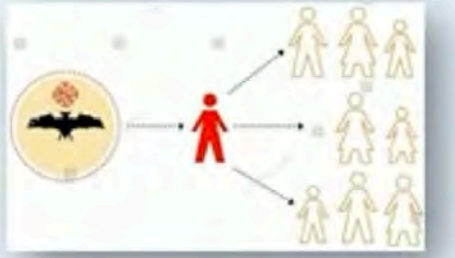
## CONCLUSION

1. Biologics is efficacy and safe for children with psoriasis.
2. Switching between TNFα antagonists, or switching from TNFα antagonists to IL-17A antagonists are both effective and safe.
3. Extending the dosing interval is safe for most patients.

- *Fungal infections of the scalp - current treatment algorithm*
  Prof. Jacob Mashiah (Tel Aviv, Israel)

# Carrier state

- **Colonization with dermatophytes without symptoms**
- Reservoir, source of transmission of disease.
- In a study 32% of families with an infected child had at least one carrier, of whom 13% still positive six months later
- Asymptomatic carriers are source of transmission:
  - Household members, residential schools, day-care cent
- More likely with anthropophilic species – minimal infla
- May persist 6w-6m in 10-25% untreated carriers



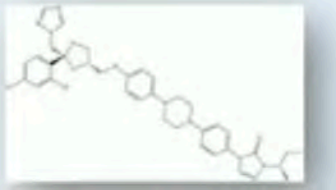
- **Screening within the family**
  - Systemic treatment is indicated only if clinical signs exist
  - Asymptomatic contacts should use antifungal shampoos
- **Contaminated objects treatment**

- **Management**
  - Children receiving treatment can attend school
  - Not necessary to have haircut, or to wear a hat
  - Topical antifungal shampoo is advised In order to prevent spread and for better cure

Pomeranz et al, A
Gupta AK et al, pediatric
Aharaz et al, J Eur Acad Derm
2021

# Tinea Capitis Treatment

- **Griseofulvin**
  - Has served as first-line therapy for more than 40 years because of its efficacy, safety
  - Decrease in sensitivity to this agent appears to have developed.
  - Significant number of failures in those treated with 10 mg/kg per day
  - **Should be preferred for *Microsporum* infections**
- **Terbinafin**
  - The only FDA approved therapeutic alternative to griseofulvin for tinea capitis
  - **Should be preferred for Trichophyton infections**
- **Itraconazole, and fluconazole**
  - Growing evidence of their efficacy
  - One study showed suboptimal results for Fluconazole
  - May require short-course therapies than griseofulvin



# Tinea Capitis Treatment

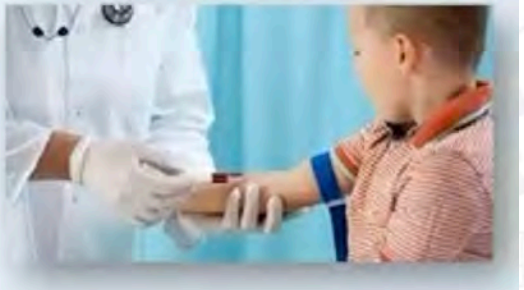
- **Kerion treatment**
  - Systemic antifungal agents + oral prednisone, 1–2 mg/kg per day for 10–14 days
  - Antibacterial agents usually not indicated, except:
    - Bacterial infection is clearly demonstrated
    - Failure of antifungal therapy

- **Dermatophytid reactions**
  - Can develop with antifungal treatment commencement
  - Often requires either topical or systemic corticosteroid therapy

- **Photodynamic therapy**
  - Alternative off-label treatment
  - In combination with topical adjuvant
  - Large thoroughly conducted clinical trials are needed

# Laboratory monitoring during antifungal treatment yes or no

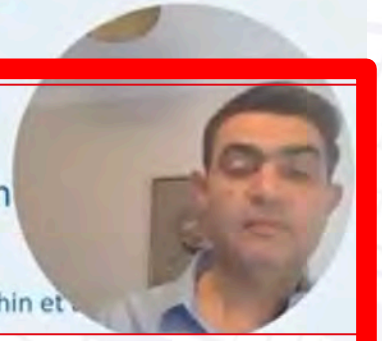
- Systemic antifungal therapy is considered safe yet can be hepatotoxic
- There is a great differences of opinion regarding the need of laboratory monitoring



- **Some recommend: Laboratory monitoring prior to treatment and every 4w:**
  - History of impaired liver function, or comorbidities affecting liver function
  - Those taking other hepatotoxic drugs

- **Our experience:**
  - 321 children, (70%) griseofulvin, (30%) terbinafine.
  - 64 (20%) had hematologic or hepatic laboratory test abnormalities
  - (96.3%) were considered as mild
  - No difference in laboratory abnormalities between griseofulvin and terbinafine groups
  - In one patient increased aminotransferases required treatment discontinuation

- **Our practice:**
  - In light of the age group of our patients and substantial, although mild, lab test abn
  - We do perform laboratory monitoring tests prior to treatment and every 4w



Aleohin et

# Introducing a Novel *SQLE* Mutation in Terbinafine-Resistant *T. indotinea* Isolates among Individuals with Recalcitrant Dermatophytosis from Iran

Mahsa Fattahi[1] Ph.D.; Shayan Zamani[1] M.D.; Alireza Firooz M.D.[1*]

1. Center for Research and Training in Skin Diseases and Leprosy, Tehran University of Medical Sciences, Tehran, Iran

und and Aim

Results

## Conclusions

Our study revealed a considerable level of terbinafine resistance in clinical samples which is a serious warning for patients vulnerable to dermatophytosis. Our findings have also revealed a different mutation pattern in the SQLE gene. Present outcome emphasizes on continuous evolution and development of novel mechanisms of terbinafine resistance in clinical *T. indotinea* isolates. Analyzing the outline of resistance of *T. indotinea* isolates could therefore make a chance for prediction of regional resistance status, and possible future epidemiological changes that can help breaking the resistance chain; either through reinforcing anti fungal stewardship guidelines or designing new antifungals with different target site.

Contact

# The Novel Treatment of Children with Recalcitrant Viral Warts using Microwave Technology

Katie Solomon & Vincent Yip
Alder Hey Children's NHS Foundation Trust, Liverpool, UK

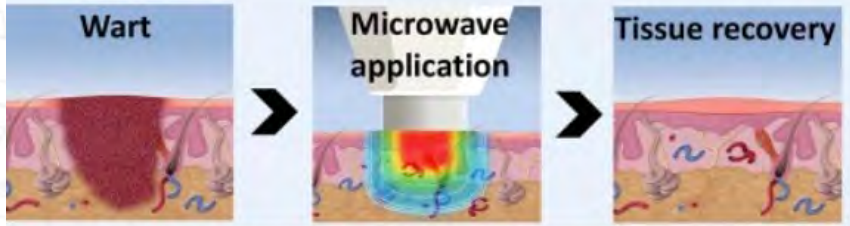



Figure 1. Microwave therapy for wart removal

| Characteristics | Resolved (n = 24) | Not Resolved (n = 11) |
|---|---|---|
| **Sex (n)** | | |
| Male | 13 (54%) | 4 (36%) |
| Female | 11 (46%) | 7 (64%) |
| **Age (years)** | | |
| Mean (Range) | 12 (6-17) | 12 (6-19) |
| **Duration of warts (months)** | | |
| Mean (median) | 29 (24) | 31 (36) |
| **Previous treatments (n)** | | |
| Topicals | 17 | 10 |
| Cantharidin | 11 | 5 |
| Cryotherapy | 2 | 1 |
| Nil | 2 | 0 |
| **Number of treatment areas** | | |
| Mean (range) | 2 (1-3) | 2 (1-4) |
| **Number of treatment sessions** | | |
| Mean (range) | 3 (1-8) | 4 (1-6) |
| **Tolerability** | | |
| Tolerated | 20 (83%) | 7 (64%) |
| Not tolerated | 4 (17%) | 4 (36%) |

- Microwave therapy is an effective and well tolerated treatment modality for recalcitrant viral warts in children.
- In our cohort, 20 patients presented with plantar warts and clearance was achieved in 70% (14/20) of cases. This compares favourably to salicylic acid and cryotherapy which achieved clearance in 31% and 34% of patients, respectively.[5]
- There were no reports of ulceration, blistering or pigmentary changes.
- An acute short-lived pain was reported during treatment that led to discontinuation in some patients. Adjusting the energy settings and duration of the device improved tolerability.
- Microwave therapy is quick, without the need for specialist pre- or post-treatment care and does not generate surgical plume which can be harmful to operators.
- Further randomised studies with larger sample sizes are warranted to confirm our findings.

# The novel treatment of children with molluscum contagiosum using microwave technology

Menno Gaastra, MD[1]
[1]Centrum Oosterwal, Comeniusstraat 3, 1817 MS Alkmaar, Netherlands

EADV CONGRESS P2139

centrum oosterwal medisch specialisten

## Summary


- Feasibility case series to use microwave technology to treat molluscum contagiosum
- 100% clearance within 1 to 2 treatments
- Only a small subset of lesions treated, but all cleared
- Quick and easy treatment modality
- Minimal acute treatment pain, no blistering, no aftercare


**Fig. 1: MC lesions on the right elbow.** Photo courtesy of D. Cronkwright B.Pod (Hons), Geelong Wart Clinic

## Introduction

- Molluscum contagiosum (MC) is an easily transmitted pox virus commonly found in children and the immunosuppressed[1]
- Multiple individual benign papules associated with itching, pain, and inflammation (Fig. 1)
- Although self-limiting, auto-inoculation can result in the lesions being present for months to years due to the virus' innate ability to hide from the host immune system[2]
- Recent Cochrane review concluded that no single intervention has been shown to be convincingly effective in the treatment of MC[3]
- No EMA/MHRA-approved treatments (Tx) available in Europe and the UK

## Results

- Atopic family history of asthma, bronchitis, hay fever, or eczema
- Failed prior Tx for their MC using different over-the-counter products.

| | | | | |
|---|---|---|---|---|
| Patient 1: | 1x | 2W, 2s, 3 repeats | ⟹ | 100% resolution |
| Patient 2: | 2x | 2W, 2s, 3 repeats | ⟹ | 100% resolution |
| Patient 3: | 2x | 2W, 2s, 4 repeats | ⟹ | 100% resolution |
| Patient 4: | 1x | 2W, 2s, 3 repeats | ⟹ | 100% resolution |
| Patient 5: | 2x | 2W, 2s, 3 repeats | ⟹ | 100% resolution |

- Systemic immune response is suggested (subset treated, all resolved)
- Microwave Tx can induce acute pain for 1-2s → Tx very well tolerated by children
- Patients & parents "very happy" with microwave therapy outcome

## Conclusion

# CHILDHOOD GRANULOMATOUS PERIORIFICIAL DERMATITIS
## *EXPLORING NOVEL APPROACHES FOR MANAGEMENT*

Madalena Pupo Correia[1], Catarina Correia[1], Sónia Fernandes[1,2], Pedro de Vasconcelos[1], Luís Soares de Almeida[1,2], Paulo Filipe[1,2]
1. Dermatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal
2. Lisbon University Clinic of Dermatology, Faculdade de Medicina da Universidade de Lisboa, Lisbon, Portugal

## INTRODUCTION

*Childhood granulomatous periorifial dermatitis* was first reported in 1970 by Gianotti *et al.* is thought to be an uncommon variant of perioral dermatitis.

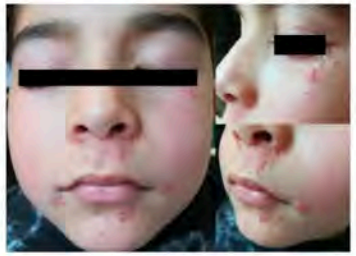
The **diagnosis** is based on clinical presentation (flesh-coloured papules without vesicles or pustules distributed by perioriificial areas of the face) and the presence of a perifollicular granulomatous infiltrate on histopathology

Due to **its benign and self-limiting course**, treatment is not mandatory.

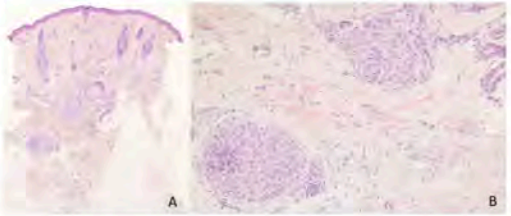
When it imposes a significant impact on the wellbeing of the child, **treatment** with topical metronidazole and, depending on age, tetracyclines and erythromycin may be efficacious. The first step in management should be discontinuation of all topical corticosteroids, as **rebound flaring** is often seen when stopping them.

## CASE REPORT

- 9-year-old portuguese boy
- Consecutive appearance of persistent asymptomatic erythematous micropapules appearing consecutively around the nose, eyes, and mouth in the last 8 months
- Previous treatments: oral clarithromycin, topical and systemic corticosteroids, pimecrolimus cream, boric acid solution, and emollients
- **Medical history**: asthma
- **Current treatments**: daily inhaled salmeterol/fluticasone and oral montelukast

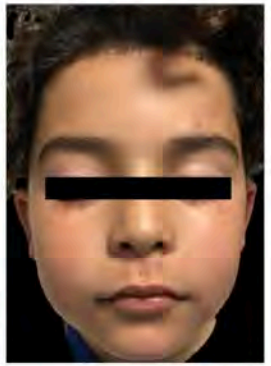


**Picture 1**. Clinical features in the first appointment at our clinic




**Picture 2**. skin biopsy from the perioral area (A - H&E, ×40), (B - H&E, ×100)

Gram stain was negative



**Picture 3**. 1 month after oral ivermectin

**DIAGNOSIS: CHILDHOOD GRANULOMATOUS PERIORIFICIAL DERMATITIS**

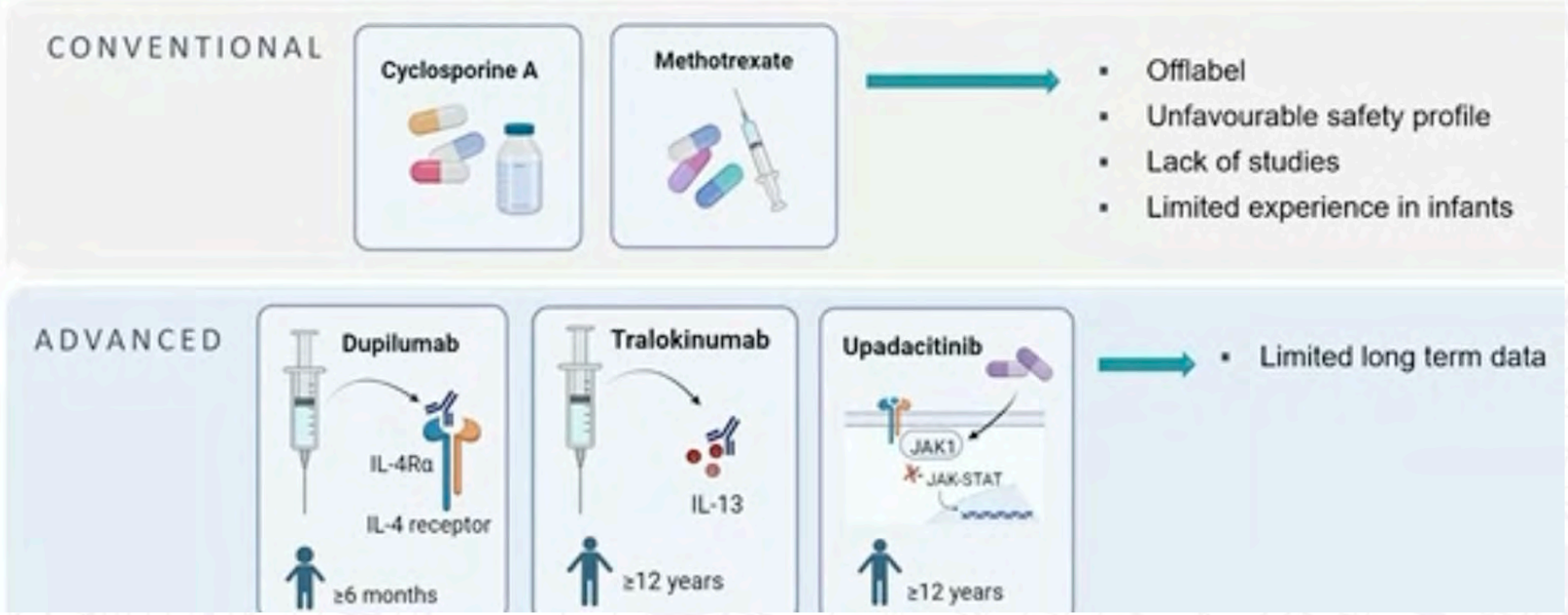
TREATMENT with topical tacrolimus and ivermectin led to significant improvement, although some perioriificial millimeter-sized papules persisted

- After adding a single oral dose of ivermectin (214 µg/kg) there was an almost complete clearance of skin lesions

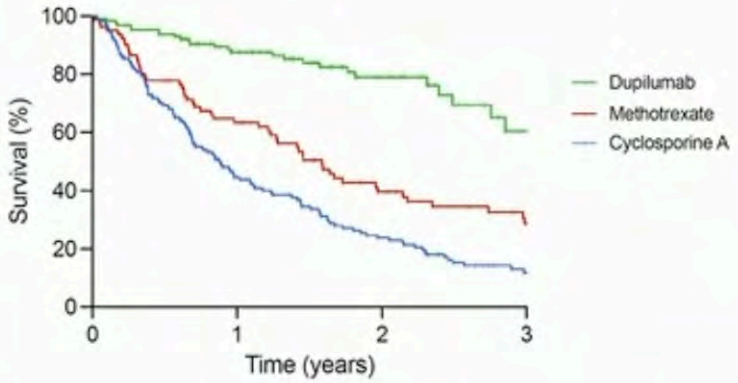
**Ivermectina oral en monodosis (214ug/kg) eficaz en refractarios a ivermectina y tacrólimus tópico**

- *Management of paediatric atopic dermatitis*
  Dr. Marlies De Graaf (Utrecht, Netherlands)

# Current systemic treatments for pediatric AD



## Overall drug survival




| Survival | Totaal |
|---|---|
| Dupilumab (n) | 128 (27 stopped)* |
| 1 year (%) | 87.6 |
| 2 years (%) | 79.0 |
| 3 years (%) | 65.1 |
| CsA (n) | 173 (138 stopped)* |
| 1 year (%) | 44.6 |
| 2 years (%) | 23.8 |
| 3 years (%) | 11.7 |
| MTX (n) | 82 (55 stopped)* |
| 1 year (%) | 63.4 |
| 2 years (%) | 39.6 |
| 3 years (%) | 28.8 |

*Censored for well-controlled disease and lost-to-follow-up.

Data of 3/5 centers are presented.

Van der Rijst et al. Manuscript in preparation.

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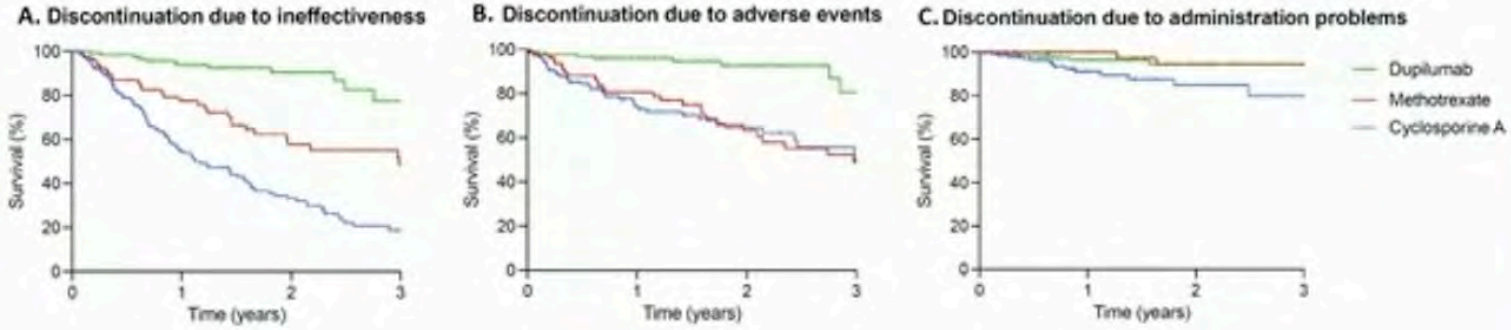
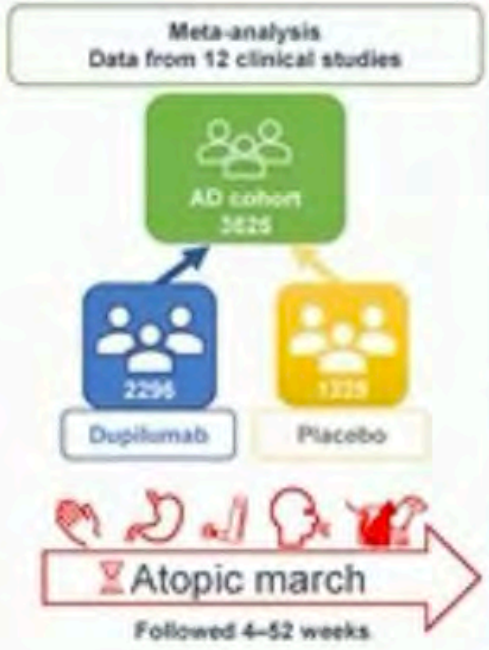
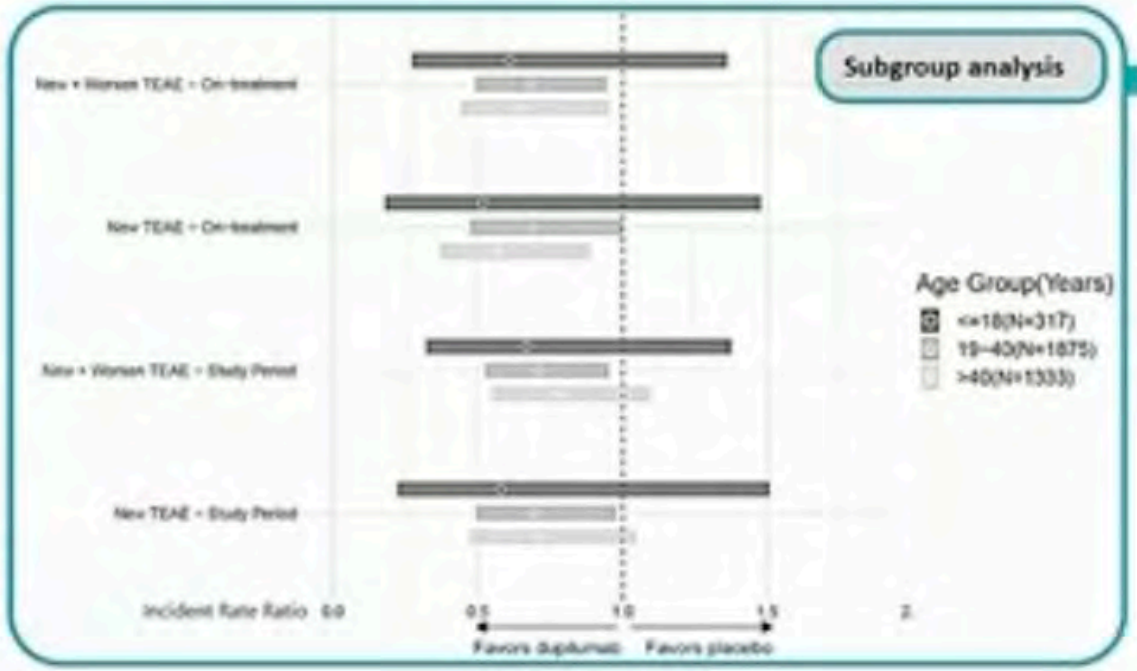
## Reasons for discontinuation



# Attenuating the Atopic March:

## Meta-analysis of the dupilumab atopic dermatitis database for incident allergic events




**Treatment benefit of dupilumab appeared greater for:**

- Younger patients (<18 years)
- Early onset of AD (<2 years)
- Those with more severe AD at baseline
- Those with baseline asthma

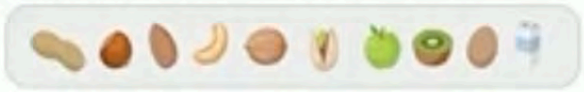
ba, et al. Attenuating the atopic march: Meta-analysis of the dupilumab atopic dermatitis database for incident allergic events. J Allergy Clin Immunol. 2023 Mar.

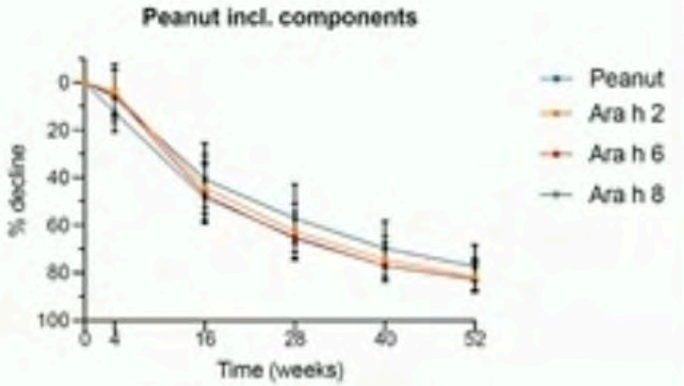
# Impact on Atopy – Food Allergy

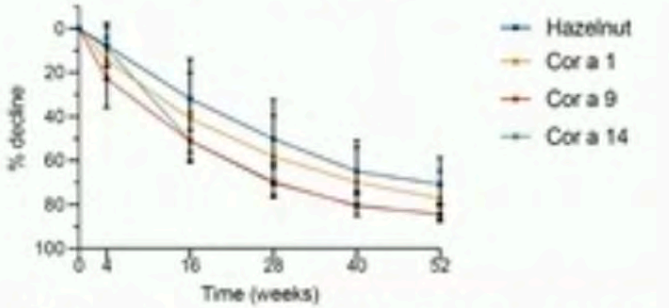
36 patients included

- N=1008 sIgE samples

**70.5%** to **82.5%** after 52 weeks





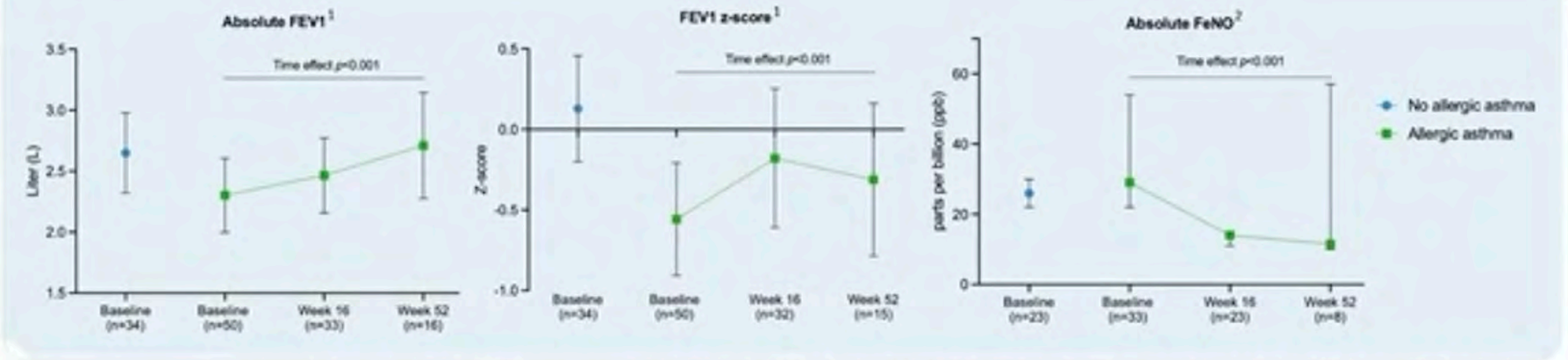

*Decline representative for all food allergens (peanut, hazelnut, cashew nut, almond, pistachio, walnut, kiwi, apple, cow's milk and hen's egg)*

*...n der Rijst et al. Manuscript in preparation.*

# Impact on Atopy – Asthma

84 patients included

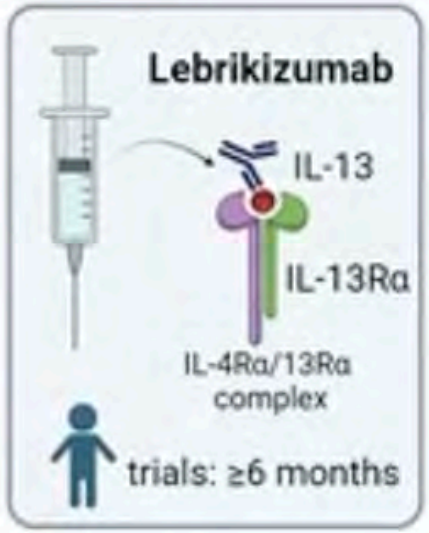
- **59.5%** (n=50) diagnosed with allergic asthma
  - 7/50 (14%) patients with newly diagnosed allergic asthma (median age: 12.0 [range: 4-17])




[1]Bars represent means and the 95% CI. [2]Bars represent medians and the 95% CI. FEV1, Forced Expiratory Volume in 1 second; FeNO, Fractional exhaled Nitric Oxide; Ppb, parts per billion. P-values based on overall likelihood ratio tests for time.

*Van der Rijst et al. Manuscript in preparation.*

# Future for pediatric patients with AD: lebrikizumab




**Recent publication**:

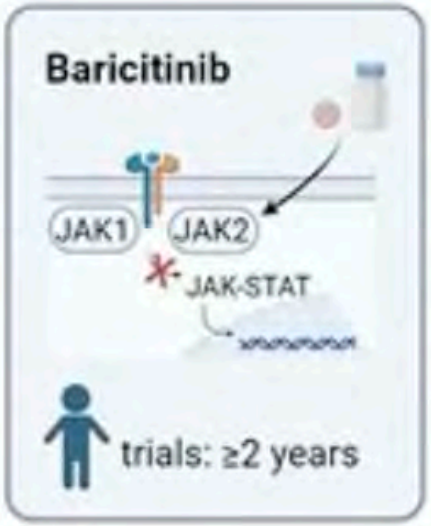
Paller et al. 2023. Trials: ADvocate 1, ADvocate 2, Adhere

- Lebrikizumab 250 mg Q2W
- ≥12-17 years (n=206)
- 52 weeks of treatment
- 2.4% AEs leading to treatment discontinuation, 2.4% SAEs

➡ 81.9% achieved EASI-75 at W52


r AS, et al. Safety and Efficacy of Lebrikizumab in Adolescent Patients with Moderate-to-Severe Atopic Dermatitis: A 52-Week, Open-Label, Phase 3 Study. Dermatol Ther (Heidelb). 2023

# Future for pediatric patients with AD: baricitinib

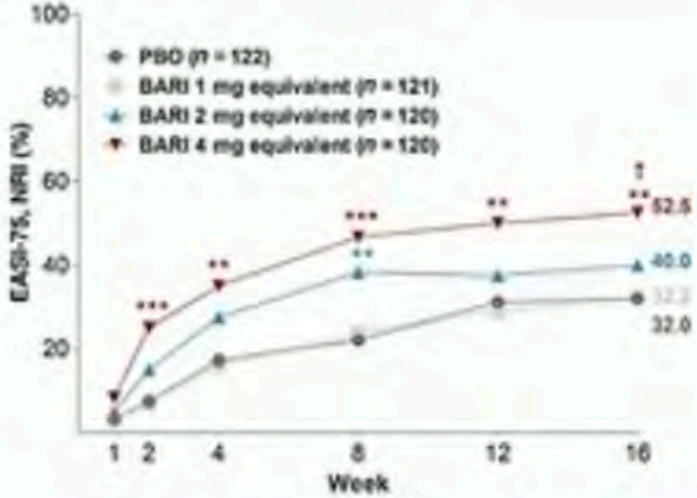



**Recent publication**:

Torrelo et al. 2023. Trial: BREEZE-AD PEDS

- Baricitinib 1mg/2mg/4mg vs placebo
- ≥2-17 years (n=483)
- 16 weeks of treatment
- 0.6% AEs leading to treatment discontinuation, 1.1% SAEs

➡ 32.2-52.5% achieved EASI-75 at W16




Paller AS, et al. Safety and Efficacy of Lebrikizumab in Adolescent Patients with Moderate-to-Severe Atopic Dermatitis: A 52-Week, Open-Label, Phase 3 Study. Dermatol Ther (Heidelb). 2023

# SleeP in INfants with early-onset atopic Dermatitis by Longitudinal Evaluation
# The SPINDLE study

O'Connor C [1,2], Ventura S [1,2], O'Sullivan M, [1] Irvine A [1,3], Murray D [1,2], Hourihane J [1,4], Murphy M [5], Boylan G [1,2]
1 INFANT Research Centre, University College Cork, Cork 2 Department of Paediatrics and Child Health, Cork University Hospital, Cork
3 Dermatology, CHI at Crumlin; Clinical Medicine, Trinity College Dublin 4 Paediatric Allergy, CHI at Temple St; Paediatrics, Royal College of Surgeons of Ireland, Dublin
5 Dermatology, South Infirmary Victoria University Hospital; Medicine, University College Cork

ucc
Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

Infant

ICAT
Irish Clinical Academic Training

## RESULTS – QUANTITATIVE

### INFANT SLEEP - QUANTITATIVE

| 6 months | Sleep latency (min) | Waking (n) | Total sleep time (hours) | 'Major problem' (%) |
|---|---|---|---|---|
| Cases (n=32) | 22.3 | 3.5 | 13.1 | 16.1% |
| Controls (n=31) | 15.8 | 1.9 | 13.8 | 5.4% |
| | p<0.05 | p<0.05 | p<0.05 | p<0.05 |

Babies with eczema wake 2x overnight as babies without eczema

### MATERNAL SLEEP - QUANTITATIVE

Mother sleep less, take longer to fall asleep

| 6 months | Sleep latency (min) | Time in bed (hours) | Total sleep time (hours) | Sleep efficiency (%) |
|---|---|---|---|---|
| Cases (n=32) | 27.1 | 8.3 | 6 | 72 |
| Controls (n=31) | 12.8 | 8.38 | 7.3 | 88 |
| | p<0.05 | | p<0.05 | p<0.05 |

Fathers – no difference

## RESULTS – QUALITATIVE

**Afectación sueño, tanto pacientes como padres**
**Carga indirecta de enfermedad**

inflammatory cytokine analysis using tape stripping. In addition to the skin barrier assessments, clinical severity scoring and filaggrin mutational testing was performed for cases.

BMC Pediatrics

STUDY PROTOCOL Open Access

### Study protocol: assessing SleeP IN infants with early-onset atopic Dermatitis by Longitudinal Evaluation (The SPINDLE study)

Cathal O'Connor, Alan D. Irvine, Deirdre Murray, Michelle Murphy, Jonathan O'B Hourihane and Geraldine Boylan

Trial registration

clinicaltrials.gov NCT05031754, retrospectively registered on September 2nd, 2021.

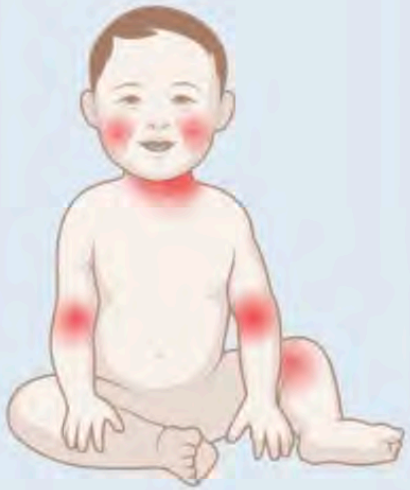
# Atopic dermatitis in childhood and subsequent pubertal development: A nationwide cohort study

Camilla Lomholt Kjersgaard, MD[1], Andreas Ernst, MD, PhD[1,2], Lea Lykke Harrits Lunddorf MD, PhD[1], Linn Håkonsen Arendt MD, PhD[1,3], Nis Brix MD, PhD[1,4], Onyebuchi A. Arah, MD, PhD [1,5], Mette Deleuran, M
[1]Department of Public Health, Research Unit for Epidemiology, Aarhus University, Aarhus, Denmark. [2]Department of Urology, Aarhus U
[4]Department of Clinical Genetics, Aarhus University Hospital, Aarhus, Denmark [5]Department of Epidemiology, Fielding School of Public H

AEDV2023 Highlights BERLIN

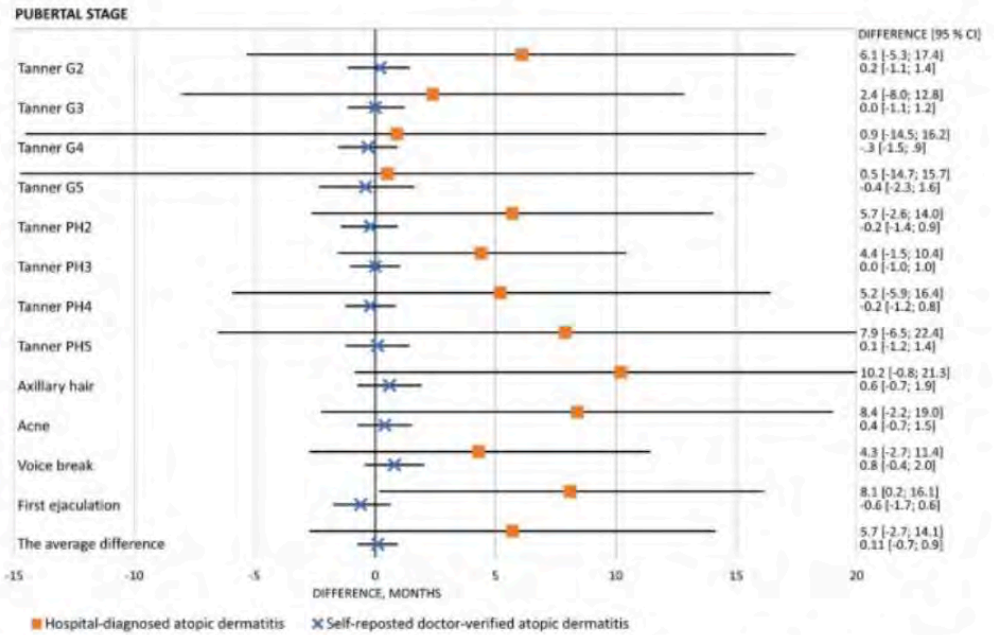
Boys with hospital-diagnosed **atopic dermatitis** had a later **pubertal development** than their unaffected peers

**No efecto en niñas**



## RESULTS - preliminary

**Age difference in months in pubertal development according to atopic dermatitis among 7,563 boys in the Puberty Cohort, Danish National Birth Cohort, Denmark, 2012-2021**




Notes: Estimated age differences in pubertal development with 95 % confidence intervals (CIs). The reference was boys without atopic dermatitis and the analyses were adjusted for maternal age at menarche, maternal body mass index (BMI), maternal smoking during pregnancy, cohabitation of parents during pregnancy, and socioeconomic status of parents. G2-5, genital stages 2-5; PH2-5, pubic hair stages

## CONCLUSION

Boys with hospital-diagnosed atopic dermatitis had a later pubertal development than their unaffected peers, but with confidence intervals including the null. We did not find any relationship between atopic dermatitis and pubertal development in girls and self-reported doctor-verified atopic dermatitis in boys.

# Long-Term Efficacy and Safety of Dupilumab Treatment in Children Aged 6 Months to 5 Years with Severe Atopic Dermatitis Enrolled in an Open-Label Extension Study

Amy S. Paller[1,2], Andreas Pinter[3], Lawrence F. Eichenfield[4,5], Lara Wine Lee[6], Roland Aschoff[7], Jacek Zdybski[8], Christina Schnopp[9], Amy Praestgaard[10], Ashish Bansal[11], Brad Shumel[11], Randy Prescilla[10], Mike Bastian[12]

[1]Northwestern University Feinberg School of Medicine, Chicago, IL, USA; [2]Ann and Robert H. Lurie Children's Hospital, Chicago, IL, USA; [3]University Hospital Frankfurt am Main, Frankfurt am Main, Germany; [4]University of California, San Diego, CA, USA; [5]Rady Children's Hospital, San Diego, CA, USA; [6]...; ...unich, Germany;

## RESULTS (CONT.)

**Table 2. Patient treatment exposure.**

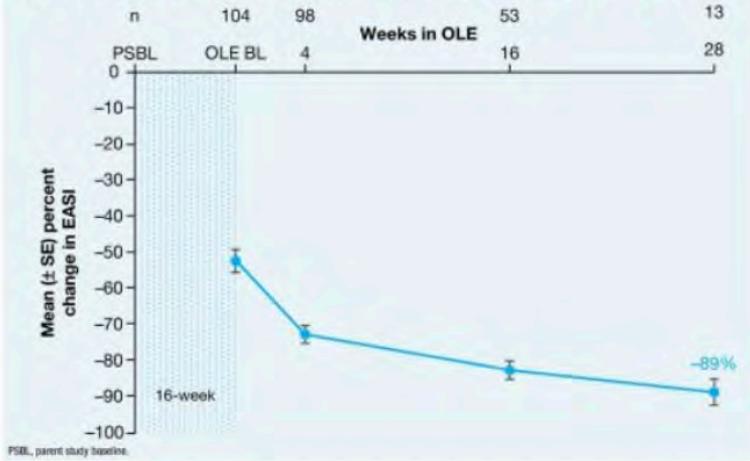
| | Dupilumab 200/300 mg q4w (N = 104) |
|---|---|
| Treatment exposure, mean (SD), weeks | 17.4 (7.3) |
| Patients with overall treatment exposure, n (%), weeks | |
| 4 to <16 weeks | 46 (44.2) |
| 16 to <28 weeks | 47 (45.2) |

**Table 3. Summary of TEAEs.**

| | Dupilumab 200/300 mg q4w (N = 104) |
|---|---|
| Patients with any TEAE | 55 (52.9) |
| Patients with any serious TEAE | 0 |
| Patients with any severe TEAE | 2 (1.9) |
| Patients with any TEAEs related to treatment | 7 (6.7) |
| Patients with any TEAEs leading to permanent discontinuation | 1 (1.0) |

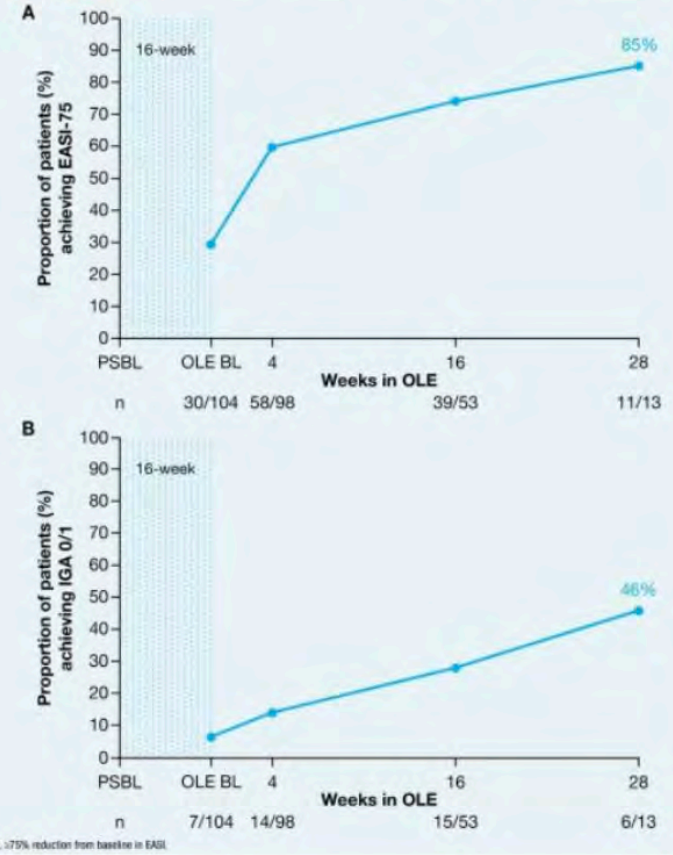
All data are expressed as n (%), nP/100PY, number of patients per 100-patient years; TEAE, treatment-emergent adverse event.

**Figure 1. Percent change in EASI score from PSBL to Week 28 of the OLE.**




PSBL, parent study baseline.

**Figure 2. Proportion of patients achieving (A) EASI-75 and (B) IGA 0/1 through to Week 28 of the OLE.**




EASI-75, ≥75% reduction from baseline in EASI.

## CONCLUSIONS

- Long-term dupilumab treatment showed sustained improvement of AD signs in children aged 6 months to 5 years with severe AD
- Consistent with results seen in adults, adolescents, and children aged 6 years and older, long-term treatment with dupilumab in children aged 6 months to 5 years with severe AD showed an acceptable safety profile

**Buenos resultados a largo plazo en subgrupo de 6m a 5 años (ya aprobado)**

# Dupilumab Reduces Inflammatory Biomarkers in Patients Aged 6 Months to 17 Years With Moderate-to-Severe or Severe Atopic Dermatitis

Lisa A. Beck[1], Antonella Muraro[2], Mark Boguniewicz[3,4], Zhen Chen[5], Peter Zoob[5], Ainara Rodríguez Marco[6]

[1]University of Rochester Medical Center, Rochester, NY, USA; [2]Food Allergy Referral Centre, Padua University Hospital, Padua, Italy; [3]National Jewish Health, Denver, CO, USA; [4]University of Colorado School of Medicine, Denver, CO, USA; [5]Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; [6]Sanofi, Madrid, Spain

INTRODUCTION | RESULTS

**Posibilidad reducción inflamación sistémica: ¿reversión de la marcha atópica?**

## RESULTS

**Figure 1. Percent changes in serum TARC/CCL17 levels over time among patients aged (A) 6 months to 5 years, (B) 6 to 11 years, and (C) 12 to 17 years.**

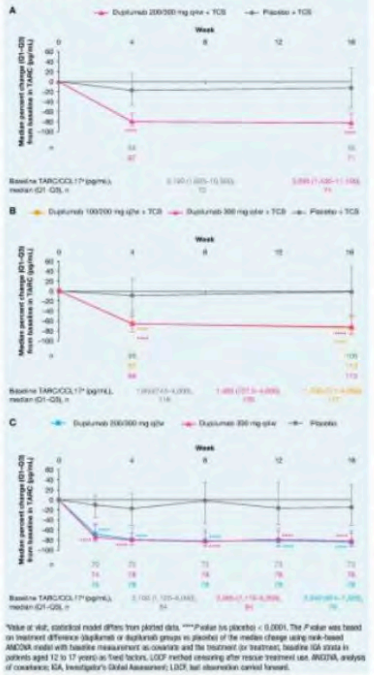


**Figure 2. Total IgE levels over time among patients aged (A) 6 months to 5 years, (B) 6 to 11 years, and (C) 12 to 17 years.**

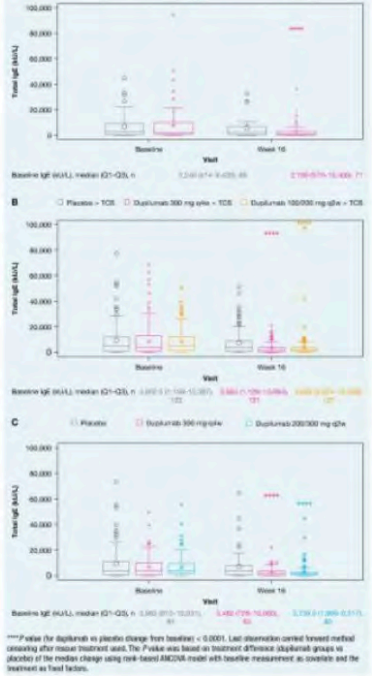


**Figure 3. Percent changes in LDH over time among patients aged (A) 6 months to 5 years, (B) 6 to 11 years, and (C) 12 to 17 years.**

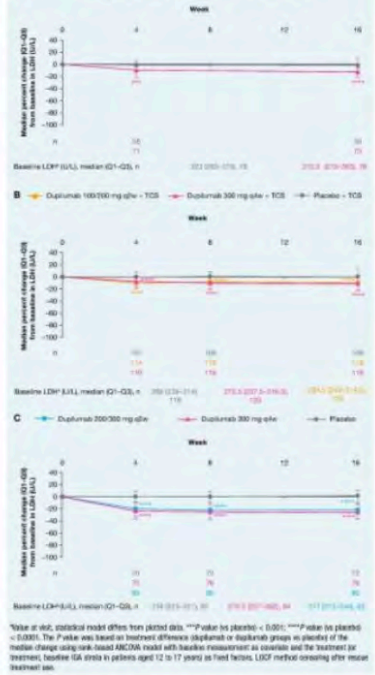
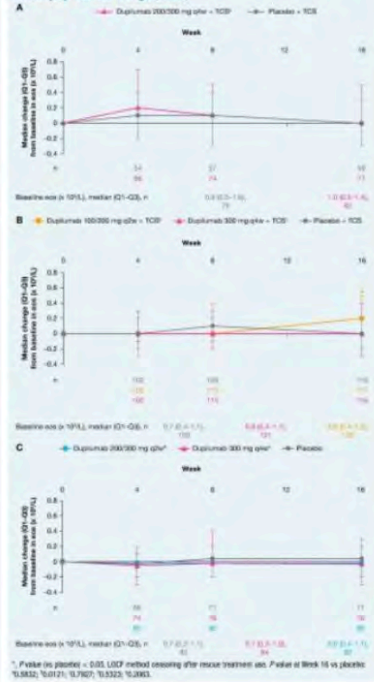


**Figure 4. Change from baseline in eosinophil levels over time among patients aged (A) 6 months to 5 years, (B) 6 to 11 years, and (C) 12 to 17 years.**



## CONCLUSIONS

- Dupilumab treatment for 16 weeks in patients aged 6 months to 17 years with moderate-to-severe or severe AD reduces levels of type 2 and general inflammatory biomarkers TARC/CCL17, LDH, and total IgE
- The changes in eosinophil levels were not clinically meaningful

# Long-Term Safety of Upadacitinib in Atopic Dermatitis Stratified by Age

Jonathan I. Silverberg,[1] Christopher G. Bunick,[2] Eric L. Simpson,[3] Linda Stein Gold,[4] Emma Guttman-Yassky,[5] Mark Boguniewicz,[6] Andrew Blauvelt,[7] Juan Francisco Silvestre Salvador,[8] H. Chih-Ho Hong,[9] Henrique D. Teixeira,[10] Smitha Suravaram,[10] Deanne Dilley,[10] Cristina Sancho,[11] Ayman Grada,[10] Kilian Eyerich[12]

[1]Department of Dermatology, The George Washington University School of Medicine and Health Sciences, Washington, DC, USA; [2]Department of Dermatology, Yale School of Medicine, New Haven, CT, USA; [3]Department of Dermatology, Oregon Health and Science University, Portland, OR, USA; [4]Henry Ford Health System, Detroit, MI, USA; [5]Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [6]Department of Pediatrics, National Jewish Health and University of Colorado School of Medicine, Denver, CO, USA; [7]Oregon Medical Research Center, Portland, OR, USA; [8]Department of Dermatology, Hospital General de Alicante, Alicante, Spain; [9]Department of Dermatology and Skin Science, University of British Columbia, and Probity Medical Research, Surrey, BC, Canada; [10]AbbVie Inc., North Chicago, IL, USA; [11]AbbVie, Madrid, Spain; [12]Department of Dermatology and Venereology, Medical Center, University of Freiburg, Freiburg im Breisgau, Germany

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**Mínimos EEAA y similar en adultos**

**Table 2. Overview of Treatment-Emergent AESI in Exposure-Adjusted Rate per 100 PY by Age Group for Patients in the United States**

| AESI | All Patients | | 12-17 years | | 18-39 years | | 40-64 years | | <65 years | | ≥65 years | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 15 mg | 30 mg | 15 mg | 30 mg | 15 mg | 30 mg | 15 mg | 30 mg | 15 mg | 30 mg | 15 mg | 30 mg |
| N | 339 | 320 | 73 | 77 | 129 | 105 | 101 | 93 | 303 | 275 | 36 | 45 |
| Exposure (PY) | 721.7 | 708.1 | 133.3 | 172.2 | 275.5 | 229.9 | 241.0 | 203.9 | 649.8 | 606.0 | 71.8 | 102.1 |
| Events (E/100 PY) | | | | | | | | | | | | |
| Serious infections | 2.4 | 2.7 | 3.0 | 0 | 2.5 | 0.9 | 1.2 | 3.9 | 2.2 | 1.7 | 4.2 | 8.8 |
| Opportunistic infection (excl. TB/herpes zoster) | 1.4 | 0.8 | 2.3 | 1.2 | 1.8 | 1.3 | 0.8 | 0 | 1.5 | 0.8 | 0 | 1.0 |
| Active TB | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Herpes zoster | 1.7 | 2.0 | 0 | 0 | 2.5 | 0.9 | 1.7 | 4.4 | 1.7 | 1.8 | 1.4 | 2.9 |
| Malignancy excl. NMSC* | 0.3 | 0.4 | 0 | 0 | 0 | 0 | 0.4 | 1.0 | 0.2 | 0.3 | 1.4 | 1.0 |
| NMSC* | 0.4 | 0.6 | 0 | 0 | 0 | 0 | 0.8 | 1.5 | 0.3 | 0.5 | 1.4 | 1.0 |
| MACE* | 0.3 | 0.1 | 0 | 0 | 0 | 0 | 0.4 | 0 | 0.2 | 0 | 1.4 | 1.0 |
| VTE* | 0.3 | 0.3 | 0 | 0 | 0 | 0 | 0.4 | 0.5 | 0.2 | 0.2 | 1.4 | 1.0 |
| Gastric perforation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| AE leading to death | 0 | 0.3 | 0 | 0 | 0 | 0 | 0 | 0.5 | 0 | 0.2 | 0 | 1.0 |

AESI, adverse events of special interest; E, event; MACE, major adverse cardiovascular event; NMSC, non-melanom… …culosis; VTE, venous thromboembolism.

*Rates shown are n/100 PY=number of patients with at least one event per 100 PY.

P0428

Presented at the
32nd European Academy of Dermatology and Venereology (EADV) Congress
Berlin, Germany • 11–14 October 2023

# A Maximum-Use Trial of Ruxolitinib Cream in Children Aged 2 to <12 Years With Atopic Dermatitis: 8-Week Analysis of Safety, Pharmacokinetics, Efficacy, and Patient-Reported Outcomes

Seth B. Forman, MD,[1] Salma H. Elfaki, MD,[2] Steve Sitar, MD,[3] Shaoceng Wei, PhD,[4] Xiaohua Gong, PhD,[4] Brett Angel, MD,[4] Howard Kallender, PhD,[4] Mark S. Lee, MD[5]

[1]ForCare Clinical Research, Tampa, FL, USA; [2]Nona Pediatric Center, Orlando, FL, USA; [3]Orange County Research Institute, Anaheim, CA, USA; [4]Incyte Corporation, Wilmington, DE, USA; [5]Progressive Clinical Research, San Antonio, TX, USA

## Efficacy

Figure 4. Efficacy Improvements Were Observed at First Post-Baseline Visit (Week 2) and Continued to Improve to Week 8 in (A) IGA-TS, (B) EASI75, (C) Itch NRS4 (in Patients Aged 6 to <12 Years), and (D) Affected BSA

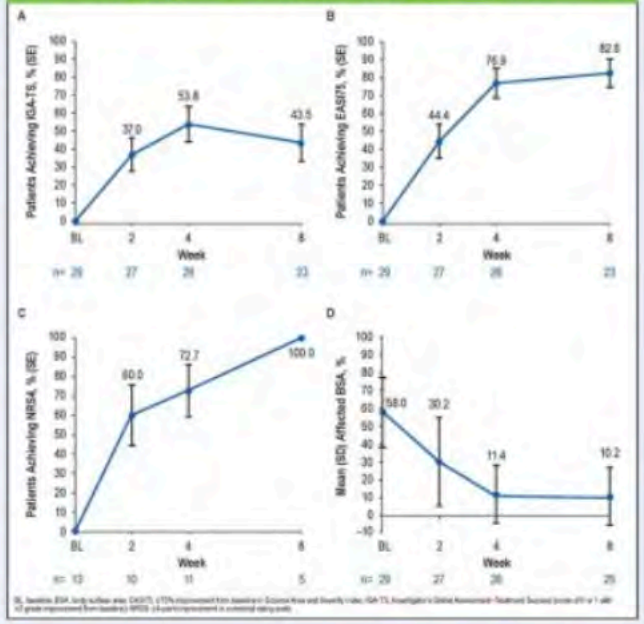
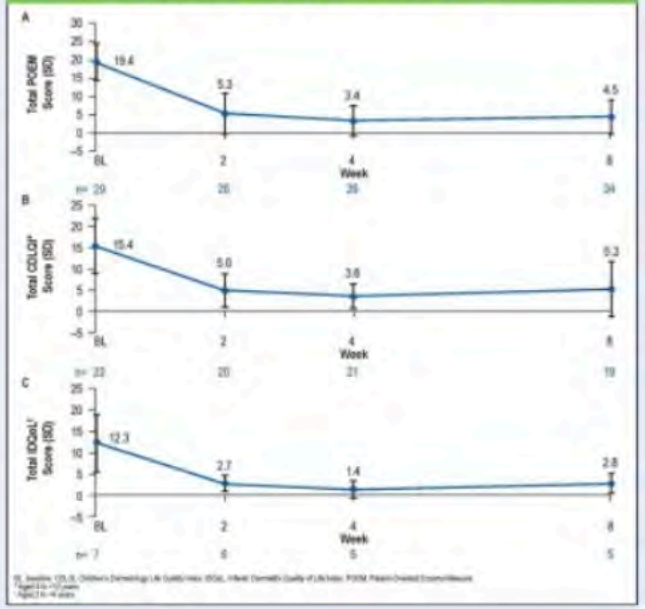



Figure 5. Median Daily Itch NRS Score Among Patients Aged 6 to <12 Years Decreased Early and Was Sustained During the 8-Week Treatment Period, Including With As-Needed Application of Ruxolitinib Cream


## PROs

Figure 7. Substantial Improvement From Baseline in Disease Severity and Quality of Life at Week 2, Sustained Through Week 8: Mean (SD) (A) POEM, (B) CDLQI,* and (C) IDQoL† Scores




## Conclusions

- Under maximum-use conditions, 1.5% ruxolitinib cream BID appears to be safe and well tolerated in patients aged 2 to <12 years with moderate or severe AD
- PK, TEAE, and hematologic data suggest that physiologically meaningful systemic JAK inhibition is highly unlikely
  - Consistent with the maximum-use trial in adolescents and adults[3]
- Ruxolitinib cream had prompt anti-inflammatory and antipruritic effects and improvement in PROs
  - Consistent with previous studies[2,6]

**En niños entre 2 y 12 años buenos resultados en efectividad y seguridad Ruxo tópico 1,5% a las 8 semanas, sin EEAA**

- *Treatment of bullous diseases in children*
  Prof. Dr. Annika Vogt (Berlin, Germany)

**Considerar clindamicina, retapamulina, Ozenoxacino**

## Systematic Review: Emerging Treatment Strategies for Impetigo

- superficial bacterial skin infection, most commonly in children 2 to 5 years of age
- 10 studies that involved 6651 participants and reported on 9 treatments in the final analysis
- rapid emergence and spread of antibiotic-resistant bacteria including MRSA
- increase in antimicrobial resistance to topical mupirocin and fusidic acid

Gahlawat G, Tesfaye W, Bushell M, Abrha S, Peterson GM, Mathew C, Sinnollareddy M, McMillan F, Samarawickrema I, Calma T, Chang AY, Engelman D, Steer A, Thomas J. Emerging Treatment Strategies for Impetigo in Endemic and Nonendemic Settings: A Systematic Review. Clin Ther. **2021** Jun;43(6):986.

## Epidemic European Fusidic Acid-Resistant Impetigo Clone (EEFIC)

- Among 518 *S. aureus* strains: 94.0% were susceptible to oxacillin
  of these: 16% were resistant to fusidic acid
  of which: 48% belonged to the EEFIC
- EEFIC: fusidic acid-resistant MSSA clone, harbouring genes encoding the exfoliatins A and/or B
  - Mostly isolated from young patients with impetigo
  - seasonal late summer peak
- 27 of the 50 impetigo-causing strains studied here were FA-R and some were co-resistant to mupirocin

Deplano A, Hallin M, Bustos Sierra N, Michel C, Prevost B, Martiny D, Yin N. Persistence of the Staphylococcus aureus epidemic European fusidic acid-resistant impetigo clone (EEFIC) in Belgium. J Antimicrob Chemother. **2023** Aug 2;78(8):2061-2065.

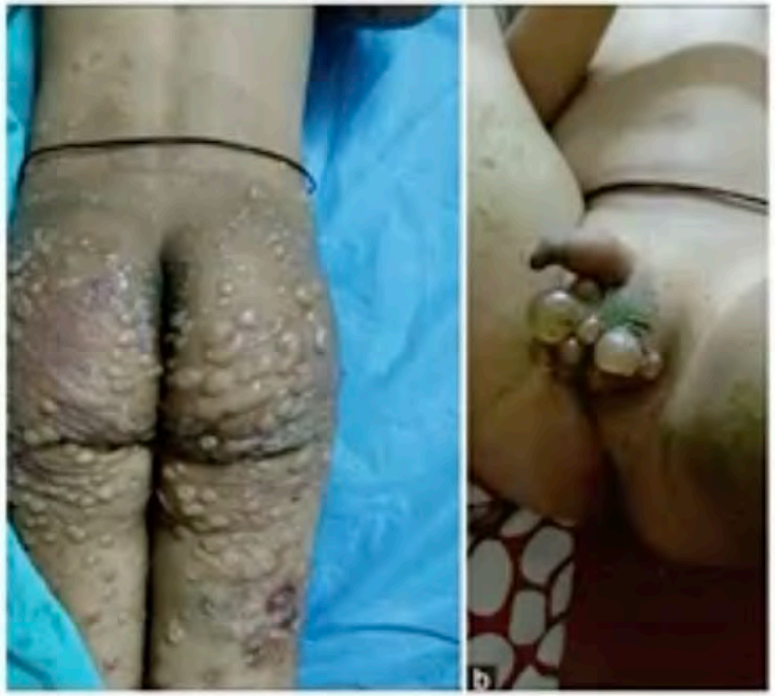
# Rare: Refractory CBDC

2-year-old Child:

History of dapsone hypersensitivity
fever, hypereosinophilia, hepatosplenomegaly, TAs

No therapeutic effects over 6 months

- systemic corticosteroids
- erythromycin, tetracyclin, flucloxacillin
- cyclosporine, methotrexate, azathioprine nicotinamide, mycophenolate
- IVVG, immunadsorption



Successful treatment with rituximab

Mitra D, Bhatnagar A, Singh GK, Sandhu S. Successful Treatment of Refractory Chronic Bullous Disease of Childhood with Rituximab. Indian Dermatol Online J. **2022** Mar 3;13(2):248-251.

**Tratamiento no establecido (Falta estudios)**

**CTCs, CyA, Ig IV**

## Toxic Epidermolytic Necrolysis

- EN generally considered drug-induced: in children: identification only in approx. 50%
- Numbers vary, letality in children: approx. 6% (lower than in adults)
- Lower incidence in children compred to adults (0,36/Mio <12 years compared to 3/Mio adults
- Children: Antiepileptics, sulfonamides, sulfasalazin, antibiotics (e.g., amoxicillin (EN vs. DRESS)

Mockenhaupt M. Schwere kutane Arzneimittelreaktionen bei Kindern [Severe cutaneous drug reactions in children]. Monatsschr Kinderheilkd. 2023;171(5):439-451. German..

Systematic review SJS, TEN in children 12 months and younger
Iriarte et al., Pediatr Dermatol. 2022 Nov;39(6):876-882

- Higher affected body surface area correlated with increased mortality
  Mortality numbers vary widely in literature 10-40 %,: secondary sepsis frequent cause of death
  Optimal therapeutic regimen yet to be established
- Most infants in that cohorte: supportive care only (60%)

- supportive: 60% survived (n=9)
- systemic corticosteroids: 60% survived, vs. Immunosuppressive care: both approx. 40% (n=5)
- IVIG 50% survived (n=2)

# Bullous Manifestations in the Context of SARS-CoV-2 Infection

≠ TEN

03/2020-04/2022 retrospective case series, 6 tertiary medical care centers

Mucobullous conditions:

RIME, SJS; TEN and positive SARS-CoV-2 test <4 weeks prior to onset

- 86% clinical diagnosis of RIME
- 100 % oral mucosal involvement, 50% ocular, 50% urogenital, 38% skin


Systemic treatment was variable:

- n=6 treated with systemic corticosteroids.
- n=2 elevated MP IgM titers: systemic antibiotics.
- n=1 oral tacrolimus
- n=1 IVIG.

Topical therapies: corticosteroids, hydrogels, and others

Miller AE et al. COVID-19 associated severe mucocutaneous blistering eruptions: A case series. Pediatr Dermatol. 2023 Aug 1. doi: 10.1111/pde.15407. Epub ahead of print. PMID: 37526023.

Ryder CY et al. Reactive infectious mucocutaneous eruption secondary to SARS-CoV-2. JAAD Case Rep. 2021 Dec;18:103-105.

# Auto-Antibodies in EB

- secondary event, as they appear to not bind to the respective skin structures?

n= 258 EB patients

- autoantibodies in ELISA in 22% of the patients against the bullous pemphigoid antigen BP180.
- titers correlated negatively with collagen VII skin expression and positively with disease severity

n=6 (2.33%) with clinical features of an autoimmune bullous disorder (AIBD)

- and positive indirect immunofluorescence (IIF) staining
- Co-existence disease-aggravating AIBD, young age

Treatment

- Challenging: immunosuppression contra-indicated in JEB and DEB
- risk for development of highly aggressive SCCs
- better understanding of B cell involvement could provide new therapeutic targets.

Lehr S, Felber F, Tantcheva-Poór I, Keßler C, Eming R, Nyström A, Rizzi M, Kiritsi D. Occurrence of autoantibodies against skin proteins in patients with hereditary epidermolysis bullosa predisposes to development of autoimmune blistering disease. Front Immunol. **2022** Jul 25;13:945176.

**Pénfigo vulgar neonatal:** tronco y cefálica, raro acral exclusivo

≠

**Penfigoide gestional neonatal**: más frecuente acral

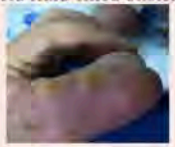
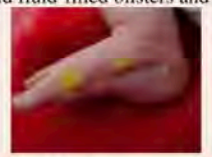
**Px excelente ambas**, si madre clínica típica no necesario biopsia en niño

EADV CONGRESS

## Acral blisters in neonates

Mnif E, Regaieg C*, Sellami K, Khanfir H*, Kolsi N*, Baklouti M, Amouri M, Masmoudi A, Ben Thabet A*, Gargouri A*, Turki H
Department of Dermatology, Hedi Chaker Hospital, University of Sfax, Tunisia
*Department of Neonatology, Hedi Chaker Hospital, University of Sfax, Tunisia

**Introduction :** **Neonatal pemphigus (NP)** and **neonatal bullous pemphigoid (NBP)** are rare and transient resulting from the passive transplacental transfer of maternal autoantibodies to fetus. We report 2 cases of NP and a case of NBP with particular clinical presentations.

| | 1er cas | 2ème cas | 3ème cas |
|---|---|---|---|
| Age | First hour of life | First hour of life | At birth |
| Clinical aspect | flaccid fluid-filled blisters and erosions  | flaccid fluid-filled blisters and erosions  | 1-Diffuse urticarial plaques<br>2- Post blistering erosions  |
| Localisation | Hands and feet | Hands and feet | 1-Tunk, face and limbs<br>2- Hands and feet |
| The mother's medical history | Followed-up for pemphigus | Followed-up for pemphigus | followed-up for gestational pemphigoid. |
| Treatment | Local care | Local care | Topical steroids |
| Diagnosis | NP | NP | NBP |

**Conclusion:**

- NP often affects the **trunk and the cephalic region**. Exclusive involvement of palms and feet is unusual.
- NP vulgaris is relatively frequent # NP foliaceus is a **very rare** entity. It may be a result of desmoglein 3 over expression in neonatal epidermis.
- Blisters in NBP, affecting 2 to 3% of newborns of mothers with gestational pemphigoid, can be located in the **trunk, limbs and acral areas**.
- The clinical aspect could wrongly point to an infectious disease hence, the importance of the mother examination and medical history screening.
- Biopsy and DIF : not recommended if the mother has typical lesions.
- NP and NBP : good prognosis / usually resolve within the first 3 to 5 weeks of life.
- No correlation between the severity of the disease in the baby and the mother. However, stabilization of the disease before conception remains essential.

# ¡¡DxD!!

## Bullous varicella in an immunocompetent infant

*I. Moubine, Fz. El Fatoiki, F. Hali, S. Chiheb*

*Department of Dermatology and venereology, Ibn Rochd University Hospital*

### Introduction

- **Varicella** is a highly contagious disease caused by the varicella zoster virus (VZV).
- It primarily affects **children** and is mostly **benign**. However, it continues to cause significant **morbidity** and even **mortality**.
- The **bullous onset** of varicella is **rare** and mostly seen in **immunocompromised** children. Herein, we report a case of bullous varicella in an immunocompetent infant.

### Observation

- An **8-month-old girl** with no prior medical history or previous drug use
- Admitted to the pediatric department with a history of **fever** and the subsequent **eruption** of **multiple bullous lesions** on the entire body. The lesions started as **vesicules** on the forehead and spread to involve the entire body.
- Her brother had a history of a concomitant varicella infection, which was successfully treated.
- Physical examination revealed **multiple vesicules** and **large erosions**, especially on the trunk, limbs, and face. Nikolsky's sign was negative. **(Figs. 1-3)**
- A laboratory investigation revealed an increased inflammatory marker. Swab cultures taken from the ruptured bullous were negative. HIV serology was negative, and the immunoglobulin levels were normal.
- The diagnosis of bullous varicella was made based on family history and clinical findings. The patient received intravenous acyclovir for 10 days with good improvement. **(Figs. 4,5)**

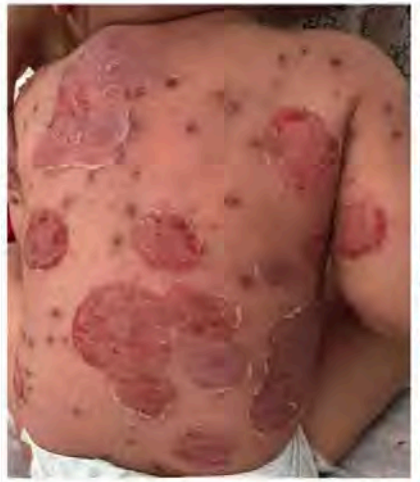


Figure 4

Figure 5

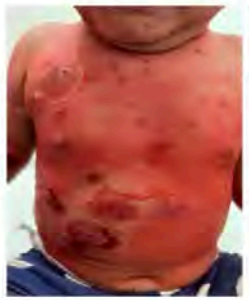


Figure 1

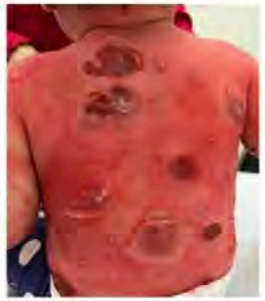


Figure 2

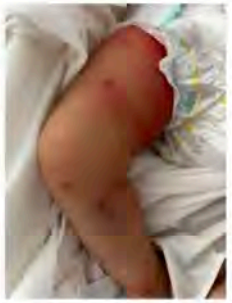


Figure 3

### Discussion

- Varicella is one of the most common viral infections in children. It may lead to some **complications**, such as **bacterial infections**, **pneumonia**, **meningitis**, **encephalitis**, cerebellar **ataxia**, and **pain syndromes**.
- The most common **cutaneous complication** of varicella is **bacterial surinfection**, which is commonly caused by Staphylococcus aureus or Streptococcus pyogenes and may worsen scarring and, in rare cases, lead to **staphylococcal** and **streptococcal toxic shock syndromes**.
- **Bullous varicella** is an extremely **rare** clinical manifestation of the disease. The exact mechanisms by which large bullae are formed are not clear; some synergistic effect between the infectious agents must occur. It has been suggested that bullous lesions are caused by secondary **bacterial infections**, most commonly ***Staphylococcus aureus.***
- **Vaccination coverage** and **adequate prophylaxis** contribute to avoiding complications in the **high-risk population**.

# *Melanoma in congenital melanocytic naevi*

Prof. Dr. Cristina Carrera (Barcelona, Spain)

# Pediatric melanomas in CMN:

| | Associated GCMN | Conventional MM | Spitz MM |
|---|---|---|---|
|  | **100% congenital nevus associated** | **80% nevus associated (any type of nevus)** | NO nevus related |
| | Childhood or any age!! | Adolescents and adults | Childhood and AYA |
|  | Giant / Multiple CMN | Nevus-prone and fair-skin | No risk-phenotype |
|  | No UVR relation | Intermitent UVR pathway (similar to adults) | No UVR relation |
|  | *NRAS* mutations | *BRAF* mutations (V600) | HRAS / Kinase fusions |

*Lu et al. J Invest Derm 2015; 135:816-823*
*Pappo et al. Cancer 2021;127:3825-3831*

- Generalmente, **adolescentes**

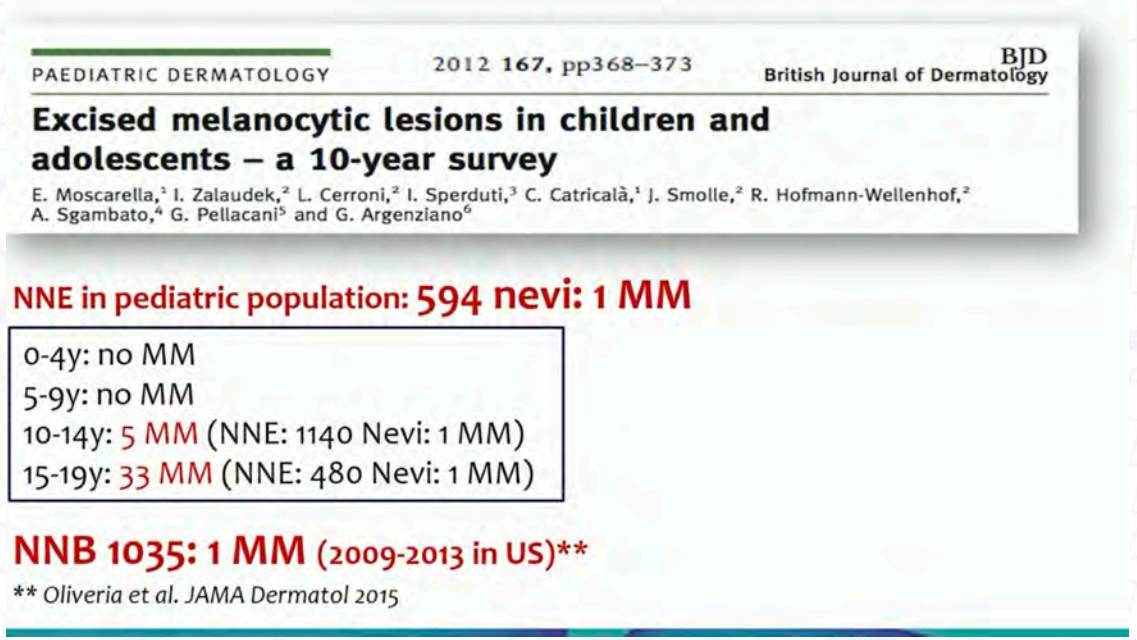
- **Tres FR aceptados de MM en NMC:**

- Gigantes

- Múltiples pequeños/medianos

- Alteraciones NRL en primeros 6 meses de vida

- En general, no necesario excisión
- Se **realizan muchas más exéresis de las necesarias**



PAEDIATRIC DERMATOLOGY 2012 167, pp368–373 BJD British Journal of Dermatology

**Excised melanocytic lesions in children and adolescents – a 10-year survey**

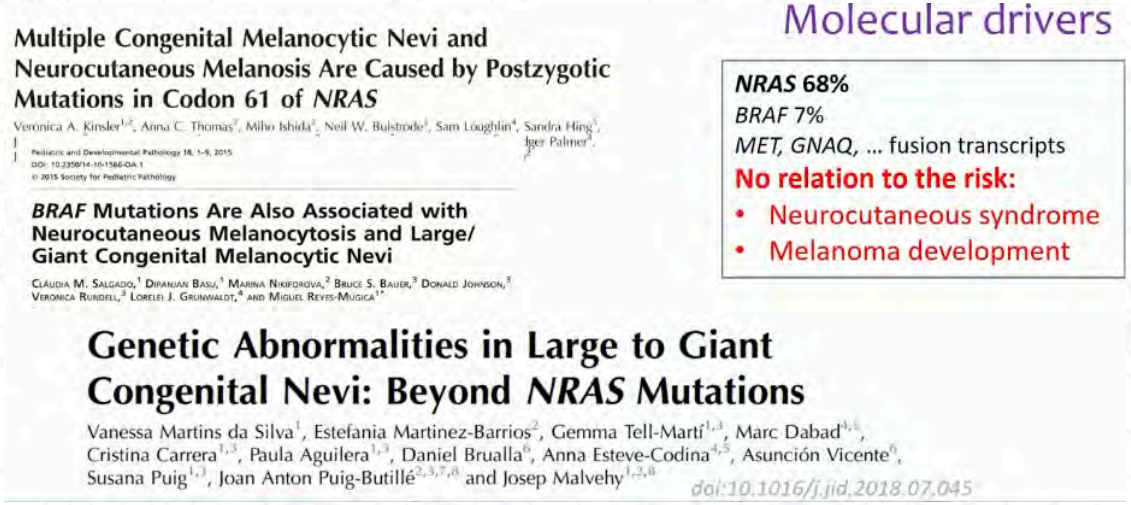
E. Moscarella,[1] I. Zalaudek,[2] L. Cerroni,[2] I. Sperduti,[3] C. Catricalà,[1] J. Smolle,[2] R. Hofmann-Wellenhof,[2] A. Sgambato,[4] G. Pellacani[5] and G. Argenziano[6]

**NNE in pediatric population: 594 nevi: 1 MM**

0-4y: no MM
5-9y: no MM
10-14y: 5 MM (NNE: 1140 Nevi: 1 MM)
15-19y: 33 MM (NNE: 480 Nevi: 1 MM)

**NNB 1035: 1 MM** (2009-2013 in US)**

** *Oliveria et al. JAMA Dermatol 2015*



Multiple Congenital Melanocytic Nevi and Neurocutaneous Melanosis Are Caused by Postzygotic Mutations in Codon 61 of *NRAS*

Veronica A. Kinsler[1,2], Anna C. Thomas[3], Miho Ishida[2], Neil W. Bulstrode[1], Sam Loughlin[4], Sandra Hing[1], Igor Palmer[3]

Pediatric and Developmental Pathology 18, 1–9, 2015
DOI: 10.2350/14-10-1566-OA.1
© 2015 Society for Pediatric Pathology

*BRAF* Mutations Are Also Associated with Neurocutaneous Melanocytosis and Large/Giant Congenital Melanocytic Nevi

Cláudia M. Salgado,[1] Dipanjan Basu,[1] Marina Nikiforova,[2] Bruce S. Bauer,[3] Donald Johnson,[3] Veronica Rundell,[3] Lorelei J. Grunwaldt,[4] and Miguel Reyes-Múgica[1,*]

Molecular drivers

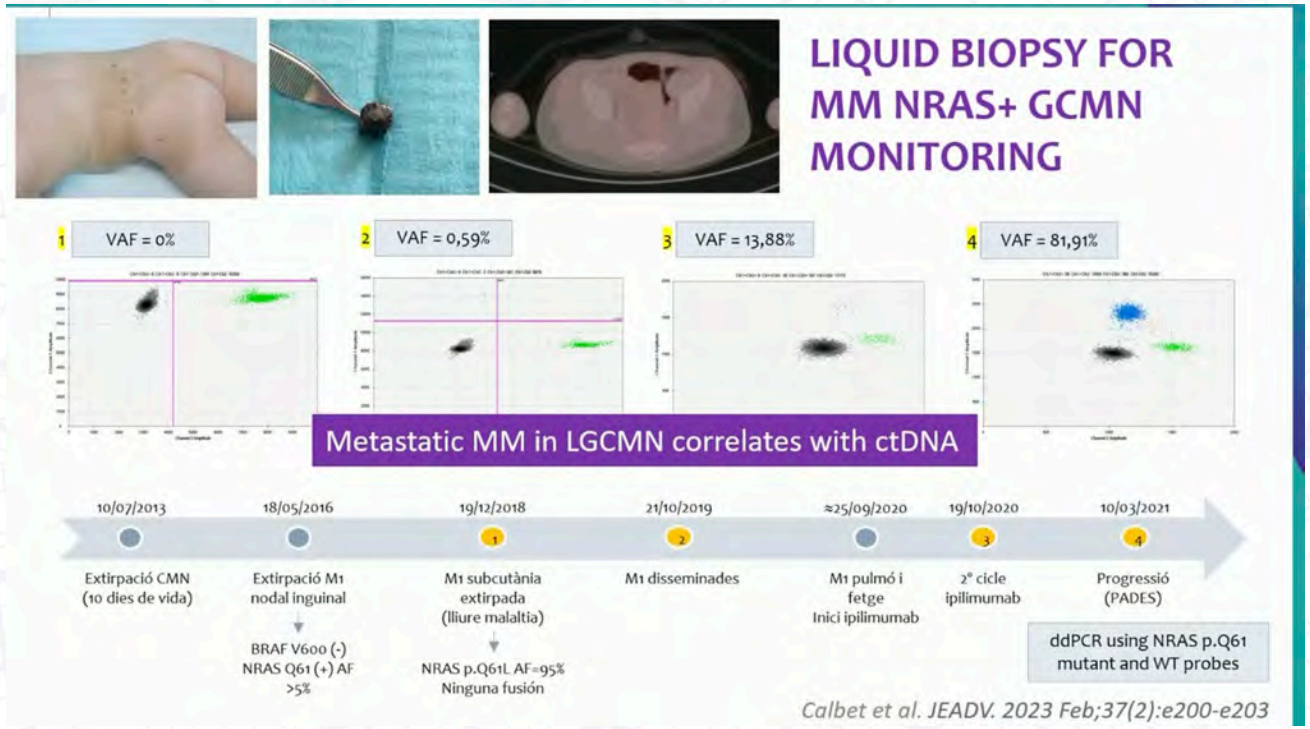
***NRAS* 68%**
*BRAF* 7%
*MET, GNAQ,* ... fusion transcripts
**No relation to the risk:**
- Neurocutaneous syndrome
- Melanoma development

Genetic Abnormalities in Large to Giant Congenital Nevi: Beyond *NRAS* Mutations

Vanessa Martins da Silva[1], Estefania Martinez-Barrios[2], Gemma Tell-Martí[1,3], Marc Dabad[3,4], Cristina Carrera[1,3], Paula Aguilera[1,3], Daniel Brualla[6], Anna Esteve-Codina[4,5], Asunción Vicente[6], Susana Puig[1,3], Joan Anton Puig-Butillé[2,3,7,8] and Josep Malvehy[1,2,8]

doi:10.1016/j.jid.2018.07.045

- **> mutación nRAS**
- **Pronósitco de MM sobre NMC: malo.**




- Problema: **nódulos sobre NMC**
- **Dificultad también en la biopsia**
- Necesidad estudio **NGS sobre biopsia**
- **Estudio BL: ayuda en la monitorización nRAS**

# Nodular lesions on giant congenital nevus: the role of molecular analysis with SNP-array.

Bordin C.[1], Tolone M.[2], Diociaiuti A.[3], Gisondi P.[1], Girolomoni G.[1], El Hachem M.[3]

[1]Section of Dermatology and Venereology, Department of Medicine, University of Verona, Verona.
[2]Department of Health Sciences, Magna Graecia University, Catanzaro.
[3]Dermatology Unit and Genodermatoses Research Unit, Bambino Gesù Children's Hospital, IRCSS, Rome.

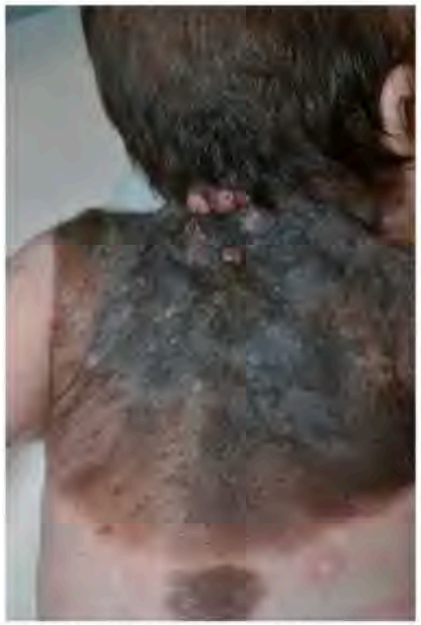


**Figure1**: patient at the age of 1 year.

**Introduction & Objectives:** We present the case of a 4-year-old patient affected by giant congenital melanocytic nevus (GCMN) of the back, extending to the head and left mandibular region with numerous satellite lesions of various sizes on the limbs, abdomen and face. MRI of the brain and spinal cord performed at one month of age was negative for neuromelanosis and the ophthalmological examination was normal. During her first years of life, she developed two nodular lesions arising from the GCMN: at the age of two months, a polypoid ulcerated nodule appeared in the nuchal region and at the age of 3 years the patient developed a new greyish nodular lesion on the dorsal interscapular region.

**Materials & Methods:** The patient underwent regular clinical and dermoscopic examination and every nodular lesion was biopsied. Both nodules were analysed through histopathological, histochemical and molecular examination (SNP-array).

**Results:** For the differential diagnosis between proliferative nodule and malignant lesion, histological examination and immunohistochemistry were performed. In both cases they were suggestive, but not decisive for melanoma. Therefore, molecular diagnosis with SNP-array was performed.

In the first lesion monosomies of various chromosomes and trisomy of chromosome 22 were highlighted, while no segmental chromosomal alterations were detected. The diagnosis was a proliferative nodule. Although the lesion was classified as benign, in consideration of the morphological aspects, a strict clinical and ultrasound follow-up was planned.

Regarding the second lesion, SNP-array showed multiple chromosomal imbalances, both aneuploidies and segmental alterations, in particular in the loci 8q.24 (MYC gain) and 1q (gain), which are

¡¡DxD!!

EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

# When faced to a congenital mass protruding from vagina, think of botryoid rhabdomyosarcoma

كلية الطب والصيدلة - مراكش
FACULTÉ DE MÉDECINE ET DE PHARMACIE - MARRAKECH

**B.BENNOUR, S.ABDEL-ILAH, M.ABOUDOURIB, S.AMAL, O.HOCAR**
Dermatology department- Arrazi hospital - Biosciences laboratory
Mohamed VI university hospital Marrakech Morocco

## Introduction

Gynaecologic neoplasms are rare in children.
Rhabdomyosarcoma (RMS) are malignant mesenchymal tumors deriving from myogenic progenitor that represents one of the most common soft tissue sarcomas of childhood.

It is often found in the genital tract of infants and young children and may be exceptionally congenital. We report a rare case of a congenital botryoid RMS.

## Case report

A female newborn presented 3 congenital papillomatous tumors in the vulvar area with vaginal and anal extension.

The histological study revealed spindle cells proliferation with high cellularity, the epidermis was hyperplastic and pseudo-sarcomatous. Immunohistochemistry showed a moderate expression of desmin, myogenin and Ki67 markers. Protein S100 was negative. The diagnosis of congenital botryoid rhabdomyosarcoma was retained.

The therapeutic management was to put the patient under chemotherapy according to the VAC protocol and to perform a tumor resection after regression of the lesions in order to avoid the anatomical damage of the ano-vulvar region.

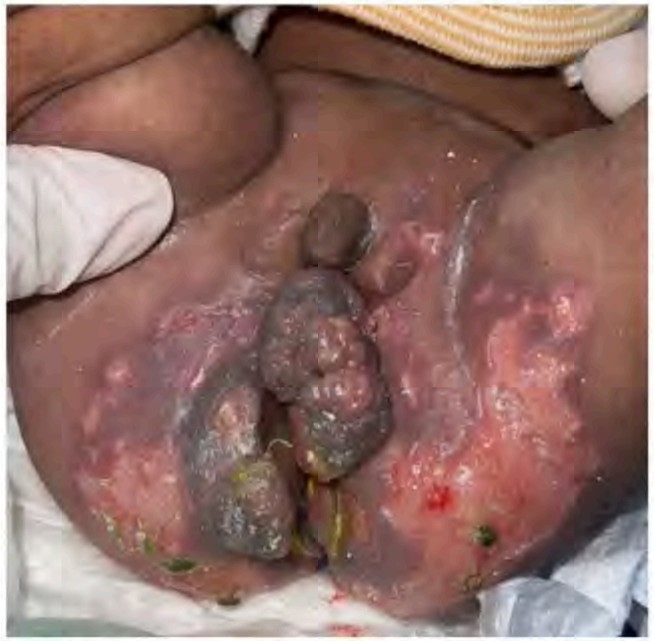


**Figure: Congenital botryoid rhabdomyosarcoma**

in which vulvar location and congenital onset were associated (1).

Four major histologic subtypes of RMS are identified:

embryonal, alveolar, pleomorphic, and sclerosing/spindle cell(2). Embryonal RMS (ERMS) is the most common type of all RMSs frequently arising in the pediatric female genitourinary tract(3). A study on 67 female children with ERMS showed that uterine RMSs were most often seen during adolescence however, vagina was the primary site in 68.4% of children between 0 and 9 years.(4)

Botryoid variant is a type of ERMS often occuring frequently in the vagina, characterized by 'grape-like' appearance caused by polypoid mass arising in submucosal tissue(5). Histological findings helps eliminate sacrococygeal teratoma neuroblastoma and Burkitt's lymphoma. Recently, authors have highlighted a variety of genitourinary ERMS associated with a somatic or a germline DICER1 mutation(6)(7). The combination of surgery and chemotherapy (Vincristine, dactinomycin, and cyclophosphamide) with or without radiotherapy or brachytherapy provides good results in early stage of genital ERMS(8)

# Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder in children: a cases series of fourteen patients

Seguí M[1], Olivares-Guerrero M[1], Noguera-Morel L[2], Hernández-Martín A[2], Colmenero I[3], Campos-Domínguez M[4], Kempf W[5], Gru A[6], Torrelo-Fernández A[2], Llamas-Velasco M[1].

[1]Department of Dermatology, Hospital Universitario de La Princesa, Madrid, Spain, [2]Department of Dermatology, Hospital Infantil Universitario Niño Jesús, Madrid, Spain, [3]Department of Pathology, Hospital Infantil Universitario Niño Jesús, Madrid, Spain, [4]Department of Dermatology, Hospital General Universitario Gregorio Marañón, Spain, [5]Department of Dermatology, University Hospital Zurich, Zurich, Switzerland, [6]Department of Pathology, University of Virginia School of Medicine, Charlottesville, Virginia, USA

**Results:** Fourteen patients were included, nine males and five females, aged between 1 and 16 years old. All patients presented as a single lesion and the most frequent location was the head. The histological findings were similar to those described in adults, with lymphoid proliferation in the papillary and reticular dermis composed of polymorphic lymphoid cells, recognizing small and medium-sized lymphocytes. The immunohistochemical study revealed a T phenotype (CD3+, CD4+, CD8-). The molecular study was positive for the monoclonal rearrangement of TCR gamma. All patients presented an indolent course with resolution after surgical treatment. In two cases, spontaneous regression was demonstrated after an incisional biopsy. In none of the cases recurrence was observed during follow-up of 38 months (2-55 months).

**Conclusions:** We present the largest case series of PCSM-LPD described in the literature in the paediatric age. As in adult populations, paediatric PCSM-LPD appears to most commonly present as a single lesion on the head or neck and have an excellent clinical prognosis, and thus further staging cannot be recommended. Surgical excision is the preferred mode of treatment, although spontaneous regression after biopsy has been described, therefore observation may be an option in these patients.

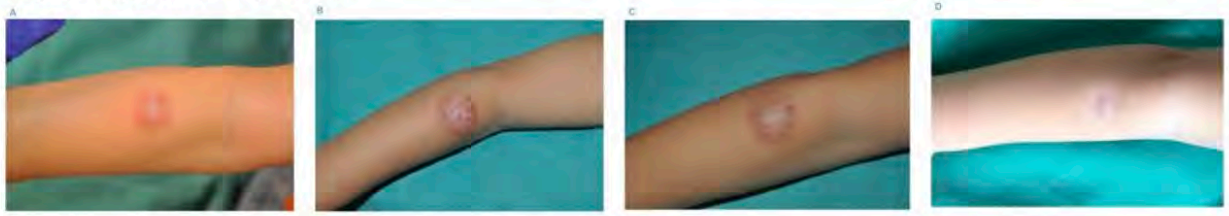


**Figure 1. Clinical images.** A) Initial clinical presentation of one of the patients: erythematous nodule on the forearm. B) 1 month after the biopsy: increase in the size of the lesion with a scar at the center and telangiectasias at the periphery. C) Two months after the biopsy: the lesion experienced spontaneous regression D) Six months after the biopsy: complete regression with a residual hypopigmented macule.

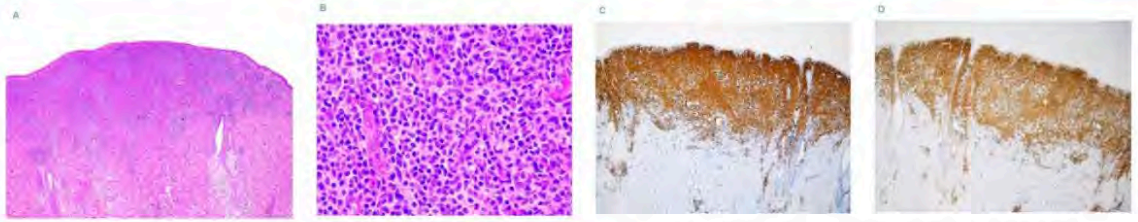


**Figure 2. Biopsy specimens.** A) At low magnification, a lymphoid proliferation is identified that diffusely occupies the papilar and reticular dermis. B) At high magnification, these small and medium-sized lymphocytes are recognized, which are pleomorphic, with elongated nuclei and a large, poorly defined cytoplasm. D) With immunohostichemistry techniques, lymphoid cells diffusely express CD3. E) As well as CD4. )

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD, Jaffe ES. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016 May 19;127(20):2375-90.
2. Plumptre IR, Said JT, Sheu Song J, Corey K, LeBoeuf NR. Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder in children: A case report and review of the literature. Pediatr Blood Cancer. 2022 Sep;69(9):e29862.

**Serie + larga de TCD4+ CP/M, español, muy recomendable**

# *Treatment of cutaneous vascular tumours*

16:20 - 16:40 CEST

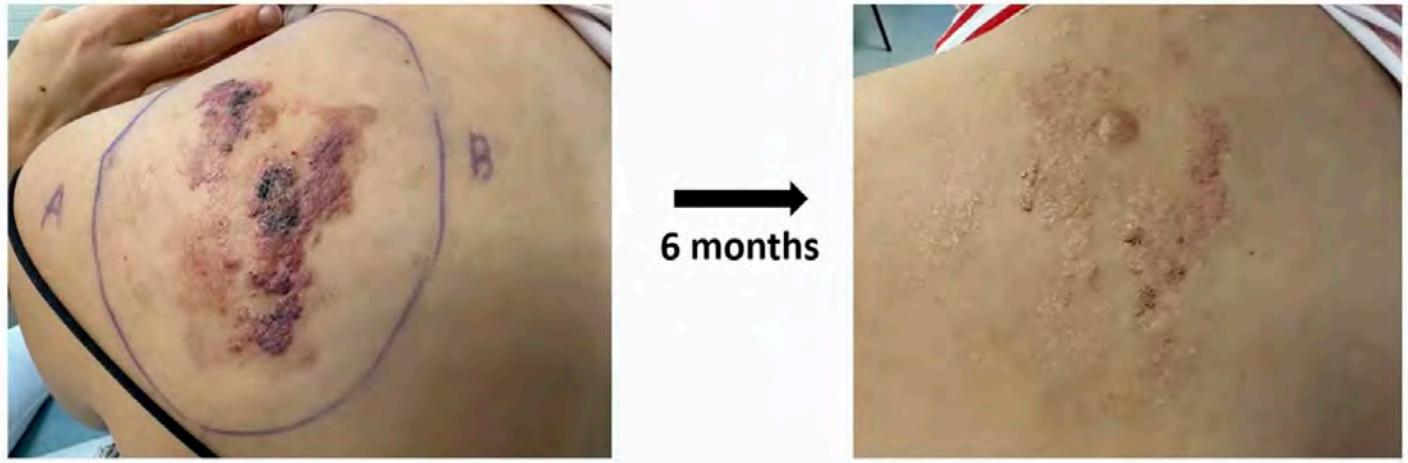
- **Sirolimus oral:**

- Mejoría **linfática**>**venosa**

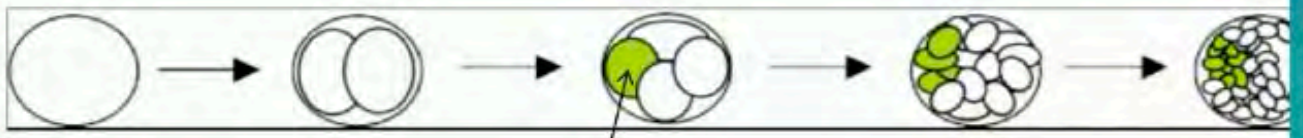
**Sirólimus tópico:**

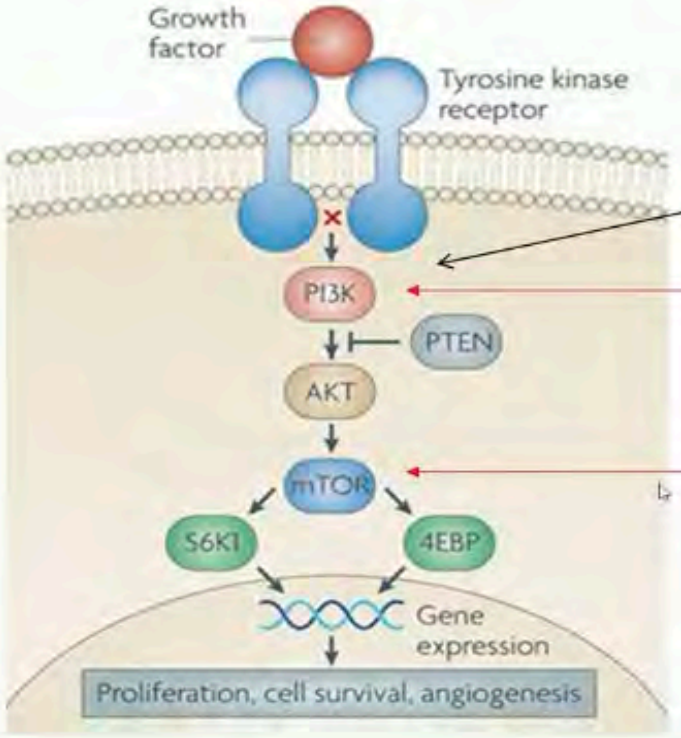
**Malf linfática microquística**

Topical sirolimus (rapamycin) 0.1% cream 1/day



# Post-zygotic gene mutations






***Mutations of PIK3CA***

**PI3K inhibitors (alpelisib)**

**mTOR inhibitors (sirolimus)**

Nature Reviews | Drug Discovery

Nature 2018

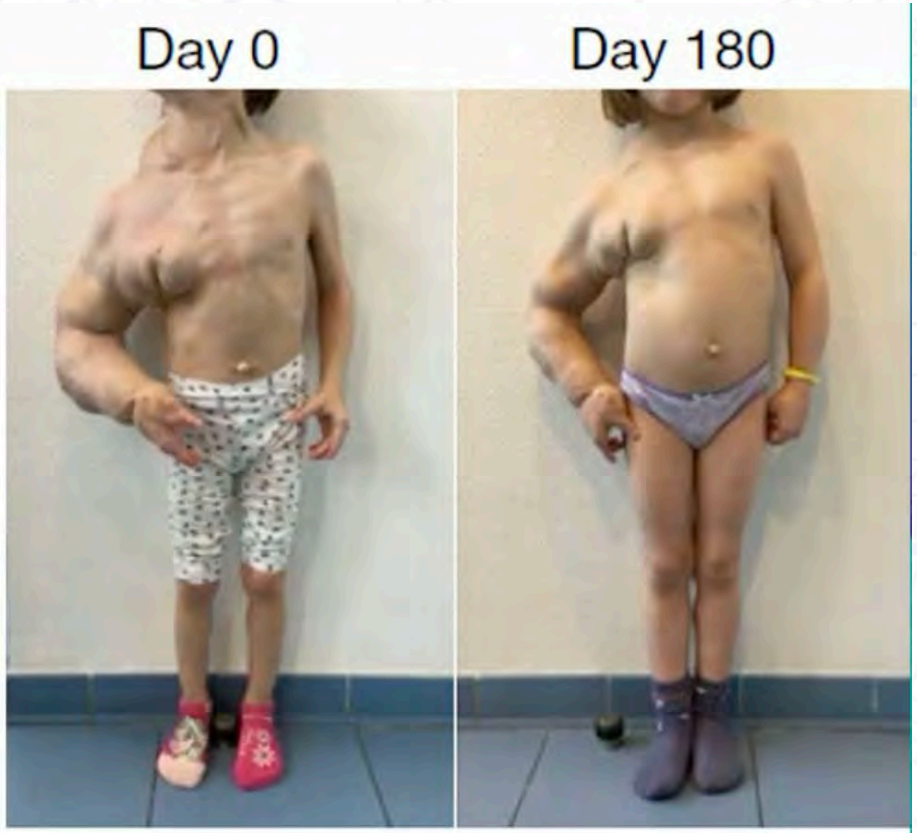
ARTICLE

https://doi.org/10.1038/s41586-018-0217-9

# Targeted therapy in patients with PIK3CA-related overgrowth syndrome

Quitterie Venot[1], Thomas Blanc[1,2,3,21], Smail Hadj Rabia[2,4,5,21], Laureline Berteloot[5,6], Sophia Ladraa[1], Jean-Paul Duong[2,7], Estelle Blanc[8], Simon C. Johnson[9], Clément Hoguin[1], Olivia Boccara[4], Sabine Sarnacki[2,3], Nathalie Boddaert[2,5,6], Stephanie Pannier[2,10], Frank Martinez[11], Sato Magassa[1], Junna Yamaguchi[1], Bertrand Knebelmann[1,2,11], Pierre Merville[12,13], Nicolas Grenier[14], Dominique Joly[1,2,11], Valérie Cormier-Daire[2,5,15], Caroline Michot[2,5,15], Christine Bole-Feysot[5], Arnaud Picard[2,16], Véronique Soupre[16], Stanislas Lyonnet[2,5,15], Jeremy Sadoine[17], Lotfi Slimani[17], Catherine Chaussain[2,17], Cécile Laroche-Raynaud[18], Laurent Guibaud[19], Christine Broissand[20], Jeanne Amiel[2,5,15], Christophe Legendre[1,2,11], Fabiola Terzi[1,2] & Guillaume Canaud[1,2,11]*

CLOVES syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal naevi, scoliosis/skeletal and spinal syndrome) is a genetic disorder that results from somatic, mosaic gain-of-function mutations of the *PIK3CA* gene, and belongs to the spectrum of *PIK3CA*-related overgrowth syndromes (PROS). This rare condition has no specific treatment and a poor survival rate. Here, we describe a postnatal mouse model of PROS/CLOVES that partially recapitulates the human disease, and demonstrate the efficacy of BYL719, an inhibitor of PIK3CA, in preventing and improving organ dysfunction. On the basis of these results, we used BYL719 to treat nineteen patients with PROS. The drug improved the disease symptoms in all patients. Previously intractable vascular tumours became smaller, congestive heart failure was improved, hemihypertrophy was reduced, and scoliosis was attenuated. The treatment was not associated with any substantial side effects. In conclusion, this study provides the first direct evidence supporting PIK3CA inhibition as a promising therapeutic strategy in patients with PROS.




***Randomized controlled trials are ongoing***

# Alpelisib for a PIK3CA- Related Vascular Anomaly

UNSW SYDNEY Australia's Global University

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## CASE REPORT

A 25-year-old female presented for review of a vascular birthmark. She reported increasing pain, bleeding, and soft tissue overgrowth within a congenital plaque on her right flank. She reported temporary symptomatic relief with cautery and debulking surgery performed years prior to presentation. Her past medical history was remarkable for cross-fused renal ectopia and endometriosis. The birthmark caused significant pain for which she had previously trialled multiple analgesics with minimal improvement. Examination revealed a geometric maroon patch measuring 35cm by 30cm. It was studded with dark vesicles, characteristic of microcystic lymphatic malformations in association with soft tissue swelling (Fig 1a).

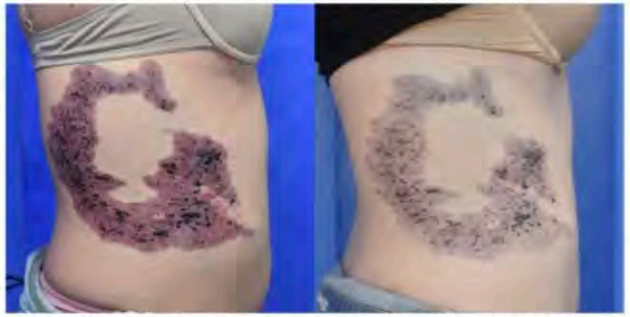

*Figure 1: PIK3CA-related vascular anomaly composed of capillary, lymphatic and venous malformations (a) at presentation and (b) two months follow up*

Incisional biopsy demonstrated dilated, thin-walled vessels

Her presentation was in keeping with a PIK3CA-related vascular anomaly composed of capillary, lymphatic and venous malformations. Given the morbidity associated with her birthmark, she was commenced on targeted treatment with a PI3K inhibitor, alpelisib 250mg once daily. At two-month follow-up, there was significant improvement with lightening of the capillary malformation and decrease in the number of microcystic lymphatic malformations (Fig 1b). Repeat MRI demonstrated reduced vascular calibre in the right flank with reduction in the tributaries of her lesion (Fig 2b). The patient no longer had associated pain with her lesion.

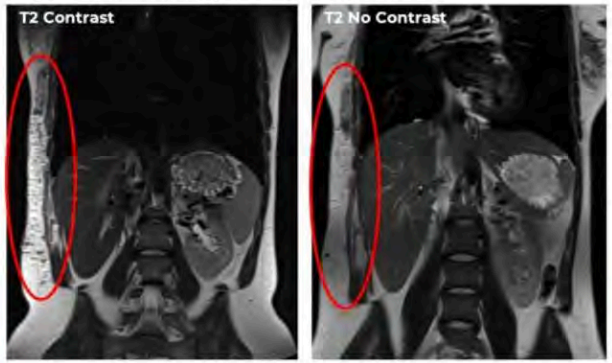


*Figure 2: MRI findings at (a) presentation and (b) four month follow up demonstrating reduction in vascular calibre and tributaries of the lesion*

## DISCUSSION

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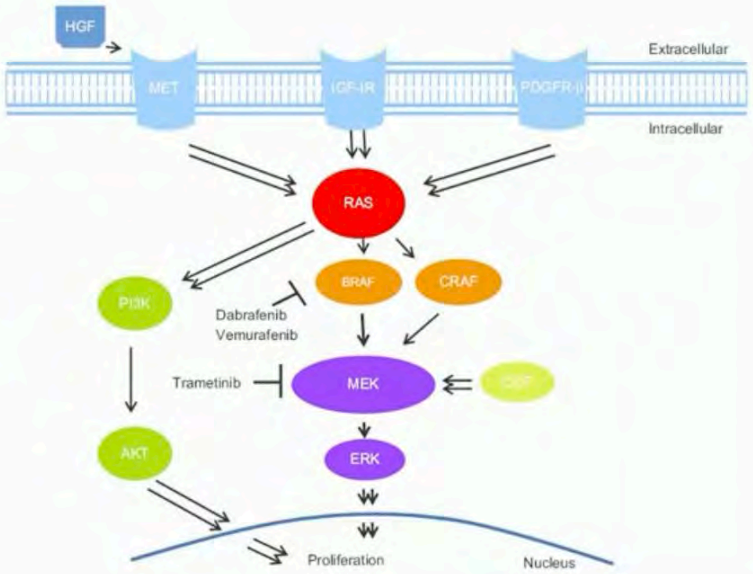
# Futuro de PROS: Alpelisib

## Hiperglucemia

# Somatic mutations identified in extracranial arteriovenous malformations




- Pathogenic variants in 78.3% of cases (n=18/23) :

MAP2K1 (Mitogen-activated protein kinase kinase 1) (n=7), KRAS (n=6), RASA1 (n=3), BRAF (n=2)

***El Sissy FN**, et al. JEADV 2022*

- Activation of the RAS/MAPK signaling pathway: a place for anti-MEK drugs (trametinib)?

***Kainthla R.** Pharmacogenomics and Personalized Medicine. 2013*
***Lekwuttikam R**, et al. JAMA Dermatol. 2019*
***Edwards EA**, et al. Pediatrics. sept 2020*

*Prospective studies are ongoing*
*(trametinib and cobimetinib,* NCT05125471)

# P0337 Successful Treatement of Angiolymphoid Hyperplasia with Eosinophilia by Propranolol

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## Introduction

Angiolymphoid hyperplasia with eosinophilia (ALHE) is a rare idiopathic condition, usually seen in adults and characterized by the presence of isolated or grouped papules, plaques or nodules in the skin of the head and neck region, specifically on the preauricular region. In the view of management, majority of related reports of therapeutic methods comprise of surgical excision, intralesional/topical/systemic corticosteroid...

In some cases, the oral propranolol was demonstrated as an alternative treatment of ALHE. Here we reported a case of a 30-year-old woman with ALHE successfully treated with propranolol.

## Case report

A 30-year-old woman, without past medical history was admitted with multiple painful papules, appeared 7 months ago, spontaneous bleeding in the auricle and the preauricular area

Physical examination revealed multiple red-brown firm dome-shape papules in the helix and antihelix, without any other cutaneous lesions. There was no local or regional lymphadenopathy, and other system examination were unremarkable and the complete blood count was normal.

Surgical removal of one of the lesions was performed and pathological examination confirmed the histological diagnosis of ALHE.

The patient was started on oral propranolol 40 mg once daily. Within 2 months, several of the lesions had decreased. Propranolol was subsequently stopped within 8 months of initiating treatment after a complete disappearance of all lesions and without any adverse effects of the medication **(Fig 1,2,3).**

Fig 1: Violaceous papules with a spontaneous bleeding.

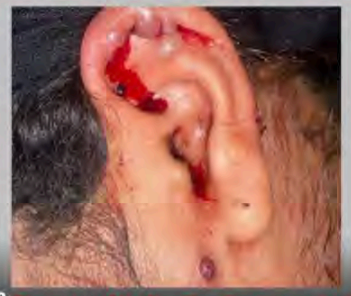

Fig 2: Regression of the bleeding after two weeks of treatment.

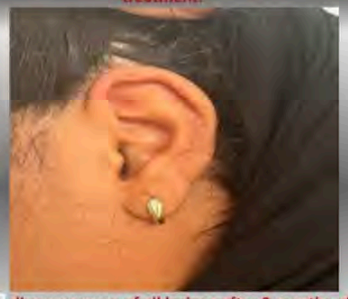

Fig 3 disappearance of all lesions after 8 months of treatment.

## Discussion

Angiolymphoid hyperplasia with eosinophilia is a benign, locally proliferating disease but the pathogenesis is not clearly understood whether it consists of a vascular neoplasm or a lymphoproliferative process.

ALHE commonly present with some symptoms, like pruritus, spontaneous bleeding and pain. This is consistent with our patient that had intense pain and bleeding. It tends to arise in the skin of the head and neck, particularly in the scalp and the periauricular area. Other features include regional lymphadenopathy and peripheral eosinophilia which is an inconstant feature as in our case.

Histologically, it is characterized by proliferation of vascular channels with inflammatory infiltrate composed of lymphocytes and eosinophils.

However, from previous case reports, surgical excision is considered as the most effective.Moreover, some reported cases showed the interesting successful treatment by oral propranolol. Although the definite mechanism remains unclear, the hypothesis has been proposed that beta-blocker-induced localized vasoconstriction, inhibition of angiogenesis and apoptosis of capillary endothelial cells.

Our case, shows that oral propranolol is one of the good therapeutic options in the treatment of ALHE with an excellent improvement in clinical presentations and symptoms and without any adverse effect.

### References

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3- Bahloul E; Ben Rejeb; Khaoula B; Ons B, et al. Successful treatment of angiolymphoid hyperplasia with eosinophilia with oral propranolol in two cases . Dermatol Ther 2021 Jul;34(4):e14994

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**Eficacia de Propranolol en hipreplasia angiolinfoide con eosinofilia**

# Mensajes para llevar a casa

AEDV2023 Highlights BERLIN

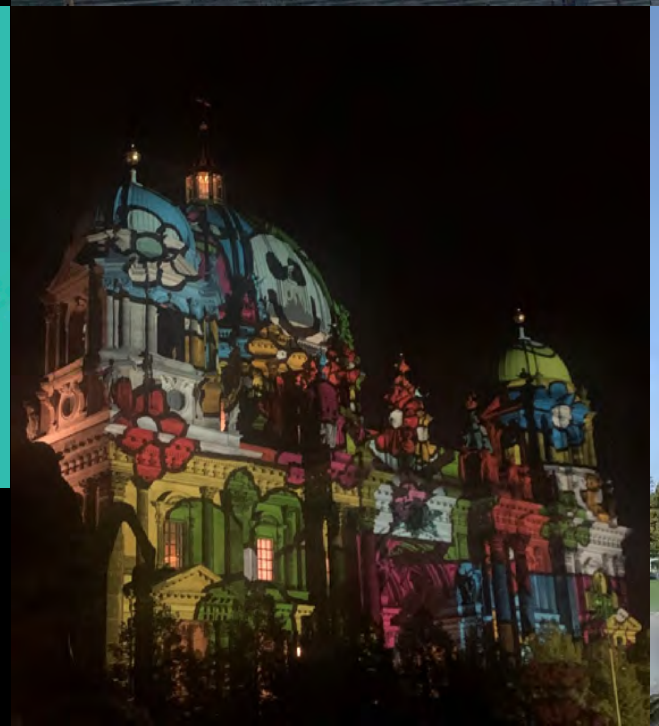
- **Fármacos biológicos en psoriasis:** 1ª línea, probablemente IL17 mejor que TNF. Nuevas moléculas en estudio.
- **Fúngicas:** siempre tenerlas presentes, tratamiento temprano evitar alopecia permanente. Griseofulvina/Terbinafina. Tratamiento convivientes.
- **DA infantil:** revolución biológica y de pequeña molécula → indicaciones, posología. ¿Posibilidad de detener o curar la marcha/Espectro atópico?
- **Ampollosas:** +F infecciosas, cuidado enfs graves (toxicodermias, AI, etc.). Post-virales simulan TEN. Ac en EB
- **Melanoma en NMC:** gigantes, satélite, alteración en SNC / 2º subgrupo: ≈ a población general, típico adolescentes mayores
- Tratamiento de **tumores vasculares cutáneos:** importancia sirólimus / alpelisib / y otras que vendrán tto dirigido

# Gracias


Miguel Mansilla Polo

Hospital Universitario y Politécnico La Fe

@mig_vec



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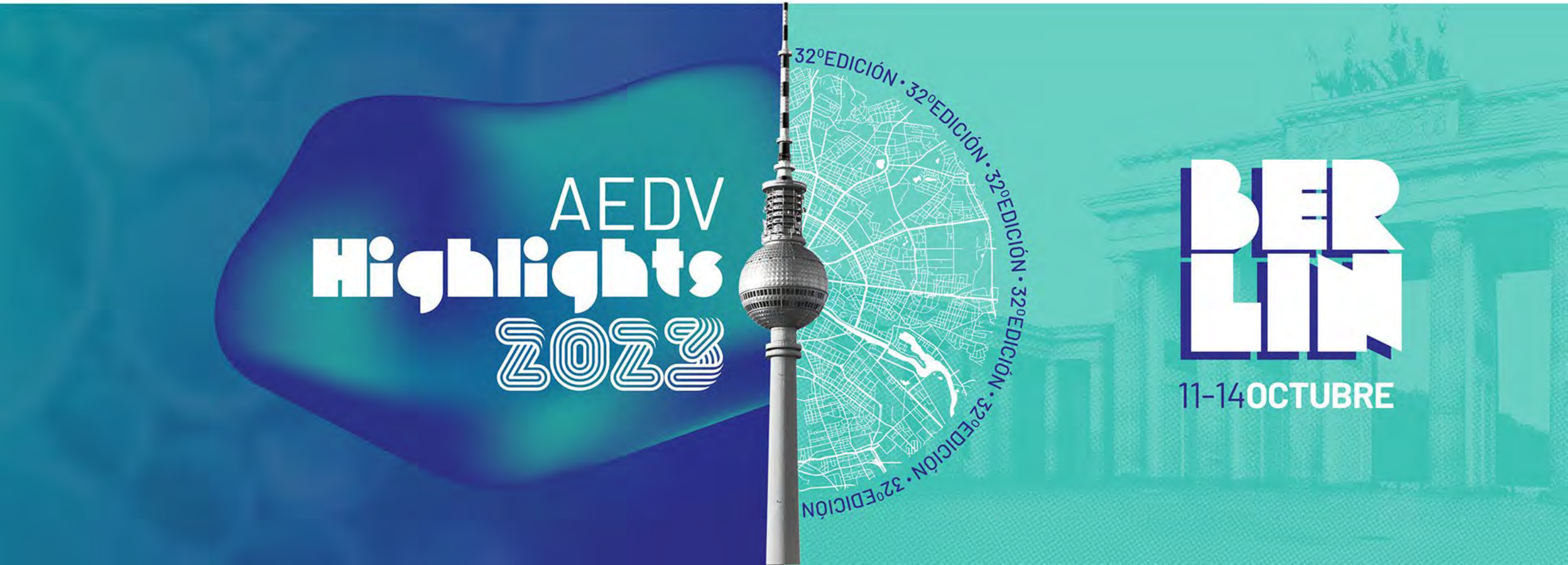

# AEDV 2023 Highlights

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