

 #WCD2019

AEDV

HIGHLIGHTS

24th World Congress of Dermatology (WCD)

10-15
JUNIO
2019

Milán



Patrocina:

janssen  Immunology
PHARMACEUTICAL COMPANIES OF 

Organiza:



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Dermatitis atópica

Dr. Pablo de la Cueva

Hospital Universitario Infanta Leonor

Patrocina:



Organiza:



Atopic dermatitis. Graham Ogg

Graham Ogg

1:33

DIVERSITY OF AD

Several variants/subtypes of AD:

- Acute vs. chronic¹
- Intrinsic (20%) vs. extrinsic (80%)²
- FLG+ vs. FLG-³
- Pediatric vs. adult⁴
- Western (European American) vs. Asian⁵
- Systemic disease associations

Most AD subtypes share type 2 activation

Global Disease Phenotype



Similar therapeutics



Different Disease Phenotypes



Require different therapeutic targets

FLG=filaggrin.

1. Gittler JK, et al. *J Allergy Clin Immunol*. 2012;130(6):1344-1354. 2. Suárez-Fariñas M, et al. *J Allergy Clin Immunol*. 2013;132(2):361-370. 3. Kezic S, et al. *Allergy*. 2011;66(7):934-940. 4. Czarnowski T, et al. *J Allergy Clin Immunol*. 2015;136(4):941-951. 5. Noda S, et al. *J Allergy Clin Immunol*. 2015;135(2):324-336.

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Atopic dermatitis. Emma Guttman

Emma Guttman 19:39

Emerging Systemic Treatments for AD

Emma Guttman-Yassky MD, PhD
 Sol and Clara Kest Professor of Dermatology
 Vice Chair, Department of Dermatology
 Icahn School of Medicine at Mount Sinai, New York, NY
 President. International Eczema Council

Is AD A Single Disease Across The Spectrum?

	American AD	Asian AD	African American AD	Pediatric AD	Psoriasis
Clinical Phenotype					
Immune Polarization	Th2 (Int>Ext, C>A) ↑↑↑ Th22 (Int>Ext, C>A) ↑↑↑ Th17 (Int>Ext, C>A) ↑↑↑ Th1 (C>>A) ↑↑↑	Th2 ↑↑↑ Th22 ↑↑↑ Th17 ↑↑↑ Th1 ↓	Th2 ↑↑↑ Th22 ↑↑↑ Th17 X (Absent) Th1 X (Absent)	Th2 ↑↑↑ Th22 ↑↑↑ Th17 ↑↑↑ Th1 X (Absent)	Th2 X (Absent) Th22 ↑↑↑ Th17 ↑↑↑ Th1 ↑↑↑
Epidermal Barrier	Epidermal thickness ↑↑ KRT16 ↑ K167 ↑ FLG, LOR, PPL ↓↓	Epidermal thickness ↑↑↑ KRT16 ↑↑ K167 ↑↑ FLG ↓ LOR ↔	Epidermal thickness ↑↑ KRT16 ↑ K167 ↑ FLG ↔ LOR ↓↓	Epidermal thickness ↑↑ KRT16 ↑↑ K167 ↑↑ FLG, LOR, PPL ↓↓	Epidermal thickness ↑↑↑ KRT16 ↑↑↑ K167 ↑↑↑ FLG, LOR, PPL ↔

Czarnowicki T, He H, Krueger JG, Guttman-Yassky E. JACI 2018

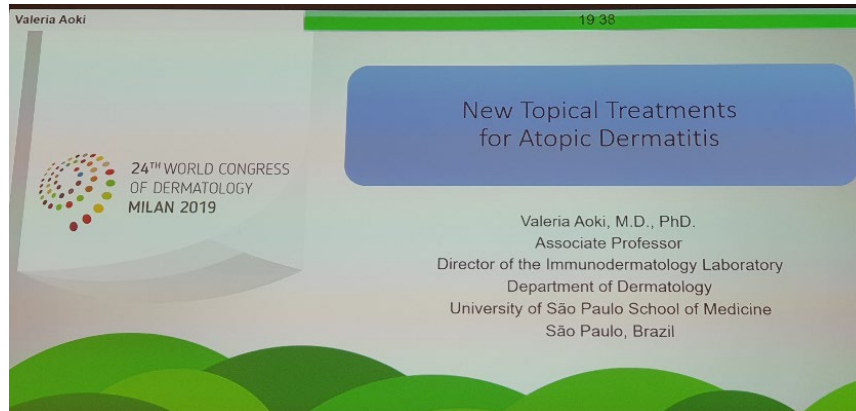
• Biologic

- Anti-IL4/13: dupilumab
- Anti-IL13: tralokinumab, lebrikizumab.
- Anti- IL31: nemolizumab.
- Anti-IL31 y anti-OncostatinM: KPL-716.
- Anti-IL22: ILV-094.
- Anti-OX40: GBR830, KHK4083.
- Anti-IL17C: MOR-106.
- Anti-IL33: ANB020.

• Oral:

- JAK Inhibitors: baricitinib (1,2), upadacitinib (1), abrocitinib (1), ASN002 (JAK/SIK).
- Anti-H4R: ZPL-389





Valeria Aoki

PDE4 Inhibitors and AD

JAK Inhibitors and AD

AMPs and AD

Prostaglandin leukotriene inhibitors and AD

TRPV1 Inhibitors and AD



Valeria Aoki 14:22

PDE4 Inhibitors and AD

Name	Primary endpoint	Phase	Trial #	N
PDE4 inhibitors:				
• Crisaborole	• ISGA d29 • ADSI/interv- adherence	• III/ • IV	• NCT02118792/02118766/ 010301508/030250663	• 763 (>2yo), 764 (>2yo) 46A, 40A
• DRM02	• Phys les assess	• II	• NCT01993420	• 21A
• OPA-15406	• Sev AE, % Success IGA	• II	• NCT02068352	• 121 (12-70 yo)
• Roflumilast	• Bas d15/SCORAD	• II	• NCT01856764	• 40A
• E6005/RVT-501	• Pharm/pruritus-EASI/Sev AE	• I/II • II	• NCT01179880/NCT146941/NCT02950922	• 76A, 78A, 157 (12-70 yo)
• Leo-29102	• EASI-wk 4	• II	• NCT01037881	• 183A

(Nygaard U et al, Dermatology 2017; Napolitano M et al 2018, Exp Rev Clin Pharm; Moyle M et al 2019 Exp Dermatol)

Valeria Aoki 14:23

JAK Inhibitors and AD

Name	Primary endpoint	Phase	Trial #	N
JAK inhibitors:				
• Ruxolitinib (JAK1/2)	• EASI-wk 4	• II/III	• NCB018424	• 307A
• Tofacitinib (JAK1/3)		• II	• NCT02001181	• 69A
• LEO124249 (JAK1/2/3/TYK2)	• EASI-wk 4	• II/III		• 327A

Momelotinib (MMB-mouse model)

(Bissonette R et al 2016; Nygaard U et al, Dermatology 2017; Napolitano M et al 2018, Exp Rev Clin Pharm; Moyle M et al 2019 Exp Dermatol)

Valeria Aoki 6:37

Antimicrobial peptides and AD

Name	Primary endpoint	Phase	Trial #	N
AMPs				
• Omiganan pentahydrochloride (synthetic cationic peptide)	• pharm/saf/tol • Clin SCORAD	• II • II	• NCT02456480 • NCT03091426	• 37 A • 80 A
• Tapinarof (AhR)	• IGA wk12	• II	• NCT02564055	• 247 (>12yo)

(Nygaard U et al, Dermatology 2017; Napolitano M et al 2018, Exp Rev Clin Pharm; Moyle M et al 2019 Exp Dermatol)

Valeria Aoki 5:09

Prostaglandin/Leukotriene Inhibitors and AD

Q301: 5-lipoxygenase inhibitor

- BID, 8 wk, double-blinded, vehicle-controlled
- 57 moderate to severe AD > 18 yo

ZPL-521: cPLA2 inhibitor

- 1% 2 wk, double-blinded, vehicle-controlled
- 57 moderate to severe AD > 18 yo

TRVP1 Inhibitors and AD

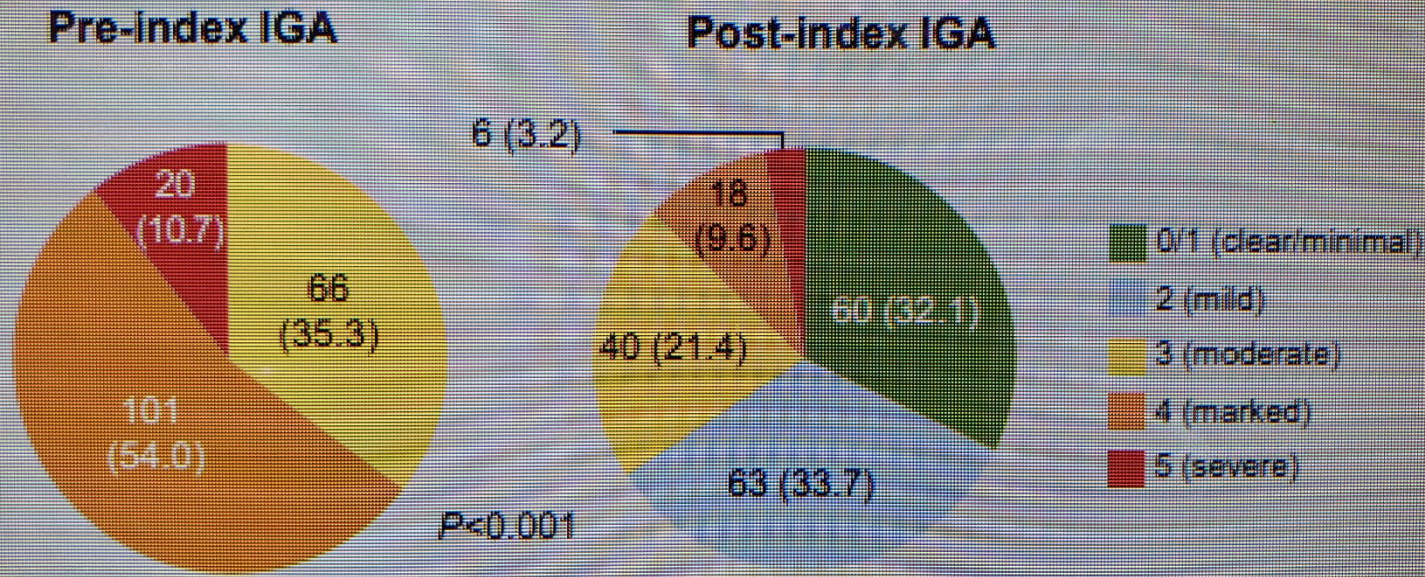
Name	Primary endpoint	Phase	Trial #	N
TRVP1 inhibitors:				
• PAC 14028	• SCORAD 4 wk/IGA wk8	• III/IV	• NCT02583022/NCT02757729	• 74A, 192A
• CT1327 (Creabilis)	• Change pruritus/VAS	• II	• NCT01808157	• 188 >12 yo



Real-World Effectiveness of Dupilumab in Atopic Dermatitis (AD): Improvement in AD Signs as Assessed by the Investigator Global Assessment (IGA) in an Electronic Medical Records Dataset

Lawrence F. Eichenfield¹, April W. Armstrong², Abhijit Gadkar³, Raymond Miao⁴, Chi-Chang Chen⁵, Dionne M. Hines⁵, Catherine McGuinness⁵, Zhen Chen³, Mandeep Kaur⁶, Andrew Korotzer³, Usha G. Mallya⁶

Figure 2. Pre-post IGA change (n, %) in patients with moderate-to-severe AD, n=187



Dupilumab in real-world clinical practice: efficacy and safety in patients with moderate to severe atopic dermatitis

S. M. Ferrucci¹, S. Tavecchio^{1,2}, F. Germinasi³, C. Moltrasio¹, L. Angileri³, E. Berti^{1,2}

Figure 2. Score improvement at week 16 (n=49)



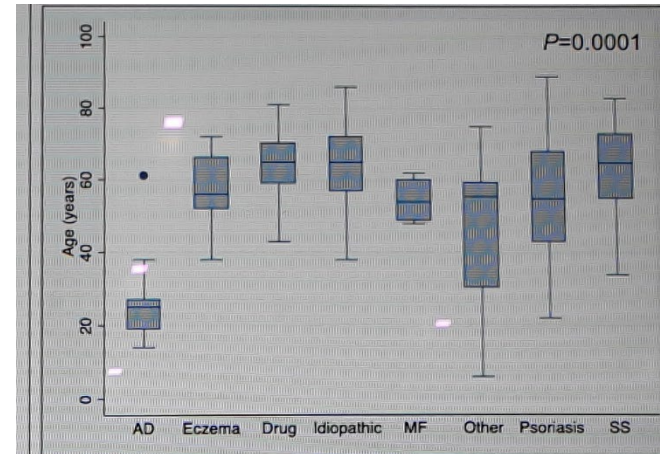
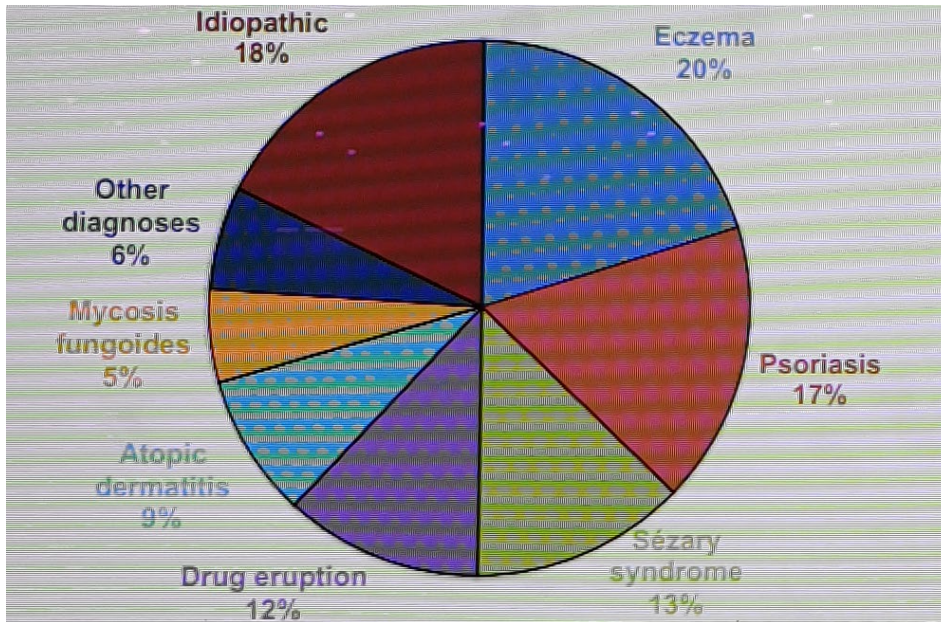


Fig.2. Ages at diagnosis according to the etiologies

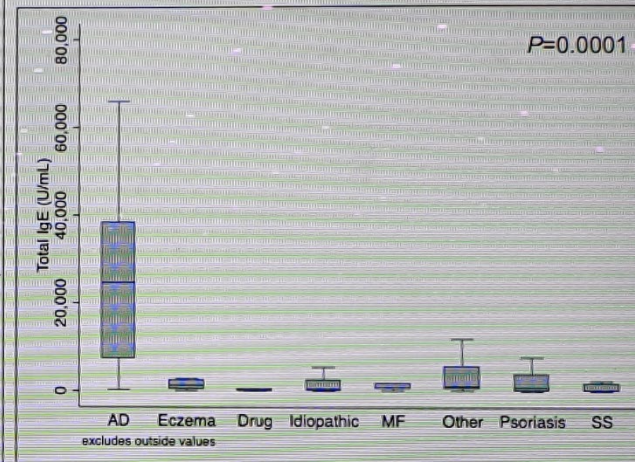


Fig.3. Total IgE at diagnosis according to the etiologies

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Urticaria

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Patrocina:



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Chronic urticaria. Treatment of the future (Ana Giménez Arnau)

Ana Gimenez-Arnau

24th WORLD CONGRESS OF DERMATOLOGY

What will the future hold? How we will treat urticaria and angioedema in 2020 and beyond

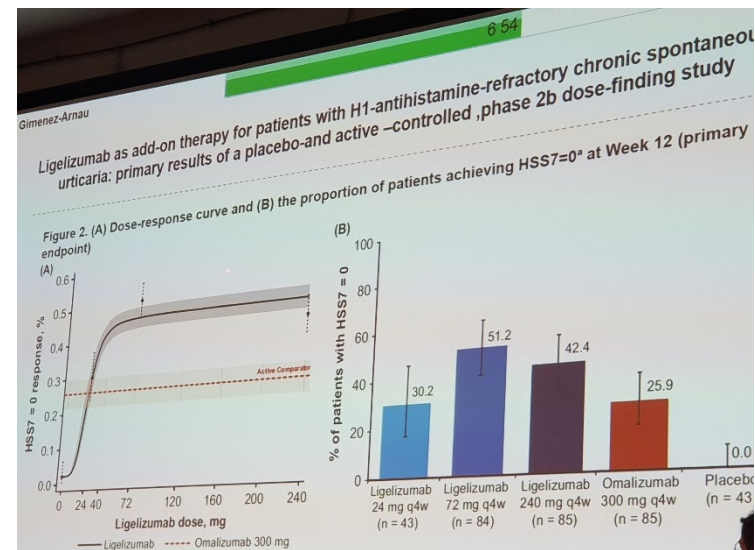
Ana M Giménez-Arnau
Dermatology. Hospital del Mar
Universitat Autònoma
Universitat Pompeu Fabra
Barcelona . Spain

Ana Gimenez-Arnau

The future of urticaria therapy Novel targets, Better treatment ?

- Do you and the patients feel comfortable with the available therapeutic tools ? Yes, much better, better than before 2014
- Why we need to develop new therapeutic tools in Chronic urticaria ?
 - Even better control of Angioedema episodes in CSU
 - Increase % of CSU patients completely controlled
 - Increase % with fast CSU complete control
 - Increase % of CSU complete remission with no relapse
 - Succeed in refractory patients to current recommended treatment
 - Develop licenced treatments for CInDUs

Target	Biological	Study Phase
CD20	Rituximab	1-2 CSU
IgE	Ligelizumab	3 CSU NCT/03437278/NCT03580356/NCT03580369/NCT02645
IgE	UB-221	1 CSU NCT03632291
Intracellular signaling mast cell	SYK-inhibitor GSK2646264	CSU and Cold Urticaria NCT02424799
Siglec-8 , mast cell	Siglec-8 inhibitor AK002	2a CU NCT03436797
T-cells -Anti CD80/CD86 - CD28	Abatacept	Pilot CU NCT00886795
IL-1β	Canakinumab	2 CSU NCT01635127
IL-1β	Rilonacept	2 Cold CU NCT02171416
BTK Inhibitor - B and Mast cells	GDC-0853 Fenebrutinib	2 CSU NCT03137069
Intracellular signaling	LOU064	NCT03693625
BTK Inhibitor - B and Mast cells	LOU064	2 CSU CLOU064A2201
IL-5, eosinophils	Benralizumab	4 CSU NCT03183024
IL-5, eosinophils	Mepolizumab	1 CSU NCT0344881
IL-4r	Dupilumab	CU Proff of concept
PGD2 receptor antagonist	AZD1981	2 NCT02031679



Chronic urticaria. Pregnancy and lactation (Emek Kocaturk)

11:57
Emek Kocaturk Goncu

CHRONIC URTICARIA AND HORMONES

- W/M = 2/1
- Disease activity changes during menstrual cycle, pregnancy, menopause, and hormone replacement therapy

.....strongly suggests that sex hormones could modulate the course of CU

10:06
Emek Kocaturk Goncu

PREG-CU: CHRONIC URTICARIA AND PREGNANCY RESULTS FROM OUR CENTER

SUMMARY

- From our 27 CU patients who experienced pregnancy,
 - CU seems to improve during pregnancy
 - Exacerbations do occur especially at the first trimester
 - May worsen after delivery
 - Preterm delivery is more common?

Emek Kocaturk Goncu

TREATMENT ALGORITHM RECOMMENDED BY THE EAACI/GA²LEN/EDF/WAO URTICARIA GUIDELINE

Second-generation H1-Antihistamines (sgAH)

Should the same treatment algorithm be used in pregnant women and during lactation?

We suggest using the same treatment algorithm with caution both in pregnant and lactating women after risk benefit assessment. Drugs contraindicated in pregnancy should not be used.	↑	> 90% consensus
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Add-on to sgAH: Ciclosporin

Exacerbation: Systemic corticosteroid (3-7 days)

Emek Kocaturk Goncu

TREATMENT OF CU DURING PREGNANCY

OMALIZUMAB

- Although this study cannot definitively establish the absence of any increased risk with omalizumab, there was no evidence of an increased risk of major congenital anomalies following exposure to omalizumab among pregnant women compared to a disease-matched cohort of pregnant women with moderate-to-severe asthma

Chronic urticaria. Pregnancy and lactation (Emek Kocaturk)

Emek Kocaturk Gocnu

TREATMENT OF CU DURING LACTATION

ANTIHISTAMINES

- 2nd gen AH are safe as the transfer rate to breast milk is minimal
- Loratadine, cetirizine, and fexofenadine are the best studied
- 1st gen AH might lead to infant irritability and drowsiness
- 2nd gen AH should be preferred
- Higher doses of loratadine and terfenadine showed very minimal transmission to the milk
- Higher doses of 2nd gen AH can be safely used during lactation

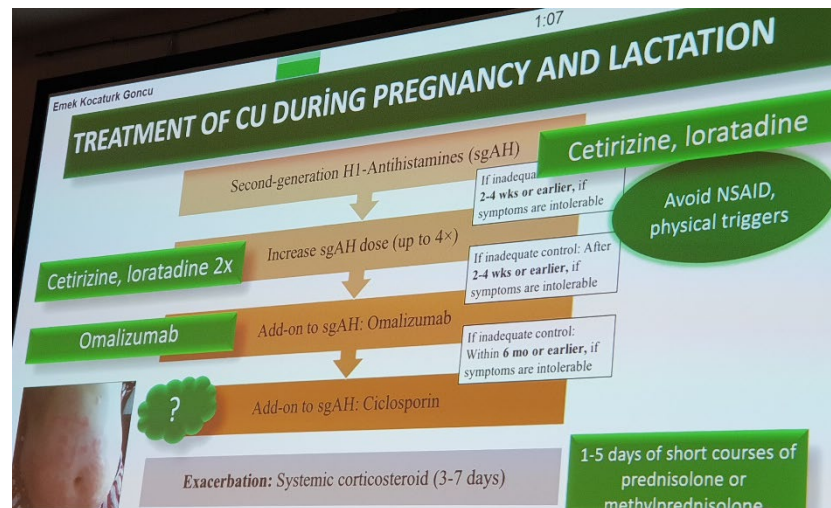
Emek Kocaturk Gocnu

TREATMENT OF CU DURING LACTATION

OMALIZUMAB

- Because omalizumab is a large protein molecule with a molecular weight of 145,058, the amount in milk is likely to be very low
- absorption is unlikely because it is probably destroyed in the infant's gastrointestinal tract
- The manufacturer reports that 186 infants have been breastfed during maternal omalizumab therapy, with no increase in infectious complications

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Milán

