

28º Congreso EADV

**AEDV**  
*Highlights*

M A D R I D

9 al 13 de octubre 2019



<https://eadvhighlights.aedv.es>

 #EADV2019

# INMUNOALERGIA CUTÁNEA

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Patrocina:

*Lilly*

Organiza:



ACADEMIA ESPAÑOLA  
DE DERMATOLOGÍA  
Y VENEREOLOGÍA

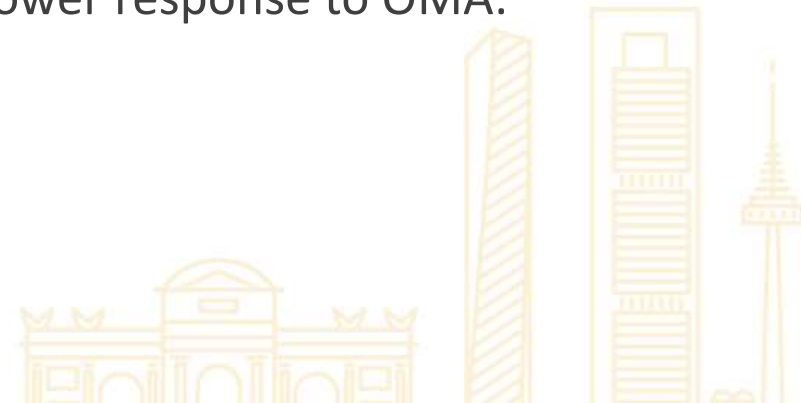


# URTICARIA

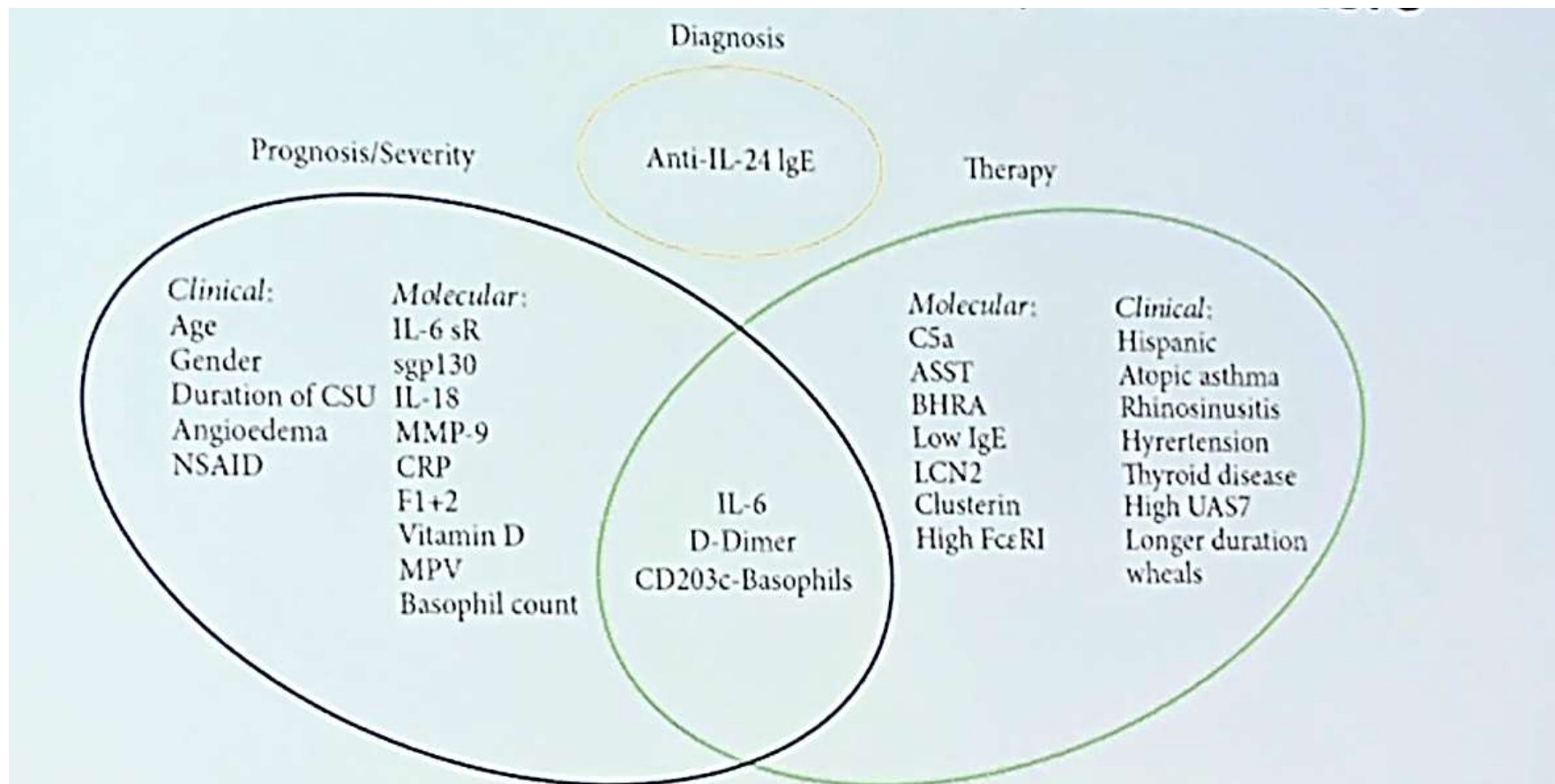


## URTICARIA – AUTOIMMUNITY

- Autoimmunity and CSU: type I and type IIb
  - Association with other autoimmune diseases: RA, LES, IBD + functional autoab inducing histamine release from mast cells or basophils
  - Many ways to explore autoimmunity: in vitro and in vivo
  - Definition of “autoimmune CSU”: **IgG autoantibodies** to FcεRI or to IgE **+ positive BAT + positive ASST** – only 8% patients have it all. Rest: partial or non AI CSU.
  - Majority of AI CSU: **↓ IgE levels and ↑ antiTPO IgG**
  - The more autoimmune features – the slower response to OMA.
    - Good response to CsA
  - Promising effect of OMA on LES and DM



# URTICARIA - BIOMARKERS



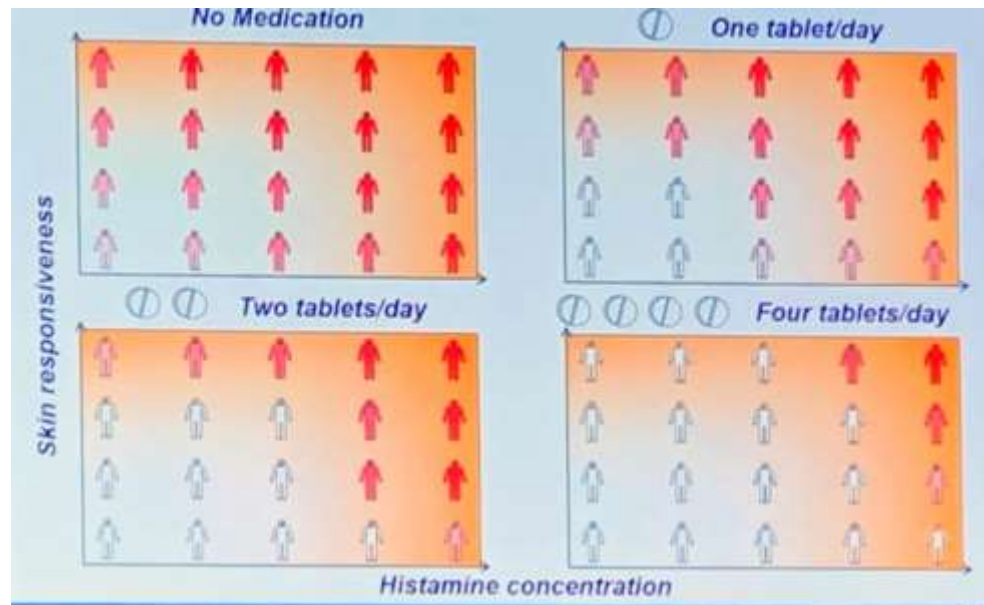
## URTICARIA - BIOMARKERS

- Biomarkers
  - **Severity:** ASST and BAT + more severe disease
  - **Duration:** Anti-thyroid antibodies, ASST and angioedema
  - **Activity:** IL6, D-dimer and CRP
  - **Treatment:**
    - **AntiH1 non responders:** ↑ Basal UAS7 and ↑ D-Dimer
    - OMA:
      - ↓ FcεRI receptor expression and very low IgE: NO RESPONDERS
      - Very low IgE, but increased at least twice – response
      - Receptor expression could be also used for CINDU
      - +ASST: SLOW RESPONDERS
      - **D-DIMER NOT USEFUL FOR PREDICTING RESPONSE TO OMA!!!!**
      - IL-31 and OMA
    - CsA: D-dimer seems to be useful (high), ASST+

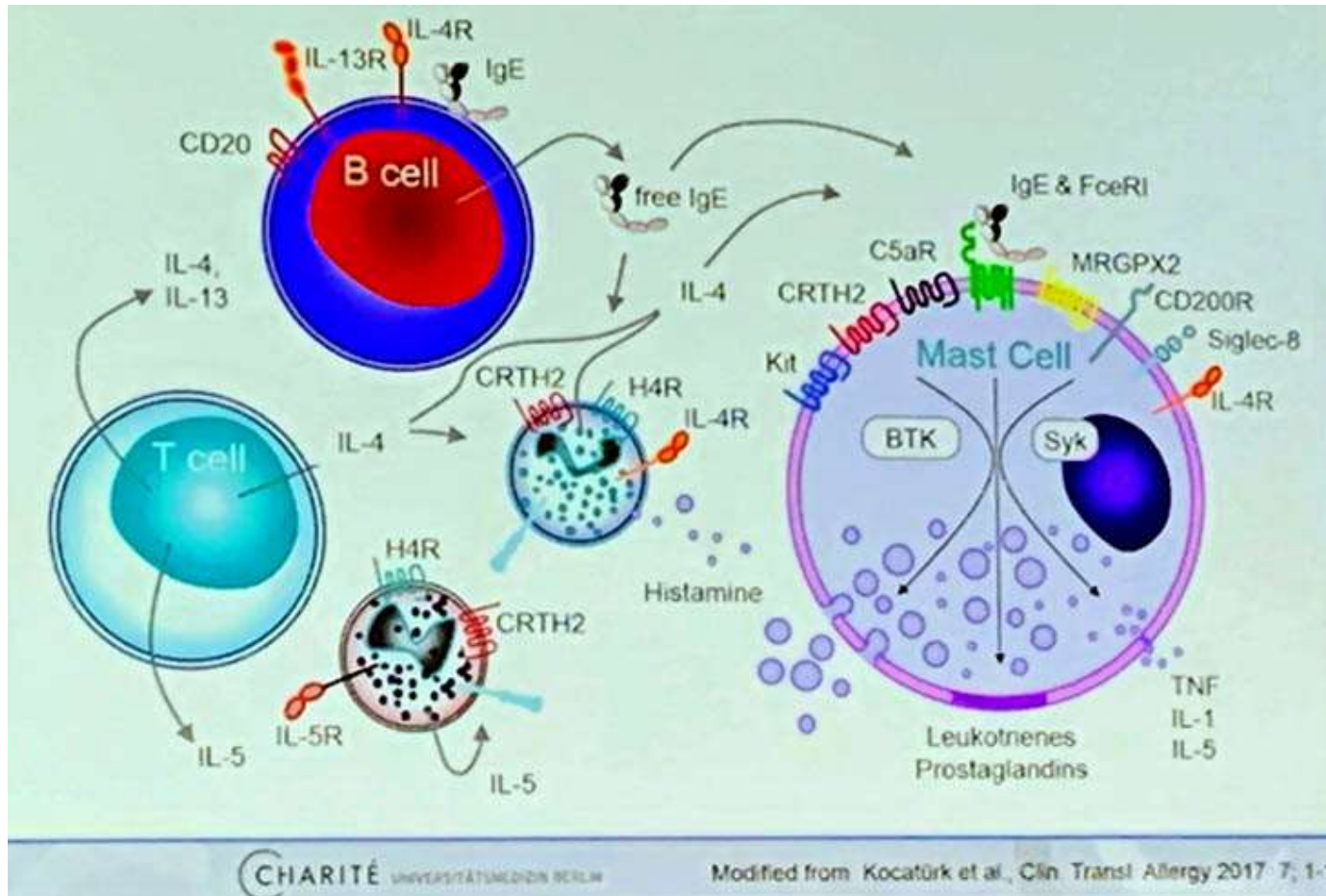


## URTICARIA – TREATMENT

- 2<sup>nd</sup> gen antiH very little sedative effect (unless you up-dose)
- Bilastine and fexofenadine** do not diffuse into the brain because of p-glycoprotein (substrates) – NOT SEDATIVES
- Cardiac safety – not a worry with 2<sup>nd</sup> gen. antiH (even when updose)

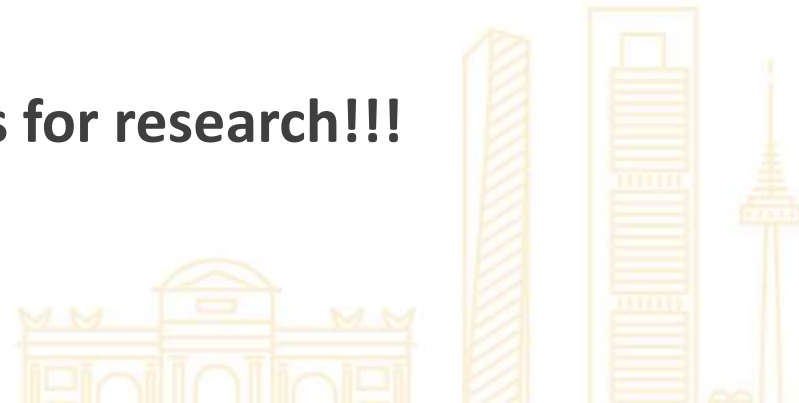


# URTICARIA NEW TREATMENTS I



## URTICARIA NEW TREATMENTS II

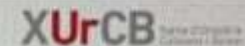
- **Ligelizumab** shows better responses than omalizumab
- **Siglec-8** – mast cell activation inhibitor
  - 61% benefit of response in UAS7 in OMA-refractory patients
- **Dupilumab** – limited evidence
- **Anti IL-5** (asthma + CSU) reslizumab, benralizumab and mepolizumab – strong benefit for CSU
- **BTK inhibitors** (intracellular molecule) - shut down mast cell
- **Syk-inhibitor** – trials ongoing
- **CINDU? Angioedema? MAS? – gaps for research!!!**





## POSTER

### OMALIZUMAB FOR THE TREATMENT OF CHRONIC INDUCIBLE URTICARIA IN 80 PATIENTS:



#### Efficacy and prognostic factors of response

Abstract: Introduction: Chronic inducible urticaria (CI-U) is a chronic allergic condition characterized by recurrent wheals and/or angioedema induced by physical or chemical stimuli. The treatment of CI-U is based on the use of antihistamines. Omalizumab is a monoclonal antibody that acts as an anti-IgE antibody. Objective: To evaluate the efficacy and prognostic factors of response to omalizumab in 80 patients with CI-U. Methods: Retrospective study of 80 patients with CI-U treated with omalizumab. Results: The response to omalizumab was evaluated in terms of the number of wheals and/or angioedema attacks per month. The response was considered as complete when there was no wheal or angioedema attack during the study period. The response was considered as partial when there was a reduction in the number of wheals and/or angioedema attacks per month. The response was considered as non-response when there was no reduction in the number of wheals and/or angioedema attacks per month. The response to omalizumab was evaluated in terms of the number of wheals and/or angioedema attacks per month. The response was considered as complete when there was no wheal or angioedema attack during the study period. The response was considered as partial when there was a reduction in the number of wheals and/or angioedema attacks per month. The response was considered as non-response when there was no reduction in the number of wheals and/or angioedema attacks per month.

### CONCLUSIONS

Our findings suggest that omalizumab is an effective treatment in patients affected by CI-U in clinical daily practice. Omalizumab up dosing may be useful in non-responder patients. The main limitation of our study is related to its retrospective nature, the few number of patients and the lack of an available activity score to compare all the subtypes of CI-U. Studies with a larger number of patients would be needed to confirm our results.





# ATOPIC DERMATITIS



## POSTERS

### A simulation study for clinical efficacy of an anti-ORAI1 antibody (DS-2741a) on atopic dermatitis using quantitative systems pharmacology (QSP) modeling for preclinical-to-clinical translation

Christina Friedrich<sup>1,\*</sup>, Takashi Ito<sup>2</sup>, Katherine Kudrycki<sup>1</sup>, Meghan Pryor<sup>1</sup>, Vincent Hurez<sup>1</sup>, Shinnosuke Yamada<sup>2</sup>, Naoki Kiyosawa<sup>2</sup>, Masatoshi Nishimura<sup>2</sup>, Ryo Atsumi<sup>2</sup>, Kiyoshi Morimoto<sup>2</sup>  
<sup>1</sup>Rosa & Co. LLC, CA, USA, <sup>2</sup>Daiichi Sankyo Co., Ltd, Tokyo, Japan \*cfriedrich@rosaandco.com

#### Conclusions

- QSP modeling provided an early indication of the potential for DS-2741a as a novel therapeutic agent in AD
- Simulations suggest that DS-2741a could show faster response and more efficacy than dupilumab in a broad spectrum of AD patients
- QSP modeling and research was regarded in-house as an alternative investigation to preclinical animal model and was leveraged to prioritize the product toward clinical trial

# POSTERS

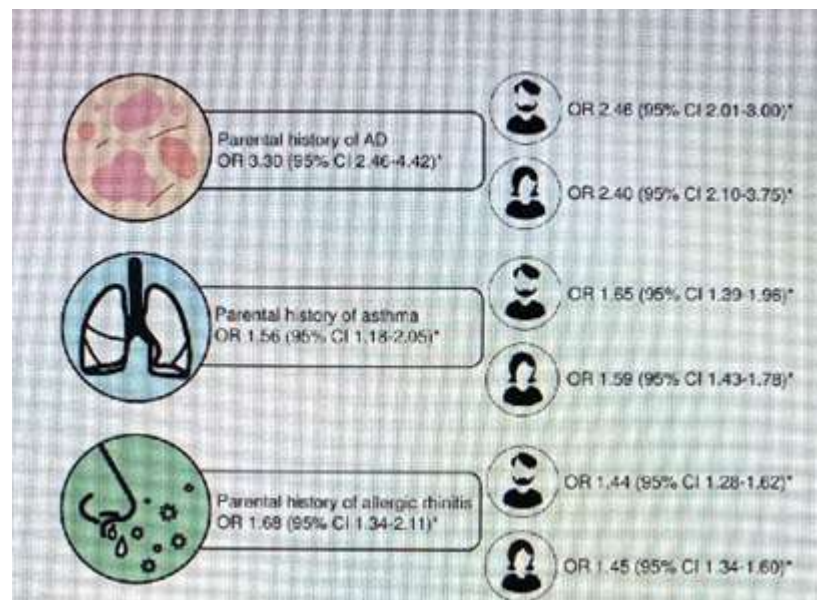


Figure 2: Association between AD and parental history of AD, asthma and allergic rhinitis overall and subdivided by parental sex. \* $p < 0.001$

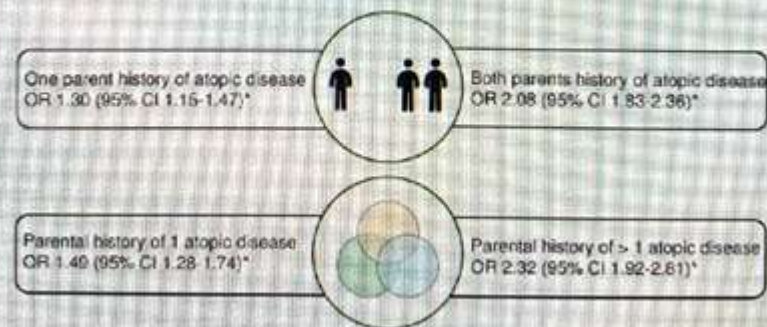


Figure 3: Dose-response relationship between AD and parental history of atopic disease. \* $p < 0.001$



# PRURITUS



## POSTERS

### IL-31 is Implicated in the Pathogenesis of Prurigo Nodularis, a Chronic Pruritic Skin Disease that can Exist Irrespective of Co-morbid Conditions (LOTUS-PN Study)

Poster P1566

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<sup>1</sup>University of Kansas School of Medicine - Wichita, <sup>2</sup>Universidad de Sevilla, <sup>3</sup>University of Colorado at Colorado Springs, <sup>4</sup>University of Colorado at Denver, <sup>5</sup>University of Colorado at Boulder, <sup>6</sup>Medical University of Lodz, <sup>7</sup>University of Cologne, <sup>8</sup>University of California, <sup>9</sup>University of Michigan, <sup>10</sup>University of Illinois at Chicago, <sup>11</sup>University of Illinois at Chicago, <sup>12</sup>University of Illinois at Chicago, <sup>13</sup>University of Illinois at Chicago, <sup>14</sup>University of Illinois at Chicago, <sup>15</sup>University of Illinois at Chicago

## CONCLUSIONS

- Prurigo nodularis is a distinct, highly pruritic chronic skin disease that is not defined by its comorbid conditions.
- Disease severity is similar regardless of absence or presence of underlying conditions
- Pruritus intensity and sleep impairment appear not to correlate with underlying condition
- IL-31 expression is related to pruritus intensity
- The OSMR $\beta$  axis is upregulated in lesional versus non-lesional skin

The OSMR $\beta$  axis (IL-31, OSM, IL-31R $\alpha$ , and OSMR $\beta$ ) may play a role in the pathogenesis of PN given its prevalent expression in PN lesional skin and represents an attractive target for further study of pharmacological intervention in PN