



Terapias Reativas e Proativas no controle da Dermatite Atópica Canina

Prof. Dr. Rafael Rodrigues Ferreira

E porque é importante saber ao menos o básico sobre imunologia?

Phase I: Reactive Therapy = Induction of Remission



BREADTH OF TARGETING

oral ± topical glucocorticoids

oclacitinib

Phase II: Proactive Therapy = Prevention of Recurrences



<

proactive topical glucocorticoids

>

allergen avoidance

±

immunotherapy

lokivetmab

oclacitinib

ciclosporin

BREADTH OF TARGETING

oral ± topical glucocorticoids

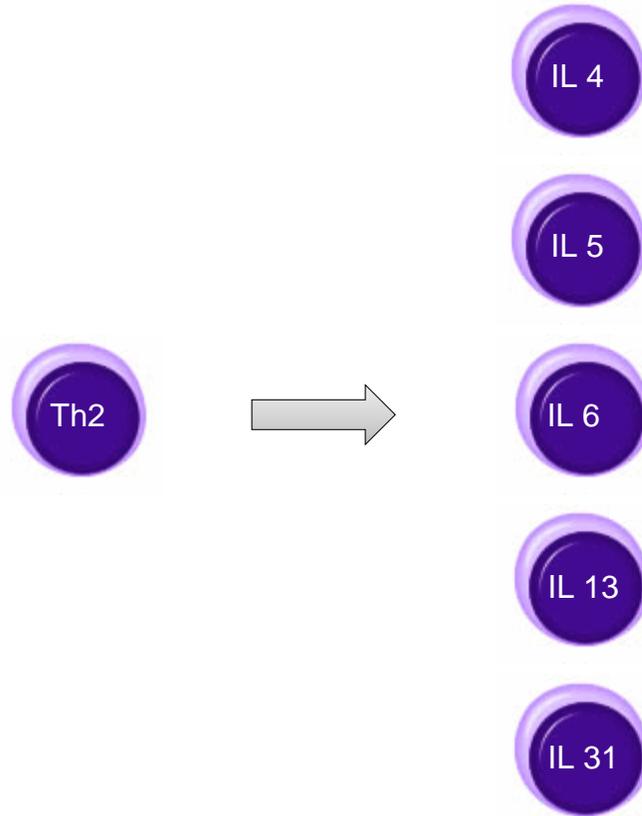
**Tratando de acordo com perfis fenotípicos e
medicina comparada**

XXVIII CONGRESO Latinoamericano DE ALERGIA, ASMA E INMUNOLOGÍA

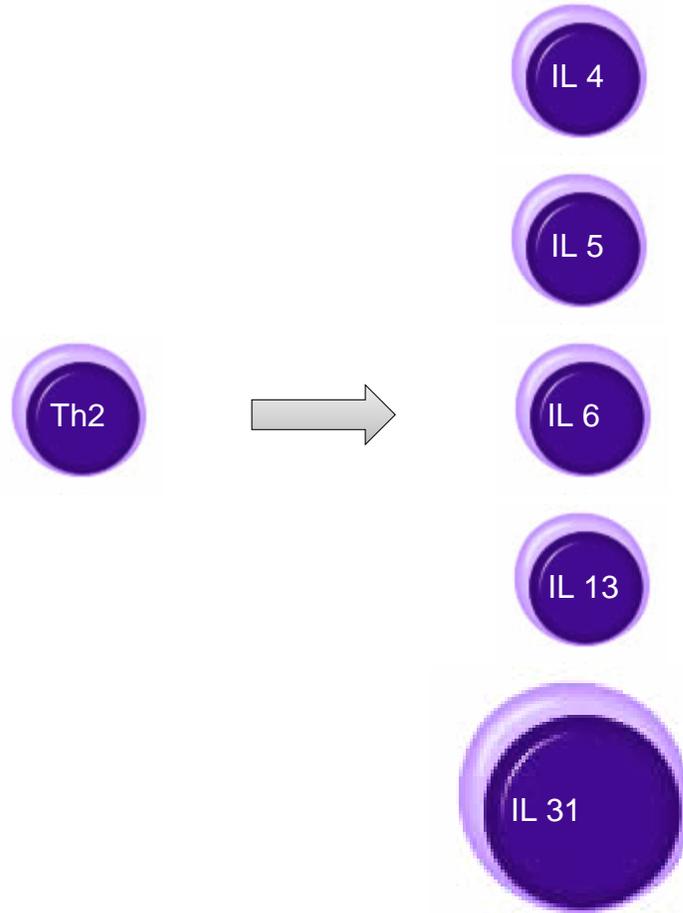
Innovación y manejo interdisciplinario
de las enfermedades alérgicas



Tipo 2



Tipo 2





Tipo 2



Phase I: Reactive Therapy = Induction of Remission

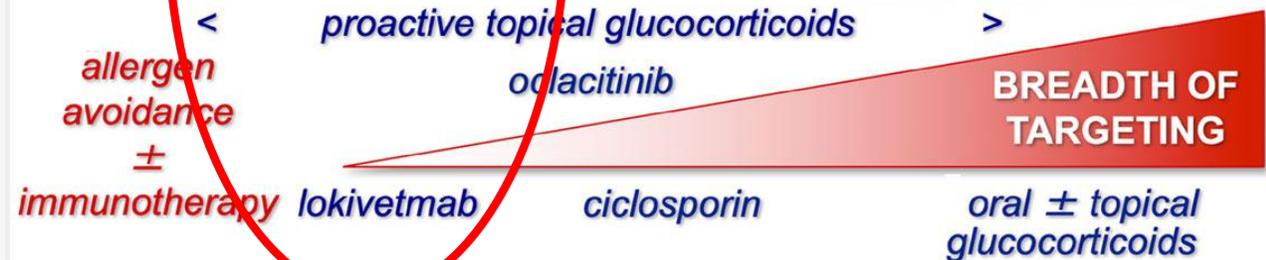


BREADTH OF TARGETING

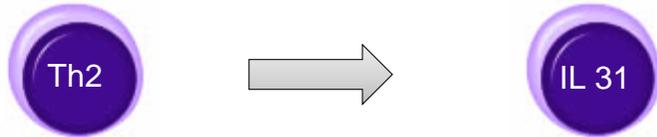
oral ± topical glucocorticoids

oclacitinib

Phase II: Proactive Therapy = Prevention of Recurrences



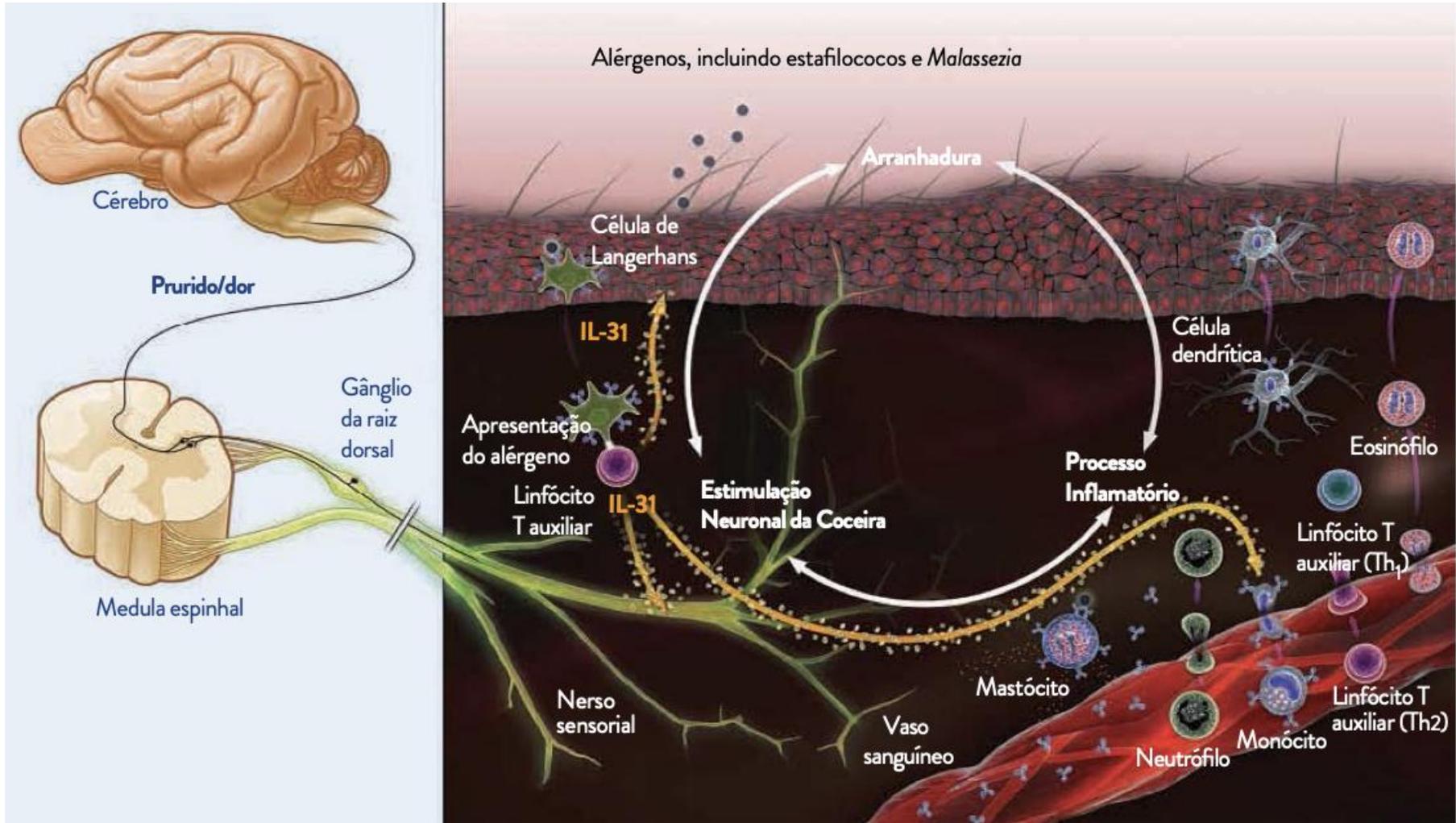
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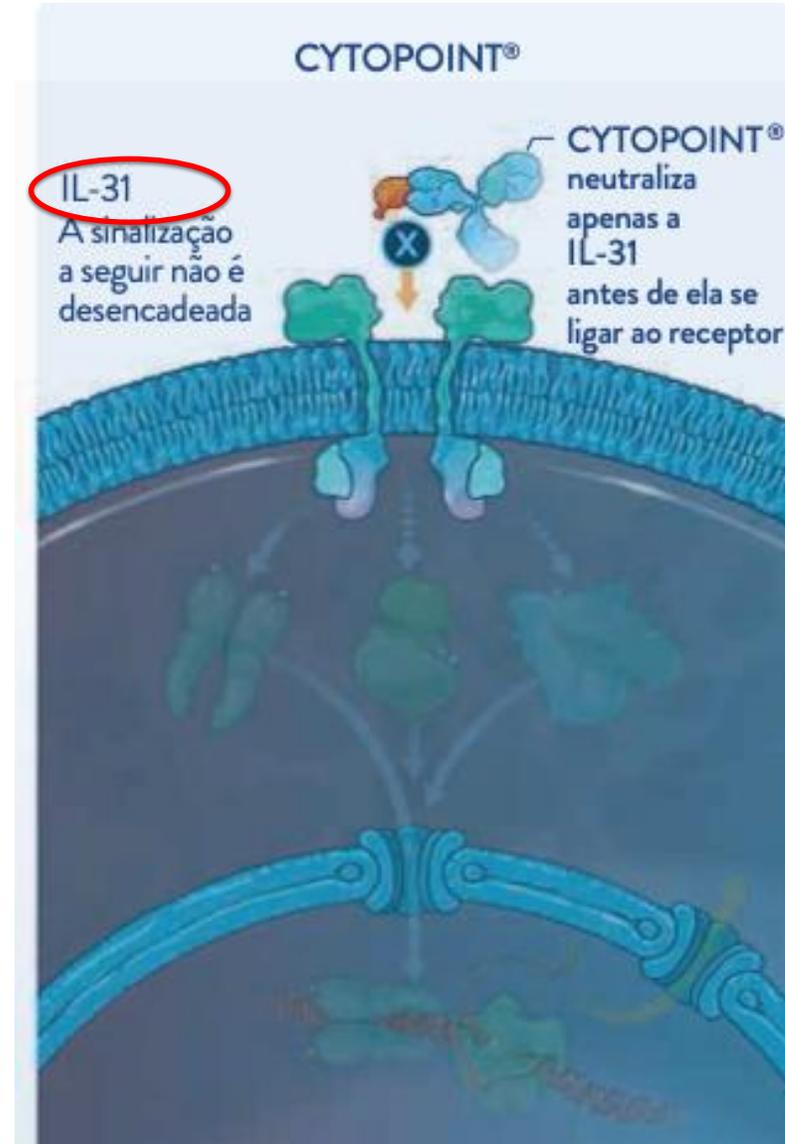
Lokivetmab

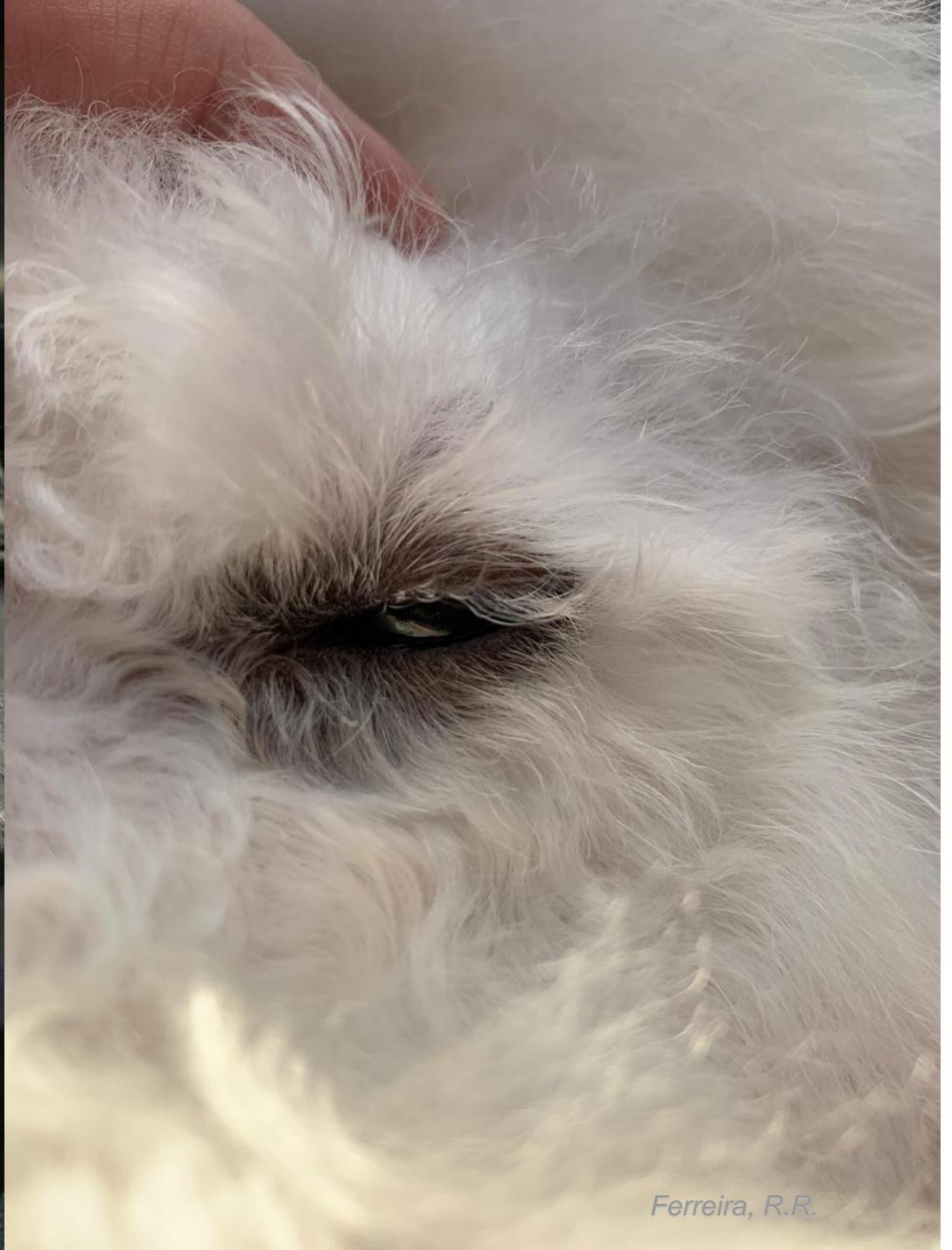
Ação contra IL 31

DOSE: 1-3mg/kg/média mensal



Tipo 2





Ferreira, R.R.



Ferreira, R.R.



E na medicina...

Aprovados pela FDA para DA

- **MAB's**

- Dupilumab (anti IL-4, IL-13)
- Nemolizumab (anti IL-31)

- **Innibidores JAK**

- Baricitinib (JAK 1 y JAK 2)
- Abrocitinib (JAK 1)
- Upadacitinib (JAK 1)

Tipo 2



GALDERMA



Nemolizumab is the First IL-31 Inhibitor for Atopic Dermatitis

Updated Dec 16, 2024 | ⌚ 5 Min Read

Kelsey Giara, PharmD, RPh

On December 13, the US Food and Drug Administration (FDA) approved [nemolizumab-ilto](#) for adolescents and adults with moderate to severe [atopic dermatitis](#) (AD; eczema) after review of a Biologics License Application (BLA) submitted in February. The FDA previously [approved](#) nemolizumab-ilto (Nemluvio) in August 2024 for the treatment of adults with prurigo nodularis, a skin condition that persistently causes hard, intensely itchy bumps on the skin.

The only biologic for AD with Q4W dosing from the start^{1,2*}

NEMLUVIO[®] OFFERS THE CONVENIENCE OF 1 INJECTION EVERY 4 WEEKS¹

NEMLUVIO

13x
a year

DUPILUMAB

26x
a year

*For pediatric patients weighing ≥ 66 lbs, dupilumab may be dosed Q4W.²

Nemluvio is a brand-name medication

Learn how to save on brand-name medications



Prescription

30mg Nemluvio (2 pens)



Choose pharmacy

Miami, FL



CVS Pharmacy

\$8,369



Walgreens

\$8,678



Walmart

\$8,810



Costco

\$9,366

Special offers



Target (CVS)

\$8,369



Walmart Neighborhood Market

\$8,810



Navarro Discount Pharmacy

\$8,369



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\$8,369



Retail price: \$17,813

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BIN 015995

PCN GDC

Group DR33

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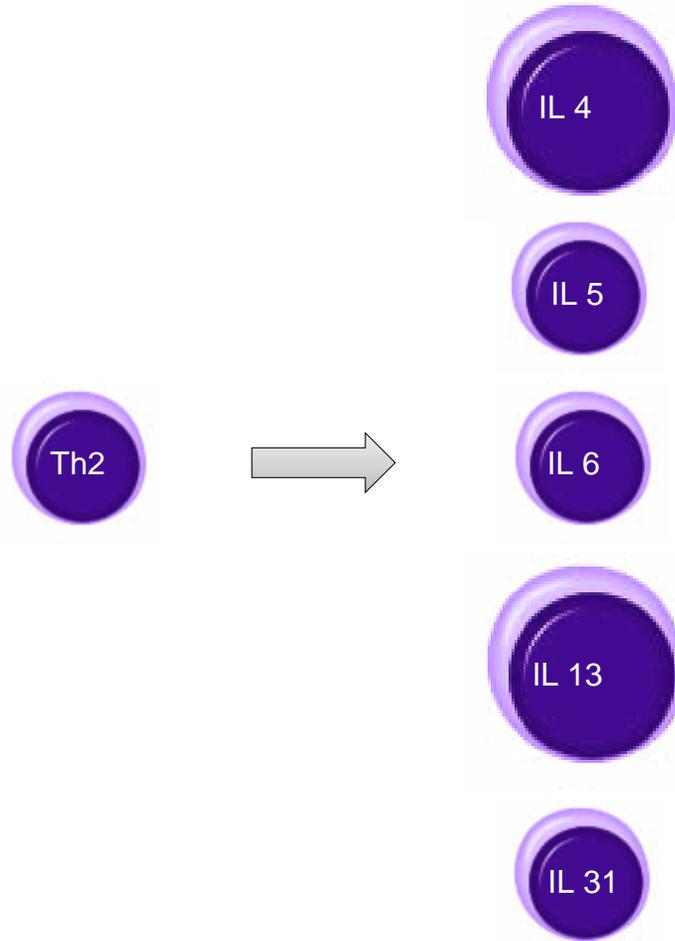
Sales tax may apply and is not included.

How to use GoodRx coupons

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Tipo 2



Tipo 2

Th2



IL 4

IL 13

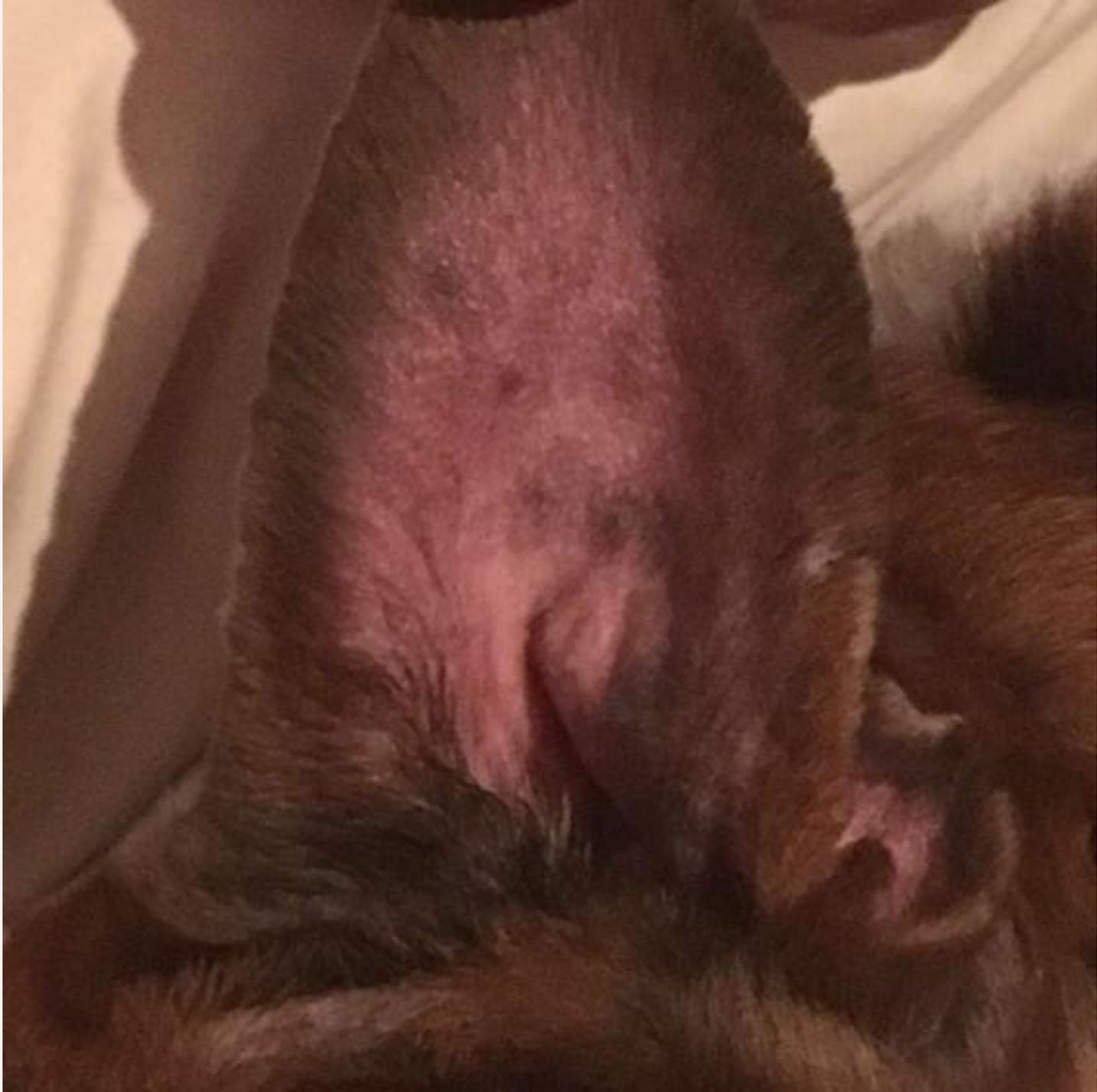












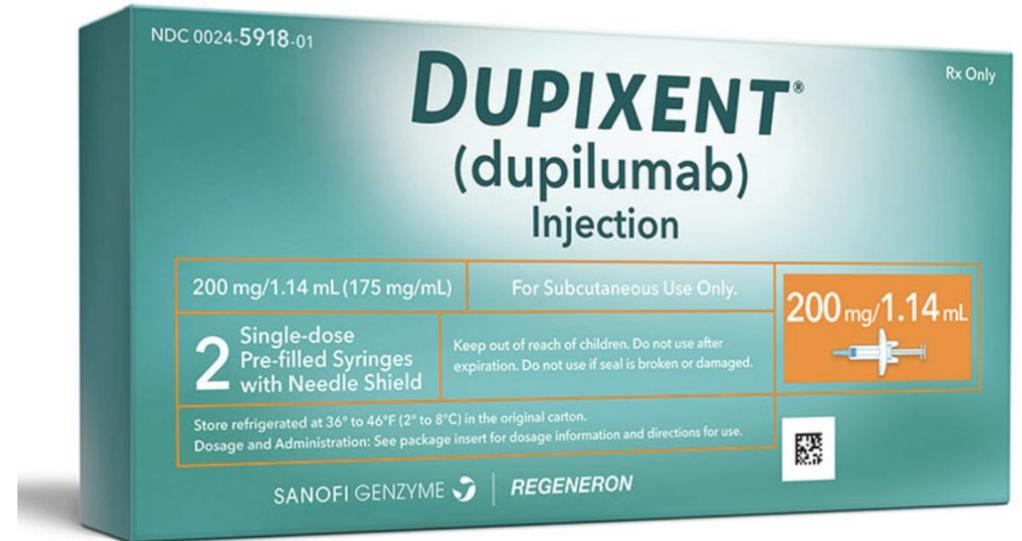








Tipo 2



Acima de 6 meses

Ação contra IL 4, IL 13

DOSE: injeções de 300mg/14d.

Medicamentos / Outras especialidades / Dupixent 300mg 2 seringas preenchidas 2ml



R\$ 13587,74

R\$ 10024,37

QUANTIDADE:

- 1 +

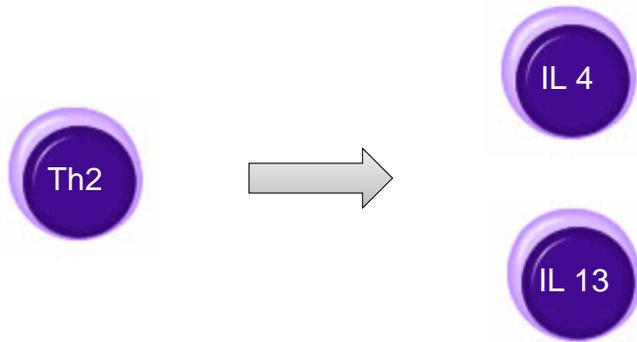
Dupixent 300mg 2 Seringas Preenchidas 2ml
Sanofi Aventis

Vendido e entregue por **4Bio Medicamentos**



Este produto é vendido e entregue por uma loja parceira e a Droga Raia garante a sua compra, do pedido à entrega.

Tipo 2



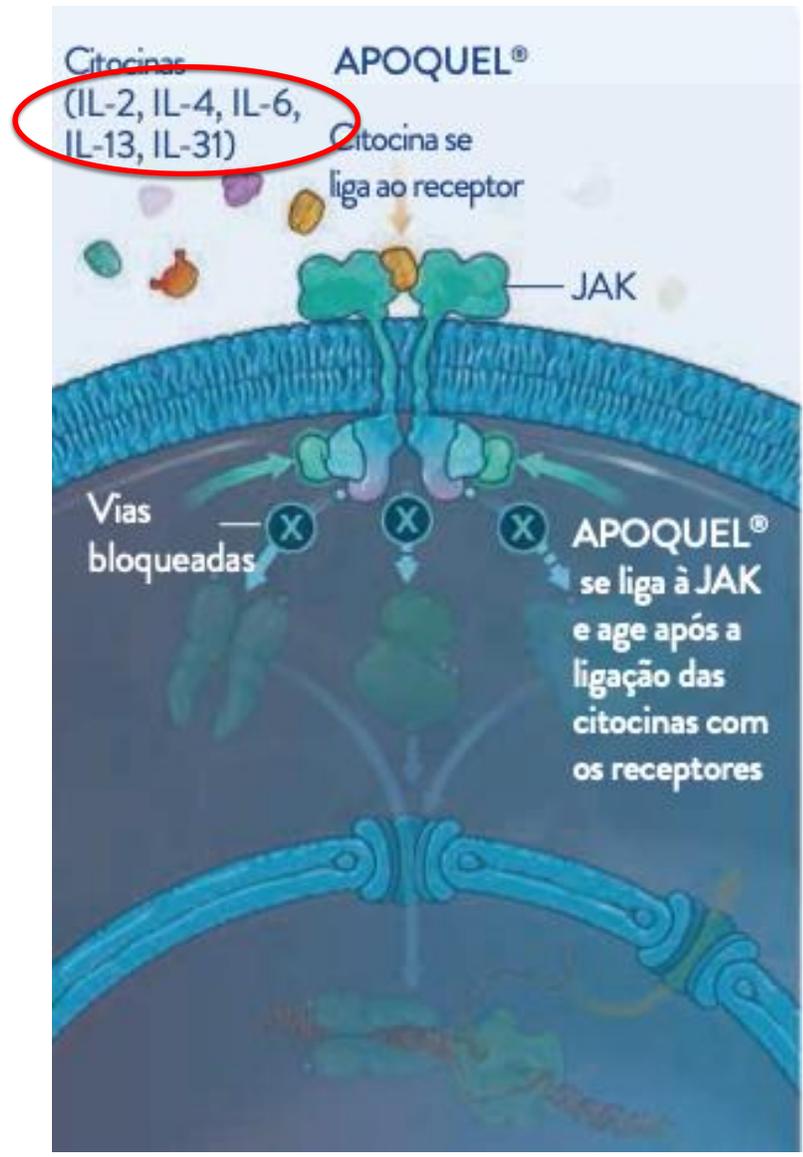
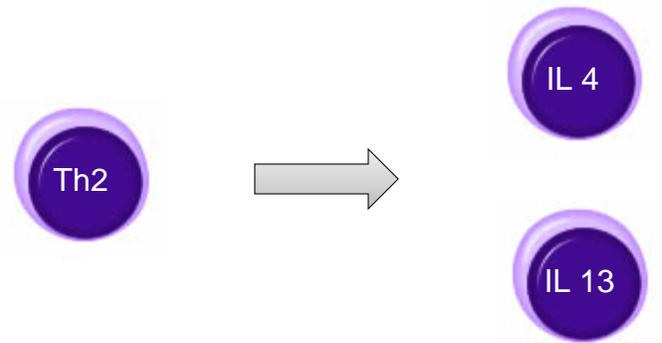
Oclacitinib

Acima de 12 meses

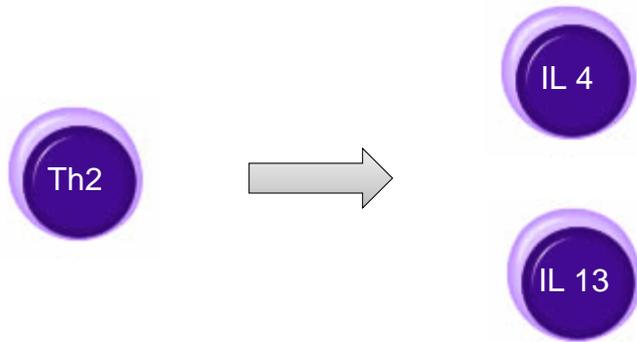
Ação contra IL 2,4,6,13,31

DOSE: 0,4-0,6mg/kg/BID/14d, depois SID

Tipo 2



Tipo 2



Ilunocitinib

Acima de 1 ano

Ação para JAK1, JAK2 y TYK2

Inibe IL2,4,6,13,31

DOSE: 0,6-0,8mg/kg/SID



Acima de 12 anos
Ação selectiva para JAK1
DOSE: 15mg/SID



Formas de entrega

Calcular frete

CEP:

Calcular

Rinvoq 15mg - Upadacitinibe - 30 comprimidos

Rinvoq

30 Comprimidos de Liberação Prolongada

Upadacitinibe

Vendido e entregue por Droga Raia

Rinvoq é indicado para o tratamento de pacientes adultos com artrite reumatoide e dermatite atópica.

RINVOQ É UM MEDICAMENTO. SEU USO PODE TRAZER RISCOS. PROCURE UM MÉDICO OU UM FARMACÊUTICO. LEIA A BULA. MEDICAMENTOS PODEM CAUSAR EFEITOS INDESEJADOS. EVITE A AUTOMEDICAÇÃO: INFORME-SE COM O FARMACÊUTICO.

VENDA SOB PRESCRIÇÃO MÉDICA.

Envie sua receita

 Desconto de laboratório

De R\$ 7876,38

Por **R\$ 1935,23** -75%

- 1 +



Arriba de 2 años

Acción selectiva para JAK1 e JAK2

DOSIS: 2 - 4mg/SID

Vida saudável / Complementos alimentares / **Olumiant baricitinibe 2mg 30 comprimidos**



~~R\$ 5222,26~~

R\$ 4344,50

QUANTIDADE:

- 1 +

Olumiant Baricitinibe 2mg 30 Comprimidos
Eli Lilly

Vendido e entregue por **4Bio Medicamentos**



Este produto é vendido e entregue por uma loja parceira e a Droga Raia garante a sua compra, do pedido à entrega.



Acima de 12 anos

Ação seletiva para JAK1

medicamentos / Remédios / **Cibinqo abrocitinibe 200mg 30 comprimidos**



R\$ 11377,51

QUANTIDADE:

R\$ 4124,35

CIBINQO Abrocitinibe 200mg 30 Comprimidos
Cibinqo
30 Comprimidos Revestidos
Abrocitinibe

Vendido e entregue por Droga Raia

CIBINQO® (abrocitinibe) é indicado para o tratamento de dermatite atópica moderada a grave, em adultos e adolescentes acima de 12 anos, candidatos à terapia sistêmica, podendo ser utilizado com ou sem a associação de terapias tópicas para dermatite atópica.





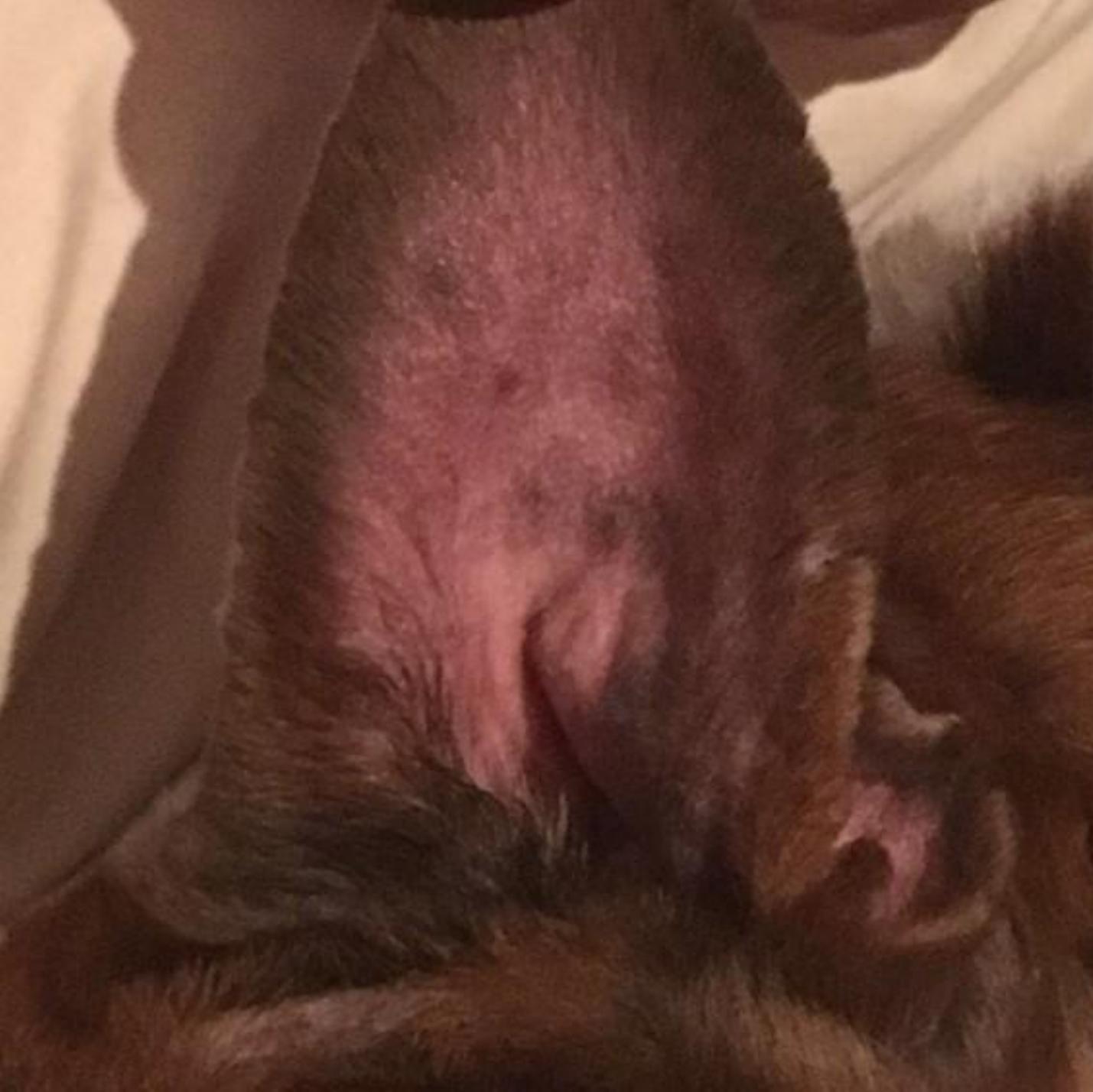
















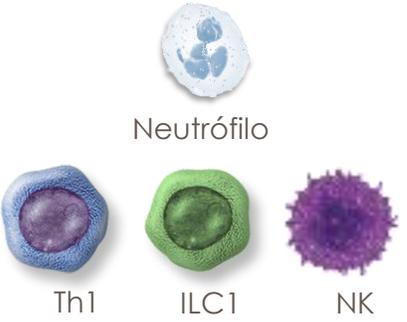
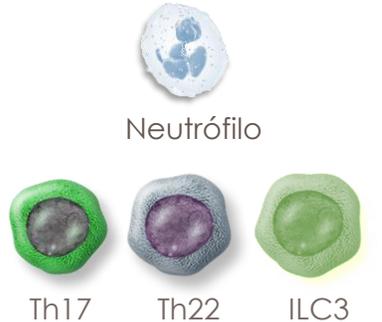




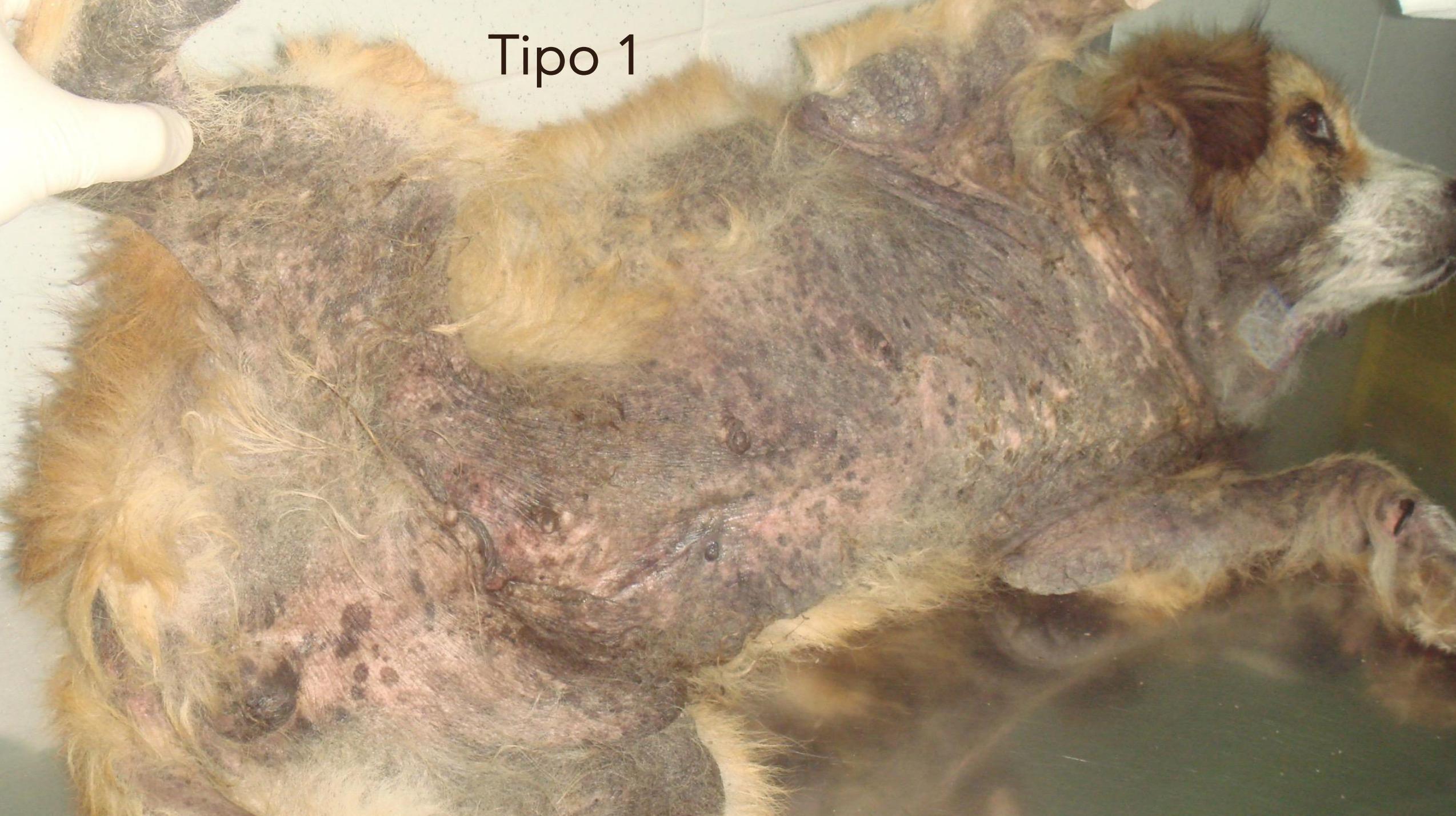




PARA RESPONDER A UMA VARIEDADE DE PATÓGENOS, O SISTEMA IMUNOLÓGICO CONTA COM TRÊS TIPOS CONHECIDOS DE RESPOSTA IMUNE

| Via inflamatória | Tipo 1 | Tipo 2 | Tipo 3 | | | | | | | | | | | | | | |
|---|--|--|---|------|-------|------|-----|---|------|------|-------|-------|--|-------|------|-------|-------|
| Células imunes primárias^{1,2} |  <p>Neutrófilo</p> <p>Th1 ILC1 NK</p> | <p>Doenças Inflamatórias</p>  <p>Th2 ILC2 Mastócito</p> <p>T_{fh} Basófilo Eosinófilo</p> |  <p>Neutrófilo</p> <p>Th17 Th22 ILC3</p> | | | | | | | | | | | | | | |
| Çitocinas chave¹⁻³ | <table border="1"> <tr> <td>IL-17</td> <td>IFNγ</td> <td>IL-6</td> </tr> <tr> <td>IL-12</td> <td>IL-2</td> <td>TNF</td> </tr> </table> | IL-17 | IFN γ | IL-6 | IL-12 | IL-2 | TNF | <table border="1"> <tr> <td>IL-4</td> <td>IL-5</td> </tr> <tr> <td>IL-13</td> <td>IL-31</td> </tr> </table> | IL-4 | IL-5 | IL-13 | IL-31 | <table border="1"> <tr> <td>IL-17</td> <td>IL-6</td> </tr> <tr> <td>IL-22</td> <td>IL-23</td> </tr> </table> | IL-17 | IL-6 | IL-22 | IL-23 |
| IL-17 | IFN γ | IL-6 | | | | | | | | | | | | | | | |
| IL-12 | IL-2 | TNF | | | | | | | | | | | | | | | |
| IL-4 | IL-5 | | | | | | | | | | | | | | | | |
| IL-13 | IL-31 | | | | | | | | | | | | | | | | |
| IL-17 | IL-6 | | | | | | | | | | | | | | | | |
| IL-22 | IL-23 | | | | | | | | | | | | | | | | |
| Alvos^{1,3} | <p>Vírus</p> <p>Bactérias intracelulares</p> <p>Células cancerígenas</p> | <p>Alérgenos</p> <p>Parasitas</p> | <p>Bactérias extracelulares</p> <p>Fungos</p> | | | | | | | | | | | | | | |
| Doenças (exemplos)⁴⁻⁶ | <p>Psoríase</p> <p>Artrite psoriática</p> | <p>DOENÇAS INFLAMATÓRIAS TIPO 2:</p> <p>Dermatite atópica</p> <p>Rinite alérgica</p> <p>Asma</p> <p>Polipose nasal</p> <p>Esofagite eosinofílica</p> <p>Alergia alimentar</p> | <p>Psoríase</p> <p>Artrite psoriática</p> | | | | | | | | | | | | | | |

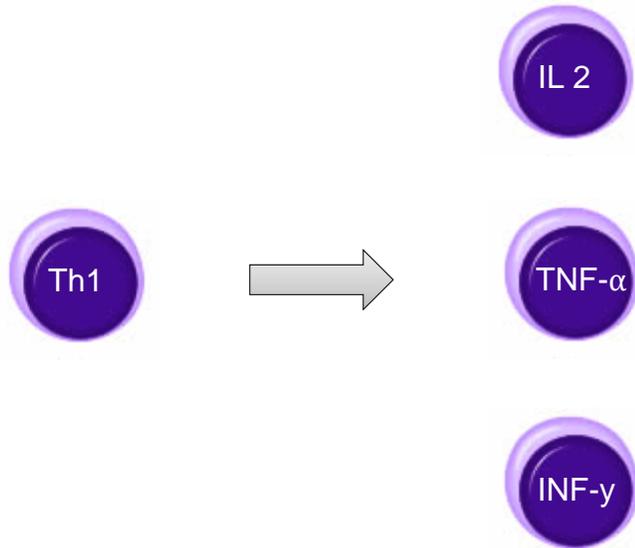
Tipo 1











Cyclosporine in Veterinary Dermatology

Brian S. Palmeiro, VMD

Vet Clin Small Anim 43 (2013) 153–171
<http://dx.doi.org/10.1016/j.cvsm.2012.09.007>

MECHANISM OF ACTION

CsA, a calcineurin inhibitor, is an immunosuppressive medication that inhibits T-cell activation.¹ CsA binds to the intracellular protein cyclophilin-1; the cyclophilin-CsA complex inhibits calcineurin, preventing the dephosphorylation/activation of nuclear factor of activated T cells (NFAT).² NFAT helps regulate the production of several important proinflammatory cytokines including interleukin (IL)-2, IL-4, interferon (IFN)- γ , and tumor necrosis factor (TNF)- α .¹ Inhibition of IL-2, a potent T-cell growth promoter and activator, is most commonly implicated as the main mechanism of immu-

Ciclosporina

Microemulsificada

5mg/kg/sid/3-4 sem. (Con prednisona /
Oclacitinib)

5mg/kg/sid (Sin prednisona / Oclacitinb)

Review

Life-long diseases need life-long treatment: long-term safety of ciclosporin in canine atopic dermatitis

 OPEN ACCESS

Tim Nuttall, BVSc, BSc, Cert VD, CBiol, MIBiol, PhD, MRCVS¹, Douglas Reece, DVM² and Elizabeth Roberts, DVM, PhD, DABT²

 Author Affiliations

E-mail for correspondence tim.nuttall@ed.ac.uk

Abstract

Ciclosporin (Atopica; Novartis Animal Health) has been licensed for canine atopic dermatitis (AD) since 2002. Adverse events (AEs) have been reported in 55 per cent of 759 dogs in 15 clinical trials, but are rare in pharmacovigilance data (71.81 AEs/million capsules sold). Gastrointestinal reactions were most common, but were mild and rarely required intervention. Other AEs were rare (≤ 1 per cent in clinical trials; < 10 /million capsules sold). Hirsutism, gingival hyperplasia and hyperplastic dermatitis were rarely significant and resolved on dose reduction. Ciclosporin decreases staphylococcal and *Malassezia* infections in AD, and at the recommended dose is not a risk factor for other infections, neoplasia, renal failure or hypertension. The impact on glucose and calcium metabolism is not clinically significant for normal dogs. Concomitant treatment with most drugs is safe. Effects on cytochrome P450 and MDR1 P-glycoprotein activity may elevate plasma ciclosporin concentrations, but short-term changes are not clinically significant. Monitoring of complete blood counts, urinalysis or ciclosporin levels is not justified except with higher than recommended doses and/or long-term concurrent immunosuppressive drugs. Ciclosporin is not a contraindication for killed (including rabies) vaccines, but the licensed recommendation is that live vaccination is avoided during treatment. In conclusion, ciclosporin has a positive risk-benefit profile for the long-term management of canine AD.













Ferreira, R.R.



- Primer dia de consulta



•Cuatro semanas después...



•Siete semanas...



•Doce semanas...

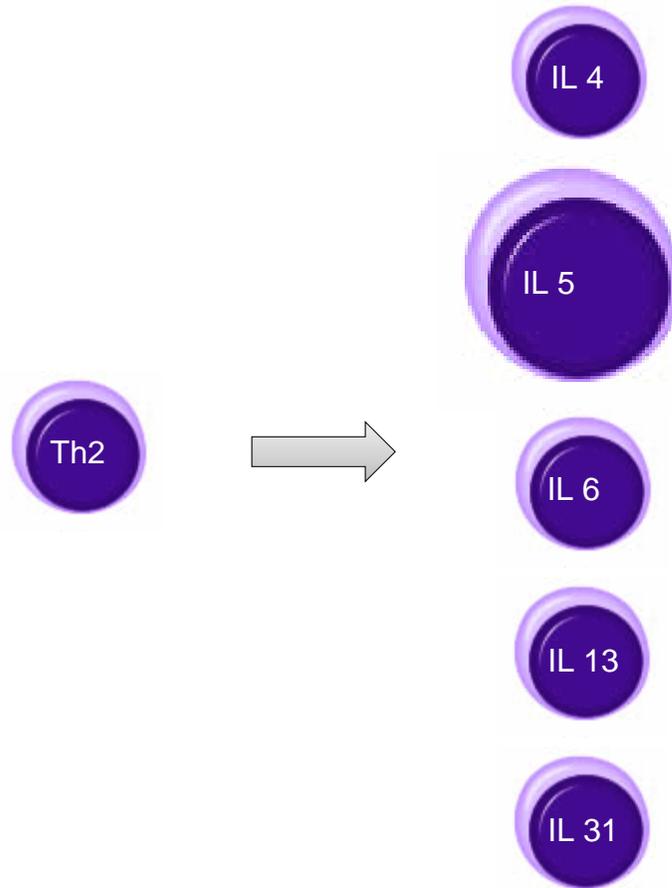


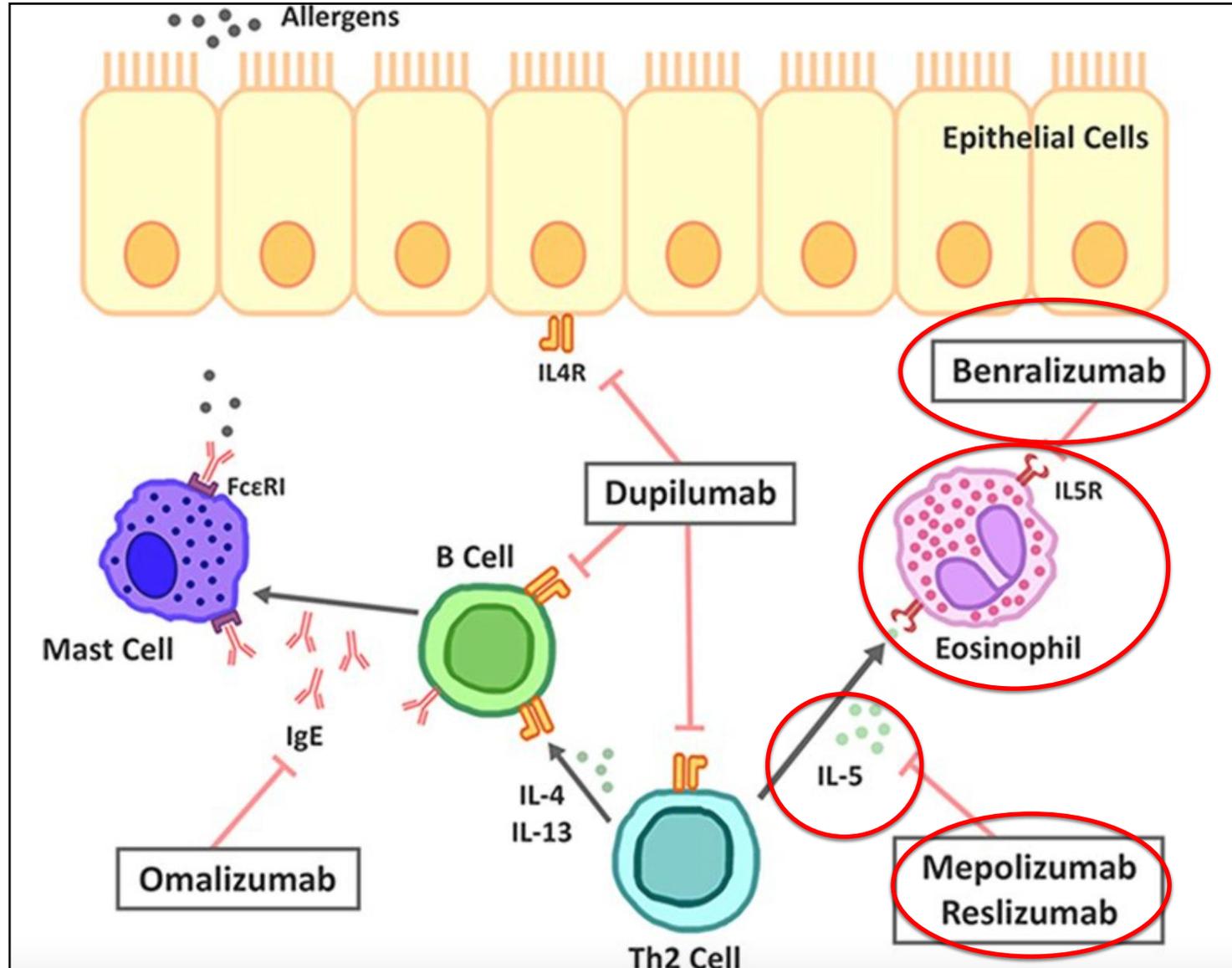
•16 semanas...

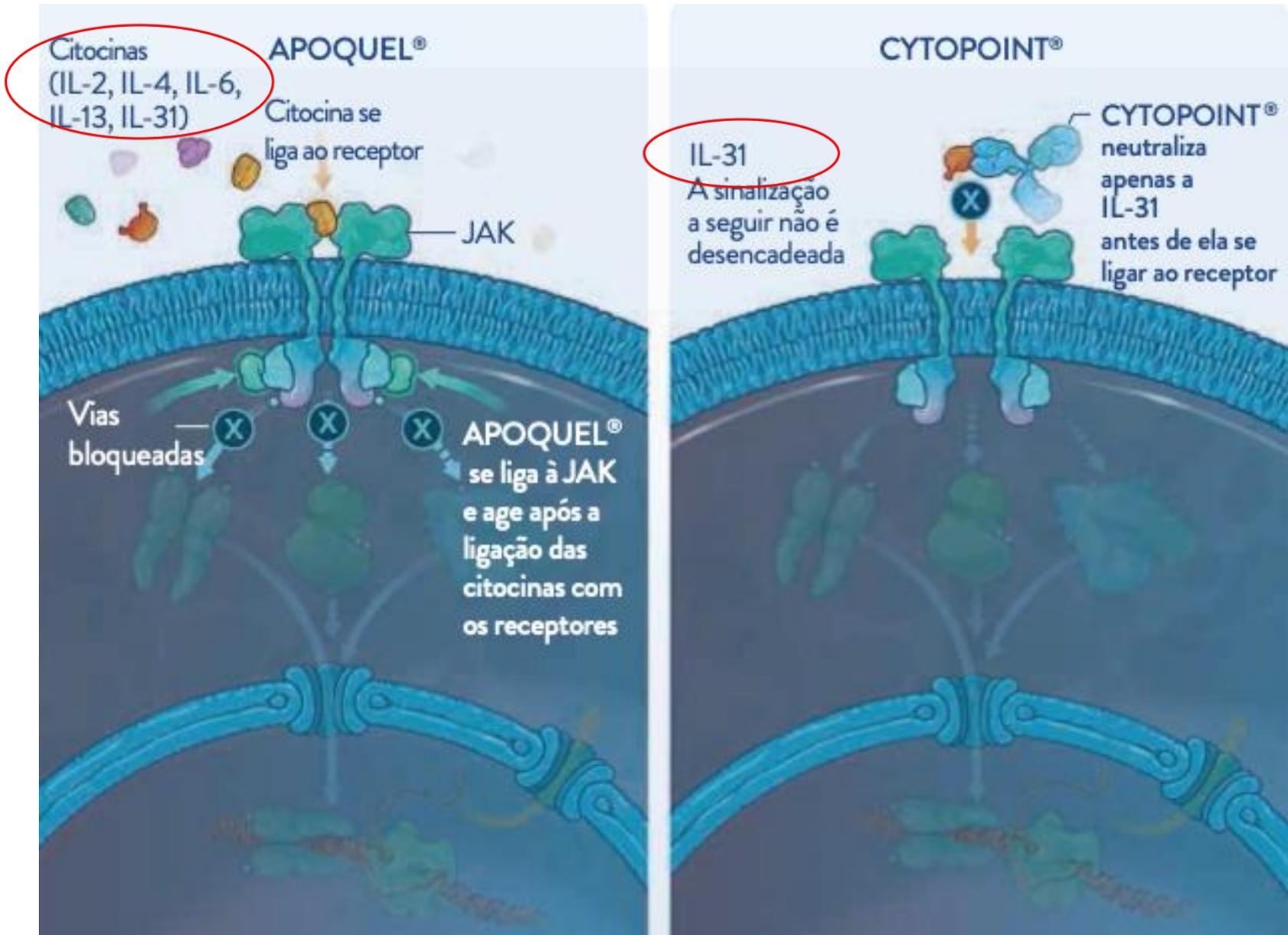
- Actualmente...



Tipo 2







Citocinas
(IL-2, IL-4, IL-6,
IL-13, IL-31)

APOQUEL®

Citocina se
liga ao receptor

JAK

Vias
bloqueadas

APOQUEL®
se liga à JAK
e age após a
ligação das
citocinas com
os receptores

CYTOPOINT®

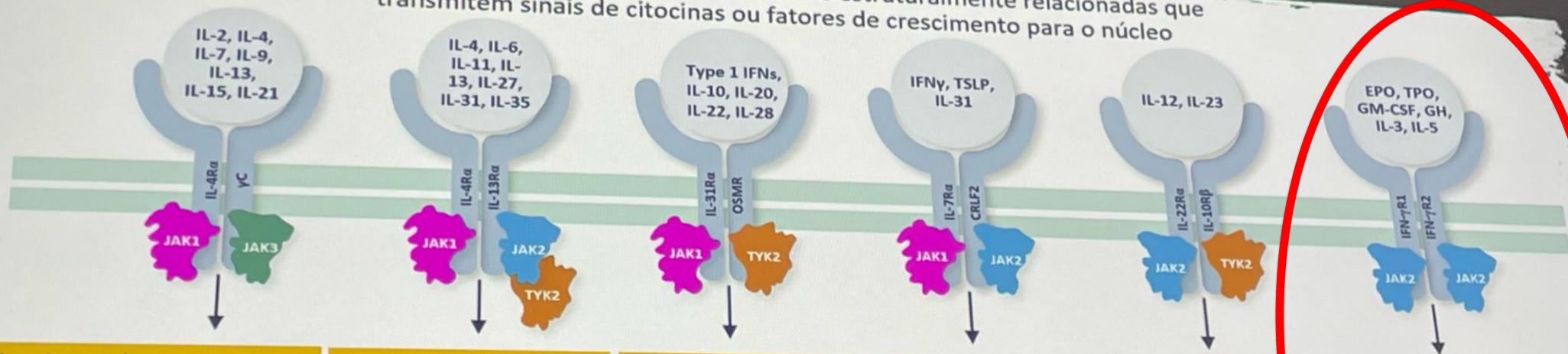
IL-31

A sinalização
a seguir não é
desencadeada

CYTOPOINT®
neutraliza
apenas a
IL-31
antes de ela se
ligar ao receptor

JAKS SÃO MOLÉCULAS DE SINALIZAÇÃO INTRACELULAR QUE DESEMPENHAM PAPEL EM UMA AMPLA GAMA DE FUNÇÕES BIOLÓGICAS¹⁻⁶

A família JAK consiste em quatro isoformas estruturalmente relacionadas que transmitem sinais de citocinas ou fatores de crescimento para o núcleo



- Crescimento/maturação de células linfóides
- Proliferação de linfócitos e homeostase
- Diferenciação/homeostase de células T, células NK
- Comutação de classe de célula B
- Inflamação

- Diferenciação de células T virgens
- Homeostase das células T
- Inflamação
- Granulopoiese

- Antiviral
- Inflamação
- Antitumoral

- Antiviral
- Inflamação
- Anti-micobacteriano

- Imunidade inata
- Diferenciação/proliferação de células Th17
- Inflamação

- Eritro/mielopoiese
- Produção de megacariócitos/plaquetas
- Crescimento
- Desenvolvimento mamário

Cyclosporine in Veterinary Dermatology

Brian S. Palmeiro, VMD

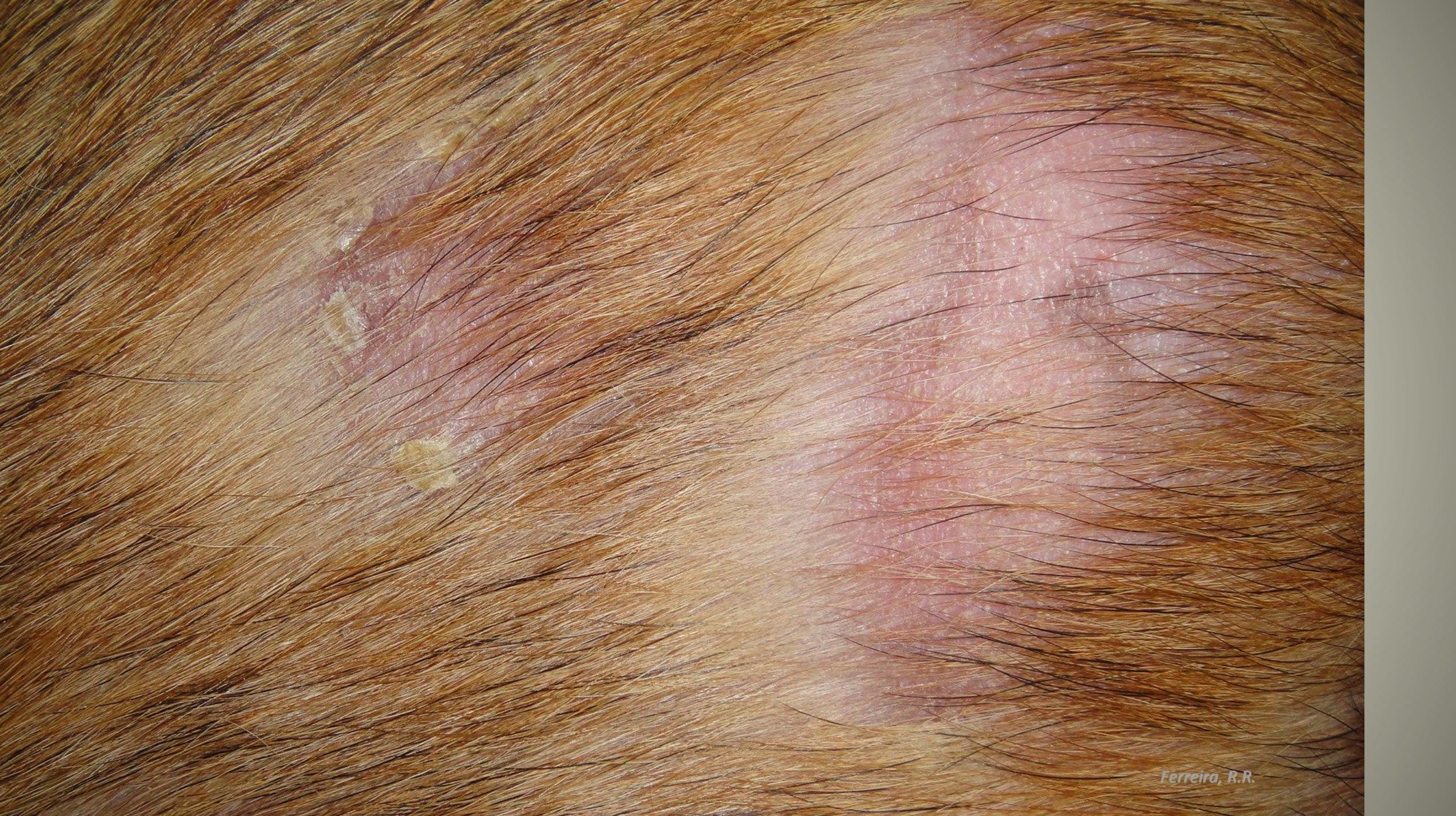
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Ferreira, R.R.



Terapia reativa

Prednisona, prednisolona - 0,5 - 1mg/kg/SID

Terapia proativa

Prednisona, prednisolona - 0,5 - 1mg/kg/72h

Conclusões

Para escolher melhor as medicações

- Conhecer ao menos o básico de imunologia
- Conhecer as medicações e as interleucinas que cada uma inibe
- Conhecer os Perfís Fenotípicos

Resumo dos Fenótipos de DA

Europeus-Americanos DA¹⁻⁴



Asiáticos DA¹⁻⁴



DA em pacientes pediátricos⁴⁻⁶



Africanos-Americanos DA¹⁻⁴



Todos os subtipos de DA compartilham uma ativação robusta da via Tipo 2¹⁻⁶

Annals

of Allergy, Asthma & Immunology

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PRACTICE PARAMETERS · [Volume 132, Issue 3, P274-312, March 2024](#) · [Open Access](#)

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Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE– and Institute of Medicine–based recommendations

[AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel](#) · [Derek K. Chu, MD, PhD](#)  ^{*,†}  · [Lynda Schneider, MD](#) [‡]  · ... · [Elissa Abrams, MD](#) ^{*****} · [Dennis Ledford, MD](#) ^{†††††} · [Derek K. Chu, MD, PhD](#) ^{*,†}... [Show more](#)

| INTERVENTION | SEVERITY | RECOMMENDATION | STRENGTH | CERTAINTY |
|--|----------------------------|---|-----------------------------|------------------------------------|
| ELIMINATION DIETS <p>Oykhman et al Systematic review</p> | MILD MODERATE SEVERE | We suggest against the use of elimination diets | <p>Conditional against</p> | <p>Low certainty evidence</p> |
| ALLERGEN IMMUNOTHERAPY <p>Best evidence for dust mite allergy</p> <p>Yepez Nuñez & Chu et al Systematic review</p> | MILD MODERATE SEVERE | We suggest adding allergen immunotherapy If refractory, intolerant, or unable to use mid potency topical treatments | <p>Conditional in favor</p> | <p>Moderate certainty evidence</p> |
| | MILD MODERATE SEVERE | We suggest against adding allergen immunotherapy See conditions to consider, e.g. comorbidities, values and preferences | <p>Conditional against</p> | <p>Moderate certainty evidence</p> |
| SYSTEMIC TREATMENTS <p>Consider if refractory, intolerant, or unable to use mid to high potency topical treatment</p> <p>Consider if refractory, intolerant, or unable to use mid to high potency topical treatment and systemic treatment inclusive of a biologic recommended above</p> <p>See conditions to consider, e.g. comorbidities, risk factors, values and preferences, and exceptional circumstances</p> <p>Chu et al Network meta-analysis</p> | MILD MODERATE SEVERE | BIOLOGICS / MONOCLONAL ANTIBODIES DUPILUMAB We recommend adding dupilumab Age 6mo+ | <p>Strong in favor</p> | <p>High certainty evidence</p> |
| | MILD MODERATE SEVERE | TRALOKINUMAB We recommend adding tralokinumab Age 12yo+ | <p>Strong in favor</p> | <p>High certainty evidence</p> |
| | MILD MODERATE SEVERE | UVB TREATMENT We suggest adding clinic-based narrow band UVB treatment | <p>Conditional in favor</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | ABROCITINIB, BARICITINIB, OR UPADACITINIB We suggest adding one of these three JAK inhibitors Age varies: 12 or 18 yo+ Suggested daily doses: Abrocitinib 100-200 mg Baricitinib 2-4 mg Upadacitinib 15-30 mg | <p>Conditional in favor</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | BARICITINIB 1 mg DAILY We recommend against adding baricitinib 1 mg daily | <p>Strong against</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | AZATHIOPRINE We suggest against adding azathioprine | <p>Conditional against</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | CYCLOSPORINE We suggest adding cyclosporine Shared-decision making should determine whether to start therapy at high dose (5mg/kg) or low dose (3 mg/kg) | <p>Conditional in favor</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | METHOTREXATE We suggest against adding methotrexate | <p>Conditional against</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | MYCOPHENOLATE We suggest against adding mycophenolate | <p>Conditional against</p> | <p>Low certainty evidence</p> |
| | MILD MODERATE SEVERE | SYSTEMIC CORTICOSTEROIDS We suggest against systemic corticosteroids for all patients with atopic dermatitis | <p>Conditional against</p> | <p>Low certainty evidence</p> |

Conclusiones

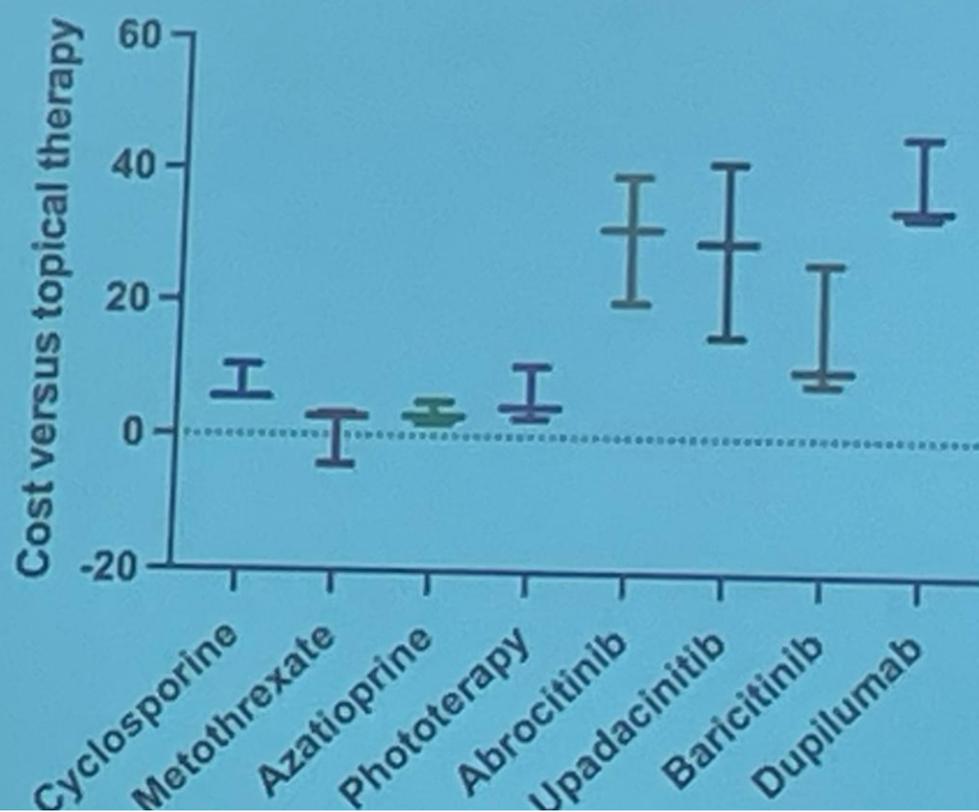
| Terapias sistémicas DA | Nuevas | Tradicionales |
|------------------------|--------|---------------|
| Eficacia | 😊😊😊😊😊 | 😊😊 |
| Efectividad | 😊😊😊😊 | 😊😊😊 |
| Costo | 😞 | 😊 |
| Adherencia | 😊¿? | 😊¿? |
| Preferencia médicos | 😞😊 | 😞😊 |
| Preferencia pagador | 😞 | 😊😊😊 |
| Preferencia pacientes | 😊😊😊 | 😞 |

Costo: Sistémicos tradicionales versus nuevos

Datos sistema SISPRO Colombia

Tradicionales
(media 185 USD)

Nuevas
(media 1058 USD)



\$

14 a 45
veces más
costosas

Eficacia: Terapias tradicionales versus nuevas:

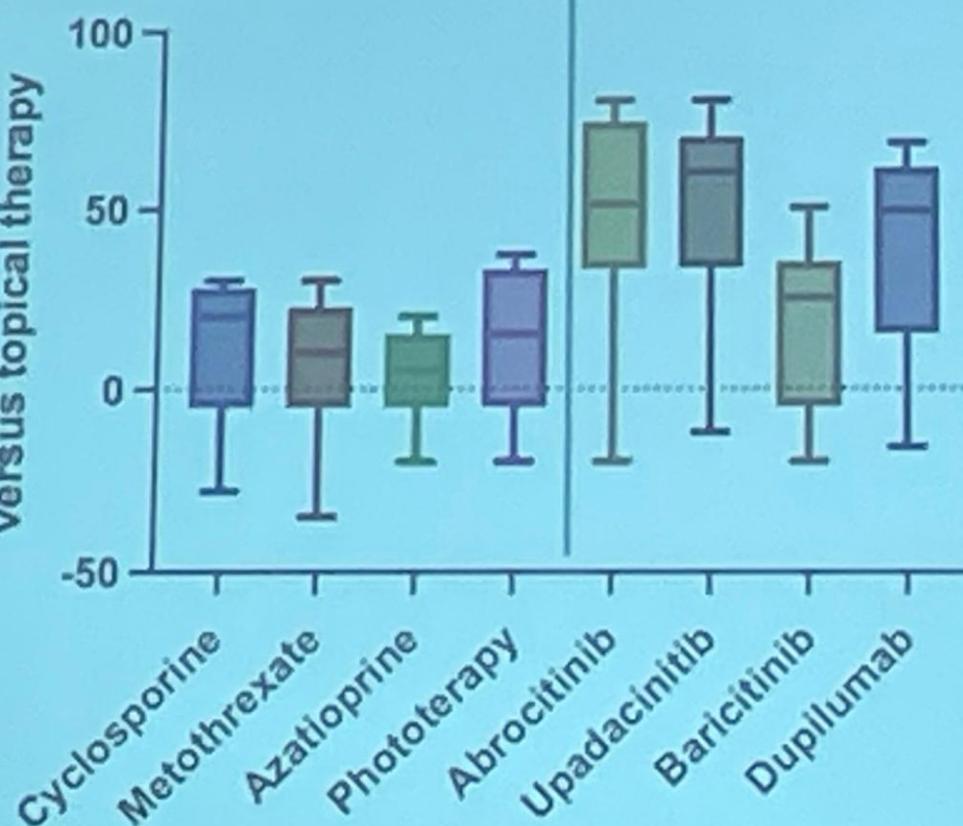
Estudios publicados en JACI, Dermatitis
Choi A, et al. JACI 2023; 152(6):1470
Sánchez J, et al. en preparación



Tradicionales
IQR -7 a 45 %

Nuevas
IQR 5 a 91%

Difference in change of EASI
versus topical therapy



Tradicionales 28%



Nuevas 76%



OBRIGADO

A scenic photograph of a sunset over the ocean. The sun is a bright, glowing orb on the horizon, casting a shimmering path of light across the water. The sky is filled with soft, golden clouds. In the foreground, the dark silhouettes of trees and a rocky coastline are visible against the bright light of the sunset. The word "OBRIGADO" is written in large, bold, black capital letters across the top center of the image.