ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Dupilumab significantly improves patient reported outcomes in pediatric AD patients < 12 years of age

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Introduction: Dupilumab has proven to be effective in improving patient-reported outcomes and has safety data for atopic dermatitis (AD) in pediatric patients in clinical trials. Few real-world studies are available to show the treatment effect on patient-reported disease symptoms and quality of life (QoL) in children with moderate-to-severe AD. **Method:** PEDISTAD (NCT03687359) is an ongoing, international, longitudinal, observational 5-year registry study in patients aged 6 months to 11 years with moderate-to-severe AD that is inadequately controlled by topical prescription therapies. This interim analysis assesses the effect of dupilumab on Patient-Oriented Eczema Measure (POEM) and on QoL using Children's Dermatology Life Quality Index (CDLQI), for up to 3 years. Overall safety was also evaluated. **Results:** A total of 214 patients received dupilumab (median treatment observation period: 16.1 months; accumulated 3-year discontinuation rate: 13.3%). The proportion of patients with severe/very severe disease (POEM score > 17 [range 0–28]) decreased from 63.2% at therapy start to 16.3% at last observation. The mean (± SE) POEM score also decreased with dupilumab use, from 17.9 ± 0.5 at therapy start to 9.1 ± 0.7 at last observation. Similarly, the mean (± SE) CDLQI score decreased with dupilumab use, from 12.9 ± 0.5 at therapy start to 7.3 ± 0.7 at last observation. 24% of patients had adverse events, including 2.4% serious adverse events. **Conclusion:** Dupilumab significantly improved patient-reported symptoms of AD and QoL in children aged 6 months to 11 years in real-world daily practice.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Dupilumab treatment normalizes skin barrier function in children aged 6 to 11 years with moderate-to-severe atopic dermatitis

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Introduction: This analysis reports the effect of dupilumab (DPL) treatment in patients aged 6-11 years with moderate-to-severe atopic dermatitis (AD) on skin barrier function, clinician- and patient-reported outcomes. **Methods:** In the PELISTAD open-label study (NCT04718870), patients aged 6-11 years with moderate-to-severe AD were treated with DPL for 16 weeks (300 mg every 4 weeks: ≥ 15 kg to < 30 kg; 200 mg every 2 weeks: ≥ 30 kg to < 60 kg) and matched with healthy volunteers. Transepidermal water loss (TEWL) was assessed longitudinally after skin tape strippings (STS) from lesional and nonlesional skin of AD patients treated with DPL and from healthy skin. Eczema Area and Severity Index (EASI) and Children's Dermatology Life Quality Index (CDLQI) were assessed during the same periods. **Results:** The median TEWL after 5 STS significantly decreased after 16 weeks of DPL treatment in the lesional and nonlesional skin of patients with AD ($P < 0.0001$ for lesional skin, and $P < 0.05$ for nonlesional skin, *vs* Day 1). At Week 16, median TEWL after 5 STS in nonlesional skin reached levels comparable to those of healthy skin ($P = 0.266$). Mean (standard deviation [SD]) EASI went from 37.7±11.1 at Day 1 to 10.7±10.3 at Week 16 and mean (SD) CDLQI from 18.4±7.3 to 4.5±2.8 between Day 1 and Week 16. Out of 23, 21 patients reported treatment-emergent adverse events. None were serious, severe, or led to treatment discontinuation. **Conclusion:** DPL treatment normalizes skin barrier function, and improves clinician- and patient-reported outcomes in patients aged 6-11 years with moderate-to-severe AD.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Maintenance of patient well-being and perception of treatment effect in dupilumab-treated patients transitioning from every other week to monthly doses

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Introduction: Patients with moderate-to-severe atopic dermatitis (AD) suffer from a high burden of disease and the patient's assessment of response to treatment is an important factor in the long-term management and treatment adherance for this chronic condition. **Methods:** Adults with moderate-to-severe AD that previously participated in SOLO 1/2 (NCT02277743/NCT02277769; 300 mg every 2 weeks for 16 weeks) and achieved a 75% reduction from baseline in Eczema Area and Severity Index and/or an Investigator's Global Assessment score of 0/1 at Week 16 were enrolled in this phase 3 study (LIBERTY AD SOLO-CONTINUE, NCT02395133). Patients were randomized to dupilumab monotherapy 300mg every 4 weeks (q4w; n = 41), dupilumab monotherapy 300mg every 8 weeks (q8w; n = 39), or placebo (n = 39) for an additional 36 weeks. Possible responses to perception of well-being and perception of treatment effect included: poor, fair, good, very good, and excellent. **Results:** After 36 weeks on monotherapy with dupilumab q4w/q8w, 56.1%/38.5% of patients responded "very good" or "excellent" in their assessment of well-being, and 58.5%/48.7% considered the treatment effect "very good" or "excellent" compared with 12.8% and 15.4% of patients on placebo. The differences between dupilumab q4w/q8w and placebo at Week 52 were significant for well-being (P<0.0001/P<0.05) and treatment effect (P<0.0001/P<0.01). Overall safety was consistent with the known dupilumab safety profile. **Conclusions:** Most optimally responding patients who were subsequently randomized to continue dupilumab 300mg q4w monotherapy for an additional 36 weeks rated both their well-being and perception of treatment effect as "very good" or "excellent" over 9 months of maintenance treatment.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Imunoterapia específica com alérgenos no tratamento da dermatite atópica em pacientes pediátricos: o que as mais novas evidências demonstram

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Introdução: A dermatite atópica (DA) é crônica e recidivante, se apresenta com pele seca e pruriginosa em pacientes com história pessoal ou familiar de atopia. Afeta 20% das crianças do mundo e possui altos custos e morbidade. A fim de reduzir os sintomas da exposição natural ao alérgeno, é empregada a imunoterapia específica com alérgenos (SIT), em quantidades progressivas do alérgeno até a hipossensibilização. Esta revisão visa responder a pergunta científica: quais as opções de SIT para DA em crianças, sua segurança e efetividade? **Métodos:** Revisão bibliográfica com base na Scientific Electronic Library Online (SciELO), Biblioteca Virtual em Saúde (BVS) e PubMed Central com os Descritores em Ciências da Saúde (DeCS) "Immunotherapy AND pediatric AND atopic dermatitis". Foram encontrados 117 artigos dos últimos 5 anos, sendo excluídos os artigos duplicados, que não respondessem a pergunta científica, revisões, editoriais, relatos de caso e experiência e artigos que não estão disponíveis na íntegra, restando 6 como amostra. **Resultados:** Identificou-se que a SIT provoca níveis séricos aumentados de imunoglobulina G4 específica. O uso da SIT mostrou melhoras na gravidade e manifestações clínicas, além da prevenção de novas sensibilizações. A eficácia é mantida após o fim do tratamento e melhorada com tratamento prolongado. As opções de SIT são esquemas via sublingual ou subcutânea, com maior evidência a via sublingual, principalmente para ácaros. Os efeitos adversos, em geral, são leves e transitórios. Ainda que necessite de mais estudos, é apropriada a indicação de SIT para pacientes com DA que possuem resposta insuficiente ao tratamento e alergia a alérgenos aerotransportados dependentes de IgE. **Conclusão:** A SIT em pacientes pediátricos com DA demonstra melhora clínica, redução na gravidade da doença e de novas sensibilizações. Ainda que a escassez de estudos revele a necessidade de mais pesquisas, em casos específicos, é uma boa escolha de tratamento da DA.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Teste de contato em crianças com dermatite atópica

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Introdução: Pacientes com Dermatite Atópica (DA) podem ter uma Dermatite de Contato Alérgica (DCA) associada e que pode contribuir para o agravamento do quadro cutâneo. **Métodos:** Estudo transversal descritivo, em ambulatório específico para DA, com 26 crianças selecionadas de acordo com critérios estabelecidos para a suspeita de DCA. Aplicou-se um teste de contato (TC) com 30 substâncias, com leituras após 48 e 96h. A bateria de TC englobou 20 substâncias da bateria pediátrica brasileira (BP), nove substâncias acrescentadas seguindo revisões da literatura sobre TC em crianças com DA, e vaselina como controle negativo. **Resultados:** Dos 26 pacientes testados, de três a 17 anos, 21 (80,8%) eram meninas e cinco (19,2%) meninos. Em 23 (88,5%) o TC foi positivo (TCP) para ao menos um alérgeno e 14 (53,8%) pacientes apresentaram polissensibilização. Em 21 (80,7%) pacientes identificamos relevância clínica. Os principais alérgenos foram: níquel (34,6%), azul disperse (30,8%), fragrâncias mix (26,9%), neomicina (23,1%), cloreto de cobalto (23,1%), bicromato de potássio (23,1%) e timerosal (23,1%). Dezenove (73%) pacientes apresentaram TCP para substâncias contidas em produtos de cuidados com a pele ou de uso terapêutico tópico, havendo correlação clínica (Teste exato de Fisher p = 0,013). Seis substâncias testadas não estão presentes na BP, porém representam de 7,7 a 15,4% dos TCP. Um paciente testou positivo para o controle vaselina, o principal veículo usado para os alérgenos do TC. **Conclusão:** Devemos suspeitar de DCA em pacientes com DA que apresentam distribuição atípica do eczema ou nos quais a terapêutica piora o eczema ou não parece controlar os sintomas. A significativa sensibilização encontrada, sugere que a realização de TC em pacientes com DA deve ser ampliada. A BP pode não ser suficiente para o diagnóstico de DCA em pacientes com DA. Alérgenos como fragrâncias, álcool de lanolina, bronopol e formaldeído podem estar presentes em produtos de uso terapêutico tópico.

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Dupilumab treatment in patients with hand and foot atopic dermatitis: results from a phase 3, randomized, double-blind, placebo-controlled trial

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Background: Atopic dermatitis (AD) of the hands and/or feet is often chronic, difficult to treat, and substantially impacts patient quality of life. We investigated the efficacy/safety of dupilumab in patients with hand and foot (H/F) AD using dedicated/validated clinical and patient-reported instruments. Type of study: Phase 3 trial. **Methods:** The phase 3, randomized, double-blind LIBERTY-AD-HAFT (NCT04417894) trial enrolled patients ≥ 12 years with moderate-to-severe (Investigator's Global Assessment [IGA] 3/4) H/F AD. Patients were randomized to dupilumab monotherapy 300mg q2w in adults; 200/300 mg every 2 weeks in adolescents, or placebo for 16 weeks. The primary endpoint was IGA (H/F) 0/1 score at Week 16. Safety/tolerability was assessed. **Results:** The 133 patients enrolled were randomized to dupilumab (n = 67) or placebo (n = 66). At Week 16, the primary and all secondary endpoints were met. Significantly more patients in the dupilumab *vs* placebo group achieved IGA 0/1 (40.3% *vs.* 16.7%; P = 0.003; primary endpoint) and ≥ 4-point improvement in the H/F Peak Pruritus Numerical Rating Scale (52.2% *vs.* 13.6%; P < 0.0001; a key secondary endpoint). Dupilumab-treated patients experienced significant improvement in percent change from baseline in the modified Total Lesion Sign Score for H/F lesions *vs* placebo (LS mean [SE] –69.4 [5.8] *vs.* –31.0 [5.9]; P < 0.0001) and Hand Eczema Severity Index (LS mean [SE] –74.8 [6.3] *vs.* –39.9 [6.2]; P < 0.0001). The most common TEAEs (≥ 10%) were nasopharyngitis (16% *vs.* 11%) and dermatitis atopic (5% *vs* 18%). **Conclusions:** Dupilumab significantly improved signs and symptoms in patients with H/F AD and had an acceptable safety profile.

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ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Efficacy and safety of dupilumab with topical corticosteroids in children aged 6 months to 5 years with severe atopic dermatitis

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Introduction: Atopic Dermatitis (AD) has a negative and multidimensional impact in infants and young children. The efficacy and safety of Dupilumab was assessed in LIBERTY AD PRESCHOOL in children aged 6 months to 5 years with moderate-to severe AD. **Methods:** Patients aged 6 months to 5 years with moderate-to-severe AD were enrolled in the phase 3 LIBERTY AD PRESCHOOL (NCT03346434; part B) study. Patients received dupilumab 200/300 mg every 4 weeks (200 mg: weight 5 to < 15 kg; 300 mg: 15 to < 30 kg), or placebo for 16 weeks; low-potency topical corticosteroids were administered from Day -14. **Results:** At week 16, dupilumab-treated patients had significantly greater percent reduction from baseline in Eczema Area and Severity Index *vs* placebo (LS mean [SE] –67.0 [3.5] *vs.* –39.2 [3.6]; P < 0.0001) and Worst Scratch/ Itch Numerical Rating Scale *vs.* placebo group (LS mean [SE] –41.8 [5.4] *vs.* 0.5 [5.4]; P < 0.0001). Dupilumab resulted in significant improvement in quality-of-life outcomes *vs* placebo (LS mean [SE]), reported as change from baseline to Week 16 in Children's Dermatology Life Quality Index (–9.1 [1.1] *vs.* –2.6 [1.2]; P < 0.0001), and Infant's Dermatitis Quality of Life (–9.1 [1.3] *vs.* –0.6 [1.1]; P < 0.0001). Treatment-emergent adverse events were reported in 66.7% of dupilumab-treated patients (conjunctivitis cluster: 6.4%) and 73.8% of the placebo group (conjunctivitis events: 0%). No dupilumab-related adverse events were serious or led to discontinuation. **Conclusion:** Dupilumab significantly improved AD signs, symptoms, and quality of life in children aged 6 months to 5 years with severe AD. The safety profile was consistent with that seen previously in adults, adolescents, and children aged > 6 years.

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