

Background and importance

Atopic dermatitis (AD) is a chronic inflammatory dermatological condition that often requires systemic treatments when topical therapies are insufficient. Previously, the only available systemic treatments were immunosuppressants. However, recently, monoclonal antibodies and oral small molecule therapies have been approved, offering more targeted and effective treatment options with fewer side effects.

Aim and objectives

To analyze whether the different therapeutic options could be considered as equivalent therapeutic alternatives (ETA) in AD.

Material and methods

A systematic search was conducted in PubMed, including randomized, double-blind, phase 2-3 controlled trials that assessed systemic therapies combined with topical corticosteroids (TCS). Efficacy was measured as a 75% reduction in the Eczema Area and Severity Index (EASI75) at week 16. The analysis was performed using RStudio® software (v 4.04) to estimate Bayesian statistics, with placebo as the reference. ETA guidelines (1) were applied to determine therapeutic positioning, using a delta value of 12% as the maximum acceptable non-inferiority margin, based on Blauvelt et al. 2021 (2).

Results

Six studies were included. All therapies showed favorable reductions in EASI75 compared to placebo, with statistically significant differences. As upadacitinib 30mg demonstrated the most favorable outcomes (0.51 [0.44;0.58]), a subsequent analysis was performed to compare its efficacy against the other therapeutic alternatives. As shown in Figure 1, abrocitinib 200mg (-0.07 [-0.19; 0.05]) and dupilumab 300 mg weekly (-0.10 [-0.20; 0.00]) showed the most similar efficacy result; in fact, statistically difference was not shown.

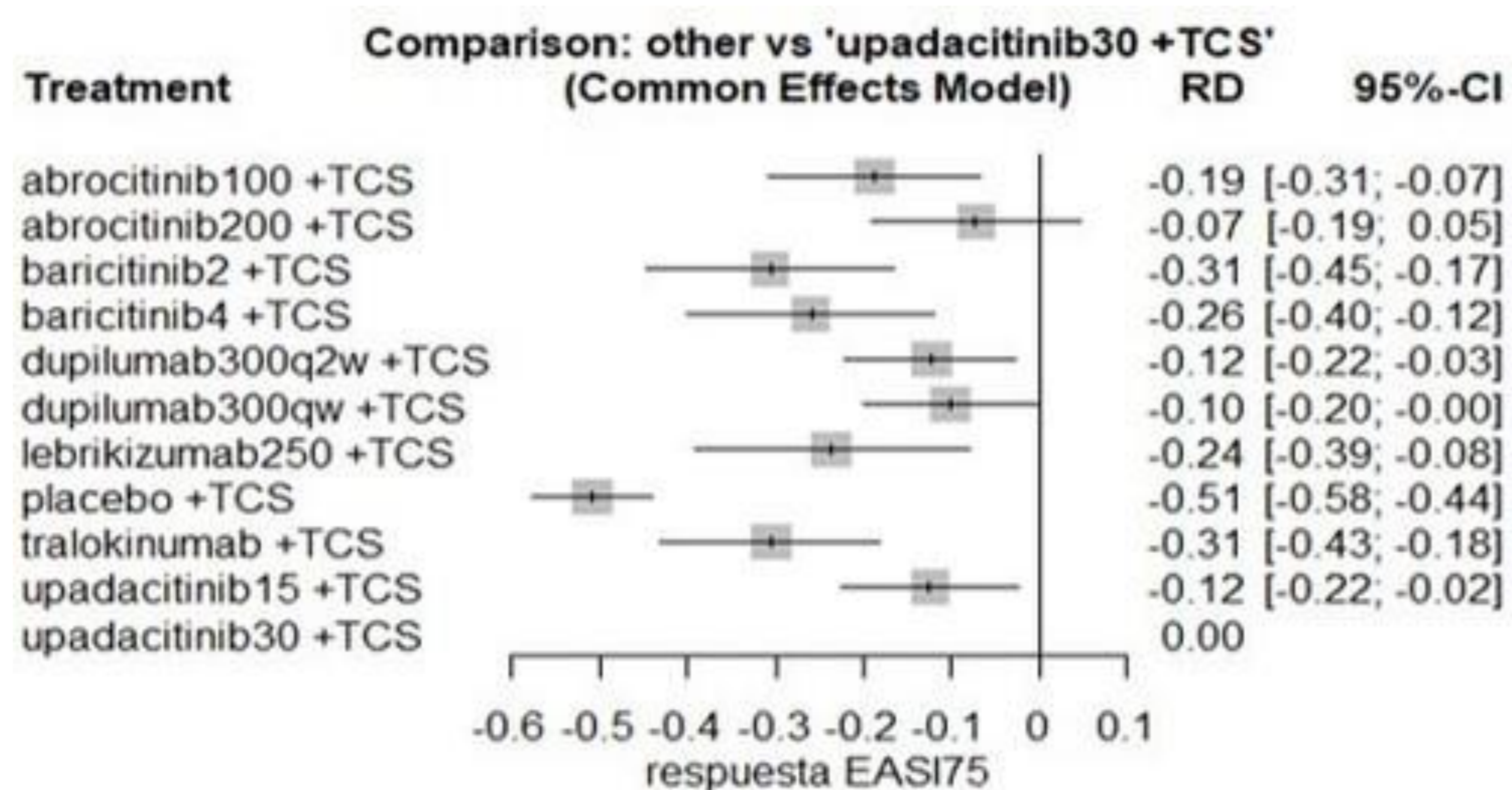


Figure 1. Forest-plot of the decrease in EASI75 response. Comparator: Upadacitinib 30mg+TCS. RD: risk difference. 95% CI: 95% confidence interval

Conclusion and relevance

This study identifies upadacitinib, abrocitinib and weekly-dupilumab as highly effective options. However, according to the Pharmacovigilance Risk Assessment Committee (PRAC) recommendations about JAK inhibitors (JAKi) safety and the unapproved weekly-dupilumab dose, only biweekly dupilumab, lebrikizumab and tralokinumab are considered viable ETAs.

References

- (1) Alegre Del Rey EJ, Fénix Caballero S, Castaño Lara R, Sierra García F. Assessment and positioning of drugs as equivalent therapeutic alternatives. *Med Clin(Barc)*.2014;143(2):85-90.doi:10.1016/j.medcli.2013.11.033
- (2) Blauvelt A, Teixeira HD, Simpson EL, Costanzo A, De Bruin-Weller M, Barbarot S, et al.Efficacy and Safety of Upadacitinib vs Dupilumab in Adults with Moderate-to-Severe Atopic Dermatitis: A Randomized Clinical Trial. *JAMA Dermatol*. 1 de septiembre de 2021;157(9):1047-55.

