Comparison of Efficacy of Targeted Therapies without Topical Corticosteroids for Moderate to Severe Atopic Dermatitis: Systematic Review and Network Meta-analysis

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INTRODUCTION

• Targeted therapies for patients with moderate to severe atopic dermatitis (AD) have been recently evaluated in multiple randomized controlled trials (RCTs), but comparative efficacy evidence among these therapies is limited.
• Reported here are network meta-analysis (NMA) results comparing efficacy, measures of skin clearance and itch among targeted therapies as monotherapy without concurrent topical corticosteroids (TCS).

METHODS

SYSTEMATIC LITERATURE REVIEW

• We conducted a systematic literature review (SLR) that searched the Cochrane Central Register of Controlled Trials, MEDLINE, Embase, Latin American and Caribbean Health Science Information database, Global Resource of Eczema Trials database, and clinical trial registries up to October 2020.
• English-language RCTs (phase III and IV) with ≥8 weeks of systemic immunomodulatory treatment for moderate to severe AD were included, as well as case studies up to the most recently available publication date.
• The SLR adhered to Preferred Reporting Items for Systematic Reviews and Meta-analyses for Network Meta-analyses guidelines.
• All studies selected by the SLR and included in the NMA were critically appraised based on methodologies using quality tool validated by the NMA in accordance with NICE recommendations.
• Studies were evaluated on multiple domains of bias: random sequence generation, allocation concealment, blinding of participants, blinding of investigators, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential sources of bias that may affect internal or external validity and generalizability of the study.

NETWORK META-ANALYSIS

• Prespecified efficacy outcomes were: Investigator Global Assessment score of 0 or 1 (clearly or almost clear) at ∆NRS≥4, EASI ≥50, PASI ≥25 at baseline (EASI-50, PASI-25), and PASI ≤10 at follow-up (PASI-10).
• For IGA 0 / 1, response rates were greatest for upadacitinib 30 mg, followed by abrocitinib 200 mg, followed by dupilumab 300 mg (Table 1).
• For EASI-50, response rates were greatest for upadacitinib 30 mg, followed by abrocitinib 200 mg, and dupilumab 300 mg (Figure 4).
• For EASI-75, EASI-90, and ∆NRS≥4 response rates were greatest for upadacitinib 30 mg, followed by abrocitinib 200 mg, followed by dupilumab 300 mg (Table 1).
• For IGA 0 / 1, NNT and SUCRA estimates were most favorable for upadacitinib 30 mg, followed by abrocitinib 200 mg, and dupilumab 300 mg (Table 1).
• For EASI-75, EASI-90, and ∆NRS≥4, response rates were greatest for upadacitinib 30 mg, followed by abrocitinib 200 mg, followed by dupilumab 300 mg (Table 1).

RESULTS

Table 1. Number needed-to-treat and SUCRA at primary endpoint evaluation (Bayesian NMA fixed-effects results)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>EASI-75</th>
<th>EASI-90</th>
<th>ΔNRS≥4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Abrocitinib 200</td>
<td>23.2%</td>
<td>26.6%</td>
<td>15.7%</td>
</tr>
<tr>
<td>Abrocitinib 200</td>
<td>9.2%</td>
<td>10.2%</td>
<td>7.5%</td>
</tr>
<tr>
<td>Abrocitinib 200</td>
<td>4.7%</td>
<td>5.6%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

LIMITATIONS

• Some heterogeneity was observed in baseline characteristics and placebo response rates across the analyzed trials. Adjusted models were tested but were not selected based on relevant fit statistics.

CONCLUSIONS

• Among targeted therapies used as monotherapy without concurrent TCS, upadacitinib 30 mg was the most effective therapy for patients with moderate to severe AD, followed by abrocitinib 200 mg, dupilumab 300 mg and placebo.

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REFERENCES

• The discrepancy between the numbers of records (n=6) and number of unique studies (n=9) is because three of the publications included, as well as data from two upadacitinib trials (Measure Up 1 and Measure Up 2) were counted.

Figure 3. IGA 0 / 1 vs ΔNRS≥4 response rate estimates and SUCRA for primary efficacy endpoints (Bayesian NMA fixed-effects results)