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Efficacy and safety of coacillium in children and adolescents with moderate to severe alopecia areata: a randomised, double-blind, multicentre, phase 2-3 trial

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Introduction & Objectives:

Alopecia areata (AA) is an autoimmune mediated disease characterized by rapid onset of hair loss often with chronic relapsing course. There is only one approved treatment for adults with severe AA, alopecia totalis (AT) and alopecia universalis (AU). No treatment is approved for children, adolescents or for patients with a moderate form of AA, albeit early-onset of AA may have a less favorable prognosis. We investigated the efficacy and safety of coacillium in children and adolescents with moderate to severe AA. Coacillium is a botanical drug composed of Allium cepa, Citrus limon, Theobroma cacao and Paullinia cupana.

Materials & Methods:

A randomised, double-blind, multicentre, phase 2–3 trial, RAAINBOW, was conducted at 12 sites in 4 countries. Patients aged 2 to 18 years with Severity of Alopecia Tool (SALT) score of 25-50 (moderate AA) and 50-95 (severe AA) were randomly assigned to coacillium 22.25% twice-daily (coacillium group), or placebo (placebo group) (2:1). The treatment period of 24 weeks was followed by a treatment-free period of 24 weeks to evaluate disease relapse after treatment discontinuation. No concomitant treatment for AA was allowed. Protocol details are registered with ClinicalTrials.gov, NCT03240627.

Results:

A total of 107 patients were randomly assigned to coacillium (71) or placebo (36). Average age was 11 years old, mean time since onset of disease was 3 years, 45% were female, 60% had severe AA, 40% moderate AA, 52% experienced their first episode of AA and 48% their second flare or more. The primary endpoint was the relative change in SALT score. After 24 weeks of treatment, the average change in coacillium group (+22.87%) was statistically significantly superior to the placebo group (-8.00%) (p<0.0001). 73% of coacillium-treated subjects who completed the 24 weeks treatment period responded to treatment. Of those, 96% kept improving after treatment discontinuation, while 4% only experienced disease relapse within the 24 weeks treatment-free period. At week 24, the percentage of patients with a SALT score of 20 or less was 21.2% in coacillium group and 5.3% in the placebo group (p=0.0031). Improvement of CDLQI was consistent with treatment effect; at week 48, CDLQI change in coacillium group was -2.52 while change in placebo group was +0.83 (p=0.0313). No serious adverse event was reported in the coacillium group. All other AEs were mild or moderate, local and transient.

Conclusion:

In this phase 2-3 trial involving children and adolescents with moderate to severe alopecia areata, coacillium cutaneous solution 22.25% twice-daily was superior to placebo after 24 weeks of treatment and well tolerated.
Discontinuation of drug treatment triggered merely no disease relapse. Coacillium might be a suitable treatment option for children and adolescents with moderate to severe alopecia areata.
Efficacy and Safety of Coacillium in Children and Adolescents with Moderate to Severe Alopecia Areata: a Randomised, Double-blind, Multicentre, Phase 2-3 Trial

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OBJECTIVE
- Coacillium cutaneous solution is a botanical drug composed of Allium cepa, Citrus limon, Theobroma cacao and Paullinia cupana. Its multiple components have shown to act positively on both hair follicle cycling and EC activation.
- We investigated Coacillium safety and efficacy in children and adolescents with moderate to severe AA.

METHODS
- **Study design**
  - RAANBOW study is an international, double-blind, placebo-controlled, randomised, multi-centre study (Figure 1).
  - Patients received twice-daily Coacillium cutaneous solution or placebo for 24 weeks.
  - The treatment period was followed by a 24-weeks treatment-free follow-up to assess disease relapse.
  - No concomitant treatment for AA was allowed.
- **Key eligibility criteria**
  - Patients were aged 2-18, with a diagnosis of AA, and hair loss involving 25-50% (moderate) or 50%-95% (severe) of the scalp, with a current AA episode duration of 6 months to 3 years.
  - Hair loss was measured by Severity of Alopecia Tool (SALT) (Olsen, 2004).

Endpoints
- Primary endpoint is the relative change in SALT after 24 weeks of treatment.
- Change in CDLQI, EQ-VAS and duration of treatment effect from end of treatment after 12 weeks and 24 weeks of treatment-free period were evaluated.
- Percentage of patients achieving SALT ≤ 20 was measured post-hoc.

Statistical analysis
- All analyses were conducted with two-sided significance level of 0.05 on relative change in SALT score as the dependent variable, and treatment, visit, and treatment-by-visit-interaction as fixed effects, and baseline SALT score (severity) as covariate.

RESULTS
- At baseline, mean SALT score was 58.9 and was generally consistent across treatment groups (Table 1).

Table 1: baseline characteristics

<table>
<thead>
<tr>
<th>Item</th>
<th>Total</th>
<th>Coacillium</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (ITT)</td>
<td>107</td>
<td>71 (66%)</td>
<td>36 (34%)</td>
</tr>
<tr>
<td>N (FAS)*</td>
<td>62</td>
<td>42 (68%)</td>
<td>20 (32%)</td>
</tr>
<tr>
<td>Severe</td>
<td>37 (60%)</td>
<td>24 (57%)</td>
<td>13 (65%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>25 (40%)</td>
<td>18 (43%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Average SALT at V1</td>
<td>58</td>
<td>56.1</td>
<td>61.8</td>
</tr>
<tr>
<td>Average age</td>
<td>11</td>
<td>11.1</td>
<td>10.1</td>
</tr>
<tr>
<td>Time since onset of AA</td>
<td>3 years</td>
<td>3.3 years</td>
<td>2.5 years</td>
</tr>
<tr>
<td>Female</td>
<td>34 (55%)</td>
<td>22 (52%)</td>
<td>12 (60%)</td>
</tr>
<tr>
<td>Patients with severe flares</td>
<td>30 (48%)</td>
<td>21 (50%)</td>
<td>9 (45%)</td>
</tr>
</tbody>
</table>

* FAS population consists of patients assessed as SALT 25-95 at baseline by both investigator and independent expert.

- Mean change in Coacillium group was 22.87% (P<0.0031; improvement).
- Mean change in placebo group was 8.00% (P=0.0453; worsening).
- Difference was statistically significant (P<0.0001).
- Change in SALT score was positively correlated by change in CDLQI and EQ-VAS.
- To our knowledge, Coacillium is among the first drugs to show sustained remission off-treatment in an autoimmune-mediated disease, without immune-altering side-effects.
- Coacillium might be a suitable treatment option for children and adolescents with moderate to severe alopecia areata.
- Larger trials are warranted.

CONCLUSION
- Coacillium was superior to placebo, and well tolerated.
- Most drug-responders experienced durable response during the 6-months treatment-free follow-up period.
- To our knowledge, Coacillium is among the first drugs to show sustained remission off-treatment in an autoimmune-mediated disease, without immune-altering side-effects.
- Coacillium might be a suitable treatment option for children and adolescents with moderate to severe alopecia areata.
- Larger trials are warranted.