**Efficacy and safety of ingenol mebutate gel in field treatment of actinic keratosis on full face, balding scalp or approximately 250 cm² on the chest: a Phase III, randomized, controlled trial**

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**Background**
- Ingenol mebutate (IngMeb; Picato®) is indicated for the topical treatment of actinic keratosis (AK) in areas of skin up to 25 cm².
- Two or three consecutive days of treatment with IngMeb provides clinically relevant clearance of AK lesions on the face/scalp (0.015% gel) and trunk/axillae (0.05% gel) when compared with vehicle gel; in addition, treatment effects of IngMeb gel are maintained long term.1
- However, some patients may require treatment of AK over areas of skin larger than 25 cm².

**Study objective**
- To compare the efficacy and safety of IngMeb 0.027% gel with vehicle gel, as a field treatment in patients with AK, when applied once daily for three consecutive days on the full face, balding scalp or ~250 cm² on the chest (clinical trial identifier: NCT02361216).

**Methods**
- Phase III, randomized, parallel-group, double-blind, vehicle-controlled, eight-week trial in patients with AK (Figure 1).
- Patients were eligible if they had 5–20 clinically typical, visible and discrete AK lesions within a selected treatment area of sun-damaged skin on either the full face, full balding scalp (~250 cm²) or a contiguous area of (~250 cm²) on the chest.

**Results**

**Patient population**
- In total, 729 patients were randomized to receive IngMeb 0.027% gel (n=552) or vehicle gel (n=177). The median age was 67.5 years, most patients were male (73.4%), all were white, and 95.6% of patients had Fitzpatrick skin type I–III (Table 1). Median AK count at baseline was 12 (range 5–56).
- No differences were reported for the Side Effects or Convenience domains.

**Table 1. Baseline demographics and disease characteristics**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Median (Range)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teen</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>Young</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Middle 17–22</td>
<td>75</td>
<td>100</td>
</tr>
<tr>
<td>Middle 23–35</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Middle 36–64</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>Older 65+</td>
<td>16</td>
<td>1</td>
</tr>
</tbody>
</table>

**Cosmetic outcomes:**
- Overall, 'much improved' or 'somewhat improved' reported by 92% patients receiving IngMeb vs 18% for vehicle.
- Overall satisfaction: 'much improved' or 'somewhat improved' reported by 94% patients receiving IngMeb vs 10% for vehicle.

**Limitations**
- Since LSRs were observed during the study, with early onset and rapid resolution, these receiving active treatment could potentially be identified.

**Conclusions**
- IngMeb 0.027% gel was superior to vehicle as a field treatment on full face, balding scalp or ~250 cm² on the chest in patients with AK, although it was less efficacious for the treatment of AK on the scalp.
- AKCLEAR 75 and 100, and percent reduction in lesion count were similar at Weeks 4 and 8, suggesting a maximal treatment effect of IngMeb by Week 4.

**Physician- and patient-reported outcomes**
- Patients were eligible if they had 5–20 clinically typical, visible and discrete AK lesions within a selected treatment area of sun-damaged skin on either the full face, full balding scalp (~250 cm²) or a contiguous area of (~250 cm²) on the chest.
- In total, 729 patients were randomized to receive IngMeb 0.027% gel (n=552) or vehicle gel (n=177). The median age was 67.5 years, most patients were male (73.4%), all were white, and 95.6% of patients had Fitzpatrick skin type I–III.

**Table 2. Most frequent AEs**

<table>
<thead>
<tr>
<th>General disorders and administration site conditions</th>
<th>IngMeb 0.027% (gel)</th>
<th>Vehicle (gel)</th>
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<tbody>
<tr>
<td>Application-site pain</td>
<td>350</td>
<td>40.8%</td>
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<td>Application-site discomfort</td>
<td>22</td>
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<tr>
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<tr>
<td>Eyelid edema</td>
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<td>2.9%</td>
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**References**

5. ACCURATE (original protocol: investigational https://www.ncbi.nlm.nih.gov/pubmed/20611056

**Figure 1. Trial design**

**Figure 2. AKCLEAR 75 by visit**
- Treatment-related AEs (TRAEs) were experienced by 73.8% and 9.1% of patients in the IngMeb and vehicle groups, respectively. Serious AEs occurred in 1.3% vs 1.1% of patients receiving IngMeb or vehicle, respectively; none were treatment-related.
- The most frequently reported AEs occurring in ≥2% patients receiving IngMeb 0.027% gel included application-site pain and application-site pruritus (Table 2).

**Figure 3. Reduction in AK lesion count by visit**
- For IngMeb, reduction in AK lesion count from baseline at Week 8 was 78.7% (95% CI, 73.6–77.3) vs 12.7% (95% CI, 3.0–21.4) with vehicle. A similar effect was observed at Week 4.

**Figure 4. Composite LSR profile**
- Mean AKCLEAR scores peaked at Day 4 (IngMeb 0.027% gel, 10.8; vehicle, 1.6), rapidly declined and returned to minimal levels by Week 4.

**Figure 5. TSGM scores**
- The lower efficacy of IngMeb observed on the scalp vs face/chest corresponded with lower LSR scores in this area.

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**Notes:**
- All randomized (N = 729)
- Week 8 data are displayed in Figure 4 (Table 2).
- AKCLEAR 75 and 100, and percent reduction in lesion count were similar at Weeks 4 and 8, suggesting a maximal treatment effect of IngMeb by Week 4.
- The safety profile of IngMeb, for both LSRs and AEs, was as expected.
- IngMeb was also associated with higher levels of patient satisfaction and cosmetic outcomes compared with vehicle.

**Acknowledgments**
- IngMeb 0.027% gel was superior to vehicle as a field treatment on full face, balding scalp or ~250 cm² on the chest in patients with AK, although it was less efficacious for the treatment of AK on the scalp.
- For IngMeb, AKCLEAR 75 was 63.4% (95% CI, 58.8–67.9) for the face/chest (n=435) and 44.1% (95% CI, 36.0–53.3) for the scalp (n=114); respective values in the vehicle group were 9.5% (95% CI, 0.5–18.6; n=144) and 3.1% (95% CI, 0.0–12.2; n=22).
- In total 729 patients were randomized to receive IngMeb 0.027% gel (n=552) or vehicle gel (n=177). The median age was 67.5, most patients were male (73.4%), all were white, and 95.6% of patients had Fitzpatrick skin type I–III. In the IngMeb group, AKCLEAR 75 and 100, and percent reduction in lesion count were similar at Weeks 4 and 8, suggesting a maximal treatment effect of IngMeb by Week 4.
- The safety profile of IngMeb, for both LSRs and AEs, was as expected.
- IngMeb was also associated with higher levels of patient satisfaction and cosmetic outcomes compared with vehicle.

**References**