Vitiligo Biomarker CXCL10 Correlates With Clinical Response in the Phase 2 Randomized, Double-Blind, Vehicle-Controlled TRU-EV Mechanism of Action Study

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Presented at: Revolutionizing Alpsea Area, Vitiligo, and Eczema (RAVE) 2024
Chicago, IL, USA; June 9–10, 2024

Introduction

- Ruxolitinib (Levaxa) is a JAK1/2 inhibitor
- CXCL10 has shown to correlate with disease severity in vitiligo
- Ruxolitinib cream application reduced serum levels of CXCL10 in a phase 2 study

Methods

- To evaluate treatment-associated changes in local and systemic biomarkers (particularly CXCL10), correlate changes in key biomarkers with regression efficacy, and assess the safety and tolerability of ruxolitinib cream

Objectives

- To evaluate treatment-associated changes in local and systemic biomarkers (particularly CXCL10), correlate changes in key biomarkers with regression efficacy, and assess the safety and tolerability of ruxolitinib cream
- Assess safety and tolerability of ruxolitinib cream

Patients and Study Design

- Adult patients aged 18 y with nonmucosal vitiligo with depigmented areas covering >50% total body surface area (BSA), involving >0.5% BSA on the face and >60% BSA on nonfacial areas, were randomized to 1 of 2 ruxolitinib cream twice daily (SGD) or vehicle cream for 24 weeks (Figure 1)
- Application was limited to <25% BSA
- Patients who completed the double-blind period were eligible to enroll in the 28-week open-label treatment extension in which all patients were switched to open-label ruxolitinib cream at Week 24

Results

- A total of 60 patients were randomized to ruxolitinib cream or vehicle
- Baseline demographics and clinical characteristics were similar between treatment groups (Table 1)

Table 1. Demographics and Baseline Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Vehicle (n=30)</th>
<th>RUX Cream (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) (mean [SD])</td>
<td>47.1 (7.3)</td>
<td>44.2 (7.2)</td>
</tr>
<tr>
<td>Male (%)</td>
<td>15 (50.0)</td>
<td>15 (50.0)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>13 (43.3)</td>
<td>25 (83.3)</td>
</tr>
<tr>
<td>T-BSA, mean (SD), %</td>
<td>12.3 (9.5)</td>
<td>13.6 (10.7)</td>
</tr>
<tr>
<td>Frequency of itch (y, n)</td>
<td>11 (36.7)</td>
<td>21 (70.0)</td>
</tr>
<tr>
<td>≥3% BSA on &lt; facial area (%)</td>
<td>8 (26.7)</td>
<td>20 (66.7)</td>
</tr>
<tr>
<td>Baseline T-VASI (mm)</td>
<td>15.3 (6.0)</td>
<td>12.5 (0.7)</td>
</tr>
<tr>
<td>≥50% T-BSA (mm)</td>
<td>12 (40.0)</td>
<td>13 (44.8)</td>
</tr>
<tr>
<td>Disease duration, median (0–52.9) (y)</td>
<td>3.0 (0.1–52.9)</td>
<td>2.9 (0.1–52.9)</td>
</tr>
<tr>
<td>Precision (y, %)</td>
<td>79 (21.0)</td>
<td>53 (17.8)</td>
</tr>
</tbody>
</table>

- Five differentially expressed proteins (adjusted P<0.05) were identified in serum and skin of patients with vitiligo

Differentially Expressed Serum Proteins

- Four differentially expressed proteins (adjusted P<0.05) were identified in serum and skin of patients with vitiligo
- Three differentially expressed proteins (adjusted P<0.05) were identified in skin and serum of patients with vitiligo

CXCL10 Levels

- Protein levels of CXCL10 in serum (Figure 3) and mRNA levels of CXCL10 in skin (Figure 4) were significantly reduced at Week 12 among patients who applied ruxolitinib cream versus baseline

Figure 3. Protein Levels of CXCL10 in Serum

Figure 4. mRNA Levels of CXCL10 in Lesional and Nonlesional Skin

Clinical Response

- Patients applying ruxolitinib cream had a significant mean (SD) reduction in T-VASI from baseline in the ≥3% BSA group at Week 12 (–32.9 [33.6]) and total VASI (T-VASI) at Week 17 (–42.1 [31.7]) compared with vehicle treatment (Figure 5, Table 3)

Correlation of Clinical Levels With Clinical Response

- Most systemic proteins did not correlate or only weakly correlated with VAS response
- T-VASI scores correlated significantly with CXCL10 levels in skin and serum (Table 3, Figure 5)

Safety

- Ruxolitinib cream was generally well tolerated through 1 year of treatment (Table 3); no serious treatment-related adverse events were reported

Table 3. Treatment-Emergent Adverse Events

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Conclusions

- These data are consistent with the role of the interferon gamma-CXCL10 axis as a central mediator of vitiligo pathogenesis
- CXCL10 levels were significantly reduced in serum and lesional skin 12 weeks after application of ruxolitinib cream SGD
- VAS was significantly reduced at Week 12, and T-VASI was significantly reduced at Week 17
- Reductions in both serum and skin CXCL10 levels significantly correlated with VASI improvement
- Correlation was strongest in lesional skin (local effect) compared with serum
- CXCL10 may be an early biomarker of effective treatment with ruxolitinib cream

Further biomarker analyses are pending

References

Disclosures

- The authors declare no conflicts of interest. This study was supported by Incyte Corporation
- The study was conducted in compliance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards
- The study was registered at ClinicalTrials.gov (NCT04968326)
- All authors approved the final version of the manuscript

Acknowledgments

- The authors thank all the patients who participated in this study
- The authors also thank the study investigators, study coordinators, and other study personnel for their contributions to the study

Appendix A

- Additional information and appendices are available in the full manuscript

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Figure 8. Safety Data

Table 1. Demographics and Baseline Clinical Characteristics

Table 2. Correlation of Clinical Scores With CXCL10 Levels

Table 3. Treatment-Emergent Adverse Events

Table 4. Differentially Expressed Serum Proteins

Table 5. Safety Data

Figure 1. Study Design

Figure 2. Flowchart of Differentially Expressed Serum Proteins

Figure 3. Protein Levels of CXCL10 in Serum

Figure 4. mRNA Levels of CXCL10 in Lesional and Nonlesional Skin

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