Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 (TYK2) Inhibitor, Compared With Placebo and Apremilast in Moderate to Severe Psoriasis: Integrated Laboratory Parameter Results From the Phase 3 POETYK PSO-1 and PSOYK PSO-2 Trials

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Introduction

Deucravacitinib is a novel oral tyrosine kinase 2 (TYK2) inhibitor that allosterically inhibits TYK2 with subnanomolar affinity, leading to the regulation of cytokine signaling in T cells and other immune cells. Deucravacitinib was significantly more efficacious than placebo and apremilast and was well tolerated in patients with moderate to severe plaque psoriasis.

Objective

The primary aims assessed the effects of deucravacitinib on hematologic, lipid, and chemistry parameters in blood in the POETYK trials.

Methods

Study designs

POETYK PSO-1 (NCT03718941) and POETYK PSO-2 (NCT03717775) were Phase 3, 52-week, double-blind, randomized, placebo- and active comparator (apremilast) controlled trials conducted globally. Figure 1A

- enrolled patients with moderate to severe plaque psoriasis (BSA, Triglyceride and CPK elevations were the most common Grade 3 laboratory abnormality) over 12 weeks to receive placebo or apremilast or deucravacitinib 6 mg once daily, apremilast 30 mg twice daily during Weeks 0–1
- blind withdrawal treatments occurred at Week 16 and Week 24
- patients receiving apremilast were switched to placebo at Week 24
- patients receiving apremilast who failed to meet trial-specific efficacy thresholds (PASI 50 in PSO-1; PASI 75, ≥75% reduction from baseline in PASI; QD, once daily; ULN, upper limit of normal.

Laboratory assessments over Weeks 0–16

Standard laboratory parameters in blood were evaluated in patients enrolled in PSO-1 who received placebo or apremilast and was well tolerated in patients with moderate to severe plaque psoriasis

Results

Patient population

469 to 1,020 patients were randomized in PSO-1 and PSO-2, respectively, and were included in this analysis

Laboratory assessments over Weeks 0–16

- Overall, no clinically important trends were observed in any of the assessed laboratory parameters
- Laboratory parameters remained within normal ranges for most patients throughout both trials

Table 1. Grade ≥3 laboratory abnormalities, Weeks 0–16

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Grade ≥3</th>
<th>PSO-1 (N=666)</th>
<th>PSO-2 (N=1,020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT increased</td>
<td>144/666</td>
<td>0.0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>AST increased</td>
<td>134/666</td>
<td>0.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>CPK increased</td>
<td>164/666</td>
<td>0.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Triglyceride increased</td>
<td>164/666</td>
<td>0.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Uric acid increased</td>
<td>134/666</td>
<td>0.0%</td>
<td>0.2%</td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>58/666</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Hematocrit decreased</td>
<td>134/666</td>
<td>0.0%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

POETYK PSO-1 and PSO-2 pooled data; Weeks 0−16 vs Weeks 0−12; sPGA, static Physician’s Global Assessment score of 0/1.

No clinically relevant cumulative trends were observed in any assessed laboratory parameters in PSO-1 patients

Conclusions

- Patients receiving deucravacitinib treatment showed no meaningful changes in multiple hematologic, chemistry, and lipid parameters in the blood over Weeks 0−16 in 2 large Phase 3 trials
- Discontinuations due to laboratory abnormalities were rare and balanced across treatment groups
- No trends were evident for any laboratory parameter with continued deucravacitinib treatment over 52 weeks
- These results suggest that routine laboratory monitoring is not warranted during deucravacitinib treatment

References


Acknowledgments

We would like to thank the patients and investigators who participated in these trials.

Relationships and Activities

SB, EC, JK, and JT: Speaker: AbbVie, Eli Lilly, Janssen, Novartis, Regeneron, and Sanofi Genzyme

SB: Industry sponsorship, travel and expenses: Amgen; Advisory board, principal investigator, and lecture fees: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, and Sanofi Genzyme.

EC: Industry sponsorship, academic research and travel support: AbbVie; Advisory board: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Pfizer, Sun Pharma, Taiho, 2X Biologics; consultant fees: AbbVie, Boehringer Ingelheim, Janssen, Novartis, Pfizer, Sun Pharma, Taiho.

TV: Advisory board, principal investigator, and lecture fees: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, Sanofi Genzyme, and Sun Pharma

SB, EC, JT, and TV: Industry sponsorship, travel and expenses: Amgen; Advisory board: AbbVie, Almirall, Amgen, Biogen Idec, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Eisai, Eli Lilly, Galapagos, Galderma, Janssen-Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche-Posay, Sanofi Genzyme, and Sun Pharma

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Table 2. Laboratory abnormality adverse events leading to discontinuation, Weeks 0–16

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No (%)</th>
<th>PSO-1 (N=666)</th>
<th>PSO-2 (N=1,020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT increased</td>
<td>1/1020</td>
<td>0.0%</td>
<td>0.0%</td>
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<tr>
<td>AST increased</td>
<td>2/1020</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>CPK increased</td>
<td>2/1020</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
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<td>2/1020</td>
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<td>Hematocrit decreased</td>
<td>2/1020</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
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</table>

Figure 2. Hematologic parameters, Weeks 0−16

Figure 3. Lipid and chemistry parameters, Weeks 0−16

Figure 4. Hematologic parameters in patients receiving deucravacitinib (PSO-1), Weeks 0−52

Figure 5. Lipid and chemistry parameters in patients receiving deucravacitinib (PSO-1), Weeks 0−52

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