SAFETY PROFILE OF THE ADJUVANT RECOMBINANT ZOSTER VACCINE (RZV) IN IMMUNOCOMPROMISED POPULATIONS: AN OVERVIEW OF 6 TRIALS

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BACKGROUND AND AIM

- Immunocompromised (IC) populations are at increased risk of herpes zoster (HZ) and its related complications.
- RZV demonstrated >68% efficacy against HZ in autologous hematopoietic stem cell transplant (auHSCT) recipients ≥18 years of age (YOA).

AIM of the overview:
We present the pooled safety data across 6 clinical trials in IC populations:
- auHSCT recipients, phase II, NCT01610414
- Renal transplant (RT) recipients, phase II, NCT01890148
- auHSCT recipients, phase I/II, NCT01903198

METHODS

- All 6 studies were randomized, observer-blinded, placebo-controlled.
- Reactogenicity data are pooled across the 6 studies and other safety data are presented by study.
- Unsolicited AEs, SAEs and fatal SAEs by age group are available across the different IC populations.

RESULTS

- As expected, most solicited symptoms were more frequently reported in the RZV group than in the Placebo group.
- Pain, fatigue, headache, myalgia, shivering and fever were reported more frequently in the RZV 18–49 YOA vs Placebo ≥50 YOA.
- The percentage of study participants with fatal SAE was comparable between RZV and Placebo groups.
- Most of these fatal SAEs were related to the underlying diseases specific to each study population.
- In the auHSCT study, reactogenicity data are pooled across the 6 studies and other safety data are presented by study.

CONCLUSIONS

- Reactogenicity symptoms were more frequent after RZV than Placebo and in younger age groups. The majority of symptoms were mild to moderate in intensity and short in duration.
- The frequency of unsolicited AEs and SAEs (including vaccination-related by investigator assessment) were similar between the RZV and Placebo groups. Most of the reported AEs and SAEs (including fatal SAEs) were in the context of underlying diseases and therapies.
- Overall, the safety data presented here together with the efficacy in auHSCT recipients’ and the immunogenicity data across populations (see immunogenicity data in presentation #4, Adult Vaccines Session) support a favorable benefit-risk profile of vaccination with RZV in IC adults.

The extensive safety data summarized here provides useful medical information for the prevention of HZ in a broad range of populations with an impaired immune system due to underlying diseases or therapy.

REFERENCES


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DISCLOSURES: MLC, MC, FR, JJS, FTS are employees of the GSK group of companies and declare financial and non-financial relationships and activities. ABD, AR, and GS were employees of GSK group of companies at the time this study was designed, initiated and conducted and was interpreted. AR, AG, and GS hold shares in the GSK group of companies. JJS reports personal fees during the conduct of the study and outside the submitted work from the GSK group of companies.

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SUPPLEMENTARY MATERIALS

SAFETY PROFILE OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE (RZV) IN IMMUNOCOMPROMISED POPULATIONS: AN OVERVIEW OF 6 TRIALS

Demographic characteristics

<table>
<thead>
<tr>
<th>IC populations, study reference</th>
<th>Gender (Male, Female)</th>
<th>Race (White, Black, Other)</th>
</tr>
</thead>
<tbody>
<tr>
<td>auHSCT</td>
<td>RZV</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>37.1</td>
<td>37.4</td>
</tr>
<tr>
<td></td>
<td>63.9</td>
<td>62.6</td>
</tr>
<tr>
<td>HM</td>
<td>59.0</td>
<td>59.2</td>
</tr>
<tr>
<td></td>
<td>40.8</td>
<td>40.8</td>
</tr>
<tr>
<td>RT</td>
<td>28.8</td>
<td>31.3</td>
</tr>
<tr>
<td></td>
<td>71.2</td>
<td>68.9</td>
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<tr>
<td>ST</td>
<td>40.2</td>
<td>40.0</td>
</tr>
<tr>
<td></td>
<td>59.8</td>
<td>60.0</td>
</tr>
<tr>
<td>HIV</td>
<td>93.2</td>
<td>95.9</td>
</tr>
</tbody>
</table>

Solicited adverse events (AEs)

Grade 3 was defined as follows: pain that prevented normal activity; >100 mm diameter for redness and swelling; symptoms that prevented normal activity for headache, myalgia, fatigue and gastrointestinal symptoms; fever >39.0 °C (axillary/oral temperature). Among systemic AEs, fatigue, headache (all, related), myalgia, shivering, and fever (all, related) were reported more frequently in the RZV ≥50 YOA group than in the RZV ≤50 YOA group.

AEs by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC)

Unsolicited AEs by MedDRA SOC

Fatal SAEs by MedDRA SOC

Supplementary materials

IC, immunocompromised; RZV, the adjuvanted recombinant zoster vaccine; auHSCT, autologous hematopoietic stem cell transplant recipients; HM, hematological malignancy patients; RT, renal transplant recipients; ST, solid tumors patients; auHSCT, HSCT phase 1 study; HM, human immunodeficiency virus-infected adults. In the auHSCT study, the 2-dose group received 1 placebo dose and 2 RZV doses and the 3-dose group received either 3 RZV doses or 3 placebo doses.

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Background: Immuno-compromised (IC) populations are at increased risk of herpes zoster (HZ) and its related complications. RZV demonstrated >98% efficacy against HZ in autologous hematopoietic stem cell transplant (HSCT) recipients ≥18 years of age (YOA). Here we present the safety data across all clinical trials in IC populations: autologous HSCT recipients, HIV-infected adults, renal transplant recipients, patients with solid tumor and patients with hematological malignancies.

Methods: All 6 studies (Table 1) enrolled IC adults ≥18 YOA in RZV and Placebo groups. Safety was evaluated in the total vaccinated cohort (TVC). Solicited adverse events (AEs) were collected for 7 days and unsolicited AEs for 30 days after each dose. Serious AEs (SAEs), and potential immunemediated diseases (pIMDs) were collected from dose 1 until 1 year post-last dose or study end (for causally related [assessed by investigator] and fatal SAEs). Data are presented by age group: 18–49 YOA and ≥50 YOA. Reactogenicity data are pooled across the 6 studies and other safety data are presented by study.

Results: 1587 (RZV) and 1529 (Placebo) adults were included in the pooled TVC. Solicited AEs were more frequently reported in the RZV than Placebo group. Pain, fatigue, headache, myalgia, shivering and fever were reported more frequently in the RZV 18–49 YOA than in the RZV ≥50 YOA (Figure 1). Solicited AEs were mostly mild/moderate and lasted ≤3 days and grade 3 solicited AEs lasted ≤2 days (median duration). Across studies, the percentage of adults reporting ≥1 unsolicited AE was similar between RZV (18–49 YOA: 37.4–84.0%; ≥50 YOA: 36.9–88.4%) and Placebo (18–49 YOA: 31.4–89.4%; ≥50 YOA: 30.1–89.4%) (Figure 2). Overall, the percentage of adults with ≥1 SAE (Figure 3), causally related SAEs, fatal SAEs and pIMDs was similar between RZV and Placebo and between age groups. Overall, no safety concern was identified.

Conclusion: Reactogenicity symptoms were more frequent after RZV than placebo, and in younger age groups but no safety concern was identified. Most of the reported AEs and SAEs were in the context of underlying diseases and therapies. Overall our data support a favorable benefit-risk profile of vaccination with RZV in IC adults.

Funding: GlaxoSmithKline Biologicals SA

Table 1. Clinical trials with immuno-compromised populations included in our analysis

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Study Type</th>
<th>Study Design</th>
<th>Regimen Details</th>
<th>Study Type and Registration Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–49 YOA</td>
<td>Randomized</td>
<td>Placebo-controlled</td>
<td>2 doses (at months 0 and 1–2): 2 RZV doses or 2 placebo doses</td>
<td>NCT02058589</td>
</tr>
<tr>
<td>≥50 YOA</td>
<td>Randomized</td>
<td>Placebo-controlled</td>
<td>3 doses (at months 0, 1, 2): 3 RZV doses or 3 placebo doses</td>
<td>NCT01165203</td>
</tr>
</tbody>
</table>

N, number of patients/subgroup receiving at least 1 dose of RZV or placebo (total vaccinated cohort [TVC]) in each study; N, number of patients receiving 1 placebo dose followed by 2 RZV doses whom were additionally included into the RZV group in the pooled TVC. YOA, years of age; RZV, recombinant zoster vaccine; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplant recipients; SAE, serious adverse event; pIMD, potential immunemediated disease; RT, renal transplant recipients; SE, solid tumors patients; HIV+, human immunodeficiency virus; RZV, recombinant zoster vaccine; YOA, years of age.

Figure 1. Percentage of participants with solicited local and systemic AEs, reported across 6 pooled studies (7 days post-vaccination, overall participant, pooled total vaccinated cohort)

Figure 2. Percentage of participants reporting ≥1 unsolicited AE 30 days post-vaccination per study (total vaccinated cohort)

Figure 3. Percentage of participants reporting ≥1 SAE from dose 1 until 1 year post-last dose per study (total vaccinated cohort)