SAFETY AND REACTOGENICITY OF THE ADJUVANTED RECOMBINANT ZOSTER VACCINE: EXPERIENCE FROM CLINICAL TRIALS AND POST-MARKETING SURVEILLANCE

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Background

Shingles is a common painful disease that occurs in approximately 1 in 3 people in the US.1 Adults aged 60 years and older and patients who are immunocompromised are at increased risk of developing shingles.1,2

Methods

Adults were randomized 1:1 to receive the recombinant zoster vaccine (RZV) or placebo (2 dose series, see QR code for details)∗.2

Results

In clinical trials, the incidence and nature of serious adverse events (SAEs) and fatal adverse events (AEs) were similar in the RZV and placebo groups. Reactogenicity symptoms occurred more frequently with RZV than with placebo. Following the first year of post-marketing surveillance, the safety profile of RZV is consistent with that observed in clinical trials.

The incidence of serious adverse events (SAEs), potential immune-mediated diseases (pIMDs), and death was similar in the RZV and placebo groups.

Conclusions

Data support a favorable benefit-risk profile for RZV and its administration to adults 50 YOA and older and to immunocompromised adults 18 YOA and older at increased risk of HZ. Patients should be informed about the adverse reactions they may experience after receiving RZV.

SUMMARY

The majority of solicited adverse events (AEs) were of mild to moderate intensity, with a median duration of 1-3 days.∗

Post-marketing surveillance data were consistent with ZOE trials. 95.3% of 15,683 spontaneous reports of adverse events were considered non-serious. Most commonly reported AEs were consistent with the reactogenicity profile of the vaccine observed in clinical trials.

22.9% of spontaneous reports were linked to vaccination errors.

∗Figure shows data for any severity of adverse events. †Data from the pooled safety analyses of the ZOE 50 and ZOE 70 clinical trials. §Gastrointestinal symptoms. ¶Human immunodeficiency virus. **Humoral malignancies. ††Renal/renal transplant. ¶¶Renal transplant, HIV recombinant zoster vaccine, SR, and panhans, 10A years of age.

*Figure shows data for any severity of adverse events. **Fatal AE was considered possibly related to RZV, the patient (SR YOA) had previous medical history of stable immune-mediated thrombocytopenia, severe cutaneous reaction and was diagnosed with acute Myeloid Leukemia. There was also one Fatal event in the NR study claimed by the investigator as possibly related however the company did not consider it related.

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Information on QR-code

POST-MARKETING SURVEILLANCE

STUDIES IN OLDER ADULT POPULATIONS

- ZOE-50 trial (NCT01655777) with 15,417 adults ≥50 years of age (YOA) and ZOE-70 trial (NCT01652299) with 13,900 adults ≥70 YOA.
- Conducted in 18 countries in Europe, North America, South America, Asia and Oceania.

STUDIES IN IMMUNOCOMPROMISED POPULATIONS

- Autologous hematopoietic stem cell transplant (NCT01615944).∗∗ I/N=1646
- Hematological malignancies (NCT01764474), N=562
- Renal transplant (RT, NCT02058189), N=294
- Solid tumors (ST, NCT01798256), N=232
- Human immunodeficiency virus (NCT01525601), N=123

From 10 October 2017 to 10 February 2019, 9,323,118 vaccine doses distributed

12719
# Study design and patient population in clinical trials of RZV in older adults and immunocompromised populations

<table>
<thead>
<tr>
<th>Study design and trial registration number</th>
<th>Study location</th>
<th>Vaccination schedule</th>
<th>Patient characteristics</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized, phase 3, placebo-controlled</td>
<td>18 countries in Europe, North America, South America, Asia and Australia</td>
<td>2-dose schedule</td>
<td>RZV</td>
<td>14,645*</td>
</tr>
<tr>
<td>ZOE-50, NCT01165177</td>
<td>28 countries</td>
<td>First dose at Month 0 followed by a second dose 2 months later</td>
<td>Placebo</td>
<td>14,660*</td>
</tr>
<tr>
<td>ZOE-70, NCT01165229</td>
<td>77 centers worldwide</td>
<td>Dose 1: 50−70 days after transplant</td>
<td>RZV</td>
<td>922</td>
</tr>
<tr>
<td>Randomized, phase 3, placebo-controlled</td>
<td>Belgium, Canada, Czech Republic, Finland, Italy, Panama, Republic of Korea, Spain, Taiwan</td>
<td>Dose 2: 1−2 months after Dose 1</td>
<td>Placebo</td>
<td>924</td>
</tr>
<tr>
<td>NCT01610414</td>
<td>2-dose schedule</td>
<td>Doses administered 1−2 months apart during or after full cancer therapy course</td>
<td>RZV</td>
<td>283</td>
</tr>
<tr>
<td>Randomized, phase 3, placebo-controlled</td>
<td>2-dose schedule</td>
<td>Dose 1: 1−2 months post-transplant</td>
<td>Placebo</td>
<td>279</td>
</tr>
<tr>
<td>NCT01767467</td>
<td>Dose 2: 1−2 months after Dose 1</td>
<td>2-dose schedule</td>
<td>RZV</td>
<td>132</td>
</tr>
<tr>
<td>Randomized, phase 3, placebo-controlled</td>
<td>2-dose schedule</td>
<td>Doses administered 1−2 months apart. First dose was given either prior to or at the start of the chemotherapy cycle. Second dose was given with a subsequent chemotherapy cycle.</td>
<td>Placebo</td>
<td>132</td>
</tr>
<tr>
<td>NCT02058589</td>
<td>3-dose schedule at Months 0, 2 and 6</td>
<td>3-dose schedule</td>
<td>RZV</td>
<td>117</td>
</tr>
<tr>
<td>Randomized, phase 2/3, placebo-controlled</td>
<td>Germany, USA, UK</td>
<td>3-dose schedule</td>
<td>Placebo</td>
<td>115</td>
</tr>
<tr>
<td>NCT01165203</td>
<td>3-dose schedule</td>
<td>3-dose schedule</td>
<td>RZV</td>
<td>74</td>
</tr>
</tbody>
</table>

N: number of participants in the total vaccinated cohort. The total vaccinated cohort for safety included all participants with at least 1 documented dose. HIV: human immunodeficiency virus; HSCT: hematopoietic stem cell transplant; RZV: recombinant zoster vaccine.

*Pooled total vaccinated cohort from ZOE-50 and ZOE-70

†Phase 1/2 study (NCT00920218) was also conducted in a similar population; data not included.

‡Participants were vaccinated during a cancer therapy course (each dose at least 10 days before and after any cancer therapy) or after the full cancer therapy course (first dose between 10 days and 6 months after therapy).

§Participants were stratified (4:1) according to the timing of the first RZV or placebo dose with respect to the start of the first (or occasionally second) cycle of a chemotherapy course: first vaccination 8−30 days before the start of a cycle (pre-chemotherapy groups) or first vaccination within 1 day of the start of a cycle (on-chemotherapy groups). Participants received their second vaccination with a subsequent chemotherapy cycle.
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Other Medically Relevant Events From First Vaccination to Study End (TVC)

<table>
<thead>
<tr>
<th>Clinical trial</th>
<th>Specific AE of interest</th>
<th>RZV n/N (%)</th>
<th>Placebo n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>auHSCTa</td>
<td>Malignancy relapse</td>
<td>239/922 (26%)</td>
<td>253/924 (27%)</td>
</tr>
<tr>
<td>HIV</td>
<td>Worsening of HIV condition</td>
<td>9/74 (12%)</td>
<td>5/49 (10%)</td>
</tr>
<tr>
<td>Hematologic malignancies</td>
<td>Relapse or progression of original malignancy</td>
<td>45/283 (16%)</td>
<td>58/279 (21%)</td>
</tr>
<tr>
<td>Renal transplantb</td>
<td>Biopsy proven rejection</td>
<td>4/132 (3%)</td>
<td>7/132 (5%)</td>
</tr>
</tbody>
</table>

Other Medically Relevant Events From First Vaccination to Study End (TVC)

- One of four rejections in the RZV group and seven of seven rejections in the placebo group occurred in patients at low risk of rejection. n = number of subjects experiencing event; N = number of subjects in each group
- auHSCT = autologous hematopoietic stem cell transplant; TVC = total vaccinated cohort, included all participants who received at least 1 dose of study vaccine or placebo

Authors information and disclosures

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- AM, JF, MC and PW are employed by the GSK group of companies. AM, JF and PW hold shares in the GSK group of companies. The authors declare no other financial and non-financial relationships and activities.

References