The Adjuvanted Recombinant Zoster Vaccine (RZV) Confers Long-term Protection Against Herpes Zoster: Interim Results of an Extension Study (ZOSTER-049) of Two Clinical Trials (ZOE-50 and ZOE-70)

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Disclosures

- AH is employed by the GSK group of companies
- CB is a consultant for Aixial (on behalf of GSK); MS, PP are employees, AS is a former employee of the GSK group of companies and declare financial and non-financial relationships and activities; AS also holds GSK stock options or restricted shares; JD-D is board member, scientific research study investigator, advisor or review panel member for the GSK group of companies and MSD; GK is a consultant for Keyrus (on behalf of GSK); JCT and C-J Yu have no real or apparent conflicts of interest to disclose.

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**Background:** herpes zoster (shingles) is caused by varicella zoster virus

Varicella zoster virus (VZV)

VZV latent in ganglia

VZV reactivation due to failed immune control

Acute herpes zoster (HZ)

- unilateral vesicular rash
- severe pain

Complications
- postherpetic neuralgia
- herpes zoster ophthalmicus
- other

Prevention through vaccination

Adjuvanted Recombinant Zoster Vaccine (RZV)

**Antigen** recombinant VZV glycoprotein E

**Adjuvant System** AS01\textsubscript{B}

\textsuperscript{1} Centers for Disease Control and Prevention. MMWR. 2008 May;57(RR-5):1–30.

**AS01\textsubscript{B},** adjuvant system containing 3-O-desacyl-4’-monophosphoryl lipid A (MPL, 50 μg), Quillaja saponaria Molina, fraction 21 (QS-21, 50 μg) and liposome.
Background: ZOE-50 and ZOE-70 parent studies

Vaccination schedule

<table>
<thead>
<tr>
<th>ZOE-50(^1) (NCT01165177) (\geq 50\ YOA)</th>
<th>Randomization 1:1</th>
<th>M0</th>
<th>M2</th>
<th>Mean follow-up period (years ± SD)</th>
<th>Vaccine efficacy against herpes zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=7,698</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>97.2% (93.7–99.0)</td>
</tr>
<tr>
<td>N=7,713</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>ZOE-70(^2) (NCT01165229) (\geq 70\ YOA)</th>
<th>Randomization 1:1</th>
<th>M0</th>
<th>M2</th>
<th>Mean follow-up period (years ± SD)</th>
<th>Vaccine efficacy against herpes zoster</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=6,950</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>89.8% (84.2–93.7)</td>
</tr>
<tr>
<td>N=6,950</td>
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</tbody>
</table>

RZV was efficacious, highly immunogenic, and had a clinically acceptable safety profile


\(\checkmark\) vaccination with RZV/placebo; RZV, adjuvanted recombinant zoster vaccine; YOA, years of age; SD, standard deviation; M, month; N, number of participants. Values in parentheses represent 95% confidence intervals.
**Zoster-049 (NCT02723773):** phase IIIb, open-label, multi-center, long-term FU study

We report interim results of the extension study (Zoster-049) after at least 2 years of follow-up (starting and ending \( \approx 5.1 \) and 7.1 years, respectively, following initial vaccination).

To assess VE, historical control estimates were used, as there was no concurrent placebo/control group.

- **AIM**

Blood sampling; FU, follow-up; N, maximum number of participants; M3, one month post-second RZV dose; Y, year; DLP, data lock point; VE, vaccine efficacy against herpes zoster; mTVC, modified total vaccinated cohort including participants who received both RZV doses and did not develop a confirmed HZ episode for 1 month after second dose in the ZOE-50/70 studies; ATP HI subset, according-to-protocol subset of ZOE-50/70 for humoral immunity persistence; ATP CMI subset, according-to-protocol subset of ZOE-50 for cell-mediated immunity persistence.

- Sample collected only from the HI and CMI subsets.

- DLP set when the last participant had reached 2 years of follow-up. All data in the database up to that time point was included in the analysis.

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**Zoster-049 (NCT02723773):**

- **Start of ZOE-50/70**
  - August 2010

- **End of ZOE-50/70**
  - July 2015

- **Start of Zoster-049**
  - April 2016

- **DLP Y2 analysis**
  - July 2019

**Year 1**

- **Start of ZOE-50/70**
  - August 2010

**Year 2**

- **End of ZOE-50/70**
  - July 2015

**Year 3**

- **Start of Zoster-049**
  - April 2016

**Year 4**

**≥50 years of age (N=7,413)**

- Long-term VE – primary objective: mTVC (N=7,277)
- Long-term VE – secondary objective: mTVC (N=13,881)
- Humoral immune persistence: ATP HI subset (N=813)
- CMI persistence: ATP CMI subset (N=108)

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**≥50 years of age (N=7,413)**

- ≥50 years of age (N=7,413)
- \( \approx 5.1 \) years
- \( \approx 7.1 \) years (data up to 8 years post-vaccination)
Demographic characteristics: are similar across cohorts

- **Modified total vaccinated cohort**
  - Participants, N: 7,277
  - Mean age*, years ± SD: 67.2 ± 9.4
  - Gender, %: 39.3% male, 60.7% female
  - Geographical ancestry, %:
    - White: 76.5%
    - Asian: 18.7%
    - African: 0.9%
    - Other: 4.0%

- **ATP HI subset**
  - Participants, N: 813
  - Mean age*, years ± SD: 66.1 ± 9.0
  - Gender, %: 39.2% male, 60.8% female
  - Geographical ancestry, %:
    - White: 71.5%
    - Asian: 25.4%
    - African: 1.0%
    - Other: 1.9%

- **ATP CMI subset**
  - Participants, N: 108
  - Mean age*, years ± SD: 62.6 ± 8.2
  - Gender, %: 48.1% male, 51.9% female
  - Geographical ancestry, %:
    - White: 69.4%
    - Asian: 28.7%
    - African: 1.9%
    - Other: 1.9%

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ATP HI subset, according-to-protocol subset of ZOE-50/70 for humoral immunity persistence; ATP CMI subset, according-to-protocol subset of ZOE-50 for cell-mediated immunity persistence; White, Caucasian/ European and Arabic/ North African heritages; Asian, Central, East, South East Asian and Japanese heritages. *mean age at first vaccination in ZOE-50/70 trials.
VE against HZ: remained high up to ≈7.1 years (mean) post-vaccination (mTVC)

84.0% (75.9–89.8)

90.9% (88.2–93.2)

*data solely from Zoster-049 study. Values in parentheses depict 95% confidence intervals.

Primary objective

Secondary objective (up to ≈7.1 years [mean FU] post-vaccination)

≈1.1 years
Analysis performed in the pooled ZOE-50/70 and Zoster-049 populations. M3, one month post-second RZV dose. *only data from those participants who reached Year 8 up to the data lock point of this interim analysis.
Humoral immunity: plateau at ≈6-fold above the pre-vaccination level

<table>
<thead>
<tr>
<th>Year</th>
<th>Antigen geometric mean concentration (mIU/mL)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-vaccination</td>
<td>1,320.5</td>
<td>1,455</td>
</tr>
<tr>
<td>Year 1</td>
<td>17,296.9</td>
<td>1,415</td>
</tr>
<tr>
<td>Year 2</td>
<td>13,713.9</td>
<td>1,366</td>
</tr>
<tr>
<td>Year 3</td>
<td>11,524.3</td>
<td>1,301</td>
</tr>
<tr>
<td>Year 4</td>
<td>(No data)</td>
<td></td>
</tr>
<tr>
<td>Year 5</td>
<td>8,053.5</td>
<td>216</td>
</tr>
<tr>
<td>Year 6</td>
<td>8,508.7</td>
<td>806</td>
</tr>
<tr>
<td>Year 7</td>
<td>8,388.9</td>
<td>770</td>
</tr>
<tr>
<td>Year 8</td>
<td>8,538.1</td>
<td>543</td>
</tr>
</tbody>
</table>

Approximately 6-fold increase versus pre-vaccination

1. Cunningham AL, et al. N Engl J Med. 2016;375(11):1019–32. ATP HI subset, according-to-protocol subset for humoral immunity persistence; gE, glycoprotein E; N, number of participants with available results; mIU/mL, milli international unit/milliliter. Error bars depict 95% confidence interval.
gE-specific CD4[2+] T-cells: remained above baseline from Y6 to Y8 after vaccination

1. Cunningham AL, et al. *N Engl J Med*. 2016;375(11):1019–32. **ATP CMI subset**, according-to-protocol subset for cell-mediated immunity persistence; **gE**, glycoprotein E; **Min**, minimum; **Q1,Q3**, quartile 1 and 3; **Max**, maximum. Maximum value at Year 1 is 6018.8; **CD4[2+]**, T-cells expressing ≥2 markers of the 4 assessed (interferon gamma, interleukin-2, tumour necrosis factor alpha, CD40 ligand). The frequency of gE-specific CD4[2+] T-cells was assessed per 10⁶ total CD4 T-cells. *Year 5 CMI results not shown because of insufficient samples (i.e. 3) for the analysis.*

![Bar chart showing frequency of gE-specific CD4[2+] T-cells from pre-vaccination to Year 8.](chart)
Safety profile: remains clinically acceptable and no safety signal was identified

- Serious adverse events (SAEs) were consistent with the aging population of the study
- No deaths or other SAE were considered as causally-related to vaccination
- Two participants with a confirmed HZ case reported HZ-related complication
  - 1 participant experienced postherpetic neuralgia
  - 1 participant experienced disseminated HZ disease (>1 dermatome affected)

Safety was assessed in the total vaccinated cohort, that included all participants from the ZOE-50 and ZOE-70 studies who were enrolled in the Zoster-049 extension study.
Conclusions

- RZV demonstrated high (84.0%) efficacy against herpes zoster over approximately 2 years of follow-up in Zoster-049 study

- Vaccine efficacy was 84.1% at Year 8 following initial vaccination (end of observation period for the year 2 interim analysis of Zoster-049 study)

- Both humoral and cellular immune responses remained high and consistent from Year 5 until Year 8

- No safety signal was identified from Zoster-049 study start up to data lock point for this interim analysis
Key messages

- RZV remains efficacious against herpes zoster up to 7.1 years (mean) post-initial vaccination in adults ≥50 years of age
- Humoral and cell-mediated immune responses persist up to 8 years post-vaccination
- RZV is able to confer long-lasting protection
- This extension study further supports the benefit of RZV vaccination
Thank you