Is there a correlation between reactogenicity and immune responses of the adjuvanted recombinant zoster vaccine (RZV)? A post-hoc analysis

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Background

Varicella-zoster virus glycoprotein E (gE)
Adjuvant system (AS01)_
- enhances immune responses to gE
- may contribute to development of transient local or general post-vaccination reactions

Recombinant zoster vaccine (RZV)

Is the magnitude of transient local or systemic post-vaccination reactions predictive of immunogenicity and efficacy?

Reactogenicity scores calculation

Score for each symptom (maximum grade recorded over 7 days post-vaccination - univariate reactogenicity models)
Global score (sum of each maximum severity for all reported symptoms - multivariate reactogenicity models)

Multivariate (random effect) regression model adjusted for covariates - used for estimating the association between RZV’s reactogenicity and immunogenicity

Methods

Post-hoc analysis using data from the ZOE-50 (NCT01165177) and ZOE-70 (NCT01165229) phase 3 clinical trials. The immuno/reacto subset included adults ≥50 YOA vaccinated with 2 RZV doses at 2 months interval.

Results

Injection site pain was the most frequently reported symptom in the immuno/reacto subset (69% of vaccinees post-dose 1 and 63% post-dose 2). The global score of reactogenicity post-dose 2 was significantly associated with humoral immune responses (although the absolute antibody increase was minimal), while the association with cell-mediated immune responses was not statistically significant.

Global score increase by 1
Humoral immune responses
1.29-fold increase
Estimated size effect (95% CI)
-0.041 (-0.114; 0.042)
p-value
0.316

Cell-mediated immune responses
1.7-fold increase
Estimated size effect (95% CI)
-0.097 (-0.242; 0.430)
p-value
0.316

Maximum global score
post-dose 1
post-dose 2

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>Humoral immune responses</th>
<th>Cell-mediated immune responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>Median 4.70 4.72 4.73 4.74</td>
<td>Median 4.20 4.26 4.35 4.28</td>
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<tr>
<td>12 months</td>
<td>Median 4.80 4.87 4.92 4.88</td>
<td>Median 4.97 4.94 5.02 4.96</td>
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<tr>
<td>24 months</td>
<td>Median 4.18 4.21 4.21 4.14</td>
<td>Median 4.47 4.47 4.58 4.46</td>
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<tr>
<td>36 months</td>
<td>Median 4.05 4.09 4.09 4.07</td>
<td>Median 4.36 4.36 4.40 4.36</td>
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</tbody>
</table>

Pain score increase by 1
Humoral immune responses
1.1-fold increase
Estimated size effect (95% CI)
0.041 (0.016; 0.065)
p-value
0.001

Cell-mediated immune responses
1.16-fold increase
Estimated size effect (95% CI)
0.065 (-0.067; 0.201)
p-value
0.316

Maximum pain score
post-dose 2

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Conclusions

Participants with and without injection site pain developed similar levels of both humoral and cell-mediated immune responses.
There was a statistically significant correlation between injection site pain and humoral immune responses in those who had pain although this was of low magnitude and likely of no clinical significance.
The presence or magnitude of injection site pain is not generally predictive of immunogenicity.

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Affiliations, Disclosure, References: available via the QR code

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ELISA, enzyme linked immunosorbent assay; Q1/Q3, inter-quartile range