

How does frailty impact the efficacy, reactogenicity, immunogenicity and safety of the adjuvanted recombinant zoster vaccine?

A secondary analysis of the ZOE-50 and ZOE-70 studies

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BACKGROUND AND OBJECTIVES

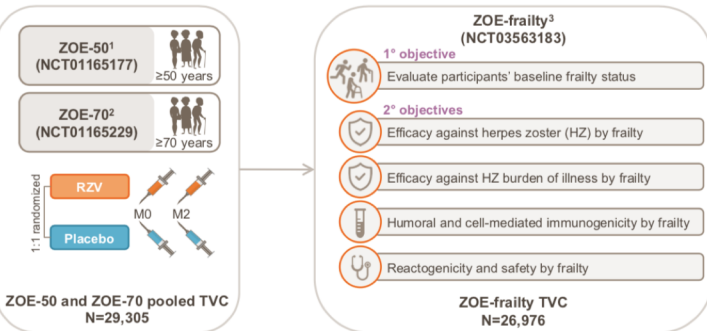
Frail older adults are more vulnerable to herpes zoster's negative impact on health and quality of life

ZOE-50 and ZOE-70 randomized controlled trials showed high efficacy of adjuvanted recombinant zoster vaccine (RZV) in older adults



Our aim: Retrospective evaluation of frailty in ZOE-50/70 participants based on collected health status data and patient reported outcomes

Some treatments and vaccines are less effective in frail older adults



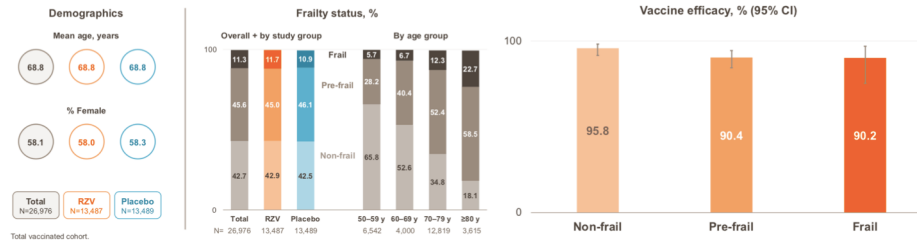
We retrospectively evaluated frailty in ZOE-50/70 participants. TVC = Total Vaccinate Cohort; M = month

METHODS: Measures

- Vaccine efficacy:** $VE = (1 - \frac{\text{herpes zoster incidence in RZV group}}{\text{herpes zoster incidence in placebo group}}) \times 100$
- Humoral immunogenicity:** anti-glycoprotein E (gE) ELISA
- Cell-mediated immunogenicity:** flow cytometry → frequencies of CD4+ T cells expressing ≥2 activation markers (IFN-γ, IL-2, TNF-α, CD40 ligand) after ex vivo stimulation with gE
- Reactogenicity:** solicited AEs in random subset (7 days after each dose)
- Safety:** unsolicited AEs (30 days after each dose), unsolicited AEs with medically attended visit (8 months post-dose 1), SAEs (14 months post-dose 1), deaths and pIMDs (entire study)

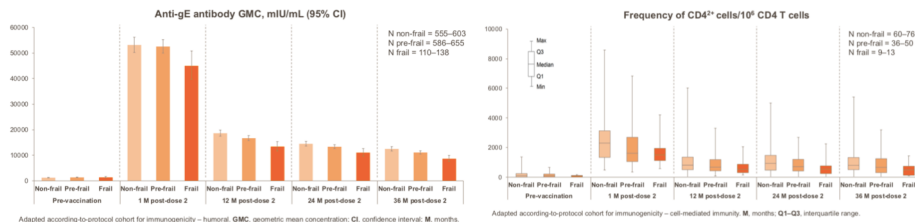
RESULTS: DEMOGRAPHICS, FRAILTY AND VE

Demographics and frailty were balanced between RZV and placebo groups and frailty increased with age. Vaccine efficacy against herpes zoster was >90% across frailty categories.

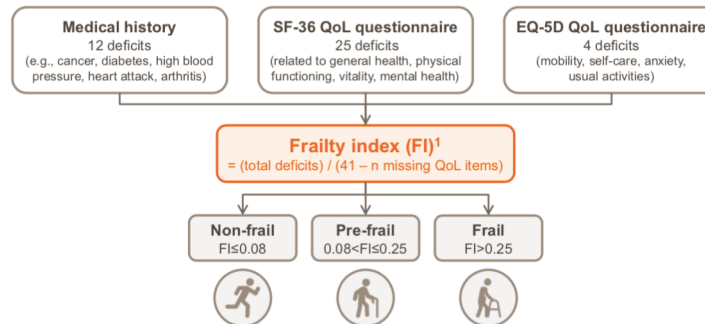


RESULTS: IMMUNOGENICITY

RZV induced robust, persistent anti-gE antibody and gE-specific CD42+ responses across frailty categories.

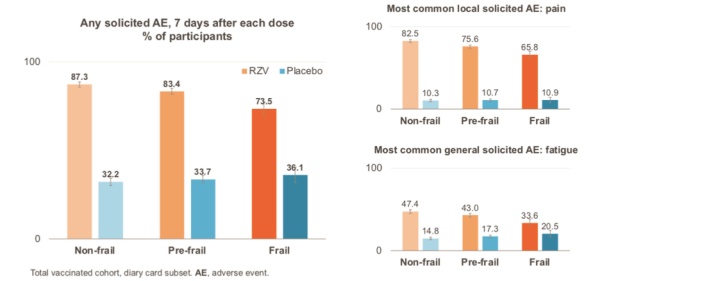


METHODS: Determination of Frailty Index and categories



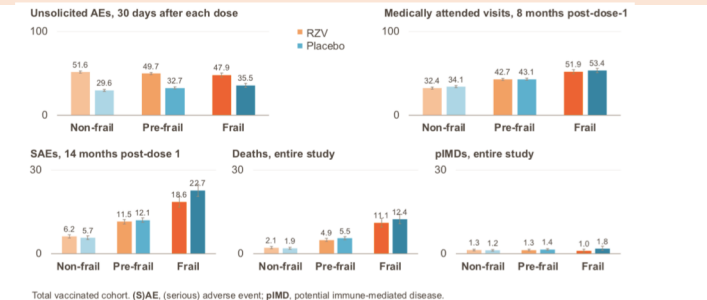
RESULTS: REACTOGENICITY

Reactogenicity decreased with increasing frailty in RZV recipients



RESULTS: SAFETY

Unsolicited medically attended visits and serious adverse events increased with frailty and were balanced between placebo and RZV groups.



CONCLUSIONS

- The relatively nonrestrictive in/exclusion criteria in the parent ZOE studies resulted in a range of participants that included frail and pre-frail older adults.
- Vaccine efficacy was high (>90%) across frailty subgroups. Immunogenicity was robust and there was no safety signal in relation to frailty.
- RZV significantly reduces the risk of herpes zoster and is safe to use across the spectrum of frailty.**
- A frailty index was readily calculated based on data sometimes collected in randomized trials for vaccines and other interventions. Frailty could thus be considered retrospectively in other studies even where a frailty measure was not included up front.

SF-36, Short Form-36; EQ-5D, EuroQol-5D; QoL, quality of life. 1. Curran et al. Hum Vaccin Immunother 2019;15:2960-8.

