

Effect of Recombinant Zoster Vaccine on Incident Dementia Diagnosis in Adults Aged ≥ 76 Years in Finland: Trial Protocol

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Background

- There is evidence of an association between **herpes zoster (HZ) and an increased risk of dementia**^{1,2}, and between **vaccination** against HZ and **a reduced risk of dementia**.²⁻⁵
- However, evidence is limited to retrospective observational designs that prevent the ability to infer causality.
- Finland provides a unique opportunity to gather more robust evidence by conducting a **large pragmatic randomised controlled trial** because:
 - **HZ vaccination** is not currently part of the national immunisation program
 - Existing community-based health clinics facilitate **vaccination delivery**
 - Nationwide, population-based health and social registers enable **comprehensive, passive, and long-term follow-up of dementia** with little loss to follow-up^{6,7}

Implications

This trial provides an opportunity for **timely, high-quality and robust evidence generation** on the effect of RZV on the rate of incident dementia diagnosis.

Findings could have major implications for **further targeted research** and for **public health** in Finland and worldwide.

Objectives

PRIMARY OBJECTIVE

To assess the effect of RZV on the rate of **incident dementia diagnosis** among adults aged ≥ 76 years, compared to placebo

SECONDARY OBJECTIVE

To assess the effect of RZV on the rate of **incident Alzheimer's disease (AD) diagnosis** among adults aged ≥ 76 years, compared to placebo

PRIMARY ENDPOINT

Incident dementia
diagnosis post-first dose
of RZV or placebo

SECONDARY ENDPOINT

Incident AD diagnosis
post-first dose of RZV or
placebo

See QR code for operational definitions for all objectives

Eligibility Criteria

 Inclusion criteria:

- Consenting citizens living permanently in Finland and aged ≥ 76 years at enrolment

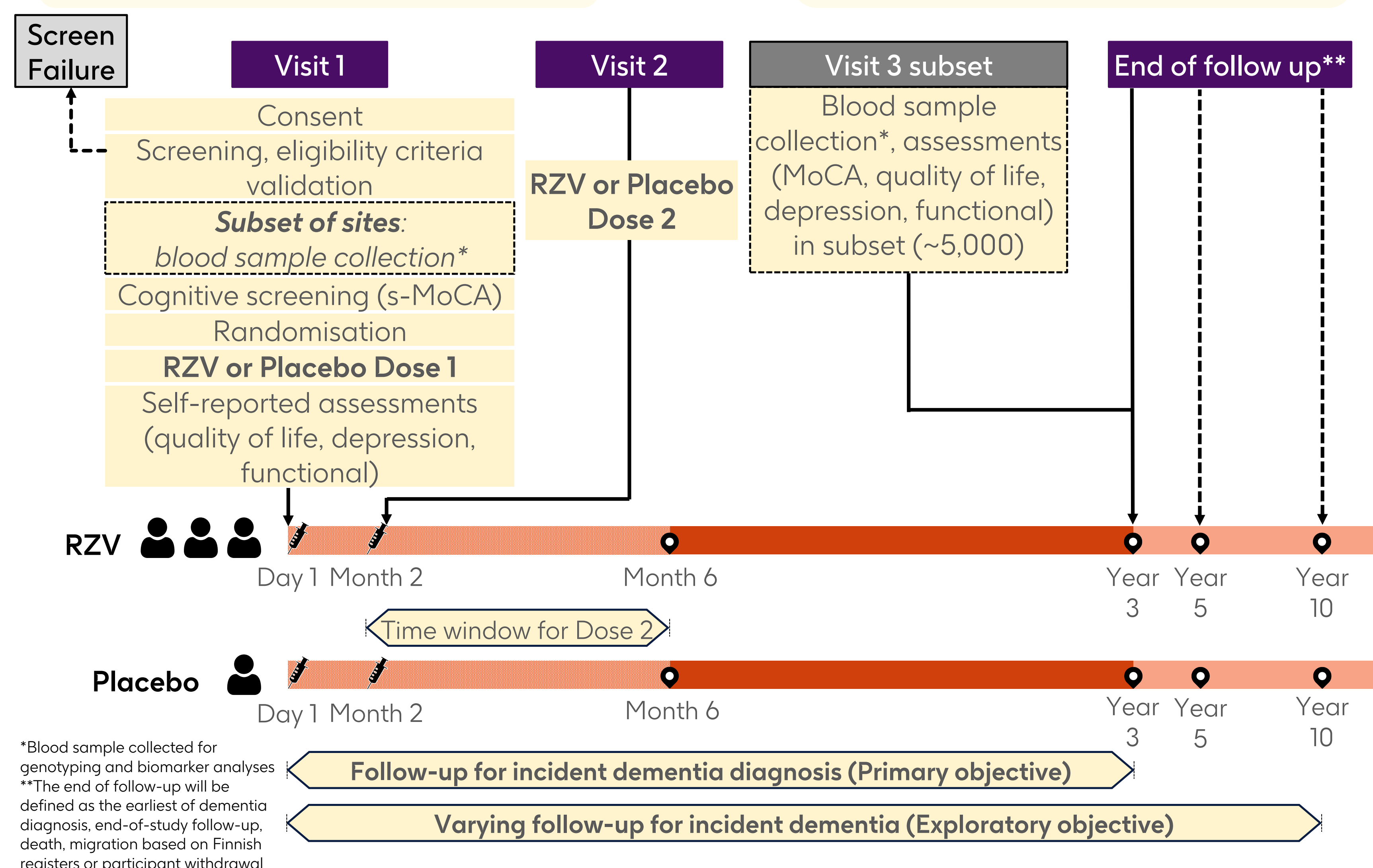
 Exclusion criteria:

- ▶ No prior **shingles vaccination**
- ▶ No prior **dementia diagnosis** or ongoing investigation for dementia
- ▶ No **severely immunocompromising conditions**
- ▶ Not concurrently participating in **another clinical trial**
- ▶ No known systemic **hypersensitivity to RZV components**
- ▶ Not living in **nursing facility**

Study Design

- Trial size: 33,609 participants
- Enrolment initiated: 31 March 2026
- Interventional, Phase IV
- Observer-blind
- Randomised: RZV vs Placebo (3:1)
- 2 doses within 2-6 months per RZV SmPC

- Passive follow-up for clinical endpoints via comprehensive & linkable Finnish health & social care registers
- Primary read-out trigger (n=1,614 dementia cases & ≥3 years average follow-up)



*Blood sample collected for genotyping and biomarker analyses
**The end of follow-up will be defined as the earliest of dementia diagnosis, end-of-study follow-up, death, migration based on Finnish registers or participant withdrawal

Abbreviations

AD: Alzheimer's disease; FVR: Finnish Vaccine Research; HZ: herpes zoster; s-MoCA: short Montreal Cognitive Assessment; RZV: recombinant zoster vaccine; SmPC: Shingrix summary of product characteristics

References

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