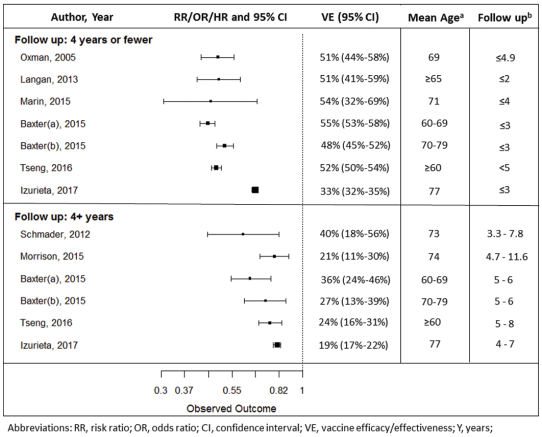
immunocompetent recipients ≤ 60 years old. Selected articles were abstracted, independently reviewed, and discrepancies adjudicated. We attempted to locate relevant unpublished work and contacted authors for additional data, where necessary. Measures of association were illustrated on a forest plot and converted to VE (1-hazard ratio or risk ratio or odds ratio).

Results. We screened 1302 articles; 17 underwent full text review and 8 met inclusion criteria and were abstracted for this review. Selected studies included 1 phase III randomized controlled trial, 2 quasi experimental and 5 observational studies. One experimental and 5 observational studies estimated VE during the period from vaccination up to 4 years following vaccination; estimates across studies ranged from 33%-55%. Two quasi experimental and 3 observational studies estimated VE for ≥ 4 years following vaccination; estimates ranged from 19%-40%; the median estimate was 24% (Figure). Pooled VE was not calculated due to heterogeneity in length of follow up, age distribution of study subjects, as well as adjustment for factors such as underlying medical conditions.

Conclusion. Most experimental and observational studies estimate VE just above 50% during the 3 years following receipt of ZVL. Beyond 3 years, ZVL protection wanes, with most studies estimating a VE of ≤24% after 4 years. Information on overall efficacy and duration of protection from ZVL will guide policy decisions regarding its use.

Figure. Comparative VE of ZVL (Zostavax) for the prevention of herpes zoster, by length of follow-up time post-vaccination



Abbreviations: RR, risk ratio; OR, odds ratio; CI, confidence interval; VE, vaccine efficacy/effectiveness; Y, years;
[a]Mean age reported in years. If mean age was not available, age range for study participants was reported.
[b]Length of study follow-up period post ZVL vaccination in years.

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1338. Assessment of the Potential Herpes Zoster and Post Herpetic Neuralgia Case Avoidance with Vaccination in the United States

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Background. Herpes zoster (HZ), commonly referred to as shingles, is a reactivation of latent varicella zoster virus in patients previously infected. Clinical characteristics of HZ include painful rash with potential complications, including post herpetic neuralgia (PHN). Care for HZ and PHN incurs significant costs and vaccination is beneficial. The aim of this study was to compare the impact on HZ and PHN case avoidance of two HZ vaccines, an available live-attenuated zoster vaccine (zoster vaccine live [ZVL]) vs. a candidate non-live adjuvanted HZ subunit vaccine (HZ/su), in the US population.

Methods. A Markov model called ZONA (ZOster ecoNomic Analyses) was developed following two age cohorts (≥60 years to represent the current ACIP recommendation and ≥65 years to represent the Medicare population) over their lifetimes from the year of vaccination. Demographic data were obtained from the US Census, whereas HZ incidence and the proportion of HZ individuals developing PHN were derived from published US-specific sources. Age-specific vaccine efficacy and waning rates were based on published clinical trial data. Vaccine coverage for both vaccines was assumed to be 30.6% and 34.2% in the two age cohorts, respectively, based on CDC data; compliance of the second dose of the HZ/su vaccine was 69%, based on data from clinical trials and Hepatitis B seconddose completion. Sensitivity analyses demonstrated robustness of the base analysis findings.

Results. In the US, for cohorts of 66.83 million (M) persons aged 60+ and 47.76M aged 65+ it was estimated that the HZ/su vaccine would reduce the number of HZ cases by 2.12M and 1.55M in the two age cohorts, respectively, compared with 0.65M and 0.45M using the ZVL. Furthermore, the HZ/su vaccine would reduce the number of PHN cases by 0.23M and 0.18M in the two age cohorts, respectively, compared with 0.10M and 0.09 using the ZVL. The number needed to vaccinate to prevent one HZ case were 10 and 11, in the respective cohorts, using the HZ/su vaccine compared with 31 and 37, in the respective cohorts, using the ZVL.

Conclusion. Due to higher and sustained vaccine efficacy, the candidate HZ/su vaccine demonstrated superior public health impact in the US compared with the currently available ZVL.

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1339. Effectiveness of Live Zoster Vaccine in Preventing Herpes Zoster Ophthalmicus (HZO)

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Background. Herpes zoster ophthalmicus (HZO), caused by reactivation of varicella-zoster virus in or around the eye, can be severe and often results in care-seeking that may be less discretionary than for uncomplicated herpes zoster (HZ). We compared the vaccine effectiveness (VE) of live zoster vaccine against HZO with the VE against HZ overall.

Methods. Kaiser Permanente Northern California (KPNC) members enter the ongoing cohort study when age-eligible for zoster vaccine starting in 2007. Incident HZ was defined as a new diagnosis of HZ with an antiviral prescription or a positive varicella viral test. Among those, an HZO case was defined as having an HZO diagnosis during an ophthalmology visit within 30 days of the initial HZ diagnosis. VE by age at vaccination and time since vaccination was estimated using Cox regression adjusted for age, race, sex and time-varying measures of healthcare use, comorbidities and immunocompromise status. Average VE over the first 5 years following vaccination was calculated as a weighted average of annual VE estimates.

Results. During 2007–2014, ~1.3 million individuals ≥50 years of age entered the study population and 29% were vaccinated. Among 48,889 incident HZ cases, 2,858 (6%) had HZO, 87% of whom were unvaccinated. For all ages combined, VE against HZO was 72% (95% CI, 64%-79%) in year 1, similar to 68% (95% CI, 65%-70%) against HZ. VE fell in years 2, 3, 4, and 5 to 47%, 45%, 42% and 27% for HZO and to 47%, 39%, 41% and 37% for HZ. For age groups 60 – 69 and 70 – 79, where we have the most data, initial VE and waning were similar for HZO and HZ. Numbers of HZO cases for 50–59 year olds were too small to evaluate at this time. Average VE against HZO over the first 5 years following vaccination was 52% (95% CI, 42%–60%) for ages 60–69, 51% (95% CI, 39%–61%) for ages 70-79, and 39% (95% CI, 14%-57%) for ages 80+; similarly, 5-year average VE against HZ was 49%, 46%, and 44% for these 3 age groups.

Conclusion. VE against HZO was similar to VE against HZ regardless of age at vaccination or time since vaccination. Effectiveness of live zoster vaccine in preventing HZO was highest in year one with subsequent waning.

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1340. Immune Senescence Factors Associated with the Immunogenicity of a Live Attenuated Zoster Vaccine (ZV) in Older Adults

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Background. ZV confers protection against herpes zoster by increasing the cell-mediated immunity (CMI) to varicella-zoster virus (VZV). ZV immunogenicity and protection decrease with increasing age. We investigated effects of age and immune senescence on ZV immunogenicity.

Methods. 399 adults ≥50 years had VZV T-cell helper 1 (Th1) CMI measured by ex vivo VZV-stimulated IL2/IFNg ELISPOT and blood T-cell nonspecific immune senescence by flow cytometric characterization of FOXP3, CD25, IL10, TGFb, PD1, CD28, CD57 and CD31 expression before and at 1, 6 and 52 weeks after ZV. In a subset of 95 vaccinees, VZV-stimulated T cell expression of CD107, Granzyme B, FOXP3, CD25, IL10, TGFb, CD39 and PD1 were also measured. Multivariate regression analysis was used to identify independent effects of age and immune senescence on VZV Th1 CMI ($P < 0.025$).

Results. IL2+ and IL2+IFNg+ Th1 *memory* VZV CMI peaked at 6 weeks after ZV and remained elevated at 1 year. *Effectors*, including VZV-specific IFNg+ Th1, and CD8+CD107+% and CD4+/CD8+Granzyme B+% cytotoxic T lymphocytes (CTL), peaked at 1 week, but only the IFNg+ Th1 effectors remained elevated at 1 year. There was also a transient increase in blood CD8+PD1+% exhausted T cells 1

week after ZV. Independent positive effects on peak *memory* Th1 VZV CMI included the baseline CMI and negative effects included blood CD4+FOXP3+% T regulatory (Treg) and CD8+PD1+% T exhausted cells. Independent positive effects on peak *effector* Th1 VZV CMI included baseline CMI and negative effects included blood CD8+CD25+FOXP3+% Treg. Age did not have an independent effect on peak CMI. Independent positive effects on persistent (1 year) *memory* Th1 included baseline CMI and negative effects included age, blood CD4+FOXP3+% Treg and CD8+PD1+% T exhausted cells. Persistent *effector* Th1 CMI was negatively affected by age only.

Conclusion. ZV generated VZV-specific Th1 and CTL responses. The early increase of CD8+ exhausted T cells in blood suggested that CTL responses to the vaccine virus may be compromised by immune senescence. The negative of age on VZV Th1 CMI was fully mediated by immune senescence at peak response, but age had a negative effect on CMI persistence that was independent from the markers of immune senescence included in this study.

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1341. Humoral and Cellular Immunogenicity of Zoster Vaccine within One Year after Herpes Zoster

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Background. Herpes zoster vaccination is recommended to patients with a prior history of herpes zoster to prevent reactivation. However, the appropriate timing of vaccination is controversial. We compared immunogenicity of vaccine according to timing of vaccination after zoster illness.

Methods. In this prospective observational study, subjects were stratified into two groups by the vaccination timing since their zoster illness: 6–12 months (within-1 year group) vs. 1–5 years (after-1 year group). Blood samples were collected before and 6 weeks after vaccination of zoster vaccine live. Varicella-zoster virus (VZV)-specific IgG concentrations were measured by enzyme-linked immunosorbent assay. Interferon-gamma enzyme-linked immunosorbent spot (ELISPOT) assays were performed to assess VZV specific T-cell responses.

Results. A total of 59 patients (18 in the within-1 year group and 41 in the after-1 year group) were enrolled. Ages were not significantly different between groups. The baseline geometric mean titer (GMT) of VZV IgG was higher in the within-1 year group than in the after-1 year group (245.8 IU/mL vs. 124.9 IU/mL; P = 0.040). The geometric mean fold-rise (GMFR) of VZV IgG was lower in the within-1 year group than in the after-1 year group (1.42 vs. 2.46; P = 0.002). The GMT of spot forming cell (SFC) counts by ELISPOT at baseline and 6 weeks after vaccination were not significantly different between groups. The GMFRs of SFCs were also comparable.

Conclusion. Zoster vaccination within 1 year after zoster illness may have disadvantage in the aspect of humoral immune response (ClinicalTrials.gov number, NCT02704572).

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1342. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Vaccine in Older Adults Previously Vaccinated with a Live-Attenuated Herpes Zoster Vaccine: A Phase III, Group-Matched, Clinical Trial

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Background. Herpes zoster (HZ), caused by reactivation of varicella-zoster virus (VZV), typically manifests as a dermatomal rash and can lead to postherpetic neuralgia (PHN). HZ and PHN risk increase with age. Efficacy against HZ induced by a live-attenuated zoster vaccine (ZVL; Merck) declines following vaccination (21% in years 5–12 post-vaccination). To ensure protection, revaccination can be considered. Therefore, we assessed immunogenicity and safety of HZ/su, a non-live candidate vaccine containing VZV glycoprotein E (gE) subunit and $AS01_B$ adjuvant system (GSK), in adults previously vaccinated with ZVL ≥5 years before, (HZ-PreVac) compared with adults not vaccinated with ZVL (HZ-NonVac).

Methods. In this phase III, group-matched, open, multicenter study (NCT02581410), 2 parallel groups of adults ≥65 years of age (YOA) received 2 HZ/su doses 2 months apart. A co-primary objective was to compare humoral immune responses 1 month post-dose 2 (M3) in the 2 groups (non-inferiority criterion: upper limit [UL] of the 95% confidence interval [CI] for HZ-NonVac/HZ-PreVac adjusted anti-gE antibody geometric mean concentration [GMC] ratio <1.5). Humoral and cellular immune responses were evaluated at various time points. Solicited and unsolicited adverse events (AEs) were recorded for 7 and 30 days post each dose, respectively. Serious AEs (SAEs), HZ cases and potential immune-mediated diseases (pIMDs) will be recorded until study end. Here, we present data up to M3, as the study is still ongoing.

Results. 430 participants were vaccinated. M3 humoral immune responses in HZ-PreVac were non-inferior to those in HZ-NonVac and the co-primary objective was met as the UL of the 95% CI of the adjusted GMC ratio was 1.17 (Table 1). In addition, there were no apparent differences in CD4[2+] T-cell frequencies between groups (Figure 1). No clinically meaningful differences between frequencies of solicited AEs, unsolicited AEs or SAEs in the 2 groups were observed (Table 2). No SAEs considered vaccine-related by investigators, no suspected HZ cases and no pIMDs were reported up to M3.

Conclusion. HZ/su vaccination in adults ≥65 YOA who previously received ZVL stimulates strong immune responses and does not raise safety concerns.

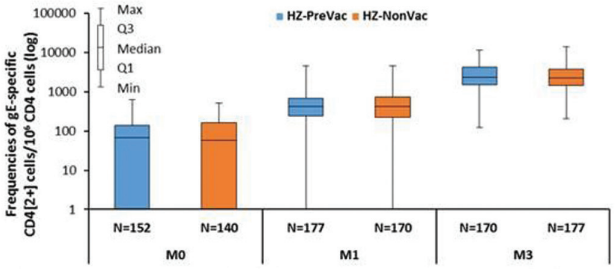
Funding. GlaxoSmithKline Biologicals SA

Table 1. Anti-gE antibody geometric mean concentrations (GMCs) and adjusted GMC ratio (HZ-NonVac over HZ-PreVac) (ATP cohort for immunogenicity)

	Timepoint	HZ-PreVac		HZ-NonVac		Adjusted GMC ratio (HZ-NonVac/HZ-PreVac)
		N	Value	N	Value	
GMC, mIU/mL (95% CI)	M0	204	1784.3 (1572.9–2024.1)	202	1408.5 (1203.3–1648.8)	
	M1	204	29959.0 (26633.6–33699.6)	202	25233.7 (22072.3–28848.0)	
	M3	204	49327.2 (45388.2–53608.1)	204	51618.5 (47224.8–56420.9)	
Adjusted* GMC, mIU/mL (95% CI)	M3	204	48589.4 (42649.4–55356.6)	204	50522.9 (44347.4–57558.4)	1.04 (0.92–1.17#)

gE, glycoprotein E; **ATP**, according-to-protocol; **HZ-PreVac**, participants ≥65 years of age (YOA) vaccinated with a live-attenuated zoster vaccine (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with available results; **CI**, confidence interval; **M0**, month 0, pre-vaccination; **M1**, month 1, 1 month post-dose 1; **M3**, month 3, 1 month post-dose 2; **IU**, international unit; **#**, co-primary objective was met (upper limit of the 95% CI for GMC ratio =1.17 [pre-defined criteria: <1.5]); *****, adjusted for group-matching variable.

Figure 1. Descriptive statistics of the frequency of gE-specific CD4[2+] T-cells (ATP cohort for immunogenicity)



gE, glycoprotein E; **ATP**, according-to-protocol; **CD4[2+]**, CD4+ T-cells expressing at least 2 activation markers (IFN-γ, IL-2, TNF-α, CD40L); **HZ-PreVac**, participants ≥65 years of age (YOA) vaccinated with a live-attenuated zoster vaccine (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with available results; **Min/Max**, minimum/maximum; **Q1**, Quartile 1 (25th percentile); **Q3**, Quartile 3 (75th percentile); **M0**, month 0, pre-vaccination; **M1**, month 1, 1 month post-dose 1; **M3**, month 3, 1 month post-dose 2.

Table 2. Frequencies of solicited and unsolicited AEs, SAEs and pIMDs (TVC)

AE		Reporting Period	HZ-PreVac		HZ-NonVac	
			N	n (% [95% CI])	N	n (% [95% CI])
Solicited Local AE	Pain	D 0–6	215	189 (**87.9** [82.8–91.9])	214	181 (**84.6** [79.0–89.1])
	Redness		215	96 (**44.7** [37.9–51.6])	214	73 (**34.1** [27.8–40.9])
	Swelling		215	50 (**23.3** [17.8–29.5])	214	37 (**17.3** [12.5–23.0])
Solicited General AE	Fatigue		215	114 (**53.0** [46.1–59.8])	214	111 (**51.9** [45.0–58.7])
	GS		215	49 (**22.8** [17.4–29.0])	214	38 (**17.8** [12.9–23.5])
	Headache		215	78 (**36.3** [29.8–43.1])	214	89 (**41.6** [34.9–48.5])
	Myalgia		215	81 (**37.7** [31.2–44.5])	214	77 (**36.0** [29.6–42.8])
	Shivering		215	51 (**23.7** [18.2–30.0])	214	37 (**17.3** [12.5–23.0])
	Fever		215	36 (**16.7** [12.0–22.4])	214	32 (**15.0** [10.5–20.4])
Unsolicited AE		D 0–29	215	78 (**36.3** [29.8–43.1])	215	52 (**24.2** [18.6–30.5])
SAE	All	From dose 1, up to 30 D post-dose 2*	215	4 (**1.9** [0.5–4.7])	215	4 (**1.9** [0.5–4.7])
	Related		215	0 (**0.0**)	215	0 (**0.0**)
pIMD			215	0 (**0.0**)	215	0 (**0.0**)

AE, adverse event; **SAE**, serious AE; **pIMD**, potential immune-mediated disease; **TVC**, total vaccinated cohort; **HZ-PreVac**, participants ≥65 years of age (YOA) vaccinated with a live-attenuated zoster vaccine (ZVL) ≥5 years earlier; **HZ-NonVac**, participants ≥65 YOA not previously vaccinated with ZVL; **N**, number of participants with a least one documented (solicited AEs) or administered (unsolicited AEs, SAEs, pIMDs) dose; **n/%**, number/percentage of participants reporting the AE at least once; **95% CI**, exact 95% confidence interval; **GS**, gastrointestinal symptoms; **Fever**, temperature ≥ 37.5°C for oral, axillary or tympanic route, or ≥ 38.0°C for rectal route; **D**, day; **D 0–6**, 7 days post each dose; **D 0–29**, 30 days post each dose; **Related**, AEs assessed by the investigator to be casually related to vaccination; **AEs** are presented as overall/participant; *****, SAEs and pIMDs will be recorded until study end.

Disclosures. **K. Grupping**, GSK group of companies: Employee, Salary; **L. Campora**, GSK group of companies: Employee, Salary; **M. Douha**, GSK group of companies: Employee, Salary; **T. C. Heineman**, GSK group of companies: Consultant and Shareholder, Consulting fee; **N. P. Klein**, GSK group of companies: Investigator, Grant recipient sanofi pasteur: Investigator, Grant recipient; Merck & Co: Investigator, Grant recipient; MedImmune: Investigator, Grant recipient; Protein Science: Investigator, Grant recipient; Pfizer: Investigator, Grant recipient; **H. Lal**, Pfizer: Employee and Shareholder, Salary and Stock as part of compensation; GSK group of companies: Employee at the time of study and Shareholder, Salary and Stock as part of compensation; **J. Peterson**, GSK group of companies: Investigator, Principal investigator fees; **L. Oostvogels**, GSK group of companies: Employee and Shareholder, Salary and Shares