

Vaccine Efficacy After One Dose of *Shingrix* in Adults ≥ 50 years of Age.

This information is provided in response to your request for information about Shingrix® (Zoster Vaccine Recombinant, Adjuvanted).

SUMMARY

- *Shingrix* is a 2-dose vaccine. No clinical studies have been conducted to assess the vaccine efficacy (VE) of 1 dose of *Shingrix*.
- Exploratory, post-hoc analyses, without *a priori* sample size calculations of 1-dose VE were conducted using data from 2 large randomized, placebo-controlled, phase III studies that were designed to assess the efficacy and safety of 2 doses of *Shingrix* in adults ≥ 50 years of age (N = 15,365) and ≥ 70 years of age (N = 17,531; pooled data from both studies).
- VE [95% confidence interval (CI)] of 1 dose of *Shingrix* in adults ≥ 50 years of age and ≥ 70 years of age (data from the pooled analysis from both studies) was 90.8% (62.1-99.00%) and 69.5% (24.9-89.1%) respectively.
- Major limitations of the 1-dose VE analyses which may impact the usefulness of this data in clinical decision making are: 1) the phase III trials were neither designed nor powered to evaluate 1-dose efficacy and 2) as $>95\%$ of the subjects went on to complete the second dose, the mean follow-up time for subjects that received 1 dose was short. The mean follow-up time for 1-dose VE across all study groups was < 90 days.
- In the 2 phase III studies, after 2 doses, solicited adverse events were more frequently reported in the groups that received *Shingrix* than in the placebo groups. Pain was the most frequently reported local reaction, fatigue and myalgia were the most reported general adverse events. Most reactions were transient and mild to moderate in intensity.
- *Shingrix* is not approved to be administered as one dose.
- Important safety information is found in the attached Prescribing Information.

BACKGROUND

Shingrix (HZ/su) is a 2-dose vaccine. No clinical studies have been conducted to assess the VE of 1 dose of *Shingrix*.

Two large randomized, observer-blind, placebo-controlled, multi-center, multinational, phase III studies were conducted to assess the efficacy and safety of 2 doses of *Shingrix* compared to placebo when administered intramuscularly according to a 0 and 2-month schedule in immunocompetent adults without prior history of herpes zoster and without prior varicella or herpes zoster vaccination. One study (ZOE-50 study)⁽¹⁾ included adults ≥ 50 years of age [N = 7698 (HZ/su group) and N = 7713 (placebo group)], the second study (ZOE-70 study)⁽²⁾ included adults ≥ 70 years of age [N = 6950 (HZ/su group) and N = 6950 (placebo group)]. In addition, data from participants ≥ 70 years of age from both studies were pooled to re-estimate vaccine efficacy (VE) in reducing the risk of HZ in a larger population as defined in the study protocol [N = 8758 (HZ/su group) and N = 8773 (placebo group)].⁽²⁾

In the 2 phase III studies, after 2 doses, solicited adverse events were more frequently reported in the groups that received *Shingrix* than in the placebo groups. Pain was the most frequently reported local

reaction, fatigue and myalgia were the most reported general adverse events. Most reactions were transient and mild to moderate in intensity.^(1,2)

ONE DOSE VACCINE EFFICACY

Exploratory, post-hoc analyses, without *a priori* sample size calculations on 1 dose VE were conducted on data from the ZOE phase III efficacy studies. The analyses included both the subjects who went on to receive dose 2 (>95% of subjects), as well as those subjects who only received dose 1.

One-dose VE in the ≥ 50 years of age (ZOE-50 study) and ≥ 70 years of age (ZOE-50-ZOE-70 pooled analysis) cohorts are presented in Table 1. VE (95% CI) of 1 dose of *Shingrix* in adults ≥ 50 years of age and ≥ 70 years of age was 90.8% (62.1-99.0%) and 69.5% (24.9-89.1%) respectively.

The following caveats and limitations, which may impact the usefulness of this data in clinical decision making, should be taken into account when interpreting these data:

- Based on phase II immunogenicity studies that confirmed the necessity of 2 doses⁽³⁾, Phase III studies were designed to solely evaluate a 2-dose series.
- In the phase III ZOE efficacy trials, exploratory, post-hoc analyses without *a priori* sample size calculations on 1 dose vaccine efficacy were conducted. The analysis included available data within the observation window of 1 dose (i.e. the 2-month time window between dose 1 and dose 2 as mandated in the study protocols) from those subjects who went on to complete dose 2 (> 95% of subjects), as well as subjects who did not receive dose 2.
- Published results from the 2 phase III studies demonstrated that > 95% of subjects received 2 doses, thus limiting the number of subjects receiving only 1 dose that could be followed over a substantial period of time.^(1,2)
- As a consequence of these two factors, the mean follow-up time for 1-dose VE across all study groups was short (< 90 days).⁽⁴⁾

Table 1. Efficacy of One Dose of *Shingrix*. Confirmed HZ Episodes During the Entire Study Period for ≥ 50 YOA and ≥ 70 YOA Cohorts⁽⁴⁾

Study	Age strata	HZ/su		Placebo		VE*,†			p-value
		N	n	N	n	(%)	95% CI		
ZOE-50	≥ 50 YOA	7695	2	7710	20	90.8	62.1	99.0	<0.0001
Pooled analysis ZOE-50- ZOE-70	≥ 70 YOA	8758	7	8773	20	69.5	24.9	89.1	0.0070

HZ = herpes zoster; HZ/su = herpes zoster subunit vaccine ; LL, UL = 95% lower and upper confidence limits; N = number of subjects included in each group; n = number of subjects having at least one confirmed HZ episode; p-value = two sided exact p-value conditional to number of cases; VE (%) = vaccine efficacy (Poisson method); YOA = years of age

*VE adjusted by age strata

†The mean follow-up time for 1-dose VE across all study groups was < 90 days.

Some information contained in this response is outside the approved Prescribing Information. This product is not approved for the use described. This response is not intended to offer recommendations for administering this product in a manner inconsistent with its approved labeling.

In order for GlaxoSmithKline to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 888-825-5249. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCE(S)

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2. Cunningham AL, Lal, H, Kovac M et al. Efficacy of the herpes zoster subunit vaccine in adults \geq 70 years of age. *N Engl J Med* 2016;375(11):1019-1032. <http://dx.doi.org/10.1056/NEJMoa1603800>. *
3. Chlibek R, Smetana J, Pauksens K et al. Safety and immunogenicity of three different formulations of an adjuvanted varicell-zoster virus subunit candidate vaccine in older adults: a phase II, randomized controlled study. *Vaccine* 2014;32:1745-1753. <http://dx.doi.org/10.1016/j.vaccine.2014.01.019>. *
4. Data on File. 2017N329366_00, 2017. *