SUPPLEMENTARY DATA

Table S1. Key Epidemiological and Quality-of-Life Inputs

Category/input	Base-case value	Range[a] Lower bound	Range[a] Upper bound	Base-case value source	Range source
Percentage of initial and recurrent HZ cases with PHN[b]	12.9%	8.5%	17.3%	Sahoo et al. (2017)[1c]	Sahoo et al. (2017)[1c]
Percentage of HZ cases with HZ-related complications [b, d]					
Ocular	3.6%	1.1%	6.0%	Sahoo et al. (2017)[1d]	Sahoo et al. (2017)[1d]
Neurological	1.8%	0.1%	3.5%		
Cutaneous	5.8%	2.7%	8.8%		
Other non-pain	0.9%	0.0%	2.1%		
QALY loss per HZ case while IC (Unvaccinated)[b]					
Without PHN	0.0144	0.0106	0.0181	Eriksson et al. (2019)[3e]	Eriksson et al. (2019)[3e]
With PHN	0.1972	0.0901	0.2879	Disutility per day from Eriksson et al. (2019)[3]; duration of PHN based on Moore et al. (2010)[4] and Oxman et al. (2005)[5f]	Lower bound: Duration of PHN based on Eriksson et al. (2019)[3]; Upper bound: Duration of PHN based on Lieu et al. (2008)[6f]
QALY loss per HZ case while IC (Vaccinated)[b]					
Without PHN	0.0047	0.0034	0.0144	Disutility per day from Eriksson et al. (2019)[3]; reduction due to RZV in Eriksson et al. (2019)[3] adjusted by values from Curran et al. (2019)[7] and Bastidas et al. (2019)[8g]	Eriksson et al. (2019)[3], Lieu et al. (2008)[6g]

Category/input	Base-case value	Range[a] Lower bound	Range[a] Upper bound	Base-case value source	Range source
With PHN	0.1972	0.1578	0.1972	Eriksson et al. (2019):[3] Assumed equal to QALY loss for unvaccinated case.	Lower bound: Assumed -20% of base-case value. Upper bound: Assumed equal to QALY loss for unvaccinated case.
Second-dose compliance for RZV	100.0%	76.0%	100.0%	Assumed[h]	Assumed[h]
Time (months) between the first and second doses of RZV	2	--	--	Assumed[i]	--

HZ = herpes zoster; IC = immunocompromised; PHN = postherpetic neuralgia; QALY = quality-adjusted life year; RZV = recombinant zoster vaccine.

Note: -- = not varied in sensitivity analysis.

[a] For the probabilistic sensitivity analysis, the beta distribution has been assumed for the purpose of sampling values for all inputs in this table. The standard errors applied in the beta distribution parameters are consistent with the reported uncertainty ranges representing 95% confidence intervals.

[b] This input applies to individuals with IC status only.

[c] This rate of PHN among incident and recurrent HZ cases was reported by Sahoo et al. (2017).[1] The rate of PHN among HZ cases was similar between incident and recurrent cases. For the uncertainty range, a 95% confidence was derived from Sahoo et al. (2017),[1] based on the number of events and the sample size.

[d] This rate of non-PHN complications among all HZ cases in HSCT recipients was reported by Sahoo et al. (2017).[1] These values were used only for generation of health outcomes; no costs due to complications other than PHN were explicitly considered in order to avoid potential double-counting with costs related to HZ from Eriksson et al. (2019)[3], which did not report costs specific to non-PHN complications. A 95% confidence interval was derived from Sahoo et al. (2017),[1] based on the number of events and the sample size.

[e] Eriksson et al. (2019)[3] estimated mean utility loss for HZ cases among HSCT patients without PHN based on assumed maximum time to HZ relief of 45 days. Loss of QALY was calculated by applying that mean utility loss (0.117) over 45 days and dividing by number of days in year (365). Derived lower bounds and upper bounds for QALY losses and from the 95% confidence intervals for mean utility loss were reported in Eriksson et al. (2019).[3] Utility losses were converted to QALY losses using the approach described for the base-case values.

[f] Eriksson et al. (2019)[3] estimated mean utility loss for HZ cases among HSCT patients with PHN, based on mean utility before PHN end date and mean utility after PHN end date. Loss of QALY was calculated by applying mean utility loss (0.186) over mean duration of PHN and dividing by the number of days in a year (365). The mean duration of PHN was from Moore et al. (2010)[4], which reported a mean duration of PHN of 12.9 months for healthy individuals aged 70 years and older. Lower and upper bounds were estimated using the same mean daily utility loss from Eriksson et al. (2019)[3] used to estimate the base-case value but applied over shorter and longer durations of PHN: 5.9 months from Eriksson et al. (2019)[3] and 18.8 months from Lieu et al.,[6] respectively.

[g] The QALY loss per acute unvaccinated HZ case among HSCT individuals derived from Eriksson et al. (2019)[3] was adjusted by the reduction in QALY loss for HZ cases in individuals vaccinated with RZV versus unvaccinated HZ cases observed in an HSCT population in Curran et al. (2019)[7] and Bastidas et al. (2019).[8] EQ-5D utility scores were reported pre-HZ and for HZ cases among RZV recipients and unvaccinated individuals from rash onset through 10 weeks after diagnosis. Average EQ-5D was calculated based on an average of the utility for the given week and the utility from the previous week (e.g., average EQ-5D for week 2 was calculated based on an average of the week 2 and week 1 utility values). Utility loss was calculated by comparing the average utility for the given week to the pre-HZ utility value. QALY losses were calculated for RZV (0.005) and placebo (0.0155), based on the utility losses estimated in each week. QALY losses were 68% lower for HZ cases among RZV recipients than for HZ cases in unvaccinated individuals. For the lower bound, we assumed that the 68% reduction in QALY loss from Curran et al. (2019)[7] was applied to the lower-bound QALY loss derived from Eriksson et al. (2019).[3] For the upper bound, it was assumed that the QALY loss for an acute vaccinated HZ case was the same as the QALY loss for an acute unvaccinated case as derived from Eriksson et al. (2019)[3] (i.e., the vaccine was assumed to have no effect on QALY loss).

[h] We have assumed 100% coverage of the second dose, based on Prosser et al.(2019)[9] assumptions and high completion rates (> 80%) of two-dose HZ vaccine in Bastidas et al. (2019).[8] The lower bound of 76% second-dose compliance was assumed from the CDC presentation on CMS data for the second dose of RZV from Dooling et al. (2019)[10] The upper bound was assumed to be the same as the base-case value (100%).

[i] We have assumed a 2-month interval between the first and second dose of RZV. The interval between first and second dose of RZV in clinical trials for IC populations was 1 to 2 months (Bastidas et al., 2019;[8] Dagnew et al., 2019;[11] Vink et al., 2019[12]).

Table S2. Model Inputs Varied in Analyses

	HSCT Population Analysis					Breast cancer population analysis	Hodgkin's lymphoma population analysis
		Range[a]					
Category/input	Base-case value	Lower bound	Upper bound	Base-case value source	Range source	Base-case value	Base-case value
Population starting age (years)	35	--	--	Assumed[b]	--	45[c]	25[d]
IC status duration (years)	5	2	5	Sahoo et al. (2017)[1e]	Assumed[e]	2[c]	2[d]
Annual incidence of initial and recurrent HZ (per 1000 person-years)	60	40	80	Sahoo et al. (2017)[1]	Sahoo et al. (2017);[1] Chen et al. (2014)[13]	17.1[c]	33.6[d]
Annual probability all-cause mortality[f]	0.0994	--	--	Arias and Xu (2019);[14] Bastidas et al. (2019);[8] Noone et al. (2018)[15g]	--	0.0217[c]	0.0284[d]
Vaccine efficacy/coverage							
Initial RZV efficacy against HZ							
One dose	58.0%	46.4%	69.6%	Assumed[h]	Assumed[h]	77.2%[h]	69.8%[h]
Two doses	72.5%	58.3%	82.4%	GSK (2020)[16i]	GSK (2020)[16i]	96.5%	87.2%
Initial RZV efficacy against PHN							
One dose	75.9%	60.7%	91.0%	Assumed[h]	Assumed[h]	77.8%[h]	77.4%[h]
Two doses	94.8%	58.3%	100.0%	Bastidas et al. (2019)[8]; GSK (2020)[16j]	Bastidas et al. (2019)[8]; GSK (2020)[16j]	97.2%	96.7%
Annual waning of RZV efficacy[f]							
One dose	18.2%	9.1%	27.3%	Assumed[k]	Assumed[k]	8.2%[k]	12.2%[k]
Two doses	9.1%	4.6%	18.2%	Bastidas et al. (2019);[8] GSK (2020)[16l]	Assumed[l]	4.1%	6.1%

HSCT = hematopoietic stem-cell transplant; HZ = herpes zoster; IC = immunocompromised; PHN = postherpetic neuralgia; RZV = recombinant zoster vaccine.

Note: -- = not varied in sensitivity analysis.

[a] For the probabilistic sensitivity analysis, the gamma distribution has been assumed for varying the IC status duration; for the probabilistic sensitivity analysis, the beta distribution has been assumed for all efficacy and waning-related inputs except for second-dose compliance, for which the uniform distribution was used. The standard errors applied in the beta distribution parameters are consistent with the reported uncertainty ranges representing 95% confidence intervals.

[b] The population was assumed to be 35 years of age at the start of the model time horizon to represent a younger HSCT population; 75% of the population in the phase 3 clinical trial were aged 50 years and older.[8]

[c] The starting age of the population was assumed to represent a younger breast cancer population and was based on National Cancer Institute (2020)[17] data, which reported that 19.7% of breast cancer diagnoses occurred in patients between the ages of 45 and 54 years. The IC status duration and annual incidence of HZ were based on Habel et al. (2013),[18] which reported the annual incidence of HZ among adults with solid tumor malignancies and by level of immunosuppression. The annual probability of all-cause death was derived from Noone et al. (2018),[15] which reported 5-year survival probability for patients with breast cancer.

[d] The starting age of the population was based on National Cancer Institute (2020)[17] data, which reported that Hodgkin lymphoma was most frequently diagnosed among adults aged 20 to 34 years. The IC status duration and annual incidence of HZ were based on Habel et al. (2013),[18] which reported the annual incidence of HZ among adults with hematologic malignancies and by level of immunosuppression. The annual probability of all-cause death was derived from Noone et al. (2018),[15] which reported 5-year survival probability for patients with Hodgkin lymphoma.

[e] Sahoo et al. (2017)[1] reported estimated HZ incidence in the 5 years following HSCT. Therefore, we assumed that the relevant period of reduced immune function also was 5 years. We assumed a lower bound of 2 years, which was similar to the length of the follow-up period observed in Bastidas et al. (2019)[8] clinical trial of HZ prevention in HSCT recipients. The IC status duration was not varied to an upper bound value, as 5 years was assumed to fully capture the duration of increased risk of HZ due to HSCT.

[f] The value shown was applied until the population returned to healthy status or until the population reached an age at which all-cause mortality (Arias and Xu, 2019)[14] was greater than the annual probability of death shown

[g] Noone et al. (2018),[15] reported the 5-year survival probability of 0.507, 0.714, 0.866, and 0.274 for multiple myeloma, non-Hodgkin lymphoma, Hodgkin lymphoma, and acute myeloid leukemia, respectively. The annual probabilities of death then were derived from the 5-year survival probability to 0.127, 0.065, 0.028, and 0.228, respectively. A weighted annual probability of death then was calculated based on the percentage of patients in the RZV autologous HSCT trial with myeloma (53.1%), non-Hodgkin lymphoma (33.1%), Hodgkin lymphoma (8.90%), and acute myeloid leukemia (2.3%) (Bastidas et al., 2019) [8]; as a simplifying assumption, these conditions were assumed to represent the total trial population, as only 2.6% of the trial population had other conditions. This value was applied until the population returned to healthy status.

[h] We have assumed a 20% relative reduction from two-dose efficacy, due to a lack of data for one-dose RZV (i.e., high second-dose compliance) in the clinical trials. We have assumed a ±20% relative change from the base-case value for the uncertainty range.

[i] Year 1 efficacy for RZV versus placebo in prevention of first or only episode of HZ was taken from the ZOSTER-002 phase 3 clinical trial of RZV in HSCT patients, as reported by GSK (2020).[16] The 95% confidence interval from GSK (2020)[16] was used for the uncertainty range.

[j] Overall efficacy against PHN over the trial follow-up period was calculated based on the PHN incidence rate ratio for the modified total vaccinated cohort (0.5 per 1,000 person-years) times the PHN incidence among the placebo cohort (4.9 per 1,000 person-years), as reported by GSK (2020)[16]. The initial efficacy against PHN then was derived by adjusting the overall efficacy of RZV against PHN, based on the relationship between the initial efficacy against HZ as reported by GSK (2020)[16] and the overall efficacy against HZ over the trial follow-up period as reported by Bastidas et al. (2019)[8]. Lower-bound initial efficacy was derived by adjusting the lower-bound overall efficacy against PHN, based on the relationship between the initial efficacy against HZ as reported by GSK (2020)[16] and the overall efficacy against HZ over the trial follow-up period as reported by Bastidas et al. (2019)[8].

[k] We have assumed a 100% relative increase from two-dose waning of efficacy, due to a lack of data for one-dose RZV (i.e., high second-dose compliance) in the clinical trials. Assumed ±50% relative change from the base-case value for the uncertainty range.

[l] Annual linear waning was estimated based on efficacy estimates in year 1 (72.5%) and years 2 and beyond (54.3%) from the ZOSTER-002 phase 3 clinical trial of RZV in HSCT patients, as reported in GSK (2020)[16]. Median follow-up in the clinical trial was 21 months (1.75 years) as reported by Bastidas et al. (2019)[8]; assuming an exponential distribution for the length of follow-up, mean follow-up was estimated to be 2.5 years. It then was assumed that year 1 efficacy was measured at the midpoint of year 1 (0.5 years), and annual waning was calculated as (72.5% – 54.3%) ÷ (2.5 – 0.5) = 9.1%. We assumed –50% and +100% relative change from the base-case value for the uncertainty range.

1 **Table S3. Key Model Inputs Used for Immunocompromised Status vs. Healthy Status for HSCT Cohort**

Category/input	Base-case value	Range		Standard error
		Lower bound	Upper bound	
HZ Incidence (IC Status)[a]				
All ages	0.06000	0.04020	0.08000	0.01015
HZ Incidence (Healthy Status)[b]				
Ages 18-49	0.00375	0.00300	0.00451	0.00038
Ages 50-59	0.00674	0.00539	0.00809	0.00069
Ages 60-69	0.00932	0.00746	0.01350	0.00154
Ages 70-79	0.01202	0.00962	0.01584	0.00159
Ages 80+	0.01278	0.01022	0.01730	0.00181
Percentage of Initial HZ cases with PHN (IC Status)[c]				
All ages	12.89%	8.51%	17.27%	2.23%
Percentage of Initial HZ cases with PHN (Healthy Status)[d]				
Ages 18-49	6.20%	4.96%	7.44%	0.63%
Ages 50-59	6.20%	4.96%	7.44%	0.63%
Ages 60-64	6.20%	4.96%	7.44%	0.63%
Ages 64-69	6.20%	4.96%	7.44%	0.63%
Ages 70-79	12.70%	10.16%	15.24%	1.30%
Ages 80+	12.70%	10.16%	15.24%	1.30%
QALY loss per unvaccinated HZ case (IC status)[e]				
All ages	0.0144	0.0106	0.0181	0.0019
QALY loss per unvaccinated HZ case (Healthy status)[f]				

Category/input	Base-case value	Range		Standard error
		Lower bound	Upper bound	
Ages 18-49	0.0025	0.0000	0.0035	0.0010
Ages 50-59	0.0050	0.0000	0.0800	0.0020
Ages 60-69	0.0100	0.0060	0.0160	0.0026
Ages 70+	0.0120	0.0070	0.0180	0.0028
QALY loss per unvaccinated HZ and PHN case (IC status)[g]				
All ages	0.1972	0.0901	0.2879	0.0505
QALY loss per unvaccinated HZ and PHN case (Healthy status)[h]				
Ages 18-49	0.0265	0.0000	0.0405	0.0103
Ages 50-59	0.0530	0.0000	0.0810	0.0207
Ages 60-69	0.1060	0.0680	0.1620	0.0240
Ages 70+	0.1560	0.1000	0.2330	0.0339
QALY loss per vaccinated HZ case (IC status)[i]				
All ages	0.0047	0.0034	0.0144	0.0028
QALY loss per vaccinated HZ case (Healthy status)[j]				
Ages 18-49	0.0025	0.0000	0.0035	0.0009
Ages 50-59	0.0050	0.0000	0.0070	0.0018
Ages 60-69	0.0100	0.0060	0.0140	0.0020
Ages 70+	0.0110	0.0070	0.0170	0.0026
QALY loss per vaccinated HZ and PHN case (IC status)[k]				
All ages	0.1972	0.1578	0.1972	0.0101
QALY loss per vaccinated HZ and PHN case (Healthy status)[l]				
Ages 18-49	0.0245	0.0000	0.0363	0.0092

Category/input	Base-case value	Range		Standard error
		Lower bound	Upper bound	
Ages 50-59	0.0490	0.0000	0.0725	0.0185
Ages 60-69	0.0980	0.0630	0.1450	0.0209
Ages 70+	0.0910	0.0580	0.1360	0.0199

HSCT = hematopoietic stem cell transplant; HZ = herpes zoster; IC = immunocompromised; PHN = postherpetic neuralgia; QALY = quality-adjusted life year.

[a] Base-case value: selected based on Sahoo et al. (2017).[1] Range and standard error: The lower bound was based on the incidence of HZ among bone-marrow or stem-cell transplant recipients aged 18 to 49 years from Chen et al. (2014)[13], which presented a lower (and therefore more conservative) estimate of HZ incidence than the lower bound of the 95% CI reported by Sahoo et al. (2017).[1] The upper bound was the upper bound of the 95% CI from Sahoo et al. (2017).[1]

[b] Base-case values: Johnson et al. (2015)[19] reported incidence rate of HZ based on 2011 claims data (estimated using ICD-9-CM code 053.xx diagnoses) from the Commercial Claims and Encounters database and the Medicare Supplemental and Coordination of Benefits database. Ranges and standard errors: Assumed –20% of the base incidence estimates for the lower bound; this was used instead of the published CIs to represent greater uncertainty around HZ incidence. The upper bound estimates were taken from Tseng et al. (2011)[20], which reported incidence based on ICD-9-CM diagnoses of HZ for an unvaccinated and healthy population of Kaiser Permanente members from 2007 to 2009; a weighted average was calculated between the reported incidence for ages 70 to 74 and 75 to 79 to derive the upper bound incidence for ages 70 to 79. Assumed +20% of base incidence for ages 50 to 59, as incidence for this age group was not reported in Tseng et al. (2011).[20]

[c] Base-case values: Sahoo et al. (2017).[1] Ranges and standard errors: Derived standard error and 95% CI from Sahoo et al. (2017)[1] based on number of events and sample size.

[d] Base-case values: Number of patients aged 70 years and older who reported more than 3 months of pain after initial HZ diagnosis, as reported by Cunningham et al. (2016).[21] For age groups under 70, GSK (2015)[22] data were used from the clinical trials to estimate the percentage of HZ cases with PHN. For ages 18 to 49, we assumed the same rate of PHN as ages 50 to 59, as Yawn et al. (2007)[23] observed rates of PHN (pain for 90 days or more) that were the same for both ages 22 to 49 and ages 50 to 59. Ranges and standard errors: Assumed a range of ±20% of the base-case values.

[e] Base-case values: Eriksson et al. (2019)[3] estimated mean utility loss for HZ cases among HSCT patients without PHN based on assumed maximum time to HZ relief of 45 days. QALY loss was calculated by applying that mean utility loss (0.117) over 45 days and dividing by number of days in year (365). A total of 363 HZ patients without PHN had utility measured before the HZ end date, and 109 had utility measured after the HZ end date. Ranges and standard errors: Derived lower bound and upper bound for QALY loss and standard errors from the 95% CI for mean utility loss reported in Eriksson et al. (2019).[3]

[f] Base-case values: Pellissier et al. (2007)[24] estimated QALY loss per unvaccinated acute HZ case based on ZBPI scores and pain duration in the SPS. Assumed half the QALY loss reported for ages 60 to 69 for the 50 to 59 age group and a quarter of the QALY loss for ages 60 to 69 for the 18 to 49 age group due to a lack of data.

Ranges and standard errors: Lower and upper bounds were estimated as the limits published in Pellissier et al. (2007).[24] For ages 18 to 49 and 50 to 59, we applied the same assumptions used to derive the base-case values but assumed no QALY loss in the lower bound. We derived standard errors for use in the probabilistic sensitivity analysis based on the assumption that the bounds for sensitivity analysis represent a 95% CI. Since the bounds were of uneven size, we used the average size between the two bounds to derive the standard error.

[g] Base-case values: Eriksson et al. (2019)[3] estimated mean utility loss for HZ cases among HSCT patients with PHN, based on mean utility before PHN end date and mean utility after PHN end date. Quality-adjusted life-year loss was calculated by applying mean utility loss (0.186) over mean duration of PHN and dividing by the number of days in a year (365). Ranges and standard errors: Lower and upper bounds were estimated using the same mean daily utility loss from Eriksson et al. (2019)[3] used to estimate the base-case value, but applied over shorter and longer duration of PHN: 5.9 months from Eriksson et al. (2019)[3] and 18.8 months from Lieu et al. (2008)[6], respectively.

[h] Base-case values: Pellissier et al. (2007)[24] estimated the QALY loss per unvaccinated acute HZ case leading to PHN based on ZBPI scores and pain duration in the SPS. Assumed half the QALY loss reported for ages 60 to 69 for the 50 to 59 age group and a quarter of the QALY loss for ages 60 to 69 for the 18 to 49 age group due to a lack of data. Ranges and standard errors: Lower and upper bounds are the limits published in Pellissier et al. (2007)[24]. For ages 18 to 49 and 50 to 59, we applied the same assumptions used to derive the base-case values but assumed no QALY loss in the lower bound. Since the bounds were of uneven size, we used the average size between the two bounds to derive the standard error.

[i] Base-case values: The QALY loss per acute unvaccinated HZ case among HSCT recipients derived from Eriksson et al. (2019)[3] was adjusted by the reduction in QALY loss for HZ cases in individuals vaccinated with RZV vs. unvaccinated HZ cases observed in an HSCT population in Curran et al. (2019)[7] and Bastidas et al. (2019)[8]. Ranges and standard errors: For the lower bound, we assumed that the 68% reduction in QALY loss from Curran et al. (2019)[7] was applied to the lower bound QALY loss derived from Eriksson et al. (2019)[3]. Upper bound assumed that the QALY loss for an acute vaccinated HZ case was the same as the QALY loss for an acute unvaccinated case derived from Eriksson et al. (2019)[3] (i.e., the vaccine was assumed to have no effect on QALY loss).

[j] Base-case values: Pellissier et al. (2007)[24] estimated the QALY loss per vaccinated acute HZ case based on ZBPI scores and pain duration in the SPS. Assumed half the QALY loss reported for ages 60 to 69 for the 50 to 59 age group and a quarter of the QALY loss for ages 60 to 69 for the 18 to 49 age group due to a lack of data. Ranges and standard errors: Lower and upper bounds for sensitivity analysis based on the limits published in Pellissier et al. (2007)[24]. For ages 18 to 49 and 50 to 59, we applied the same assumptions used to derive the base-case values but assumed no QALY loss in the lower bound. Since the bounds were of uneven size, we used the average size between the two bounds to derive the standard error.

[k] Base-case values: Eriksson et al. (2019)[3] estimated mean utility loss for HZ cases among HSCT patients with PHN based on mean utility before PHN end date and mean utility after PHN end date. QALY loss was calculated by applying mean utility loss (0.186) over mean duration of PHN and dividing by the number of days in a year (365). Ranges and standard errors: Range is from a lower bound of –20% of base-case value to an upper bound equal to the same QALY loss as unvaccinated HZ case (same as the base-case value). The standard error was calculated based on the assumption that the range reflected a 95% CI.

[l] Base-case values: Pellissier et al. (2007)[24] estimated the QALY loss per unvaccinated acute HZ case leading to PHN based on ZBPI scores and pain duration in the SPS. Assumed half the QALY loss reported for ages 60 to 69 for the 50 to 59 age group and a quarter of the QALY loss for ages 60 to 69 for the 18 to 49 age group due to a lack of data. Ranges and standard errors: Lower and upper bounds are the limits published in Pellissier et al. (2007)[24]. For ages 18 to 49 and 50 to 59, we applied the same assumptions used to derive the base-case values but assumed no QALY loss in the lower bound. Since the bounds were of uneven size, we used the average size between the two bounds to derive the standard error.

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