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Session: 152. Herpes Zoster Vaccine
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Background. Herpes zoster (HZ) develops in up to 50% of unvaccinated individuals who live to 85 years of age, accounting for more than 1 million cases of HZ annually in the United States. A live attenuated vaccine (LAV) for HZ is U.S. FDA approved for persons 50 years or older, though CDC Advisory Committee on Immunization Practices (ACIP) recommendations are only for persons beginning at age 60 years. LAV efficacy at preventing HZ is ~70% for persons 50–59 years of age, with lower efficacy in older adults, and it is efficacious in preventing post-herpetic neuralgia (PHN) beyond the HZ prevention. The efficacy of LAV after vaccination wanes over time. A new adjuvanted HZ subunit vaccine (SUV), administered as a two-dose series, has greater than 95% efficacy against HZ in persons 50–69 years of age. SUV efficacy remains greater than 90% in persons vaccinated at age 70 years and older, including the subgroup older than 80 years of age. Overall efficacy of SUV against PHN approaches 90%. The waning rate of efficacy after SUV vaccination is unknown.

Methods. To estimate the relative cost-effectiveness of SUV, LAV and no vaccination (NV) strategies, a Markov model was developed based on published trials and data on vaccine efficacy persistence, quality of life, resource utilization, costs and disease epidemiology. The perspective was U.S. societal, and the cycle length was one year with a lifelong time horizon. SUV efficacy was estimated for the base case to wane at the same rate as LAV, all persons were assumed to receive both doses of SUV, and the cost of SUV included both doses.

Results. For individuals vaccinated at age 50 years the incremental cost-effectiveness ratio (ICER) for LAV vs. NV was $142,811 per quality-adjusted life-year (QALY); at age 60 years the ICER dropped to $59,482 per QALY. The cost-effectiveness ratio of SUV approached that of LAV when the SUV cost approached $500 for persons vaccinated at age 50 years and when the cost was $400 for those vaccinated at age 60 years. The SUV cost that would result in achieving an ICER target of $100,000 per QALY for SUV vaccination vs. NV at age 50 years was $316; at age 60 years the cost was $638.

Conclusion. Vaccination at age 60 years with SUV was more cost-effective than LAV when SUV cost was ~$450 or less. Vaccination with SUV at age 50 years appeared to be cost-effective if SUV cost was ~$315 or less.

Disclosures. **All authors:** No reported disclosures.

1348. Immunogenicity and Safety of a Candidate Subunit Adjuvanted Herpes Zoster Vaccine (HZ/su) in Adults Post Renal Transplant: a Phase III Randomized Clinical Trial

Peter Vink, MD; GSK, Rockville, Maryland

Session: 152. Herpes Zoster Vaccine
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Background. The incidence rate of herpes zoster (HZ) in individuals with solid organ transplants (SOTs) is estimated as 8–9 times higher than the rate in the overall US population (3.2/1000 person-years). No vaccine is currently available to prevent HZ in immunocompromised individuals. GSK's HZ/su candidate vaccine, containing varicella-zoster virus glycoprotein E (gE) and $AS01_B$ Adjuvant System, has shown >90% efficacy for HZ prevention in immunocompetent adults ≥50 years of age (YOA). We performed a study to determine immunogenicity and safety of HZ/su in adult renal transplant (RT) recipients (RTR) on chronic immunosuppressive therapy; RT was chosen as it can be representative of SOTs due to the nature of administered immunosuppressive therapies.

Methods. In this phase III, observer-blind, multicenter study (NCT02058589), RTRs ≥18 YOA were randomized 1:1 to receive 2 doses of HZ/su or placebo intramuscularly 1–2 months apart. gE-specific vaccine response rates (VRRs) and geometric means (GMs) were assessed for humoral and $CD4^+$ cell-mediated immune (CMI) responses 1 month post dose 2 (M2). Solicited adverse events (AEs) were recorded for 7 days and unsolicited AEs and medically-attended AEs (MAEs) for 30 days after each dose. Solicited general and unsolicited AEs were also collected for 7 days prior to dose 1. Potential immune-mediated diseases (pIMDs) and serious AEs (SAEs) were recorded until 1 year post dose 2. Data from dose 1 through M2 is presented.

Results. At M2, 240 subjects (121 HZ/su; 119 placebo) were included in the humoral immunogenicity according-to-protocol (ATP) cohort. All immunogenicity success criteria were met at M2 (Table 1). VRRs for ATP humoral immune cohort and CMI sub-cohort (72 subjects: 36 HZ/su; 36 placebo) were higher in HZ/su groups. Humoral GM concentrations and CMI GM frequencies were significantly higher in HZ/su compared with placebo groups. The frequency of AEs was higher in HZ/su vs. placebo groups for solicited local AEs, but similar for solicited general AEs, unsolicited AEs, MAEs and SAEs. No pIMDs, vaccine-related SAEs or transplant rejections were reported (Table 2).

Conclusion. HZ/su was highly immunogenic in adults with RT at M2. No safety concerns were identified.

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Table 1. VRRs, GMs and GM ratios for anti-gE antibody ELISA concentrations and gE-specific $CD4^+$ T cell frequencies at M2 (ATP cohorts for humoral immunogenicity and CMI, respectively)

	HZ/su		Placebo		Adjusted ratio HZ/su:placebo
	N	Value	N	Value	
Humoral immune response (anti-gE antibody ELISA concentration)					
VRR, % (95% CI)	121	80.2% (71.9; 86.9)	119	4.2% (1.4; 9.5)	–
Adjusted* GMC, mIU/ml (95% CI)	121	19983.3 (15779.7; 25306.7)	119	1427.3 (1310.0; 1555.2)	14.00 (10.90; 17.99) p <0.0001
CMI response (gE-specific $CD4^+$ T cell frequencies)**					
VRR, % (95% CI)	28	71.4% (51.3; 86.8)	28	0.0% (0.0; 12.3)	–
Adjusted* GM, events/$10E^6$ $CD4^+$ T cells (95% CI)	28	1440.5 (1044.4; 1959.6)	28	83.5 (8.6; 181.5)	17.26 (5.92; 50.36) p <0.0001

VRR, vaccine response rate#; GM(C), geometric mean (concentration); M2, month 2 (1 month after last vaccination); ATP, according-to-protocol; N, number of subjects with available results; CI, confidence interval; IU, international units.

*adjusted for baseline values; **for the inferential analysis, the frequency of $CD4^+$ T cells producing at least two activation markers (IFN-γ, IL2, TNFα, and CD40 Ligand) upon in vitro stimulation with the antigen (induction condition) is calculated, by adding an offset of 0.5 to the number of activated $CD4^+$ T cells (numerator) divided by the total number of $CD4^+$ T cells involved (denominator).

#VRR: (i) for humoral immune response: (a) in initially seronegative subjects, the post-vaccination antibody concentration ≥4-fold the cut-off for anti-glycoprotein E (gE) (4x97 mIU/ml); (b) in initially seropositive subjects, the post-vaccination antibody concentration ≥4-fold the pre-vaccination antibody concentration; (ii) for cell-mediated immunogenicity (CMI): (a) in subjects with initial pre-vaccination T cell frequencies below the cut-off ($320/10^6$ $CD4^+$ T cells), the post-vaccination T cell frequencies ≥2-fold the cut-off ($2x320/10^6$ $CD4^+$ T cells); (b) in subjects with initial pre-vaccination T cell frequencies above the cut-off, the post-vaccination T cell frequencies ≥2-fold the pre-vaccination T cell frequencies.

Bolded values indicate that immunogenicity success criteria of primary objective (lower limit of 95% CI ≥60% for VRR – humoral) and secondary objectives (lower limit of 95% CI ≥50% for VRR – CMI, >3 for GM ratio – humoral, >1 for GM ratio – CMI) were met.

Table 2. Overall incidence of AEs (TVC)

AEs		Reporting period	n % (95% CI) HZ/su N = 132*	n % (95% CI) Placebo N=132
Solicited local		**D0–6 after each dose**	114 87.0% (80.0–92.3)	10 7.6% (3.7–13.5)
Solicited general			90 68.7% (60.0–76.5)	73 55.3% (46.4–64.0)
Unsolicited		**7D pre-dose 1**	9 6.8% (3.2–12.5)	7 5.3% (2.2–10.6)
		D0–29 after each dose	51 38.6% (30.3–47.5)	44 33.3% (25.4–42.1)
MAEs			34 25.8% (18.5–34.1)	29 22.0% (15.2–30.0)
pIMDs		**Dose 1 through 30 days post-dose 2**	0 0% (0.0)	0 0% (0.0)
SAEs	**All**		6 4.5% (1.7–9.6)	5 3.8% (1.2–8.6)
	Vaccine-related		0 0% (0.0)	0 0% (0.0)
	Biopsy confirmed allograft rejection		0 0% (0.0)	0 0% (0.0)

AEs, adverse events; TVC, total vaccinated cohort; n (%), number (percentage) of subjects with the respective AE; CI, confidence interval; MAEs, AEs with medically-attended visits; pIMDs, potential immune-mediated diseases; SAEs, serious AEs; D, day; N, number of subjects documented with ≥1 administered dose; *131 for the incidence of solicited local and general AEs.

Disclosures. **P. Vink**, GSK group of companies: Employee, Salary and stock options and stock granted

1349. Immunogenicity and Safety of a Candidate Subunit Adjuvanted Herpes Zoster Vaccine in Adults with Solid Tumors Vaccinated Before or During Immunosuppressive Chemotherapy Treatment: A Phase II/III, Randomized Clinical Trial

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Session: 152. Herpes Zoster Vaccine
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Background. No herpes zoster (HZ) vaccine for immunosuppressed individuals is currently available. GSK's candidate HZ vaccine containing recombinant varicella zoster virus glycoprotein E (gE) subunit and $AS01_B$ Adjuvant System (HZ/su) showed >90% efficacy for HZ prevention in immunocompetent adults aged ≥50 years. The HZ incidence in individuals with solid tumors (ST) receiving immunosuppressive chemotherapy (chemo) is estimated as 3–4 times higher than in the overall US population (3.2/1000 person-years). We present HZ/su immunogenicity and safety in ST adults aged ≥18 years.

Methods. In this phase II/III, observer-blind, multicenter study (NCT01798056), ST adults received 2 doses of HZ/su or placebo intramuscularly 1–2 months apart and were randomized 4:4:1:1 to receive a first dose 8–30 days (D) pre-chemo (HZ/su – HZ/su-PreC group, placebo – Pl-PreC) or on chemo start (±1 D) (HZ/su-OnC, Pl-OnC). Vaccine response rates (VRRs) and geometric means (GMs)/means were evaluated for gE humoral immune and gE-specific $CD4^+$ cell-mediated immune (CMI) responses 1 month (M2) and 12 months (M13) post-dose 2. Solicited adverse events (AEs) were recorded for 7 D and unsolicited and medically-attended AEs (MAEs) for 30 D post each dose. Potential immune-mediated diseases (pIMDs) and serious AEs (SAEs) were recorded until study end.

Results. 185 subjects (65 HZ/su-PreC, 78 Pl-PreC, 22 HZ/su-OnC, 20 Pl-OnC) were included in the according-to-protocol (ATP) cohort for humoral immunogenicity and 58 (27 HZ/su-PreC, 31 Pl-PreC) in the ATP sub-cohort for CMI. The most common ST were breast tumors (54% HZ/su, 49% placebo), followed by colorectal, lung, then other. Humoral and CMI VRRs were higher in HZ/su than Pl groups at M2 and M13. GM concentration (GMC) was highest at M2 in HZ/su-PreC. M13 GMCs were similar in the HZ/su-PreC and HZ/su-OnC groups (Table 1). The frequency of local solicited AEs was higher in HZ/su than Pl groups (Table 2); that of general solicited, unsolicited AEs, MAEs and SAEs was similar among groups (Table 3). 1 pIMD (Pl-OnC) and 23 fatal SAEs were reported. No SAE was considered vaccine-related by investigators.

Conclusion. HZ/su was highly immunogenic in ST adults receiving chemo. No safety concerns were raised.

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