1343. Persistence of Immune Response to an Adjuvanted Varicella-Zoster Virus Subunit Candidate Vaccine for up to Year 9 in Older Adults

Karlis Pauksens, MD[1]; Stephanie Volpe, MPH[2]; Tino F. Schwarz, MD[3]; Jan Smetana, MD PhD[4]; Nicole Toursarkissian, MD[5]; Lars Rombo, MD[6]; Stéphanie Ravault, PhD[7]; Marie-Pierre David, MSc[7]; Adriana Bastidas, PhD[7] and Lidia Oostvogels, MD[2]; [1]Uppsala University Hospital, Uppsala, Sweden, [2]GSK, Wavre, Belgium, [3]Central Laboratory and Vaccination Center, Stiftung Juliusspital, Wuerzburg, Germany, [4]Faculty of Military Health Sciences, University of Defence, Hradec Kralove, Czech Republic, [5]Practice Dr. Toursarkissian, Berlin, Germany, [6]Karolinska University Hospital, Stockholm, Sweden, [7]GSK, Rixensart, Belgium

Session: 152. Herpes Zoster Vaccine
Friday, October 6, 2017: 12:30 PM

Background. In the ZOE-50 and ZOE-70 clinical trials, the candidate herpes-zoster subunit vaccine (HZ/su; 50µg varicella-zoster virus glycoprotein E [gE] and $AS01_B$ Adjuvant System) demonstrated high efficacy against HZ, with limited waning over 4 years and consistent efficacy across age cohorts. In adults ≥60 years of age, the immune responses elicited by 2 HZ/su doses administered 2 months apart persisted for at least 6 years.[1] Here we report immunogenicity and safety 9 years post-initial vaccination.

Methods. This Phase IIIB, open, long-term extension study (NCT02735915) followed 70 participants who received 2 HZ/su doses in the initial trial (NCT00434577). Blood samples to evaluate the persistence of cellular (intracellular cytokine staining) and humoral (ELISA) immune responses were taken at 9 years post-initial vaccination. Limited safety follow-up was performed (1 visit).

Results. All 70 participants (mean age at dose 1: 72.3 years; 61.4% female) were included in the according-to-protocol analysis. The fold increases over pre-vaccination in the frequency of gE-specific CD4+ T-cells expressing ≥2 activation markers plateaued after 4 years post-dose 1 (year 4: 3.4, year 5: 3.0, year 6: 3.4, year 9: 3.4). Anti-gE antibody geometric mean concentrations were also stable from year 4 onwards (Table 1) and remained above the pre-vaccination value of 1213.1mIU/mL. Cellular and humoral responses at year 9 were similar across age strata (60–69, ≥70 years). No vaccine-related serious adverse events nor suspected HZ episodes were reported.

Conclusion. In adults ≥60 years of age, HZ/su-induced cellular and humoral immune responses remained above pre-vaccination levels for at least 9 years post-initial vaccination, confirming immune persistence predictions[2] based on 6-year data.

Table 1

	Pre-vaccination (95% CI)	Year 4 (95% CI)	Year 5 (95% CI)	Year 6 (95% CI)	Year 9 (95% CI)
Anti-gE antibody GMC (mIU/mL)	1213.1 (983.8–1495.9)	9643.5 (8309.7–11191.3)	9124.1 (7805.1–10666.0)	8490.5 (7292.1–9885.7)	8931.2 (7625.7–10460.3)

Disclosures. **S. Volpe**, GSK: Employee, Salary; **T. F. Schwarz**, GSK: Investigator and Scientific Advisor, Consulting fee; **J. Smetana**, GSK: Investigator, personal fees; **S. Ravault**, GSK: Employee, GSK shares and Salary; **M. P. David**, GSK: Employee, Salary and stock; **A. Bastidas**, GSK: Employee, Salary; **L. Oostvogels**, GSK: Employee and Shareholder, Salary and shares

1344. Immunogenicity and Safety of an Adjuvanted Herpes Zoster Subunit Candidate Vaccine in Adults with Hematologic Malignancies: A Phase III, Randomized Clinical Trial

Lidia Oostvogels, MD; GSK, Wavre, Belgium and the Zoster-039 Study Group

Session: 152. Herpes Zoster Vaccine
Friday, October 6, 2017: 12:30 PM

Background. Hematologic malignancy (HM) patients receiving immunosuppressive cancer therapy (ICT) are at increased risk of herpes zoster (HZ). Currently, no HZ vaccine is indicated for immunocompromised patients. The HZ subunit vaccine candidate (HZ/su), containing recombinant varicella zoster virus glycoprotein E and $AS01_B$ Adjuvant System, showed >90% efficacy and an acceptable safety profile in immunocompetent adults in all age groups ≥50 years. Here we report HZ/su immunogenicity and safety in HM adults ≥18 years of age who completed or are undergoing ICT.

Methods. In this phase III, observer-blind, multicenter study (NCT01767467), participants were randomized 1:1 to receive HZ/su or placebo (2 doses, 1–2 months apart) ≥10 days pre- or post-ICT. Humoral and cell-mediated immunogenicity (CMI) were assessed. The co-primary immunogenicity objectives were to evaluate HZ/su vaccine response rate and compare the immune response to HZ/su and placebo in participants excluding those with non-Hodgkin B-cell lymphoma (NHBCL) or chronic lymphocytic leukemia (CLL) at 1 month post-dose 2 (M2). Solicited and unsolicited adverse events (AEs) were recorded for 7 and 30 days after each dose, respectively. Serious AEs (SAEs), disease-related events and potential immune-mediated diseases (pIMDs) were recorded throughout the study. Partial safety results up to 6 months post-dose 2 are shown (partially blinded, ongoing study).

Results. Of 562 participants (283 HZ/su 283; placebo 279), (mean age 57.3 [HZ/su 56.8; placebo 57.8] years), 415 were included in the according-to-protocol (ATP) cohort for humoral immunogenicity and 132 in the ATP sub-cohort for CMI. M2 immune responses were higher in the HZ/su group (Table 1). Both co-primary immunogenicity objectives were met (Figure 1). The most frequent local and general solicited AEs were pain and fatigue, reported by 48.2% and 47.8% of all participants (per-group data remain blinded). The frequency of unsolicited AEs, SAEs and pIMDs in the 2 groups was similar (Table 2).

Conclusion. HZ/su induced robust humoral and cellular immune responses at M2 in HM adults excluding NHBCL and CLL, who completed or are undergoing ICT. No safety concerns were observed up to 6 months post-dose 2.

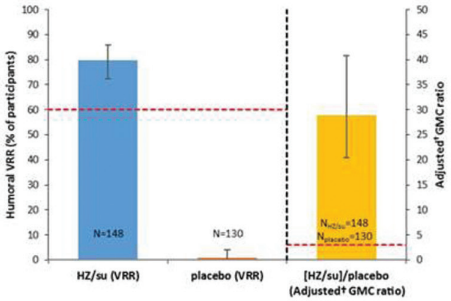
Funding. GlaxoSmithKline Biologicals SA

Table 1. Humoral and cellular immune responses at 1 month post-dose 2

	Population	HZ/su N	HZ/su Value	placebo N	placebo Value	Adjusted† GMC ratio [HZ/su]/placebo
Humoral immunogenicity (ATP cohort for humoral immunogenicity)						
VRR, % (95% CI)	All excluding NHBCL and CLL	148	79.7 (72.3*–85.9)	130	0.8 (0.0–4.2)	–
	All excluding NHBCL	184	68.5 (61.2–75.1)	165	0.6 (0.0–3.3)	
	All	217	65.0 (58.2–71.3)	198	0.5 (0.0–2.8)	
Adjusted† GMC, mIU/mL (95% CI)	All excluding NHBCL and CLL	148	22719.0 (16296.3–31673.1)	130	786.6 (711.0–870.2)	28.9 (20.4*–40.9)
Cellular immunogenicity (ATP sub-cohort for CMI)						
VRR, % (95% CI)	All	43	83.7 (69.3–93.2)	44	6.8 (1.4–18.7)	–
Frequency of gE-specific CD4[2+] T-cells, Median (Min [Q_1; Q_3] Max)	All	53	3081.9 (1.0 [1766.2; 7413.6] NP)	50	99.1 (1.0 [1.0; 268.3] NP)	–

ATP, according to protocol; **CMI,** cell-mediated immunogenicity; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; , **GMC,** (anti-glycoprotein E [gE] antibodies) geometric mean concentration; †, adjusted for baseline values; **N,** number of participants with available results; **%,** percentage of participants; **All,** all participants; **NHBCL,** participants with non-Hodgkin B-cell lymphoma; **CLL,** participants with chronic lymphocytic leukemia; **CI,** confidence interval; **IU,** international units; **CD4[2+],** CD4+ T-cells producing at least two of the four activation markers assessed (IFN-γ, IL2, TNFα, and CD40 Ligand) upon in vitro stimulation with the antigen; **Min/Max**, minimum/maximum; Q_1/Q_3, 1st/3rd quartiles; **NP**, data not published due to risk of unblinding.
*, co-primary immunogenicity objectives (criteria: [i] lower limit [LL] of 95% CI for HZ/su humoral VRR ≥60%, [ii] LL of 95% CI for adjusted GMC [HZ/su]/placebo ratio ≥3, in participants excluding those with NHBCL and CLL) were met.
VRR, vaccine response rate: **humoral,** for initially seronegative participants, antibody concentration at post-vaccination ≥4-fold the cut-off for anti-gE (97 mIU/ml); for initially seropositive participants, antibody concentration at post-vaccination ≥4-fold the pre-vaccination antibody concentration; **CMI,** for participants with pre-vaccination T cell frequencies below the threshold, ≥2-fold increase as compared to the threshold (320 Events/10^6 CD4+ T cells); for participants with pre-vaccination T cell frequencies above the threshold, ≥2-fold increase as compared to pre-vaccination T cell frequencies.

Figure 1. Humoral immune responses at 1 month post-dose 2 (ATP cohort for humoral immunogenicity) and co-primary immunogenicity objectives



ATP, according-to-protocol; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; **GMC,** (anti-glycoprotein E[gE] antibodies) geometric mean concentration; **N,** number of participants with available results; **error bars,** 95% confidence interval (CI); **†,** adjusted for baseline values.
red dashed lines, confirmatory co-primary immunogenicity objectives (criteria: [i] lower limit [LL] of 95% CI for HZ/su humoral VRR ≥60%, [ii] LL of 95% CI for [HZ/su]/placebo adjusted GMC ratio ≥3 in all participants excluding those with non-Hodgkin B-cell lymphoma [NHBCL] and chronic lymphocytic leukemia [CLL]). **VRR,** vaccine response rate: for initially seronegative participants, antibody concentration at post-vaccination ≥4-fold the cut-off for anti-gE (4x97 mIU/ml); for initially seropositive participants, antibody concentration at post-vaccination ≥4-fold the pre-vaccination antibody concentration.
This graph presents data for **all participants excluding NHBCL and CLL**.

Table 2. Frequency of adverse events (total-vaccinated cohort)

AE reporting period	HZ/su (N=283) % [95% CI] All	HZ/su (N=283) % [95% CI] Grade 3	HZ/su (N=283) % [95% CI] Related	placebo (N=279) % [95% CI] All	placebo (N=279) % [95% CI] Grade 3	placebo (N=279) % [95% CI] Related
Unsolicited AEs Days 0–29 post each dose	46.6 (40.7–52.6)	8.8 (5.8–12.8)	6.4 (3.8–9.9)	45.9 (39.9–51.9)	9.7 (6.5–13.8)	1.8 (0.6–4.1)
SAEs From dose 1 to 6 Months post dose 2	17.7 (13.4–22.6)	–	NP	21.5 (16.8–26.8)	–	NP
pIMDs From dose 1 to 6 Months post dose 2	0.7 (0.1–2.5)	–	N/A	0.4 (0.0–2.0)	–	N/A

AE, adverse event; **SAE,** serious AE; **pIMD,** potential immune-mediated disease; **HZ/su,** participants who received the herpes zoster subunit candidate vaccine; **placebo,** participants who received placebo; **N**, number of participants with ≥1 administered dose; **%,** percentage of participants who reported at least one symptom; **CI**, confidence interval; **All**, all AEs/pIMDs; **Grade 3**, severe AEs (>100 mm [redness, swelling], prevent normal everyday activities [other symptoms]); **Related**, AEs considered by the investigator as causally related to vaccination (all local solicited AEs are considered related to vaccination); **N/A**, not applicable (for this phase of analysis); **NP**, data not published due to risk of unblinding. Per-group **solicited AEs** data is not published due to risk of unblinding.

Disclosures. **L. Oostvogels**, GSK group of companies: Employee and Shareholder, Salary and Shares

1345. A Replication-Defective Herpes Simplex Virus (HSV)-2 Vaccine, HSV529, is Safe and Well-Tolerated in Adults with or without HSV Infection and Induces Significant HSV-2-Specific Antibody Responses in HSV Seronegative Individuals

Lesia Dropulic, MD[1]; Kening Wang, MD[1]; Makinna Oestreich, B.A.[2]; Harlan Pietz, BS[2]; Doreen Garabedian, BSN, RN[3]; Sinthujan Jegaskanda, PhD[2]; Kennichi Dowdell, PhD[1]; Hanh Nguyen, BS[1]; Kerry Laing, PhD[6]; David Koelle, MD[6]; Aaron Azose, BS[7]; Sally Hunsberger, PhD[8]; Keith Lumbard, MS[4]; Aiying Chen, PhD[9]; Lee-Jah Chang, MD[9]; Sanjay Phogat, PhD[9] and Jeffrey Cohen, MD[1]; [1]Laboratory of

Infectious Diseases, National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, [2]University of Minnesota Medical School, Minneapolis, Minnesota, [3]Weill Cornell Medical College, New York City, NY, [4]NIH, Bethesda, Maryland, [5]Peter Doherty Institute for Infection and Immunity, Melbourne, Australia, [6]University of Washington Medicine, Seattle, Washington, [7]Vanderbilt University Medical School, Nashville, Tennessee, [8]Biostatistics Research Branch, NIAID, Bethesda, Maryland, [9]sanofi pasteur, Swiftwater, Pennsylvania

Session: 152. Herpes Zoster Vaccine
Friday, October 6, 2017: 12:30 PM

Background. We conducted a phase 1, randomized, double-blind, placebo-controlled trial of a replication-defective HSV-2 vaccine, HSV529 (deleted for UL5 and UL29), in 60 healthy adults aged 18 to 40 years.

Methods. Subjects were enrolled in groups of 20 from 3 serogroups: HSV1+ or -/HSV2+ (group 1), HSV1+/HSV2– (group 2), and HSV1-/HSV2– (group 3). At months 0, 1, and 6, 15 subjects in each group received HSV529 intramuscularly and 5 subjects received placebo. The primary endpoint was the frequency of solicited injection site and systemic reactions from day 0 to 7 after each vaccination and unsolicited adverse events up to 6 months after the last dose.

Results. 89% of vaccine recipients experienced a mild to moderate solicited injection site reaction vs. 47% of placebo recipients (P = 0.006, 95% CI 0.129, 0.676) that did not preclude additional doses. 64% of vaccine recipients experienced solicited systemic reactions vs. 53% of placebo recipients (P = 0.44, 95% CI -0.179, 0.402). Two serious adverse events occurred in 2 participants and were assessed as unrelated to HSV529 administration. Serum neutralizing antibody titers significantly increased from baseline after 3 doses of HSV529 compared with placebo in group 3 only (P < 0.001). This increase persisted up to 6 months after the third dose of vaccine (P < 0.001). Serum and vaginal antibodies to HSV2 glycoprotein D (gD) also significantly increased after 3 doses of vaccine in group 3 subjects (P < 0.001 and P = 0.012, respectively). The mean vaginal gD titer after 3 doses was about one-third of the mean serum gD titer. In addition, the vaccine induced significant levels of HSV2-specific antibody dependent cellular cytotoxicity (ADCC) after 3 doses in group 3 subjects compared with placebo (P < 0.001). Vaccine-induced CD4 T-cell responses were detected in 46%, 27%, and 36% of subjects in groups 1, 2, and 3, respectively, one month after the third dose of vaccine. CD8 T-cell responses were detected in 8%, 18%, and 14% of subjects in groups 1, 2, and 3, respectively, at the same time point.

Conclusion. The HSV529 vaccine was safe, well-tolerated, and immunogenic, eliciting significant neutralizing, gD, and ADCC-mediating antibodies, and modest cellular immune responses in HSV seronegative individuals. NCT01915212

Disclosures. **L. Dropulic**, sanofi pasteur: Collaborator, Research support; **K. Wang**, sanofi pasteur: Collaborator, Research support; **M. Oestreich**, sanofi pasteur: Collaborator, Research support; **H. Pietz**, sanofi pasteur: Collaborator, Research support; **D. Garabedian**, sanofi pasteur: Collaborator, Research support; **K. Dowdell**, sanofi pasteur: Collaborator, Research support; **H. Nguyen**, sanofi pasteur: Collaborator, Research support; **K. Laing**, sanofi pasteur: Research Contractor, payment for conducting T cell assays; **D. Koelle**, sanofi pasteur: Research Contractor, payment for conducting T cell assays; **A. Azose**, sanofi pasteur: Research Contractor, Payment for conducting T cell assays; **A. Chen**, sanofi pasteur: Employee, Salary; **L. J. Chang**, sanofi pasteur: Employee, Salary; **S. Phogat**, sanofi pasteur: Employee, Salary

1346. Results of a Safety Pooled Analysis of an Adjuvanted Herpes Zoster Subunit Vaccine in More than 14,500 Participants Aged 50 Years or Older

Marta López-Fauqued, PhD[1]; Laura Campora, MD[1]; Frédérique Delannois, DVM[1]; Mohamed El Idrissi, MSc[1]; Edouard Ledent, MSc[2]; Javier Diez-Domingo, MD, PhD[3]; Janet McElhaney, MD[4]; Shelly McNeil, MD, FRCPC, FIDSA[5]; Ferdinandus De Looze, MBBS[6]; Wilfred Yeo, MB, ChB, MD[7]; Fernanda Tavares Da Silva, MD, ObGyn[1] and ZOE-50/70 Study Group; [1]GSK, Wavre, Belgium, [2]GSK, Rixensart, Belgium, [3]Vaccine Research Unit, Fundación para el Fomento de la Investigación Sanitaria y Biomédica, Valencia, Spain, [4]Health Sciences North Research Institute, Sudbury, ON, Canada, [5]Canadian Center for Vaccinology, IWK Health Centre and Nova Scotia Health Authority, Dalhousie University, Halifax, NS, Canada, [6]University of Queensland, Queensland, Australia, [7]School of Medicine, University of Wollongong, Wollongong, Australia

Session: 152. Herpes Zoster Vaccine
Friday, October 6, 2017: 12:30 PM

Background. The recombinant herpes zoster (HZ) subunit vaccine (HZ/su) has shown efficacy against HZ in adults ≥50 and ≥70 years of age (YOA), in two pivotal Phase III clinical trials (NCT01165177, NCT01165229). A pooled safety analysis of data from these two efficacy studies was performed, including a comparative analysis on HZ/su vs. placebo groups, to provide a comprehensive understanding of the HZ/su safety profile.

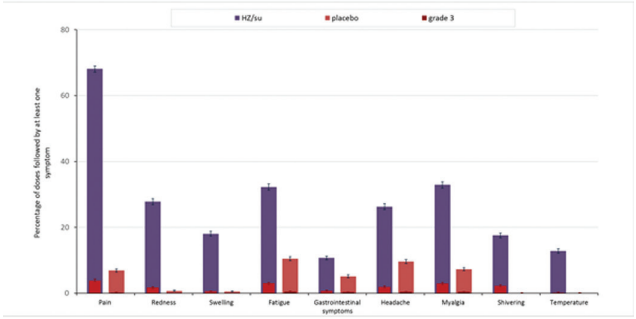
Methods. Two pivotal, randomized, placebo-controlled Phase III studies, assessed the efficacy, reactogenicity and safety of HZ/su, administered intramuscularly according to a 0, 2-month schedule. Solicited and unsolicited adverse events (AEs) were collected for 7 and 30 days after each dose, respectively; serious AEs (SAEs) for 1 year after last dose; fatal and related SAEs and potential immune-mediated diseases (pIMDs) during the entire study period. Reactogenicity was assessed in a subset of participants; safety was assessed in all vaccinated participants.

Results. 29,305 participants ≥50 YOA (HZ/su: 14,645; placebo: 14,660) were included in the pooled analysis. HZ/su was more reactogenic than placebo. Local reactions were mostly mild to moderate in intensity and transient (median duration = 3 days); the percentages of participants reporting SAEs, fatal SAEs and pIMDs were similar in both groups, at 30 days and 1 year after last dose (Figures 1 and 2). Percentages of fatal SAEs ranged between 4.3% (95% Confidence Interval [CI]: 4.0–4.7) and 4.6% (95% CI: 4.3–5.0) and pIMDs between 1.2% (95% CI: 1.1–1.4) and 1.4% (95% CI: 1.2–1.6), in HZ/su and placebo groups, respectively. In both groups, the most frequent causes of death were neoplasms, cardiac disorders, and respiratory tract infections and infestations, and most frequent pIMDs were polymyalgia rheumatica, rheumatoid arthritis and psoriasis.

Conclusion. No safety concern was identified. Together with the high efficacy against HZ (97.2% [95% CI: 93.7–99.0],[1] 91.3% [95% CI: 86.8–94.5][2]), the safety data supports a favorable benefit/risk profile of HZ/su in participants ≥50 YOA.

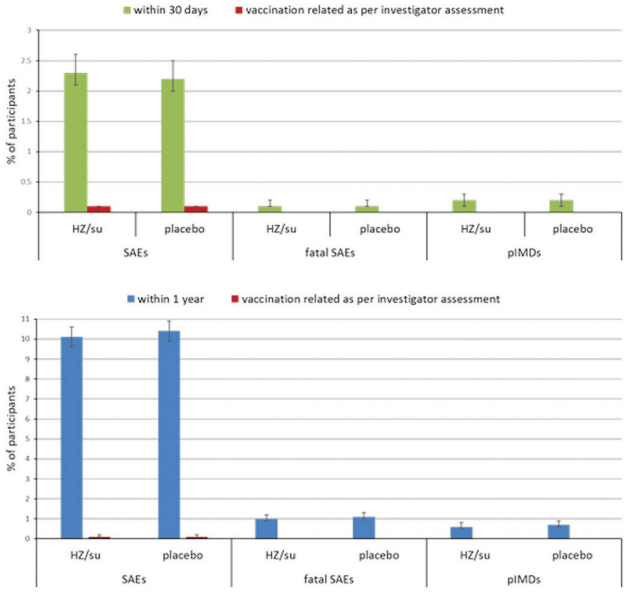
Funding. GlaxoSmithKline Biologicals SA

Figure 1: Incidence of solicited symptoms reported during the 7-day after vaccination period



Temperature is defined on oral, axillary, rectal or tympanic; Error bars depict 95% confidence intervals (CIs).

Figure 2: Overview of SAEs, fatal SAEs and pIMDs within 30 days and 1 year after last vaccination, respectively



SAEs, serious adverse events; pIMDs, potential immune-mediated diseases; Error bars depict 95% confidence intervals (CIs).

Disclosures. **M. López-Fauqued**, GSK Biologicals': Employee, Salary; **L. Campora**, GSK Biologicals': Employee, Salary; **F. Delannois**, GSK Vaccines: Employee, Salary; **M. El Idrissi**, GSK Vaccines: Employee, Salary; **E. Ledent**, GSK Vaccines: Employee, Salary; **J. Diez-Domingo**, GSK Vaccines: Consultant and Investigator, Educational support and Research grant; **J. McElhaney**, GSK Vaccines: Scientific Advisor, Speaker honorarium; **S. McNeil**, GSK/Merck: Grant Investigator, Investigator and Scientific Advisor, Consulting fee, Grant recipient, Research grant, Research support and Speaker honorarium; **F. De Looze**, GSK Vaccines: Investigator and Research Contractor, Research support; **F. Tavares Da Silva**, GSK Vaccines: Employee, restricted shares and Salary

1347. A Cost-Effectiveness Analysis of an Adjuvanted Subunit Vaccine for the Prevention of Herpes Zoster and Post-Herpetic Neuralgia

Christopher Carpenter, MD[1]; Annas Aljassem, MD[2]; Jerry Stassinopoulos, MD[3]; Giovanni Pisacreta, MBA[4] and David Hutton, PhD[5]