a NIH-funded project, the novel semisynthetic saponin TQL1055 was evaluated for its potential to augment the immunogenicity of influenza antigens.

Figure 1: TQL1055 Enhances the Antibody Response to a Recombinant Antigen Influenza Vaccine (Flublok®) and Exhibits Antigen Dose-Sparing Effects

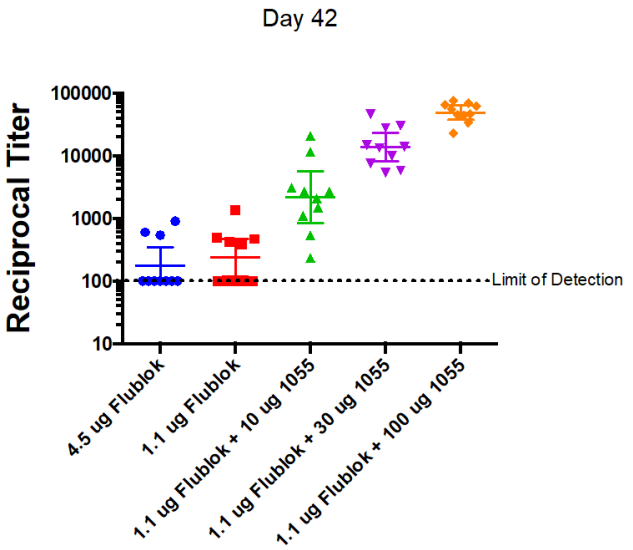
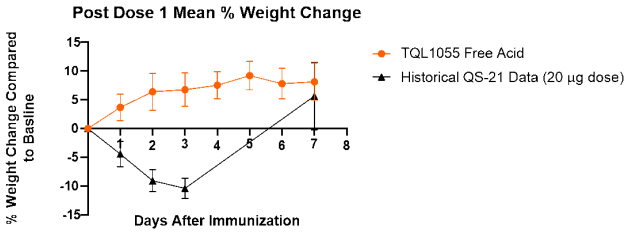


Figure 2: TQL1055 Exhibits Improved Systemic Tolerability Over QS-21.



Methods: Groups of 10 C57BL/6J mice were immunized subcutaneously (SC) with Flublok® (H3N2 antigen) alone at either a 4.5 mcg or 1.1 mcg dose, or at a 1.1 mcg dose in combination with 10, 30 or 100 mcg TQL1055 on Days 0 and 21. Sera were analyzed at days 0, 21 and 42 by ELISA for H3N2-specific IgG. Body weights were measured serially.

Results. A 2-dose series of 1.1 mcg Flublok with TQL1055 elicited anti-H3N2 antibodies in all mice. This effect was TQL1055 dose-dependent, with GMTs of 2178 in the 10 mcg group, 13674 in the 30 mcg group and 48959 in the 100 mcg group. The GMT in all TQL1055 groups was higher than the GMT of 176 in the group receiving 4.5 mcg of Flublok alone. Mice receiving TQL1055 gained weight steadily after immunization, compared with a maximum weight loss of >10% in mice receiving 20 mcg of QS-21.

Conclusion. TQL1055 exhibits robust adjuvant activity for influenza antigens, demonstrating a dose-sparing effect and improved systemic tolerability compared with QS-21. Taken together, these finding support further evaluation of its potential as an adjuvant for influenza vaccines.

Disclosures. Chloe Buzz, BS, Adjuvance Technologies (Employee) Eric Farris, PhD, Adjuvance Technologies (Employee) Sean R. Bennett, MD PhD, Adjuvance Technologies (Employee) Pat Frenchick, PhD, Adjuvance Technologies (Consultant) Tyler Martin, MD, Adjuvance Technologies (Employee, Shareholder)

1238. The Novel Semisynthetic Saponin Adjuvant TQL1055 Enhances the Antibody Response to Pertussis Vaccine with an Improved Tolerability Profile over QS-21

Chloe Buzz, BS[1]; Govind Ragupathi, PhD[2]; Sean R. Bennett, MD PhD[3]; Phil Livingston, MD[1]; Eric Farris, PhD[1]; Tyler Martin, MD[1]; [1]Adjuvance Technologies, Lincoln, Nebraska; [2]Memorial Sloan Kettering Cancer Center, New York, New York; [3]Adjuvance Technologies, Inc., Lincoln, Nebraska

Session: P-57. New Vaccines

Background. Acellular pertussis vaccines are better tolerated but less immunogenic than older whole cell vaccines. Novel adjuvants may be useful to enhance their immunogenicity. First-generation natural saponins are potent immuno-enhancers but are highly reactogenic. The novel semisynthetic saponin TQL1055 was evaluated for its potential to enhance the immunogenicity of a commercially available acellular pertussis vaccine as part of a National Institute of Allergy and Infectious Disease (NIAID) funded project.

Methods. Groups of 10 female C57BL/6J mice were immunized subcutaneously (SC) with Adacel® (containing 0.5 mcg pertussis toxin antigen) alone or in combination with QS-21 at 20 mcg/dose or TQL1055 at 50 mcg/dose on Days 0 and 28. Serum antibody titer to pertussis antigen was determined by ELISA (Alpha Diagnostics) at Days 0, 28, and 42 and geometric mean titers (GMT) in IU/mL were determined. Body weights were measured serially for 7 days after dose 1.

Results. At 28 days following dose 1, mice receiving TQL1055 had an anti-pertussis toxin IgG GMT of 8492, compared with 2263 in mice receiving QS-21 ($p = 0.005$). At Day 42, 14 days after dose 2, the GMTs increased to 18719 in the TQL1055 group and 10851 in the QS-21 group ($p = 0.0653$ vs TQL1055 dose 2; $p = 0.6038$ vs TQL1055 dose 1). Mice in the Adacel and TQL1055 groups gained weight steadily after dose 1, while mice in the QS-21 group had an average weight loss of 10% from baseline at 3 days after dose 1 ($p < 0.0001$).

Figure 1: TQL1055 Enhances the Antibody Response to Adacel® (Commercial Acellular Pertussis Vaccine) in C57BL/6J Female Mice

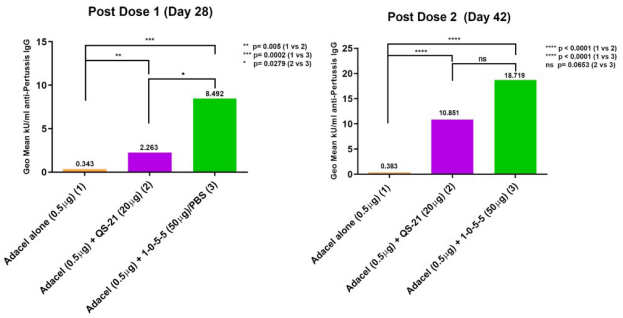
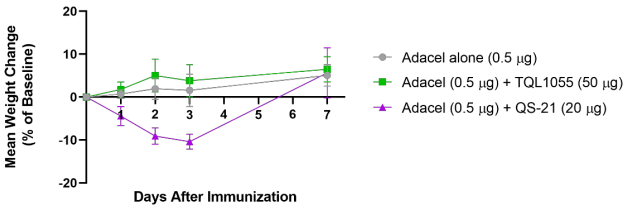


Figure 2: TQL1055 Shows Enhanced Tolerability (measured by decreased weight loss) Compared to QS-21 Following Subcutaneous Injection in C57BL/6J Female Mice



Conclusion: TQL1055 enhanced the antibody response to a commercial acellular pertussis vaccine to a greater degree than QS-21. Additionally, TQL1055 was better tolerated than QS-21, with no weight loss after vaccination. These findings suggested that TQL1055 may improve the performance of acellular pertussis vaccines without an increase in reactogenicity.

Disclosures. Chloe Buzz, BS, Adjuvance Technologies (Employee) Sean R. Bennett, MD PhD, Adjuvance Technologies (Employee) Phil Livingston, MD, Adjuvance Technologies (Consultant, Shareholder) Eric Farris, PhD, Adjuvance Technologies (Employee) Tyler Martin, MD, Adjuvance Technologies (Employee, Shareholder)

1239. Different Dose Levels of a Respiratory Syncytial Virus Maternal Vaccine Candidate (RSVPreF3) Administered to Non-pregnant Women in a Randomized Clinical Trial Are Immunogenic and Well Tolerated

Tino Schwarz, PhD[1]; Casey Johnson, DO[2]; Christine Grigat, MD[3]; Dan Apter, MD, PhD[4]; Peter Csonka, MD, PhD[5]; Niklas Lindblad, MD[6]; Thi Lien-Anh Nguyen, PhD[7]; Feng F. Gao, PhD[8]; Jyoti Soni, MA[9]; Antonella Nadia Tullio, Dr.[8]; Ilse Dieussaert, IR[10]; Marta Picciolato, PharmD, MSc[11]; Ouzama Henry, MD[8]; [1]Klinikum Wuerzburg Mitte, Standort Juliusspital, Wuerzburg, Baden-Wurttemberg, Germany; [2]Johnson County Clin-Trials, Lenexa, KS, United States, Lenexa, Kansas; [3]Clinical Research Hamburg, Hamburg, Germany, Hamburg, Hamburg, Germany; [4]VL-Medi, Helsinki, Finland, Helsinki, Uusimaa, Finland; [5]Centre for Child Health Research, Tampere University, Tampere, Finland, Tampere, Pirkanmaa, Finland; [6]University of Turku, Turku, Finland, Turku, Varsinais-Suomi, Finland; [7]GSK, Wavre, Belgium, Wavre, Brabant Wallon, Belgium; [8]GSK, Rockville, MD, United States, Rockville, Maryland; [9]GSK, Bangalore, India, Bangalore, Karnataka, India; [10]GSK, Rockville, MD; [11]GSK, Rixensart, Belgium, Rixensart, Brabant Wallon, Belgium

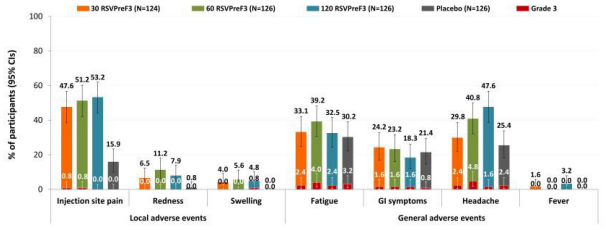
Session: P-57. New Vaccines

Background. Respiratory syncytial virus (RSV) is a leading cause of bronchiolitis and pneumonia in childhood. Maternal immunization could help to protect infants from RSV-associated infections in their first months of life. We evaluated the safety, reactogenicity and immunogenicity of the RSV maternal (RSVPreF3) vaccine candidate in non-pregnant women, at different dose levels.

Methods. In this phase I/II, observer-blind, multicenter study (NCT03674177), healthy non-pregnant women aged 18–45 years were randomized (1:1:1:1) and received 1 dose of either 30, 60 or 120 µg of RSVPreF3 vaccine (30/60/120 RSVPreF3 group) or placebo. Solicited adverse events (AEs) (until day 7 [D7] post-vaccination), unsolicited AEs (until D30 post-vaccination), hematological and biochemical laboratory abnormalities (at D8 and D31 post-vaccination) were recorded. Serious AEs (SAEs) were collected until D181 and immune responses until D91 post-vaccination. Exploratory analysis was performed at D31 to compare immunogenicity of different dose levels.

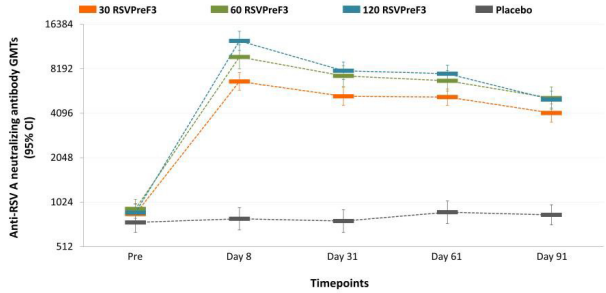
Results. 502 women were included in the exposed set. The most frequently reported solicited AEs were pain and headache (**Fig 1**). Grade 3 solicited AEs were infrequently reported. 180 women experienced unsolicited AEs; 19 reported grade 3 unsolicited AEs, among which 1 was vaccination-related (60 RSVPreF3). 3 SAEs were reported (1 in 120 RSVPreF3; 2 in placebo); none was related to vaccination. No clinically significant changes in laboratory parameters occurred. Geometric mean titers of anti-RSV A neutralizing antibody (≥ 8-fold at D8 and ≥ 5-fold until D91 vs baseline) and geometric mean concentrations of anti-RSVPreF3 IgG antibody (≥ 12-fold at D8 and ≥ 6-fold until D91 vs baseline) were boosted in all RSVPreF3 groups (**Fig 2, 3**). The 60 and 120 µg dose levels of RSVPreF3 were significantly more immunogenic than the 30 µg one.

Figure 1. Solicited adverse events until day 7 post-vaccination



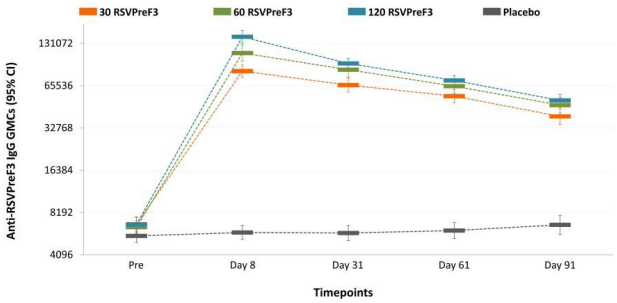
Exposed set. N, number of participants with documented dose; **CIs**, confidence intervals, represented as error bars; **30/60/120 RSVPreF3,** group of women who received 30, 60 or 120 µg of respiratory syncytial virus maternal vaccine; **GI**, gastro-intestinal; **fever**, ≥38.0 °C (regardless of the location of measurement but oral route was preferred); **Grade 3**, injection site pain defined as significant pain at rest that prevents normal every day activities, redness and swelling with diameter >100 mm, fatigue/GI symptoms/headache that prevent normal activities, fever >39.0 °C.

Figure 2. GMTs of anti-RSV A neutralizing antibody (ED60) until day 91 post-vaccination



Note: Immunogenicity analyses were performed in the per protocol set (PPS). The PPS was defined by time-point. At least 95% of the subjects in the exposed set were part of the PPS at any of the timepoints. **RSV-A**, respiratory syncytial virus A; **GMTs**, geometric mean titers; **Pre**, pre-vaccination; **CI**, confidence interval; **30/60/120 RSVPreF3,** group of women who received 30, 60 or 120 µg of RSV maternal vaccine.

Figure 3. GMCs of RSVPreF3 IgG antibody (EU/mL) until day 91 post-vaccination



Note: Immunogenicity analyses were performed in the per protocol set (PPS). The PPS was defined by time-point. At least 95% of the subjects in the exposed set were part of the PPS at any of the timepoints. **CI**, confidence interval; **IgG**, immunoglobulin G; **Pre**, pre-vaccination; **GMCs**, geometric mean concentrations; **30/60/120 RSVPreF3,** group of women who received 30, 60 or 120 µg of respiratory syncytial virus maternal vaccine.

Conclusion: All RSVPreF3 vaccine dose levels were well tolerated and no safety concerns identified. All 3 dose levels were immunogenic, with higher immune response induced by the 60 and 120 µg dose levels than the 30 µg one. These data support the further investigation of the 60 and 120 µg RSVPreF3 dose levels in pregnant women.

Funding. GlaxoSmithKline Biologicals SA

Acknowledgment. N Bulik/Q Deraedt (Modis c/o GSK) provided writing/editorial support

Disclosures. **Tino Schwarz, PhD**, **GSK group of companies** (Scientific Research Study Investigator, Speaker's Bureau) **Christine Grigat, MD**, **GSK group of companies** (Scientific Research Study Investigator) **Dan Apter, MD, PhD**, **GSK group of companies** (Research Grant or Support) **Peter Csonka, MD, PhD**, **GSK group of companies** (Scientific Research Study Investigator) **Thi Lien-Anh Nguyen, PhD**, **GSK group of companies** (Employee, Shareholder) **Feng F. Gao, PhD**, **GSK group of companies** (Employee) **Jyoti Soni, MA**, **GSK group of companies** (Employee) **Antonella Nadia Tullio, Dr.**, **GSK group of companies** (Employee) **Ilse Dieussaert, IR**, **GSK group of companies** (Employee, Shareholder) **Marta Picciolato, PharmD, MSc**, **GSK group of companies** (Employee) **Ouzama Henry, MD**, **GSK group of companies** (Employee, Shareholder)

1240. Persistence of Circulating Antibody Through 12 Months Following Vaccination With a 20-Valent Pneumococcal Conjugate Vaccine in Adults 60–64 Years of Age

Donald Hurley, MD[1]; Carl Griffin, MD[2]; Mariano Young Jr., MD[3]; Daniel Scott, MD[4]; Michael W. Pride, PhD[4]; Ingrid L. Scully, PhD[5]; John Ginis, BS[3]; Yahong Peng, PhD[3]; Kathrin U. Jansen, PhD[4]; William C. Gruber, MD[3]; Wendy Watson, MD[5]; [1]Medical Research South, LLC, Goose Creek, South Carolina; [2]Lynn Health Science Institute, Oklahoma City, Oklahoma; [3]Pfizer Inc, Collegeville, Pennsylvania; [4]Pfizer, Collegeville, Pennsylvania; [5]Pfizer Vaccine Research and Development, Pearl River, New York

Session: P-57. New Vaccines

Background. While widespread use of pneumococcal conjugate vaccines (PCVs) has reduced disease burden, expanding serotype coverage remains an unmet need in disease prevention. The 20-valent PCV (PCV20) contains capsular polysaccharide conjugates from serotypes included in the 13-valent PCV (PCV13; Prevnar 13®) as well as 7 additional serotypes. In a phase 2 study of PCV20 in adults 60–64 years of age, robust immune responses were observed at 1 month after vaccination; antibody persistence up to 12 months after vaccination from that study is described herein.

Methods. In this randomized, active-controlled, double-blind study (ClinicalTrials.gov NCT03313037), adults aged 60–64 years received a single PCV20 dose followed 1 month later by saline placebo or PCV13 followed 1 month later by 23-valent pneumococcal polysaccharide vaccine (PPSV23), which provided benchmarks for all PCV20 serotypes. Immunogenicity was assessed at baseline and at 1 and 12 months after vaccination as serotype-specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) and immunoglobulin G (IgG) geometric mean concentrations (GMCs). OPA and IgG geometric mean fold rises (GMFRs) from baseline to 12 months after vaccination were assessed.

Results. In the PCV20 group, OPA GMTs (n=185–200 at Month 12) for all PCV20 serotypes increased substantially from baseline to 1 month after vaccination and then declined by Month 12 but remained elevated above baseline. OPA GMFRs from baseline to Month 12 after PCV20 vaccination were 1.9–15.0 for the serotypes in common with PCV13 and 5.6–15.6 for the 7 additional serotypes. Similar results were observed for IgG concentrations, with GMFRs of 2.4–9.4 for the PCV13 serotypes and 3.0–15.5 for the 7 additional serotypes. At Month 12, 11 months after PPSV23 vaccination (n=162–195), OPA GMFRs were 5.3–11.5 for the 7 additional serotypes; IgG GMFRs were 5.0–10.4. Benchmarking to PCV13 serotypes in the control group was not appropriate as these subjects received both PCV13 and PPSV23, which overlap in polysaccharide composition for 12 serotypes.

Conclusion. Immune responses induced by PCV20 persisted at 12 months after vaccination in adults 60–64 years of age, further supporting the potential of PCV20 to expand serotype protection against adult pneumococcal disease.

Disclosures. Mariano Young Jr., MD, Pfizer Inc (Employee, Shareholder) Daniel Scott, MD, Pfizer (Employee, Shareholder) Michael W. Pride, PhD, Pfizer (Employee, Shareholder) Ingrid L. Scully, PhD, Pfizer Inc (Employee, Shareholder) John Ginis, BS, Pfizer Inc (Employee, Shareholder) Yahong Peng, PhD, Pfizer (Employee, Shareholder) Kathrin U. Jansen, PhD, Pfizer (Employee, Shareholder) William C. Gruber, MD, Pfizer (Employee, Shareholder) Wendy Watson, MD, Pfizer (Employee, Shareholder)

1241. PfSPZ Vaccine Administered by Direct Venous Inoculation to Prevent *Plasmodium falciparum* Malaria is as Safe as Normal Saline – a Meta-analysis of 12 Randomized Controlled Clinical Trials

LW Preston Church, MD, FIDSA[1]; [1]Sanaria Inc., Bethesda, Maryland

International PfSPZ (iPfSPZ) Consortium

Session: P-57. New Vaccines

Background. Sanaria's PfSPZ Vaccine prevents *Plasmodium falciparum* (Pf) infection transmitted in the field and by controlled human malaria infection. Safety of PfSPZ Vaccine has been demonstrated in 12 randomized, double-blind, placebo-controlled trials (RCT) varying in regimen from 3 to 5 doses over 4 to 20 weeks and in size from 18 to 332 subjects in adults in the US and EU and 5-month to 65-year-olds in 5 countries in sub-Saharan Africa. This study was conducted to analyze solicited adverse event (AE) and laboratory data by random effects meta-analysis.

Methods. PfSPZ Vaccine is composed of radiation-attenuated, aseptic, purified, cryopreserved Pf sporozoites (SPZ) administered by direct venous inoculation (DVI). Normal saline (NS) is always the placebo. Data from all completed RCTs were included as either age > 18 years (n=598) or age 5 months to 17 years (n=641). Any subject receiving at least one dose was included. A random-effects model was used to study vaccine safety and I^2 to evaluate heterogeneity. Analysis was performed for any systemic solicited AE and for the most frequently observed AEs and laboratory abnormalities. Sensitivity analyses were performed by removal of trials with zero events to evaluate potential bias.

Results. When examined individually, only 1 trial had a significant difference between PfSPZ Vaccine and NS for any AE (myalgias in adults). In the adult meta-analysis, there was no difference in the random effects risk ratios (RR) for having any vaccine-related AEs (1.40, 95% confidence interval (CI) 0.88-2.28), or for fever (0.75, 0.24-2.35), headache (1.23, 0.74-2.02), fatigue (0.72, 0.19-2.54), or myalgia (1.09, 0.26-4.68). In the pediatric meta-analysis there was no difference between the RR for PfSPZ Vaccine and NS for any AE (0.84, 0.59-1.18) or for fever (1.09, 0.44-2.69). No significant differences in the most common grade 2 or higher laboratory abnormalities – declines in hemoglobin, neutrophil or platelet count – were detected. Sensitivity analysis did not change the results.