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Background: In the pivotal clinical trials, ZOE-50 (NCT01165177) and ZOE-70 (NCT01165229), the adjuvanted recombinant zoster vaccine (RZV) showed high efficacy against herpes zoster and postherpetic neuralgia. The incidence of reported solicited events was higher in RZV compared with placebo recipients.

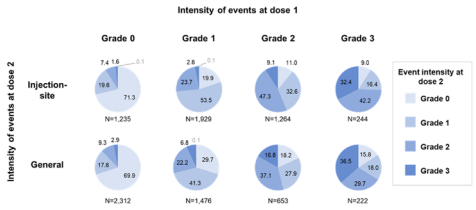
Methods: In these phase III, observer-blind, placebo-controlled trials conducted in 18 countries, adults ≥50 years of age (YOA, ZOE-50) and ≥70 YOA (ZOE-70), randomized 1:1, received 2 doses of RZV or placebo 2 months apart. Injection-site and general events were solicited for 7 days after each dose via diary cards in a participant subset. For this post-hoc analysis, ZOE-50 and ZOE-70 data from participants having completed the diary cards for both RZV doses were pooled. The intensity of each solicited event after dose 2 was stratified by the intensity of the same event after dose 1.

Results: Solicited injection-site and general events were recorded for both RZV doses by 4,676 and 4,668 vaccinees, respectively (Figure 1). Of 1,235 vaccinees with no injection-site event at dose 1, 881 (71.3%) reported no injection-site event and 20 (1.6%) reported a grade 3 event after dose 2. A total of 433 (9.3%) vaccinees reported a grade 3 injection-site event, either after dose 1 or dose 2. Of 244 vaccinees with grade 3 injection-site events at dose 1, 79 (32.4%) also reported a grade 3 event after dose 2. Of 2,312 vaccinees with no general event at dose 1, 1,617 (69.9%) reported no general event and 67 (2.9%) reported a grade 3 event after dose 2. A total of 499 (10.7%) vaccinees reported a grade 3 general event, either after dose 1 or dose 2. Of 222 vaccinees with grade 3 general events at dose 1, 81 (36.5%) also reported a grade 3 general event after dose 2. In general, vaccinees who did not experience a certain event after dose 1, did not experience this event after dose 2 either. Most vaccinees reporting a specific event at high intensity after dose 1, reported the same event at a lower intensity (or not at all) after dose 2 (Figures 2 and 3).

Conclusion: While not powered to predict event intensity of the second RZV dose, our data provides an overview of event intensity after RZV dose 2 according to the intensity of the same event experienced after dose 1.

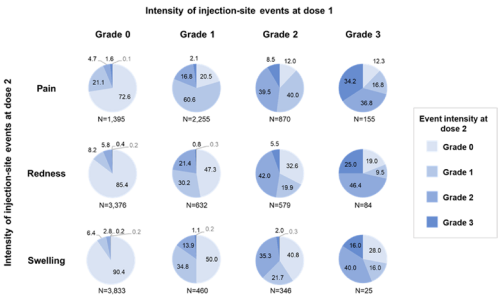
Funding: GlaxoSmithKline Biologicals SA.

Figure 1. Intensity of solicited events (injection-site and general) reported after RZV dose 2 stratified by the intensity reported after RZV dose 1



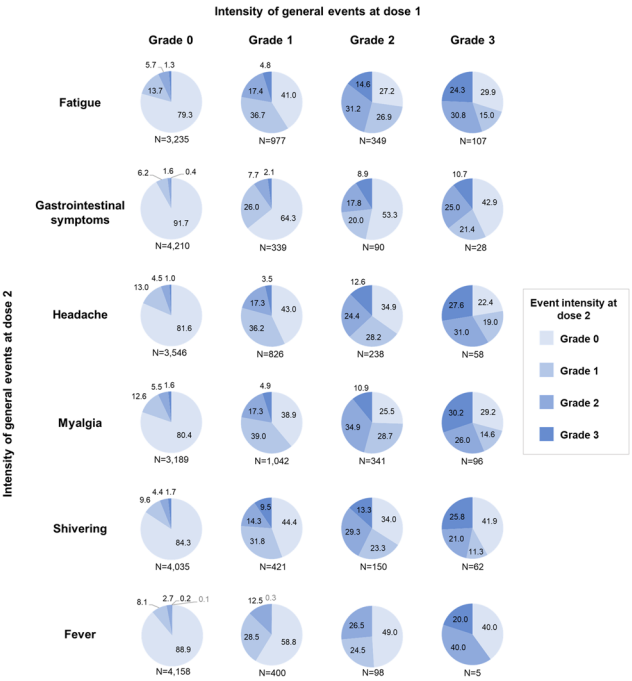
The cohort included in this analysis was a pooled subset of the total vaccinated cohorts in the ZOE-50 and ZOE-70 studies, including participants who completed a diary card after each vaccination.
Injection-site events included: pain at injection site, redness at injection site and swelling at injection site. General events included any experiences which did not occur at the site of injection of the RZV vaccine: fatigue, gastrointestinal symptoms (nausea, vomiting, diarrhea and/or abdominal pain), headache, myalgia, shivering and fever.
RZV, adjuvanted recombinant zoster vaccine; N, number of RZV vaccinees with both doses administered and corresponding event intensity following dose 1. Grey numbers represent missing values. There were 4 injection-site events and 5 general events with missing grading at dose 1 and 6 events (3 for each injection site and general) with missing grading at dose 2.

Figure 2. Intensity of solicited injection-site events reported after RZV dose 2 stratified by the intensity reported after RZV dose 1



The cohort included in this analysis was a pooled subset of the total vaccinated cohorts in the ZOE-50 and ZOE-70 studies, including participants who completed a diary card after each vaccination.
RZV, adjuvanted recombinant zoster vaccine; N, number of RZV vaccinees with both doses administered and corresponding event intensity following dose 1. Grey numbers represent missing values. Pain: grade 0, none; grade 1, mild, any pain neither interfering with nor preventing normal every day activities; grade 2, moderate, painful when limb was moved and interfered with every day activities; grade 3, severe, significant pain at rest, prevented normal every day activities. Swelling, redness: grade 0, <20 mm diameter; grade 1, ≥20 mm to ≤50 mm diameter; grade 2, >50 mm to ≤100 mm diameter; grade 3, >100 mm diameter.

Figure 3. Intensity of general events reported after RZV dose 2 stratified by the intensity reported after RZV dose 1



The cohort included in this analysis was a pooled subset of the total vaccinated cohorts in the ZOE-50 and ZOE-70 studies, including participants who completed a diary card after each vaccination.
RZV, adjuvanted recombinant zoster vaccine; N, number of RZV vaccinees with both doses administered and corresponding event intensity following dose 1. Grey numbers represent missing values. Gastrointestinal symptoms, nausea, vomiting, diarrhea and/or abdominal pain; fever, body temperature ≥37.5 °C measured by oral, axillary or tympanic route. Fatigue, gastrointestinal symptoms, headache, myalgia, shivering: grade 0, normal or none; grade 1, easily tolerated; grade 2, interfered with normal activity; grade 3, prevented normal activity. Fever: grade 0, <37.5 °C; grade 1, 37.5–38.0 °C; grade 2, 38.1–39.0 °C; grade 3, >39.0 °C.

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

2781. Statistical Modeling to Predict Maternal RSV Vaccine Efficacy from Neutralizing Titers

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Background: In the United States, respiratory syncytial virus (RSV) is the leading cause of respiratory-related hospitalization in infants. The well-studied efficacy of the prophylactic monoclonal antibody, palivizumab, at preventing RSV disease in the highest risk infants provides proof of mechanism that serum neutralizing antibody protects against RSV. The expense and burden of monthly antibody injections limit the utility of palivizumab, leaving a large unmet medical need. Maternal immunization, with transplacental transfer of antibodies to the fetus, is an alternative, highly practical approach to protect many more infants.

Methods: Levels of protection by known palivizumab serum concentrations provide a basis for predicting maternal RSV vaccine efficacy in infants based on serum neutralizing antibody titers elicited in vaccine clinical trials, using statistical modeling to compensate for differences between palivizumab prophylaxis and maternal immunization. The model adjusts for the dependency of maternal vaccine responses on pre-immunization RSV neutralizing titers, exponential decay of maternal antibodies in infants, and exponentially decreasing airway resistance (reducing RSV disease risk) as infants grow.

Results: The rates of severe RSV disease by age projected from the model match the pattern of US infant hospitalization for RSV, with a peak at 1.5 months of age. The model relates vaccine-elicited increases in maternal RSV neutralizing titers to predicted reductions in severe RSV disease in infants from 0 to 6 months of age.

Conclusion: Statistical modeling of maternal RSV vaccine efficacy based on elicited RSV neutralizing titers provides a rational basis for decision-making during RSV vaccine development.

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2782. Host Immune Response to *Enterovirus* and *Parechovirus* Systemic Infections in Children

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Background: Enterovirus (EV) and human Parechovirus (PeV) cause a range of illness including asymptomatic to systemic infections. The host immune response in children, especially the one induced by PeV, is largely unknown. The aim of this study was to determine the immune response induced by EV and PeV in cerebrospinal fluid (CSF) and plasma obtained from children with systemic infection.

Methods: Left-over CSF and paired blood samples collected from children with laboratory confirmed EV and PeV central nervous system-infection were enrolled in this study. EV/PeV-negative CSF and paired plasma from children was used as controls. Level of cytokines and chemokines were measured using a customized 21-plex ELISA panel that included 16 cytokines and 5 chemokines (Millipore, CA). Additionally, clinical characteristics of all the patients were collected to determine the potential association between the immune response and pathogenicity.

Results: Total of 74 samples were enrolled and divided into 3 groups, EV (n = 27), PeV (n = 23) and control group (n = 24). Median age of all the three groups was 2 weeks (IQR 2–4 weeks).The key analytes which had a significant difference between each groups are show in the Table. In general, EV induced more robust cytokine secretion than PeV and control group. Anti-viral response such as IFN-g was remarkably absent in both CSF and plasma in PeV group compared with EV group ($P < 0.05$). Only IL-8 was significantly higher ($P < 0.05$) in EV CSF group compared with any other groups or sample types. Level of all the chemokines measured were much higher in all the three groups but significant difference was found between PeV CSF and plasma for IP-10 and MCP-1 chemokines ($P < 0.05$).

Conclusion: In this study, we demonstrate that EV and PeV induces distinct immune response in children with systemic infections. While EV induces more robust inflammation, PeV-induced inflammation appears to be either weak or absent in CSF, but robust in plasma. The suppressed pro-inflammatory response might facilitate PeV growth and proliferation in CSF and might play a role in disease severity. Further studies are needed to fully understand the differential immune response induced by these two viruses.

Table. Comparison of cytokine levels (pg/ml) in different groups and sample types.

Analytes (pg/ml)	EV CSF (n=23) Mean ± STD	EV Plasma (n=10) Mean ± STD	PeV CSF (n=27) Mean ± STD	PeV Plasma (n=14) Mean ± STD	Control CSF (n=24) Mean ± STD	Control Plasma (n=13) Mean ± STD
IFN-γ	26.8 ± 34.83	25.1 ± 27.39	2.09 ± 1.06	11.5 ± 7.8	6.6 ± 16.3	21.4 ± 18.8
IL-6	435.5 ± 696.8	40.5 ± 65.6	3.07 ± 2.15	21.4 ± 14.9	111.3 ± 403.04	36.3 ± 18.5
TNF-α	11.7 ± 13.8	94.1 ± 46.5	1.7 ± 1.78	84.2 ± 15.5	1.66 ± 1.7	74.4 ± 51.9
IL-1Rα	869.4±1421.08	1119.6±874.7	36.4 ± 32.18	3499.9±2291.4	129.3 ± 331.7	811.9 ± 1335.5
Fractalkine	176 ± 1.62	76.3 ± 34.24	154.6 ± 17.67	442.4 ± 562.3	132.2 ± 22.9	214.8 ± 326.9
IL-8	1292.3±1760.4	31.9 ± 43.3	113.2 ± 53.6	31.9 ± 13.5	164.5 ± 235.6	38.09 ± 76.9
IP-10	11521.8±5570.6	3900±4121.2	9474.1±3911.7	9765.8±2229.2	2953.7±4576.4	2600.6±3320.9
MCP-1	6344.2±6332.3	2580.3±2344.8	3838.8±2192	7254±5021.7	1770.9±1174.7	1185.4±857.4
RANTES	339.1 ± 621.6	4187.3±1830.6	147.3 ± 312.3	3806±2166.5	227.6 ± 472.9	5816.3±3390.0

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

2783. Expansion of Monocytic Myeloid-Derived Suppressor Cells in Infants with Severe Respiratory Syncytial Virus (RSV) Infection

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Background: RSV remains a leading cause for hospitalization of infants. The mechanisms associated with the ability of RSV to suppress the induction of an adequate immune response are not well understood and represent a challenge for vaccine development. Myeloid-derived-suppressor cells (MDSCs) have been shown to suppress CD8+ T cells in patients with malignancies. These immature myeloid cells are divided into three groups: granulocytic, monocytic, and undifferentiated. Of those, monocytic MDSCs (M-MDSCs) are considered to be key regulators of inflammatory responses during acute infections. Their potential role in the immunopathogenesis of RSV infection in infants is yet to be defined.

Methods: Single-center, prospective cohort study in previously healthy infants hospitalized with severe RSV lower respiratory tract infection (LRTI) and age-matched healthy controls (HC). Nasopharyngeal swabs for RSV detection and blood samples for cell immunophenotyping were analyzed at enrollment (D1), 1-month (D30), and 6-months (D180) follow-up visits. Disease severity was assessed using a clinical disease severity score (CDSS), duration of supplemental O2, and duration of hospitalization.

Results: We enrolled 39 infants with RSV LRTI (median [IQR] age: 3.3 [1.5–5.2] months) and 5 HC (5.9 [4.5–7.2] months). Infants with RSV infection demonstrated an expansion of M-MDSCs during the acute infection (D1) that resolved to numbers comparable to those in HC at follow-up visits (Figure 1A). In addition, numbers of CD8+ T cells were significantly reduced during the acute infection (D1) in RSV-infected infants, but also returned to the HC baseline on D30 and D180 (Figure 1B). Finally, the increase in M-MDSCs numbers and decrease in CD8+ T-cell numbers were associated with worse clinical outcomes as defined by duration of supplemental oxygen (>1 day), hospitalization (>48 hours), and clinical disease severity score (CDSS, > 9) (Figure 2).

Conclusion: These findings suggest that an expansion of M-MDSCs may play a role in T-cell suppression in children with severe RSV disease. As new vaccines are being developed, it is critical to elucidate the immune suppressive mechanisms associated with RSV infection.

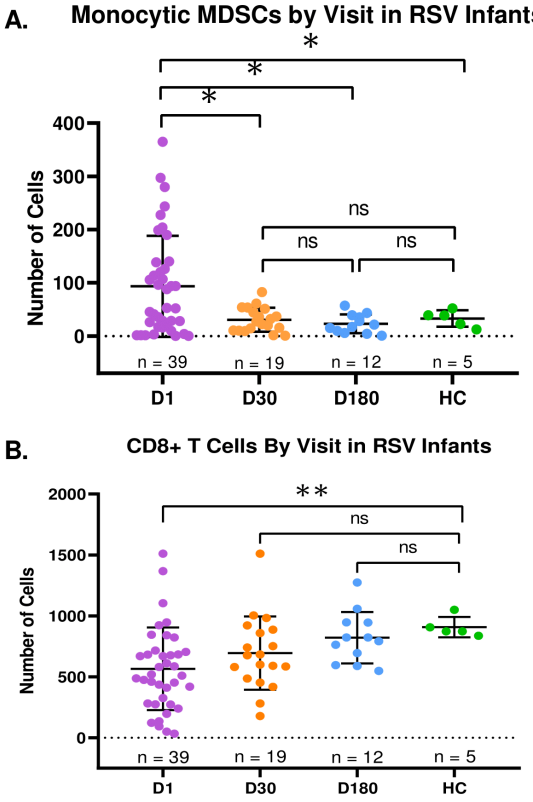

Figure 1. Number of **(A)** monocytic myeloid-derived suppressor cells (M-MDSCs) and of **(B)** CD8+ T cells in infants hospitalized with RSV LRTI (D1), and at follow up of 1-month (Day 30) and 6-months (Day 180) post hospitalization, and healthy controls (HC). (p<0.05).

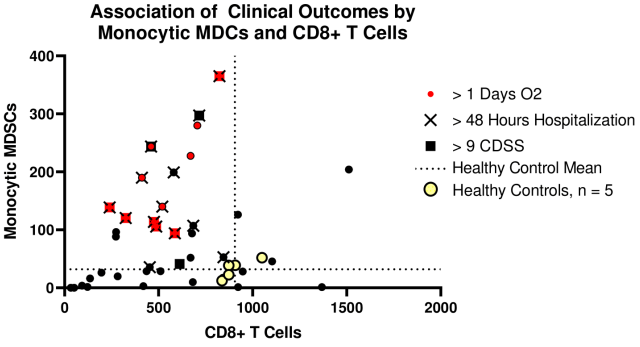

Figure 2. RSV infants profiled by numbers of monocytic myeloid-derived suppressor cells (M-MDSCs) and CD8+ T cells. Stratified by the mean number of CD8+ T cells and M-MDSCs of age-matched healthy controls (HC, dotted lines). RSV infants with higher number of M-MDSCs and lower number of CD8+ T cells (left upper quadrant) showed worse parameters of clinical disease severity. Healthy controls are plotted as a reference (yellow dots).

Disclosures: Octavio Ramilo, MD, Bill & Melinda Gates Foundation: Research Grant; Janssen: Research Grant; Merck: Advisory Board; NIH: Research Grant; Ohio Children's Hospital Association (OCHA): Research Grant; Pfizer: Advisory Board, Consultant, Lectures; Sanofi/Medimmune: Advisory Board.

2784. Increased Frontal Lobe Volume and Density in Macaques Exposed to Zika Virus In Utero

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