3. Phase 3 Pivotal Evaluation of 20-valent Pneumococcal Conjugate Vaccine (PCV20) Safety, Tolerability, and Immunologic Noninferiority in Participants 18 Years and Older

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Session: O-2. Adult Vaccines

Background. PCV20 contains the 13-valent pneumococcal conjugate vaccine (PCV13) components, and 7 additional conjugates (for serotypes 8, 10A, 11A, 12F, 15B, 22F, and 33F), extending pneumococcal serotype coverage. Key data from the pivotal Phase 3 evaluation of PCV20 in adults are presented.

Methods. Adults naïve to pneumococcal vaccination were enrolled into 3 age cohorts (≥60, 50–59, and 18–49 years of age). Participants ≥60 years received either PCV20 and saline 1 month later, or PCV13 and 23-valent pneumococcal polysaccharide (PPSV23) 1 month later (1:1 randomization, double blind). Participants 50–59 and 18–49 years received either a dose of PCV20 or PCV13 (3:1 randomization, double blind). Tolerability, safety and immunogenicity (opsonophagocytic activity [OPA] responses) were assessed.

Results. 3889 participants received vaccine. 1507 and 1490 participants ≥60 years received PCV20 or control respectively. All 20 vaccine serotypes induced robust responses and OPA geometric mean titers (GMTs) to all 13 matched serotypes were noninferior to PCV13. In addition, the OPA GMTs to 6 of the 7 additional serotypes 1 month after PCV20 were noninferior compared to the same serotypes in PPSV23. The OPA GMT of serotype 8 missed noninferiority by a very narrow margin (2-sided 95% lower bound of GMT ratio [20vPnC/PPSV23] was 0.49, with noninferiority criterion of >0.5); this is unlikely to be clinically significant given the high geometric mean fold rise of OPA titers after PCV20 (22-fold above baseline). GMTs after PCV20 in each of the younger age cohorts (18–49 years, 50–59 years) were noninferior to adults 60–64 years. The tolerability and safety profile of PCV20 was similar to PCV13.

Conclusion. Based on the robust immune responses and comparability to licensed pneumococcal vaccines, as well as bridging to the younger age group, these data support that PCV20 will be protective against pneumococcal disease due to the 20 serotypes in adults.

Disclosures. **Charu Sabharwal, MD, MPH**, **Pfizer** (Employee, Shareholder) **Xia Xu, PhD**, **Pfizer** (Employee, Shareholder) **Vani Sundaraiyer, PhD, MS**, **Pfizer** (Independent Contractor) **Yahong Peng, PhD**, **Pfizer** (Employee, Shareholder) **Lisa Moyer, BS**, **Pfizer** (Employee, Shareholder) **Michael W. Pride, PhD**, **Pfizer** (Employee, Shareholder) **Ingrid L. Scully, PhD**, **Pfizer Inc** (Employee, Shareholder) **Kathrin U. Jansen, PhD**, **Pfizer** (Employee, Shareholder) **William C. Gruber, MD**, **Pfizer** (Employee, Shareholder) **Daniel Scott, MD**, **Pfizer** (Employee, Shareholder) **Wendy Watson, MD**, **Pfizer** (Employee, Shareholder)

4. Immunogenicity of the Adjuvanted Recombinant Zoster Vaccine in Immunocompromised Adults

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Session: O-2. Adult Vaccines

Background. Immunocompromised (IC) populations are at increased risk of developing herpes zoster (HZ) due to disease- and/or therapy-induced immunosuppression. The adjuvanted recombinant zoster vaccine (RZV) has demonstrated 68.2% efficacy in preventing HZ in autologous hematopoietic stem cell transplant (HSCT) recipients and 87.2% efficacy in a post-hoc analysis in hematologic malignancy (HM) patients ≥ 18 years of age (YOA). Here we present the immunogenicity of RZV in representative IC populations.

Methods. Our analysis includes five phase I/II/III clinical trials conducted worldwide between 2010–2017 (**Table 1**) in IC populations (autologous HSCT, human immunodeficiency virus [HIV]-infected, HM, solid tumor [ST] on chemotherapy and renal transplant [RT] patients) ≥ 18 YOA. Anti-glycoprotein E (gE) antibody geometric mean concentrations (GMCs) and gE-specific CD4 T cell frequencies were descriptively evaluated by age group (18–49 YOA and ≥ 50 YOA) and overall at 1 month (M) and 12M post-last RZV dose.

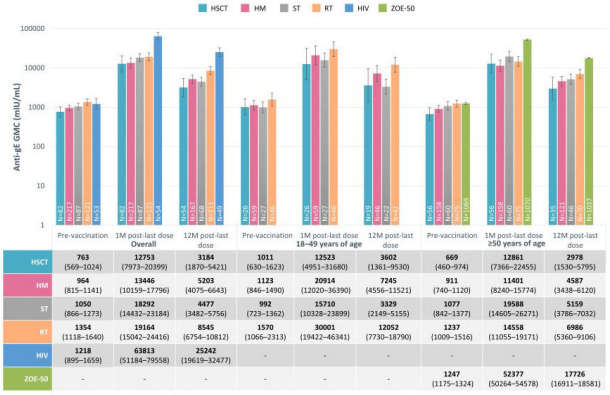
Table 1. Clinical studies with immunocompromised populations included in our analysis

Population and schedule	Study design, study years and registration numbers	Number of participants included in the ATP cohort for immunogenicity**	
		ATP for humoral immunogenicity	ATP for cell-mediated immunogenicity
HIV-infected adults ≥ 18 YOA 3 doses (at months 0, 2 and 6)	Phase I/IIa, randomized, observer-blind, placebo controlled 2010–2013 NCT01165203	3 RZV doses: 54 3 placebo doses: 37	
Autologous HSCT recipients ≥ 18 YOA (ZOE-HSCT)* 2 doses (at months 0 and 1–2)	Phase III, randomized, observer-blind, placebo-controlled efficacy study 2012–2017* NCT01610414	2 RZV doses: 82 2 placebo doses: 76	2 RZV doses: 47 2 placebo doses: 47
Hematologic malignancy patients ≥ 18 YOA 2 doses (at months 0 and 1–2)	Phase III, randomized, observer-blind, placebo-controlled study 2013–2017 NCT01767467	2 RZV doses: 217 2 placebo doses:198	2 RZV doses: 69 2 placebo doses: 63
Solid tumor patients ≥18 YOA on chemotherapy 2 doses (at months 0 and 1–2)	Phase II/III, randomized, observer-blind, placebo-controlled study 2013–2016 NCT01798056	2 RZV doses: 87 2 placebo doses: 98	2 RZV doses: 27 2 placebo doses: 31
Renal transplant patients ≥18 YOA 2 doses (at months 0 and 1-2)	Phase III, randomized, observer-blind, placebo-controlled study 2014–2017 NCT02058589	2 RZV doses: 121 2 placebo doses: 119	2 RZV doses: 36 2 placebo doses: 36

ATP, according-to-protocol; **HSCT**, hematopoietic stem cell transplant; **YOA**, years of age; **RZV**, adjuvanted recombinant zoster vaccine; **HIV**, human immunodeficiency virus; ZOE-HSCT, ZOSTER EFFICACY study in autologous HSCT recipients. *A phase I/IIa, randomized, observer-blind, placebo-controlled study (NCT00922018) conducted in autologous HSCT recipients between 2009—2012 was not included in our analysis because this phase III efficacy study enrolled a larger sample of HSCT recipients from a broader range of geographic regions. **Immunogenicity was evaluated in the ATP cohorts for immunogenicity, which included study participants who received all foreseen doses, complied with the protocol, and had available immunogenicity data. Cell-mediated immunity was evaluated in subsets, except for HIV-individuals. All studies are registered on clinicaltrials.gov and their results were previously published.

Results. The according-to-protocol cohorts for immunogenicity from the included trials are presented in **Table 1**. At 1M post-last RZV dose, anti-gE GMCs and median CD4 T-cell frequencies increased in all IC populations compared to pre-vaccination and persisted above baseline up to 12M post-last RZV dose (**Figures 1 and 2**). No meaningful differences were seen between age groups in terms of humoral (except a slight trend for stronger responses in the 18–49 YOA RT and HM patients compared to their corresponding ≥ 50 YOA group) and gE-specific CD4 T-cell responses in any of the IC populations.

Figure 1. Humoral immune responses to RZV in immunocompromised populations (adapted ATP cohort for humoral immunogenicity)



	Overall			18–49 years of age			≥50 years of age		
	Pre-vaccination	1M post-last dose	12M post-last dose	Pre-vaccination	1M post-last dose	12M post-last dose	Pre-vaccination	1M post-last dose	12M post-last dose
HSCT	763 (569–1024)	12753 (7973–20399)	3184 (1870–5421)	1011 (630–1623)	12523 (4951–31680)	3602 (1361–9530)	669 (460–974)	12861 (7366–22455)	2978 (1530–5795)
HM	964 (815–1141)	13446 (10159–17796)	5203 (4075–6643)	1123 (846–1490)	20914 (12020–36390)	7245 (4556–11521)	911 (740–1120)	11401 (8240–15774)	4587 (3438–6120)
ST	1050 (866–1273)	18292 (14432–23184)	8477 (6482–5756)	992 (723–1362)	15710 (10328–23899)	3329 (2149–5155)	1077 (842–1377)	19588 (14605–26271)	5159 (3786–7032)
RT	1354 (1118–1640)	19164 (15042–24416)	8545 (6754–10812)	1570 (1066–2313)	30001 (19422–46341)	12052 (7730–18790)	1237 (1009–1516)	14558 (11055–19171)	6986 (5360–9106)
HIV	1218 (895–1659)	63813 (51184–79558)	25242 (19619–32477)	-	-	-	-	-	-
ZOE-50	-	-	-	-	-	-	1247 (1175–1324)	52377 (50264–54578)	17726 (16911–18581)

RZV, adjuvanted recombinant zoster vaccine; **ATP**, according-to-protocol; **gE**, glycoprotein E; **GMC**, geometric mean concentration; **N**, number of participants with available results; **M**, month; **HSCT**, autologous hematopoietic stem cell transplant recipients; **HM**, hematologic malignancies patients; **ST**, solid tumor patients; **RT**, renal transplant recipients; **HIV**, human immunodeficiency virus-infected adults; **ZOE-50**, adults ≥50 years of age from the pivotal efficacy trial in older adults

Adapted ATP cohort for humoral immunogenicity includes ATP cohort with humoral immunogenicity data for each timepoint (pre-vaccination, 1M post last-dose, 12M post last-dose).

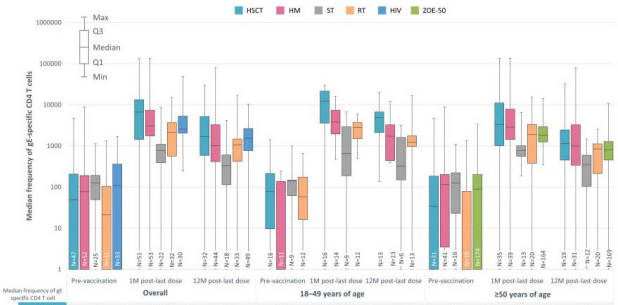
Error bars depict two-sided exact 95% confidence intervals.

HIV-infected adults were not divided by age group and immunogenicity analyses were only done overall.

The green bars display the humoral immune responses in adults ≥50 years of age from the pivotal efficacy trial (ZOE-50, Cunningham et al, 2018), which are provided here for reference.

Note: In the HSCT study (NCT01610414), anti-gE antibodies were also measured at 25M post-RZV dose 2 and found to continue to persist well above pre-vaccination levels.

Figure 2. Cell-mediated immune responses to RZV in immunocompromised populations (adapted ATP cohort for cell-mediated immunogenicity)



	Overall			18–49 years of age			≥50 years of age		
	Pre-vaccination	1M post-last dose	12M post-last dose	Pre-vaccination	1M post-last dose	12M post-last dose	Pre-vaccination	1M post-last dose	12M post-last dose
HSCT	49 (1–207)	6645 (1438–13299)	1706 (591–5207)	78 (10–214)	12366 (3591–21625)	4872 (2134–6709)	34 (1–185)	3294 (1017–11136)	1153 (454–2463)
HM	78 (1–191)	3082 (1766–7414)	1007 (416–3285)	1 (1–138)	3816 (1956–7414)	1729 (441– 3281)	115 (4–203)	2878 (1441–7864)	996 (340–3288)
ST	127 (50–192)	779 (393–1098)	333 (115–605)	142 (62–148)	653 (190–2919)	323 (150–1607)	127 (23–222)	783 (562–1015)	345 (105–595)
RT	21 (1–105)	2149 (569–3695)	1066 (425–1482)	59 (16–175)	2855 (1505–3695)	1247 (974–1765)	1 (1–79)	1909 (380–3343)	850 (215–1124)
HIV	107 (1–362)	2578 (2057–5299)	1533 (770–2643)	-	-	-	-	-	-
ZOE-50	-	-	-	-	-	-	90 (1–202)	1844 (1254–2932)	800 (454–1277)

RZV, adjuvanted recombinant zoster vaccine; **ATP**, according-to-protocol; **gE**, glycoprotein E; **M**, month; **Q1**, **Q3**, first and third quartiles; **N**, number of participants with available results; **HSCT**, autologous hematopoietic stem cell transplant recipients; **HM**, hematologic malignancies patients; **ST**, solid tumor patients; **RT**, renal transplant recipients; **HIV**, human immunodeficiency virus-infected adults; **ZOE-50**, adults ≥50 years of age from the pivotal efficacy trial in older adults.

Adapted ATP cohort for cell-mediated immunogenicity includes ATP cohort with cell-mediated immunogenicity data for each timepoint (pre-vaccination, 1M post last-dose, 12M post last-dose).

HIV-infected adults were not divided by age group and immunogenicity analyses were only done overall.

The green bars display the cell-mediated immune responses in adults ≥50 years of age from the pivotal efficacy trial (ZOE-50, Cunningham et al, 2018), which are provided here for reference.

Note: In the HSCT study (NCT01610414), cell-mediated immune responses were also measured at 25M post-RZV dose 2 and found to continue to persist well above pre-vaccination levels.

Conclusion. RZV induced robust and persistent humoral and cell-mediated immune (CMI) responses that lasted up to at least 12M post-last vaccination in all evaluated IC populations. Humoral responses in the IC populations were robust although not as strong as in the non-IC adults ≥ 50 YOA. CMI responses were mostly similar across IC populations and adults ≥ 50 YOA, with a potent response occurring even in ST patients undergoing chemotherapy. This data shows that RZV is immunogenic even in severely IC adults.

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5. How Does Frailty Impact the Efficacy, Reactogenicity, Immunogenicity and Safety of the Adjuvanted Recombinant Zoster Vaccine? A Secondary Analysis of the ZOE-50 and ZOE-70 Studies

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