Immunogenicity and Safety after One-Week Pre-Exposure Prophylaxis Regimens, Followed by a Simulated Post-Exposure Prophylaxis Regimen at One Year

***Phase III, open-label, randomized, controlled trial conducted in healthy subjects aged 2 years and older in the Philippines*.**

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Disclaimer

- The study ClinTrials.gov Identifier: NCT03700242 has been sponsored by Sanofi Pasteur
- Principals Investigators
  - Dr Beatriz P. Quiambao, MD; Research Institute for Tropical Medicine
  - Dr Jonathan G. Lim, MD; Chong Hua Hospital

- Dr Quiambao disclosure :
  - xxxxxxxxx

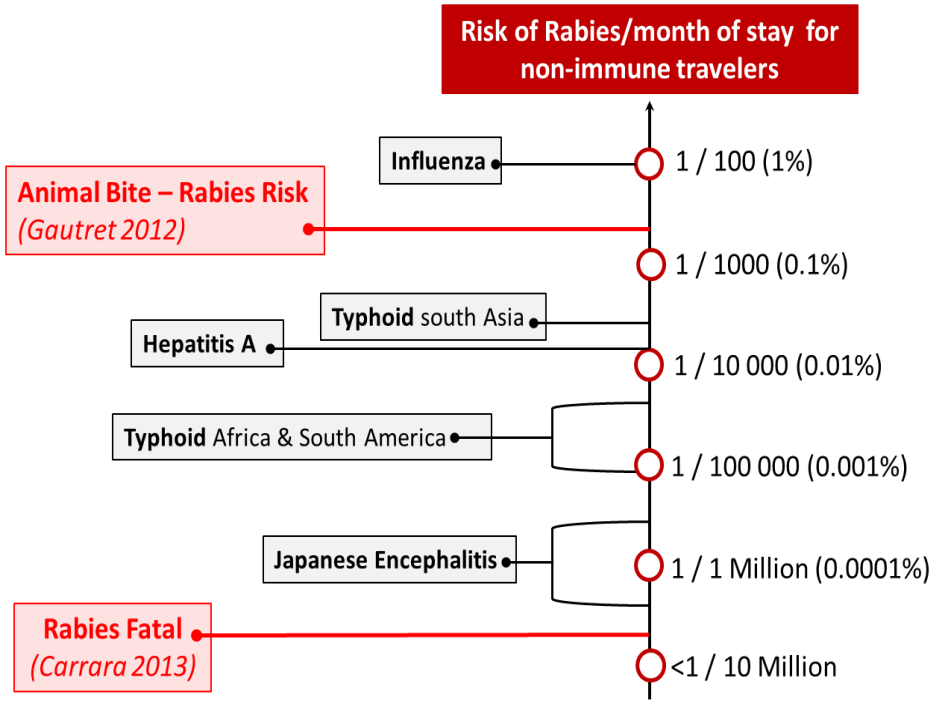
Rabies PrEP awareness and vaccination should be increased for travelers and population at frequent risk

- Risk of exposure to animal bite is high[1,2]
- WHO/ACIP recommends PrEP for travellers to rabies endemic areas
- Awareness of PrEP is low (23%) and PrEP vaccination very low (8%)[3]
- Rabies PrEP regimens are too long and complex for last minute travelers[4]
- Last minute travelers correspond to 16% of travelers[4]

Steffen R. J Trav Med. 2018; 25(1);/2. Gautret P, et al. Vaccine. 2012; 30(2):126–33./Marano C, et al. J Trav Med. 2019; 26(Suppl 1):S3–S9. /A Yates, et al, Global TravEpiNet Consortium J Travel Med. 2019; 26(6)

Vaccine-preventable disease travel-health risks

Estimated incidence per month of stay in lower-income countries[1]



Adapted from Steffen, *et al*. 2018[1]

Study rationale and objectives

- **Rational**
  - **Document One-week Pre Exposure (PrEP) regimens with SP rabies vaccines, Imovax® Rabies (HDCV) and Verorab® (PVRV)**
    - PrEP generally consists of 3 intramuscular (IM) doses given on days 0, 7, 21 or 28. PrEP regimens can be shortened in duration and number of doses required.
    - One-week PrEP regimens (D0, D7) are becoming the new standard (WHO, 2018 and ACIP 2021)

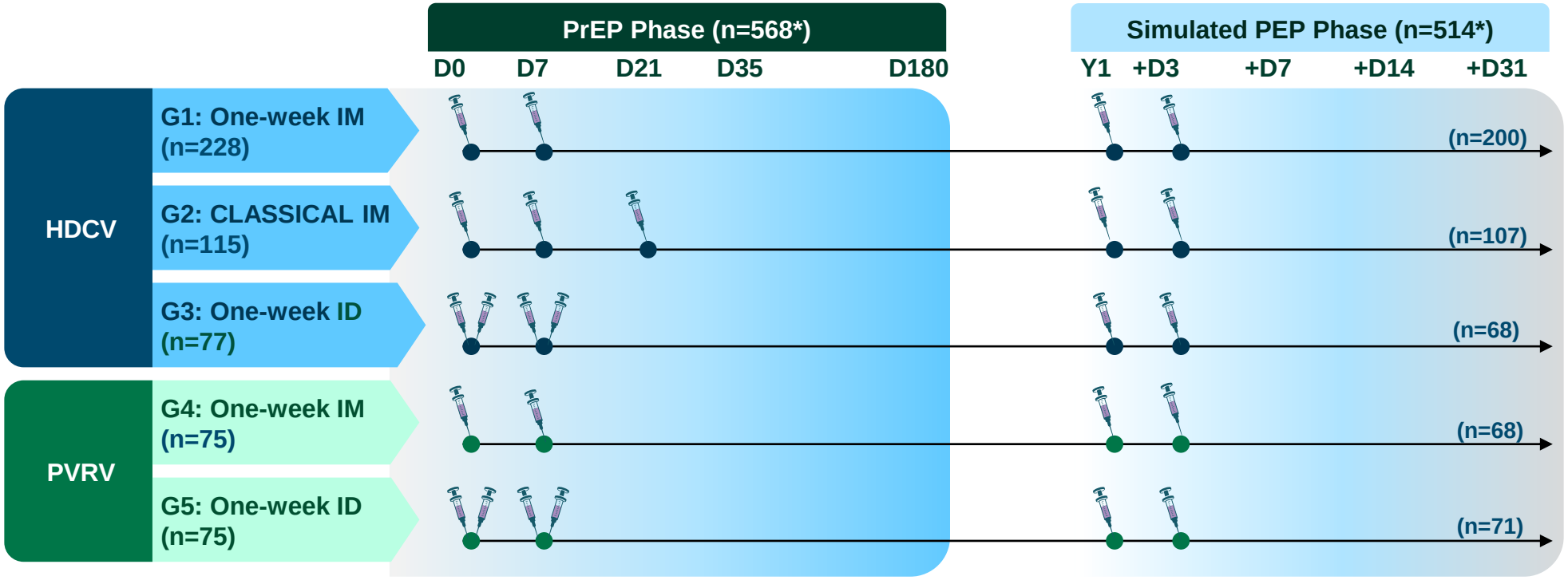
- **Primary objective:**
  - Non-inferiority of short IM PrEP (Group 1) to the reference IM PrEP (Group 2) with HDCV in terms of seroconversion* 14 days after the last PrEP vaccination

- **Secondary objectives:**
  - Immune responses measured after One-week PrEP, RVNA persistence at 6 months and 1 year
  - Boostability of One-week PrEP after simulated PEP given 1 year later
  - Safety profile of HDCV or PVRV after One-week PrEP regimens and simulated PEP given 1 year later

*Seroconversion is defined as RFFIT titer ≥ 0.5 IU/mL

Study design

- **Phase III, open-label, randomized, controlled trial, in healthy subjects aged 2-64 years in the Philippines**.
- **570** healthy subjects aged **≥ 2-64** years were randomized in **5** groups (ratio **6:3:2:2:2**)
- **Blood samples** to assess RVNA (RFFIT): at D0, D21 (D35 in G2), D180, Y1, Y1+7D,Y1+14D

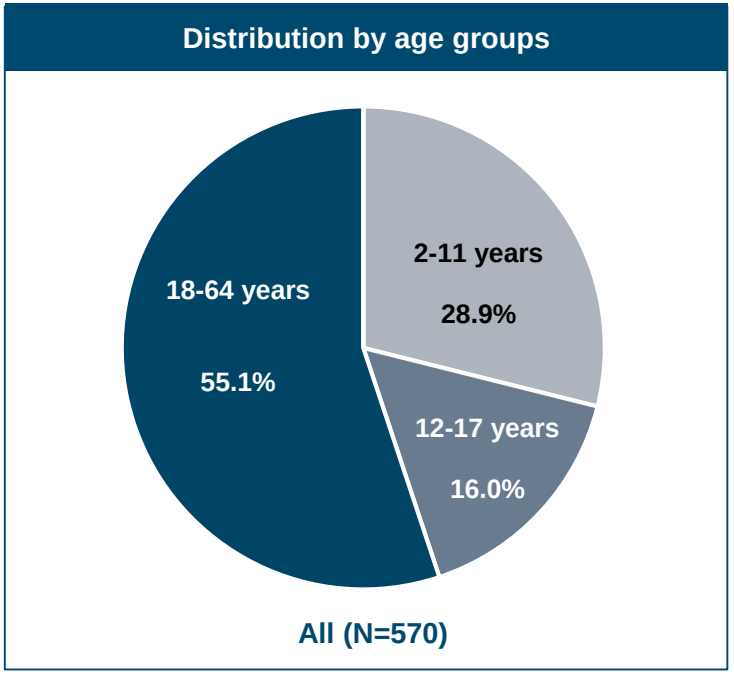


Note: one Intradermal (ID) dose = 0.1 mL, i.e., 1/10 of the Intramuscular (IM) dose for Imovax® Rabies and 1/5 of the IM dose for Verorab®.
D: Day; G: Group; Y: Year.
* Vaccinated subjects

Study population – Baseline demographics

- **Baseline demographics were comparable in all groups and were similar in the PrEP and simulated PEP vaccination phases.**

  - Male/female ratio: 47.2% male subjects and 52.8% female subjects.
  - The mean age of subjects at inclusion was 22.5 years (ranging between 2.0 and 59.0 years).
  - Majority of subjects were aged 18 to 64 years, followed by subjects aged 2 to 11 years
  - The age distribution was similar in each group.



Immunogenicity results – Primary objective

- **Non-inferiority (NI) non demonstrated between Groups 1 and 2, based on the proportion of subjects with RVNA titer ≥ 0.5 IU/mL measured at D21 (group 1) and at D35 (group 2)**

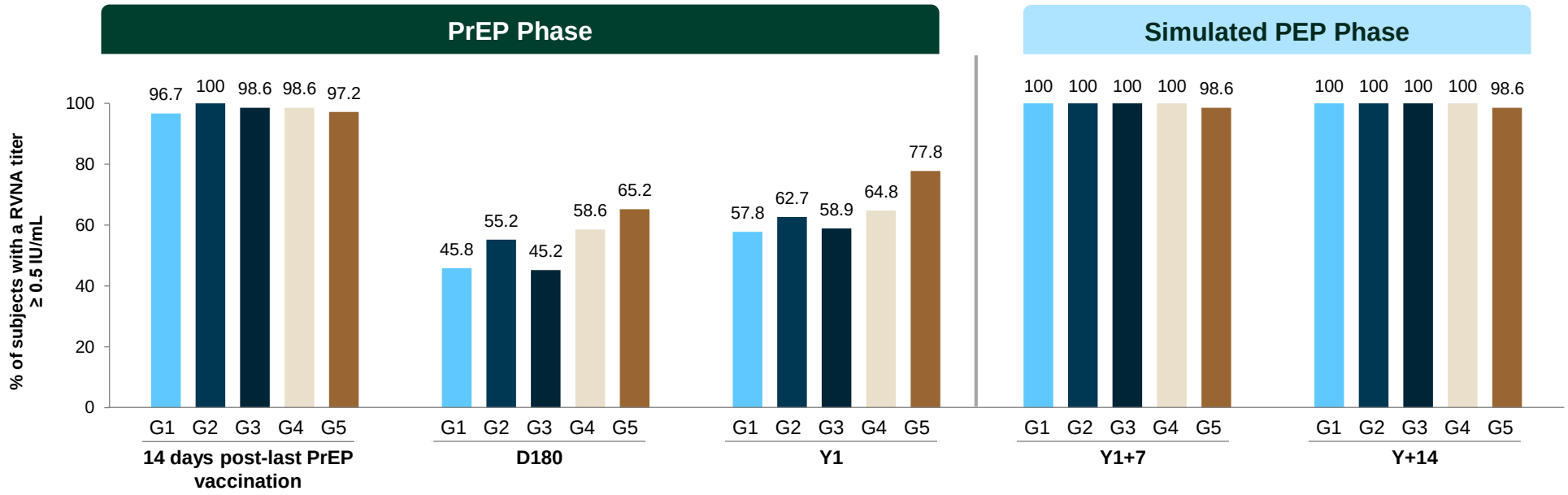
	Seroconversion at D21 (group 1) and D35 (group 2)		
	n/M	**SC%**	**(95% CI)**
Group 1 (test)	202/209	96.7%	(93.3; 98.6)
Group 2 (ref)	109/109	100%	(96.7; 100)

- **The lower limit of the two-sided 95% CI of the difference Group1 – Group 2 was below the set delta (-5%): -3.349 (-6.751; 0.464, 95% CI)**

n: number of subjects experiencing the endpoint; M: number of subjects with available data for the relevant endpoint
Note – Per Protocol Analysis Set, similar results are observed in the Full Analysis Set

Immunogenicity results – Seroconversion rates

- High rates of SRC with all one-week PrEP regimens and confirmed boostability after simulated PEP (with IM and ID routes)



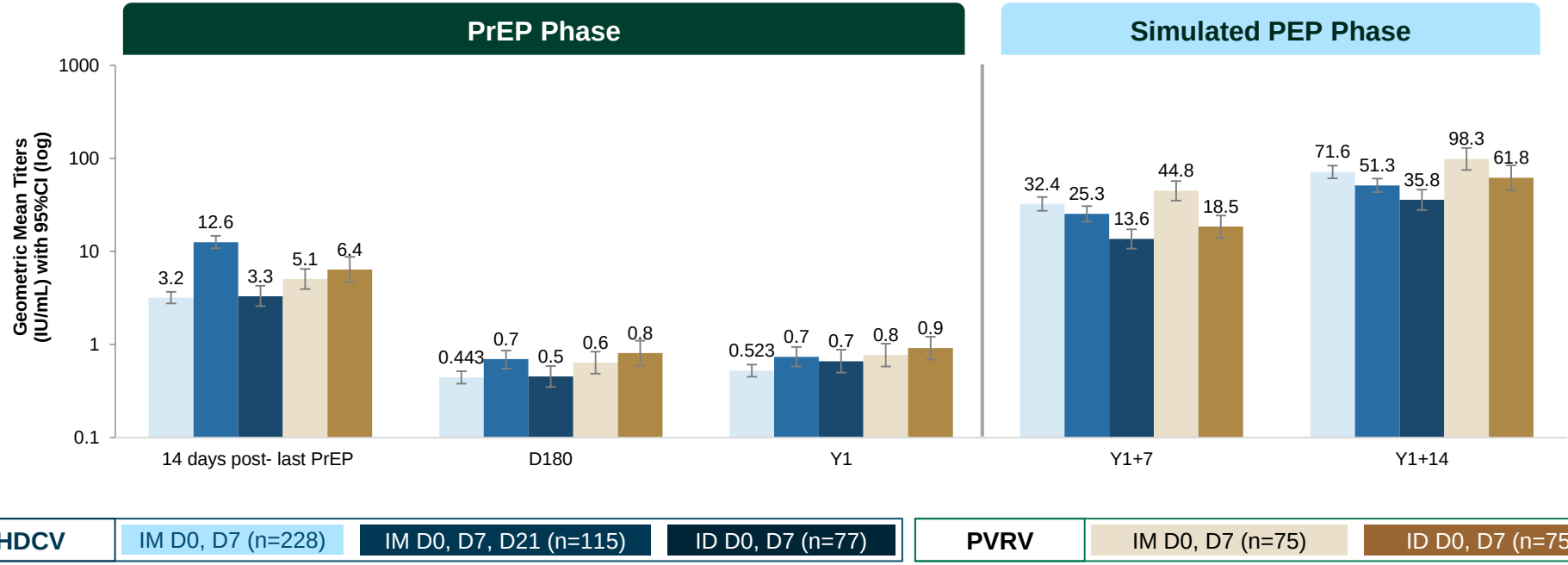
HDCV	IM D0, D7 (n=228)	IM D0, D7, D21 (n=115)	ID D0, D7 (n=77)

PVRV	IM D0, D7 (n=75)	ID D0, D7 (n=75)

- D: Day; G: Group; Y: Year. ID: intradermal; IM: intramuscular; PEP: post-exposure prophylaxis; PrEP: Pre-exposure prophylaxis; RVNA: rabies virus neutralizing antibodies.

Immunogenicity results – Geometric Mean Titers (GMTs)

- Decrease in GMTs from D14 post last injection to D180 and Y1 but strong anamnestic response after booster doses (Y1 +7/14 days) in all regimens



- D: Day; Y: Year; ID: intradermal; IM: intramuscular; PrEP: Pre-exposure prophylaxis.

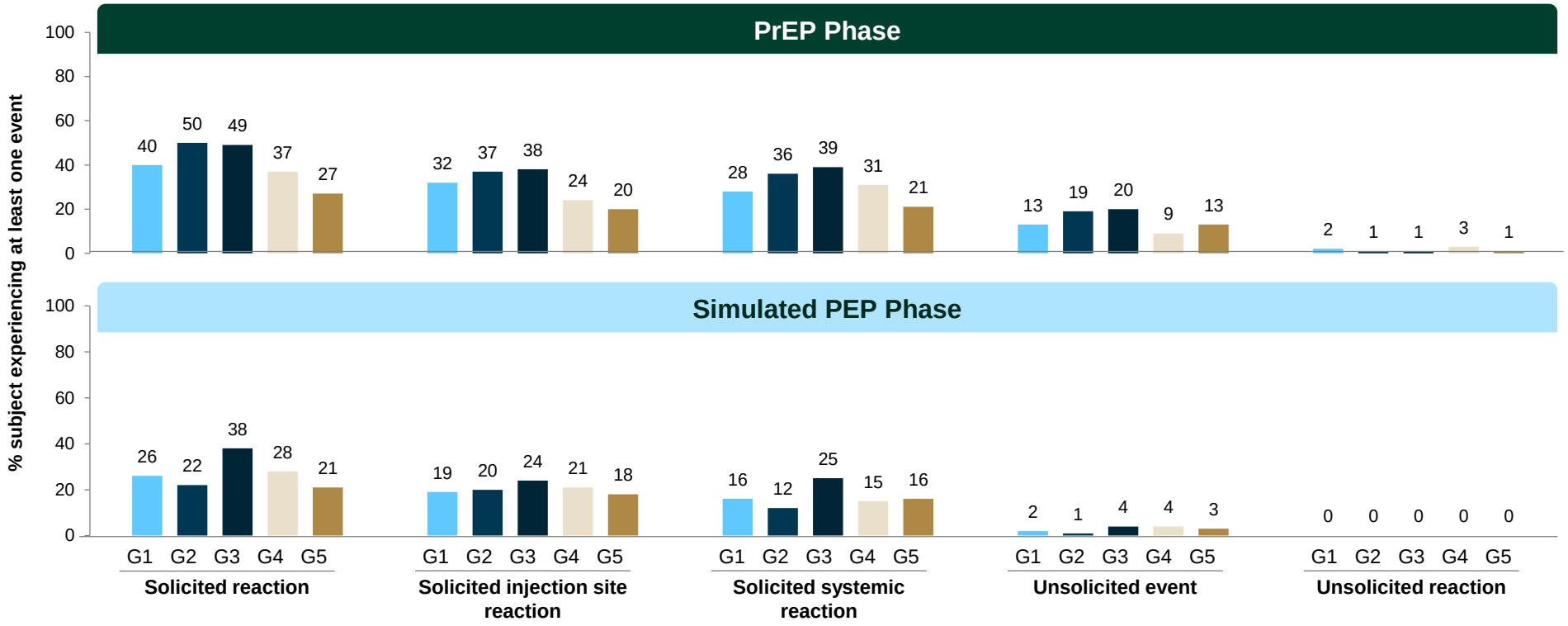
Conclusions on PrEP and PEP Immune response

- **High level seroconversion achieved with HDCV and PVRV after One-week PrEPs, with no meaningful difference between IM or ID groups and with age**
  - Seroconversion rates (SCR) varied from 96.7 to 98.6 % in one-week PrEP groups at D21 vs 100% in 3-dose PrEP at D35
  - NI not demonstrated 14 days after last injection for HDCV (group 1 vs group 2)
  - Timepoint at D21 likely too early to observe complete seroconversion (immune priming usually takes 2 to 3 weeks after immunization)

- **Ab persistence over 1 year showed the maintenance of SCRs ranging from 58-78%, with all studied regimens**

- **Boostability of one-week PrEP regimens was confirmed**
  - Simulated PEP regimens induced a very high and rapid anamnestic response in all groups measured 7 and 14 days after the first PEP dose, therefore confirming the adequate priming conferred by the one-week PrEP regimens, including in those few subjects who did not seroconvert initially.

Safety results – PrEP and PEP phases



HDCV	IM D0, D7 (n=228)	IM D0, D7, D21 (n=115)	ID D0, D7 (n=77)	PVRV	IM D0, D7 (n=75)	ID D0, D7 (n=75)

D: Day; G = Group. ID: intradermal; IM: intramuscular; PrEP: Pre-exposure prophylaxis; PEP: post-exposure prophylaxis

Conclusions on PrEP and PEP Safety

- **Overall, PrEP and simulated PEP vaccinations with HDCV or PVRV**
  - were well tolerated and safe in all groups,
  - no meaningful difference in the safety profile of IM and ID groups
  - no clinically significant differences according to the different classes of age
- **No immediate unsolicited AEs, deaths, other SAEs, or AEs leading to discontinuation were reported during the PrEP and the simulated PEP vaccination phases (during the 28 days period following vaccination)**
- **Only 3 non-related SAEs were reported outside the 28 days period following vaccination**
  - 1 death (pneumonia) and 2 other SAEs related to pregnancy, ie 1 intrauterine fetal death and 1 spontaneous abortion

Overall conclusions

- **These results of this study conducted in heathy individuals aged 2 to 64 years of age and living in The Philippines confirmed:**
  - The acceptable safety profile of the One-week IM and ID PrEP regimens evaluated with HDCV and PVRV
  - As well as the boostability of One-week IM and ID PrEP regimens, ie, their ability to induce an adequate immune priming, as confirmed by the strong anamnestic response seen in all groups after the simulated PEP vaccination.

THANK YOU!

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