First-in-human study to assess the safety and immunogenicity of an investigational respiratory syncytial virus (RSV) vaccine based on ChAd155 viral vector expressing RSV viral proteins F, N and M2-1 in healthy adults

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Disclosures

- The study was run by the Oxford Vaccine Group, which is part of the University of Oxford.
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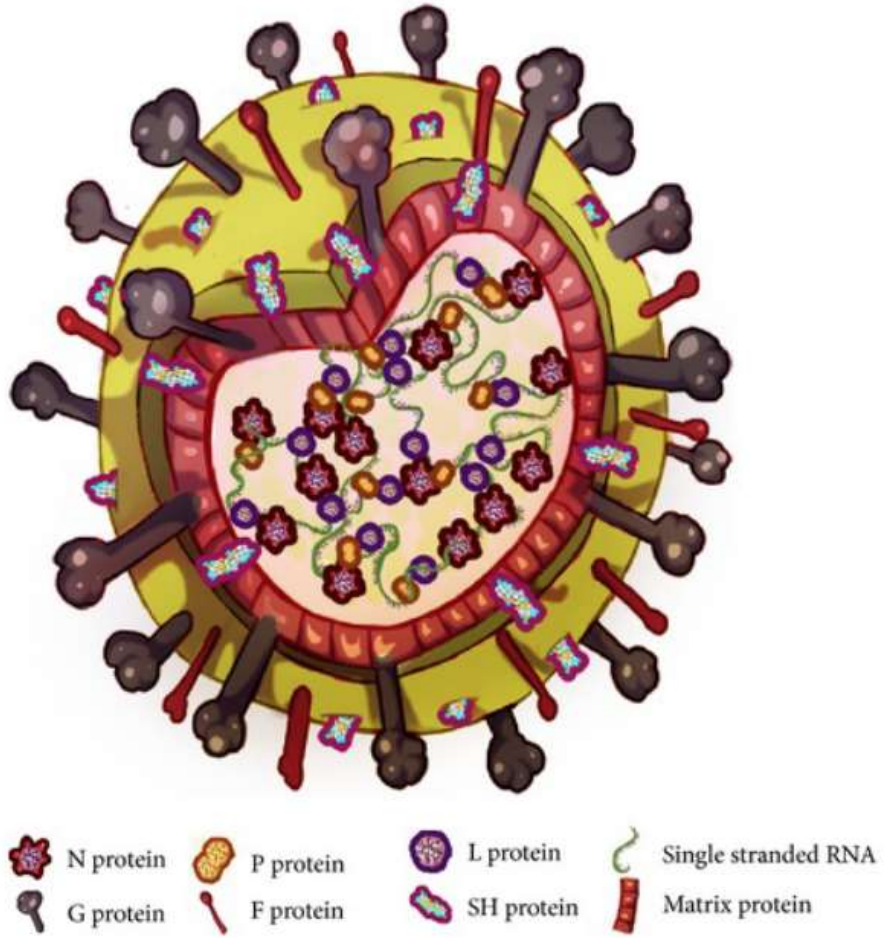
- I have no financial interests nor financial ties to GSK. I have received no compensation from GSK.

Background

Respiratory Syncytial virus (RSV) is

- most common cause of serious acute lower respiratory illness in infants and young children[1]
- significant cause of disease burden in the elderly and immunocompromised[1]
- no licensed RSV vaccines to address this significant public health need[1]
- novel vaccine against RSV infection using adenoviral vector (ChAd155) encoding for the RSV viral proteins F, N and M2-1 is being developed by GSK

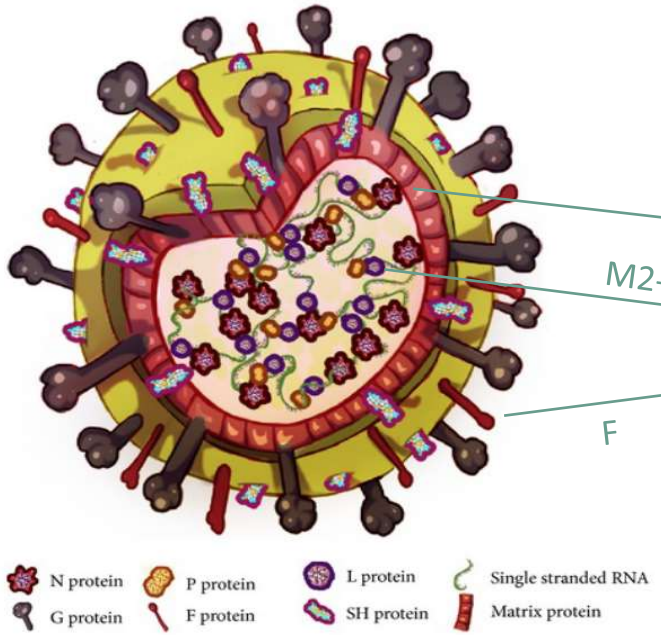


[1]PA Jorquera et al. *Expert Rev Vaccines* 2016;15:173–87

SS Bawage et al. *Adv Virol* 2013;2013. http://dx.doi.org/10.1155/2013/595768

Rationale for a viral vectored-based vaccine

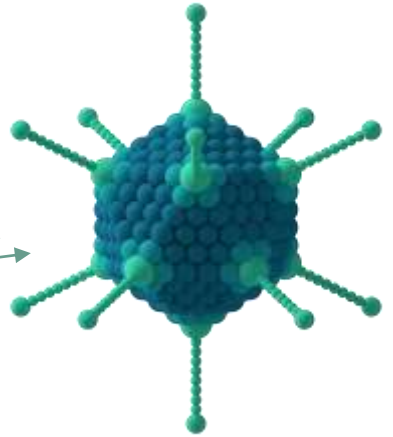
RSV



N

M2-1 (cofactor of P)

F



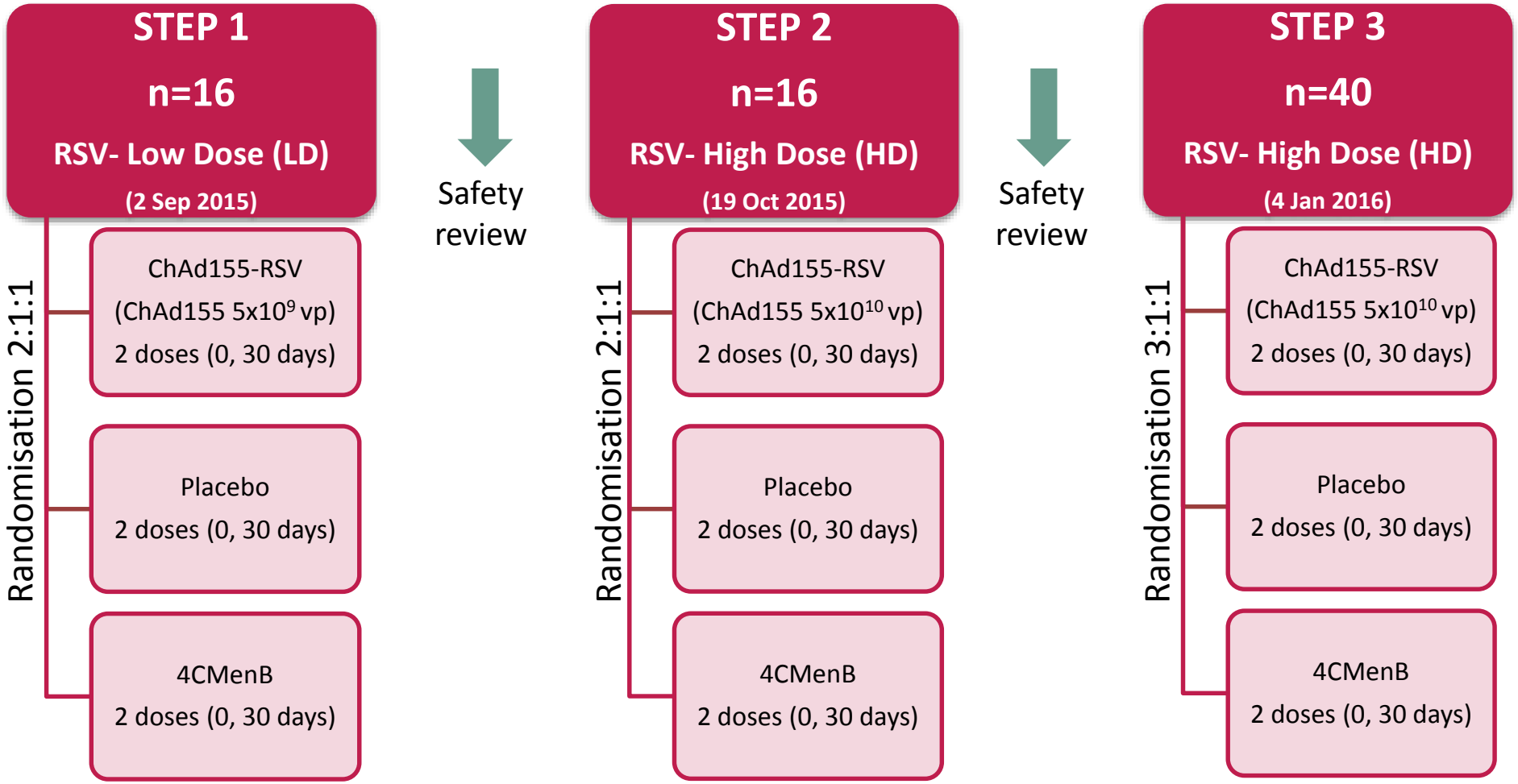
Adenoviral vector

- Both humoral and cellular RSV-specific immune responses are involved in the protection from severe disease[1]
- Adenoviral vectors have been shown to be potent inducers of CD8 T cells producing IFN gamma and antibodies against expressed antigens[2]
- Viral vectors used in the safe delivery of vaccine antigens for several infectious diseases and cancer including safe use in infants[3]

[1]MS Habibi et al. *Am J Respir Crit Care Med* 2015;191:1040–49. [2]S Colloca et al. *Sci Transl Med* 2012;4:115ra2. [3]SC Gilbert. *Vaccine* 2013;31:4241–6.

Study design

Phase I, randomised, observer-blind, controlled study (NCT02491463) in healthy adults aged 18 to 45 years



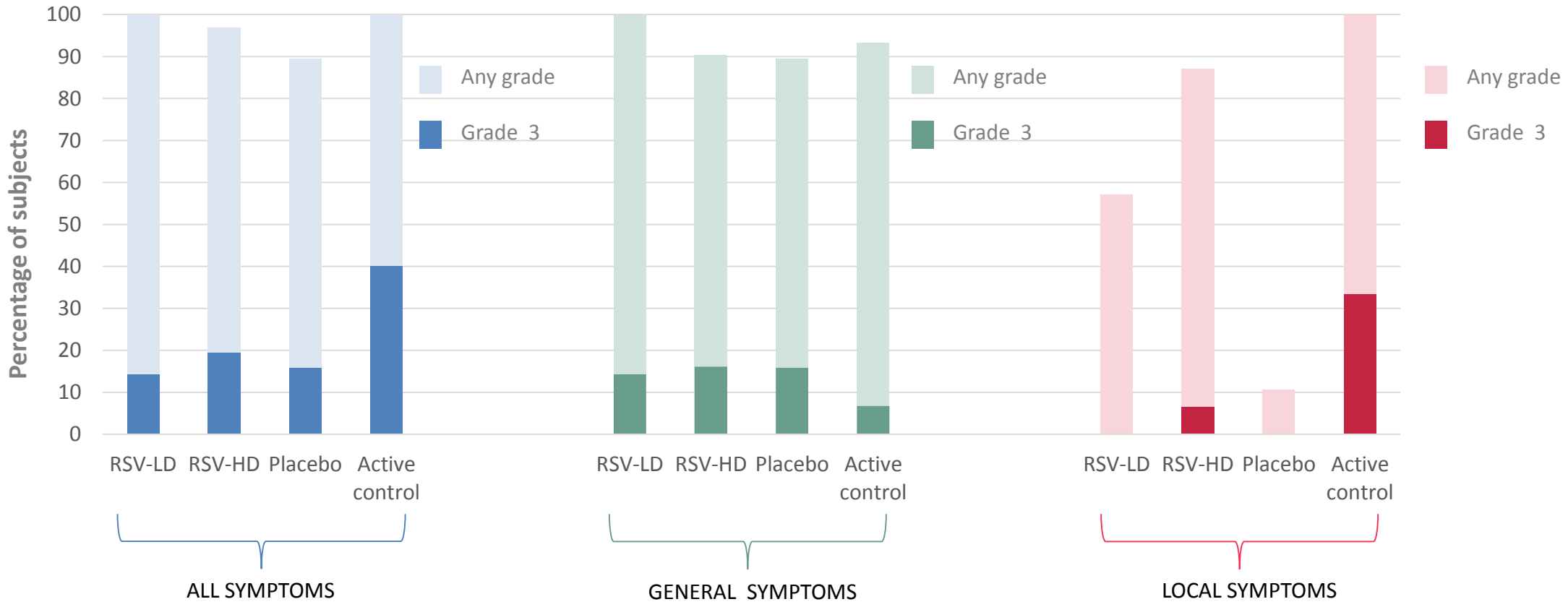
Demographic characteristics (Total vaccinated cohort)

Characteristics	RSV-LD n=7	RSV-HD n=31	Placebo n=19	Active control n=15	Total n=72
Age (years) at vaccination dose 1 Median (min-max)	28.0 (24-44)	29.0 (18-45)	29.0 (19-44)	27.0 (21-42)	28.5 (18-45)
Gender Female, n (%)	5 (71.4)	14 (45.2)	12 (63.2)	10 (66.7)	41 (56.9)
Geographic ancestry White - Caucasian / European heritage, n (%)	7 (100)	26 (83.9)	17 (89.5)	14 (93.3)	64 (88.9)

SAFETY AND REACTOGENICITY (Primary objective)

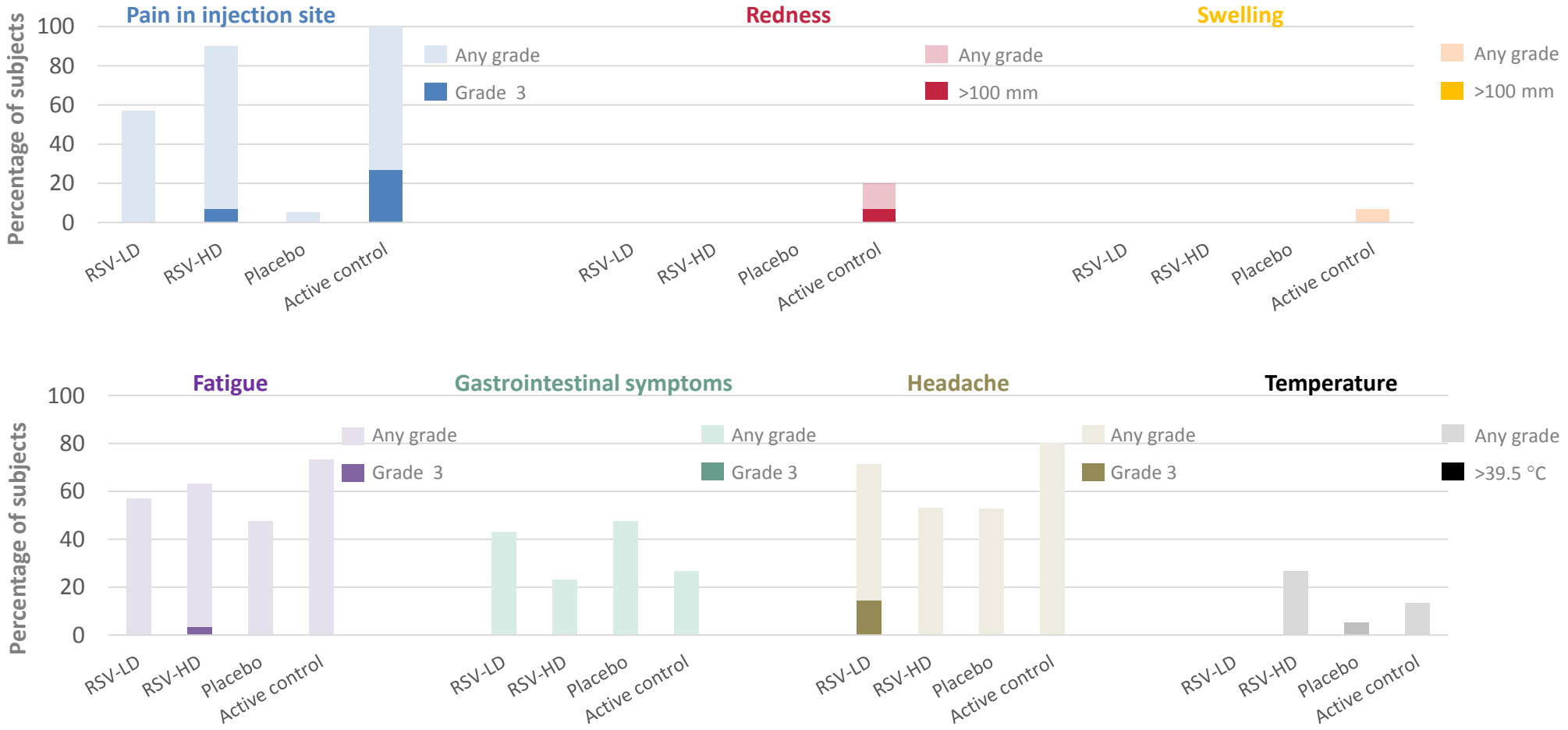
Incidence of symptoms (solicited and unsolicited) reported during the 30-day post-vaccination period, dose 1 and 2 combined

RSV-LD n= 7
RSV-HD n=30
Placebo n=19
Active control n=15



SAFETY AND REACTOGENICITY (Primary objective)

Incidence of solicited symptoms reported during the 7-day post-vaccination period, dose 1 and 2 combined



RSV-LD n= 7
RSV-HD n=30
Placebo n=19
Active control n=15

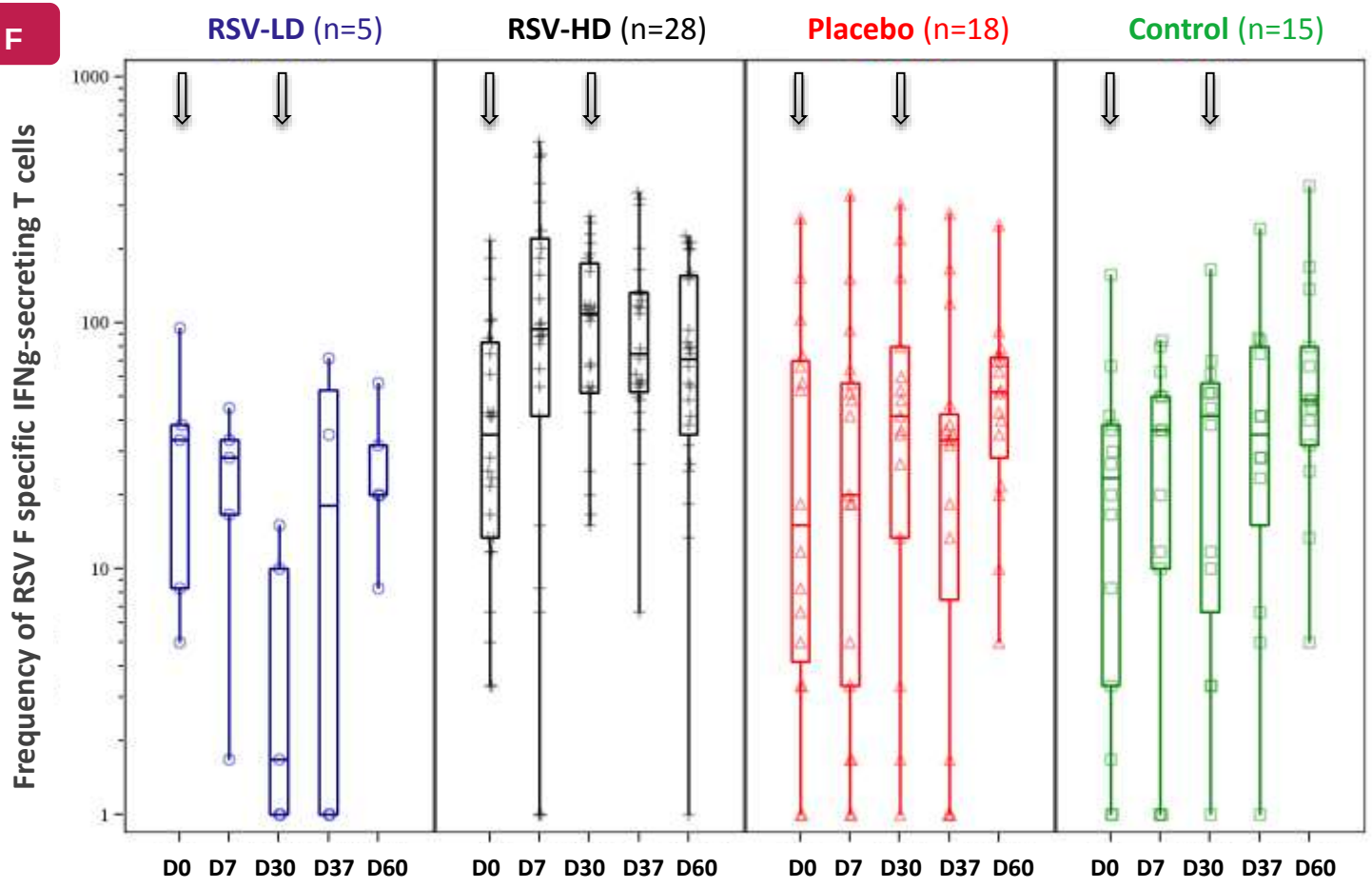
SAFETY AND REACTOGENICITY (Primary objective)

- No serious adverse events reported up to 30 days after dose 2.
- No persistent grade 3 solicited local or general adverse events reported up to 30 days after dose 2.
- No new onset of grade 3/4 toxicity in haematology or biochemistry parameters up to 30 days after dose 2.

CELLULAR RESPONSE (Secondary objective)

IFN gamma-secreting T cells (per millions of PBMC*) by ELISpot**

RSV F

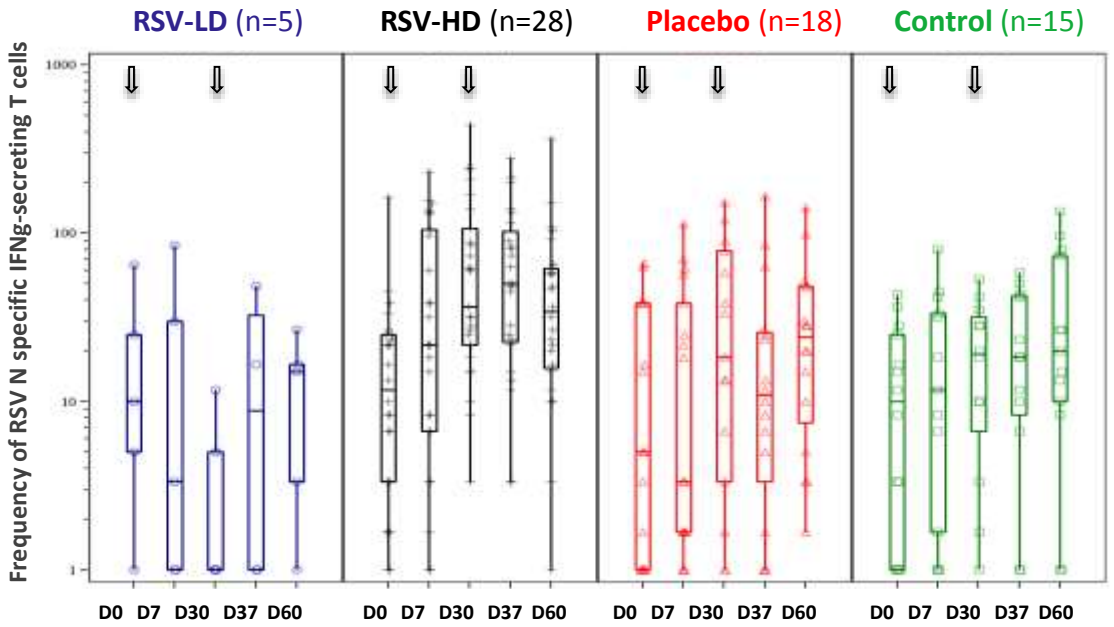


Arrows (⇩) indicate vaccine administrations

**peripheral blood mononuclear cell*
***enzyme-linked immunospot*

CELLULAR RESPONSE (Secondary objective)

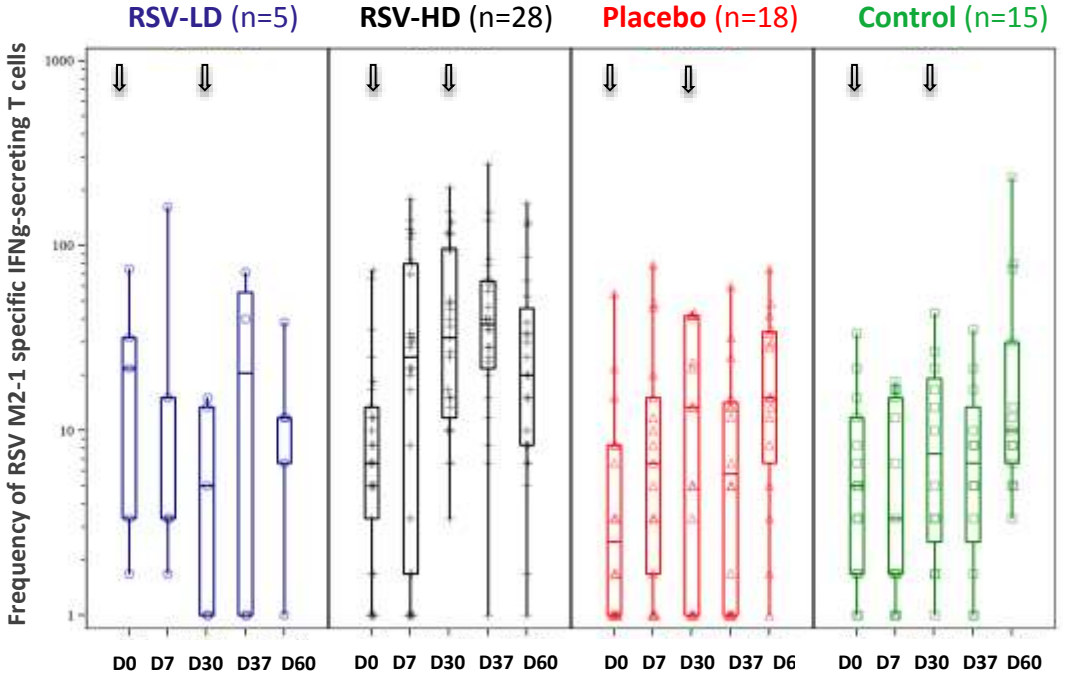
IFN gamma-secreting T cells (per millions of PBMC) by ELISpot



RSV N

Arrows (⇩) indicate vaccine administrations

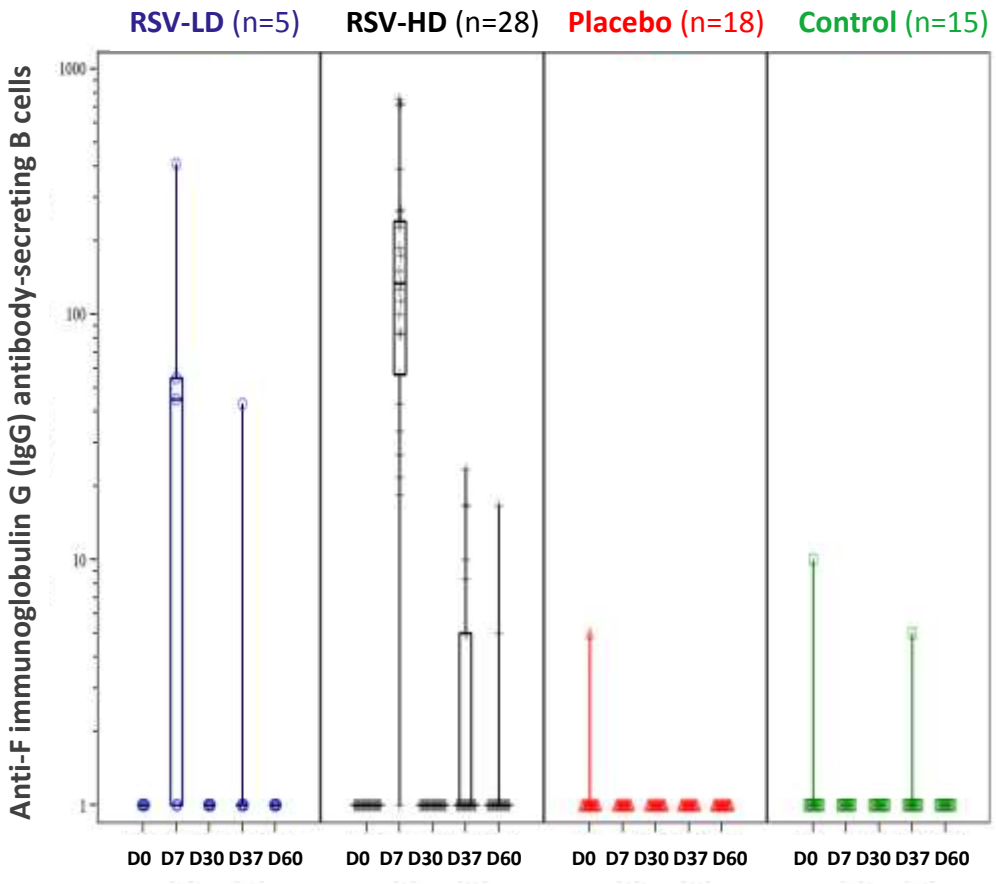
RSV M2-1



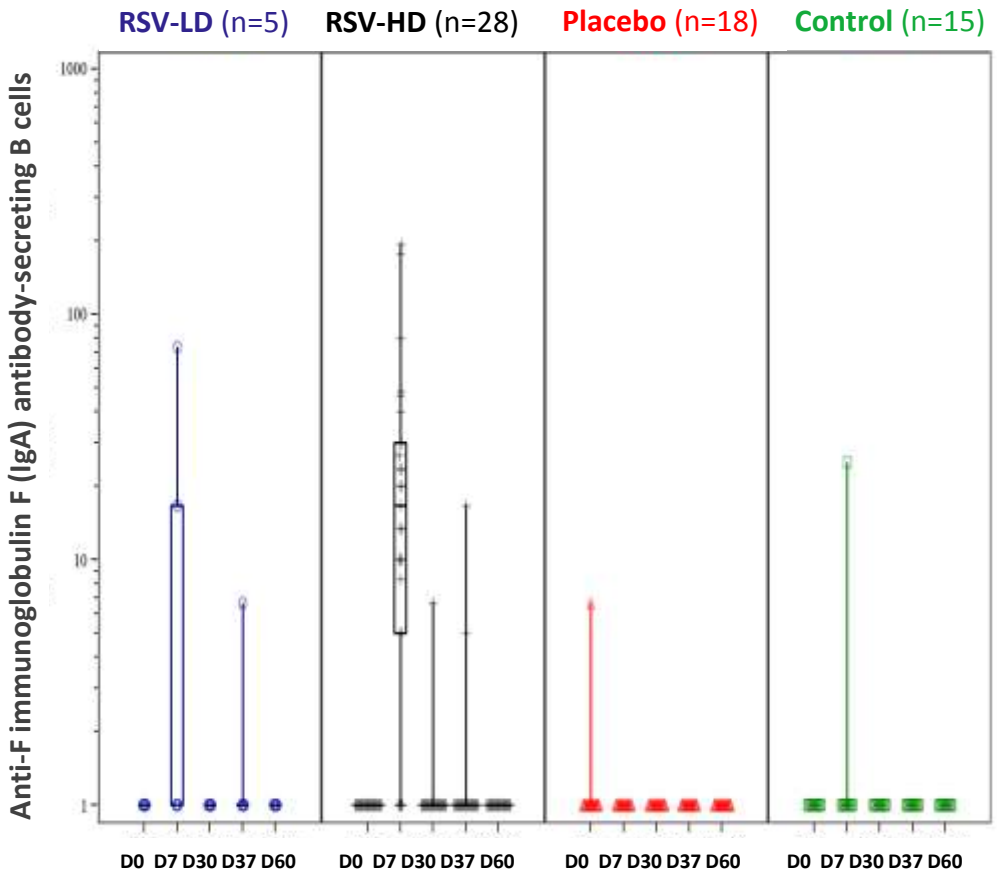
CELLULAR RESPONSE (Secondary objective)

Anti-F IgG and IgA antibody-secreting B cells (per millions of PBMC) by ELISpot

Anti-F IgG



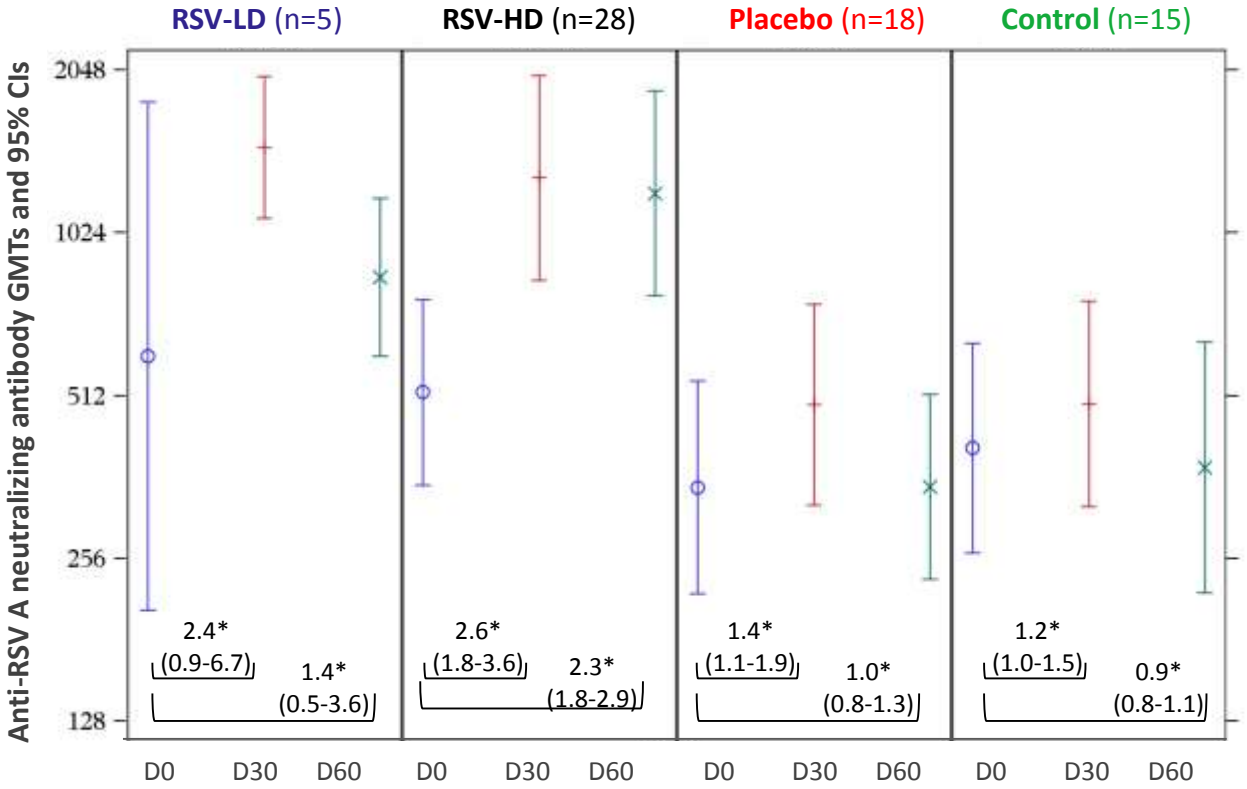
Anti-F IgA



HUMORAL RESPONSE (Tertiary objective)

GMTs and their 95% CIs for anti-RSV A neutralising antibodies

2.6-fold increase in neutralizing antibody titers (GMT from baseline) in RSV-HD after the 1st dose.



**Geometric mean titres (GMTs) (with 95% CI) of the individual ratio of anti-RSV A neutralising antibody titres at each time-point compared to pre-vaccination (D0)*

All subjects in all groups had **anti-RSV A** neutralising antibody titre ≥8 ED60

HUMORAL RESPONSE (Tertiary objective)

Vaccine response* at each post-vaccination time-point

		Vaccine response					
						95% CI	
Group	Post-vaccination timing	Pre-vaccination category (log2)	N	n	%	LL	UL
RSV-LD	D30	Total	5	1	20.0	0.5	71.6
	D60	Total	5	1	20.0	0.5	71.6
RSV-HD	D30	Total	26	15	57.7	36.9	76.6
	D60	Total	26	15	57.7	36.9	76.6
Placebo	D30	Total	18	3	16.7	3.6	41.4
	D60	Total	18	1	5.6	0.1	27.3
Active control	D30	Total	15	1	6.7	0.2	31.9
	D60	Total	15	2	13.3	1.7	40.5

* Vaccine response defined as:

- At least a 4-fold increase in pre-vaccination titre <7 log2
- At least a 3-fold increase in pre-vaccination titre in [7-8] log2
- At least a 2.5-fold increase in pre-vaccination titre in]8-10] log2
- At least 1-fold in pre-vaccination titre >10 log2.

CONCLUSIONS

- No significant safety concerns
- About 2.5-fold increase in neutralizing antibody titers (GMT from baseline) in both RSV-LD and RSV-HD after dose 1. No further increase after a booster dose
- Induction of specific IFN gamma-secreting T cells detected by ELISpot between day 7 and 30 after the first high dose of the study vaccine
- Further studies in RSV-naïve infants are needed to better assess the immune response of this candidate vaccine in the clinically relevant population.

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