Study design and initial data from a Phase 1 randomized controlled observer-blind, trial to evaluate the safety, reactogenicity and immunogenicity of a trivalent vaccine against invasive nontyphoidal *Salmonella* and typhoid fever in healthy adults in Europe

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A vaccine against invasive nontyphoidal salmonellosis (iNTS) and typhoid fever: iNTS-TCV

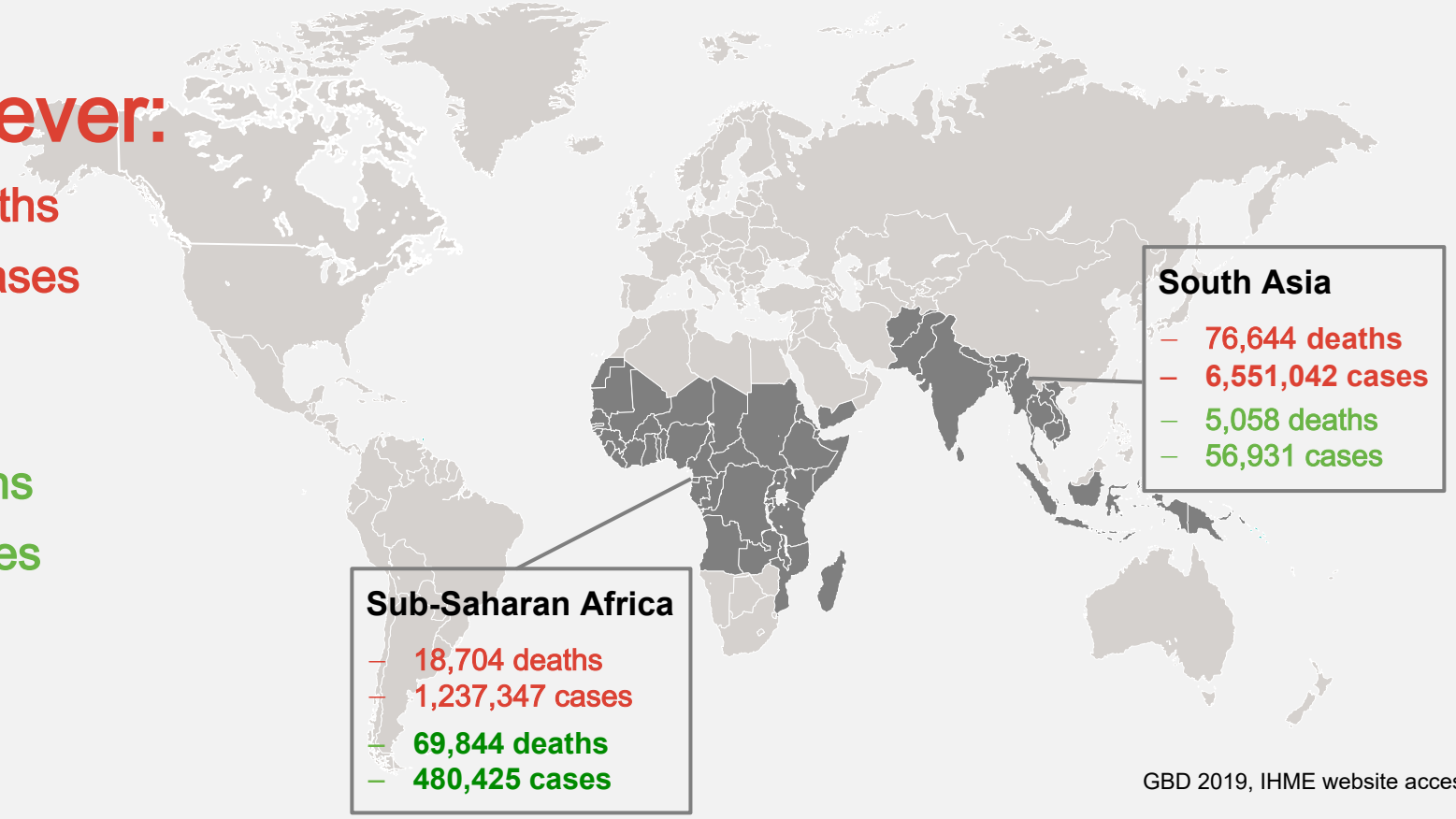
Global (2019, all ages)

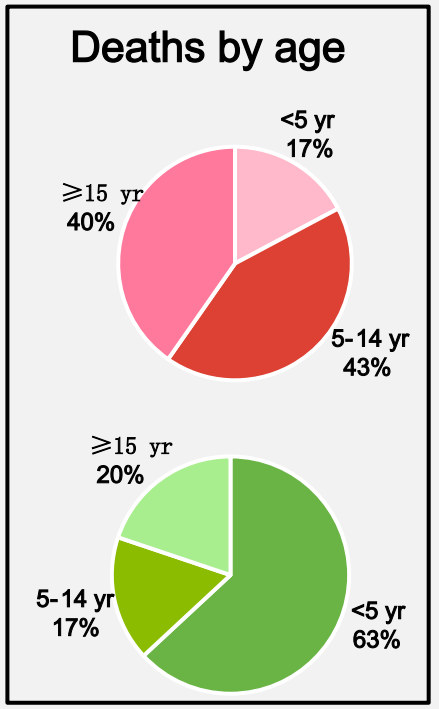
Typhoid fever:

- 110,029 deaths
- 9,237,225 cases

iNTS:

- 79,046 deaths
- 593,877 cases



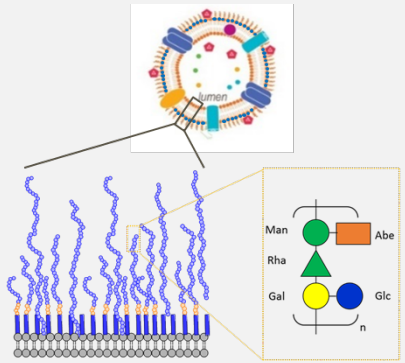


GBD 2019, IHME website accessed 11/2023

iNTS-TCV trivalent vaccine:

Combination of two technologies: GMMA + glycoconjugate

S. Typhimurium GMMA



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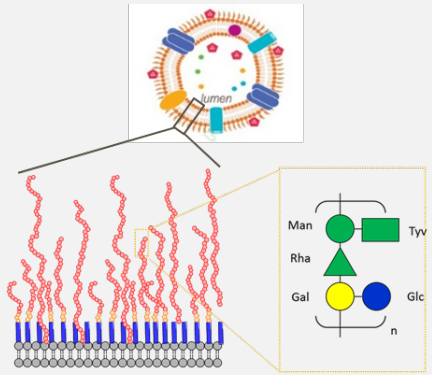
S. Enteritidis GMMA



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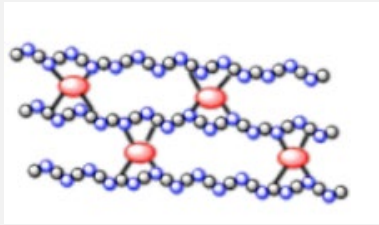
TCV component (glycoconjugate)



Vi-CRM$_{197}$ Drug Substance of a licensed vaccine, WHO PQ (Biological E Ltd)

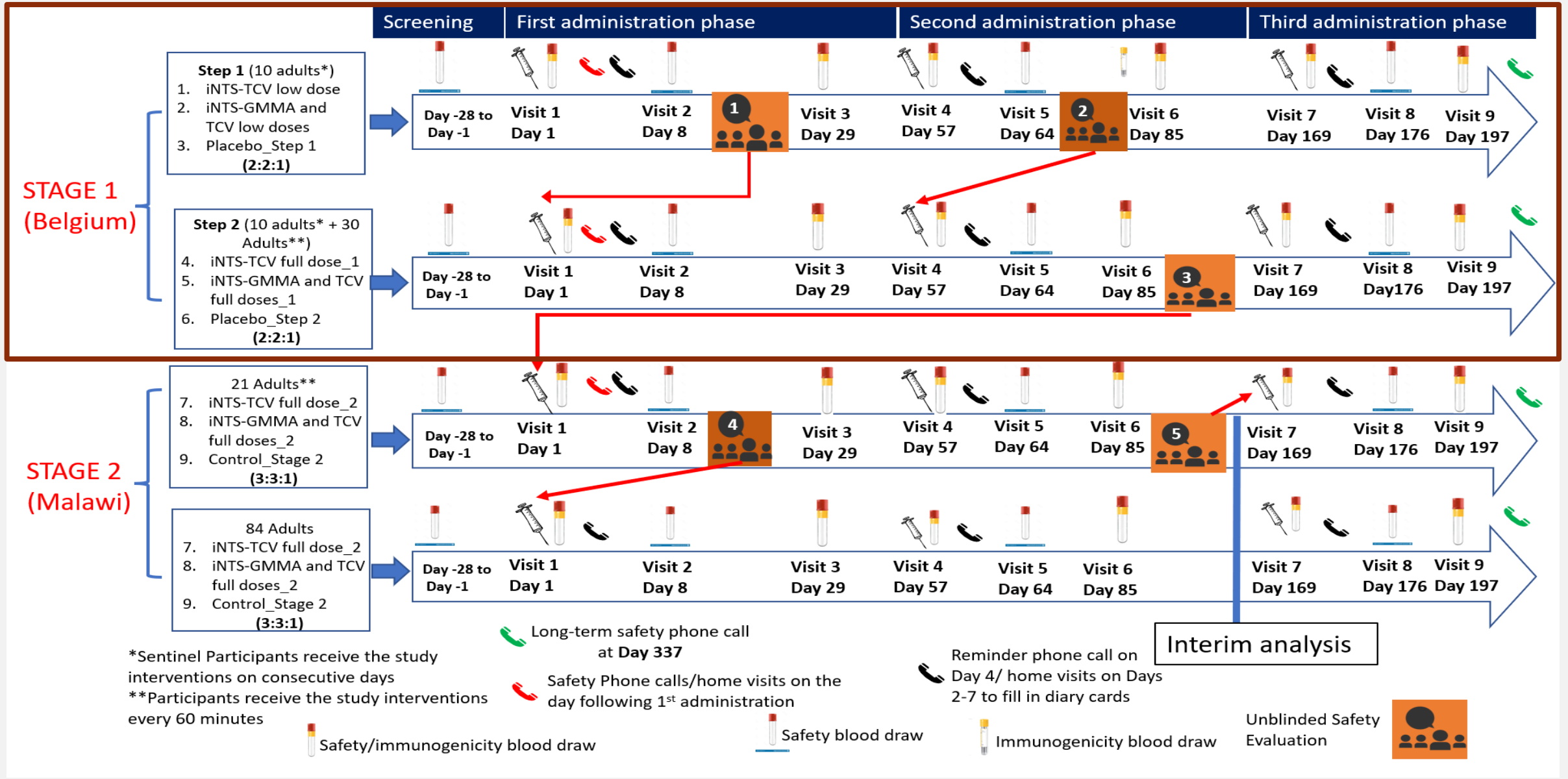
iNTS-TCV

Study Design

This is a phase 1/2a, observer-blind, randomized, controlled, two-stage, multi-country study to evaluate the safety, reactogenicity, and immune response of the trivalent vaccine against invasive nontyphoidal Salmonella (iNTS) and Typhoid Fever in healthy European and African adults.

- Planned enrolment: A total of 155 healthy adults 18–50 years of age will be randomized.
- 50 European adults were randomly assigned to 1 of the intervention groups in stage 1 while 105 African adults will be randomized in stage 2.
- Each participant will receive 2 interventions concomitantly in separate arms: iNTS-TCV and saline OR iNTS and TCV vaccines OR placebo/ controls and saline.
- Each participant will receive a study intervention per arm on Day 1, Day 57 and Day 169. Approximately 13 months participation duration.
- Schedule selected based on number of doses expected to be immunogenic in target population for primary immunization (i.e infants 6 weeks of age)
- The highest dose of the iNTS-TCV used in this trial was tested in a repeated-dose toxicology study in rabbits which showed good tolerance with no evidence of toxicity.

Study Design Overview



Study Objectives and endpoints

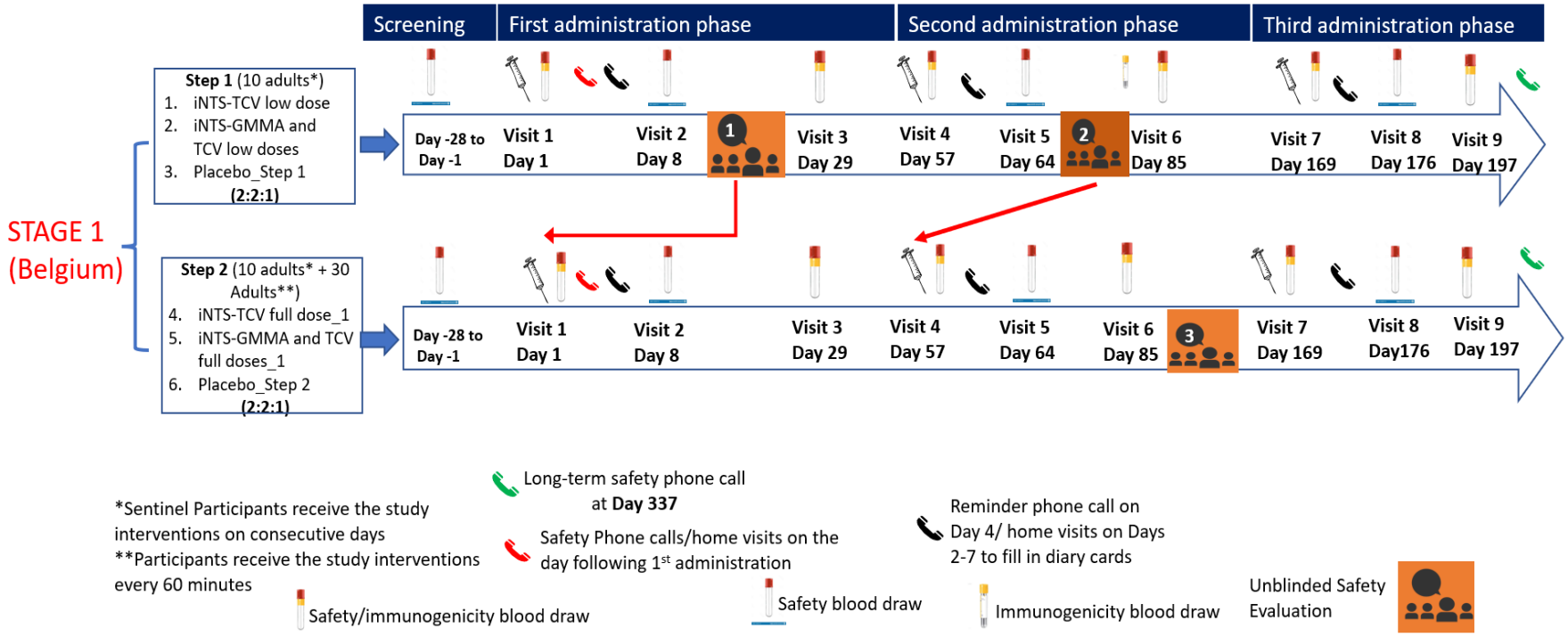
Primary Objective

Objective	Endpoint
To evaluate the safety and reactogenicity of the iNTS-TCV vaccine in healthy European/African adults	Percentage of participants with ▪ solicited administration site and systemic events during 7 days after each study intervention administration ▪ unsolicited AEs during 28 days after each study intervention administration ▪ Serious AE ▪ AEs leading to withdrawal ▪ Deviations from ranges or baseline hematological, renal and hepatic panel test

Blinded Safety data from Phase 1

Study Design Overview

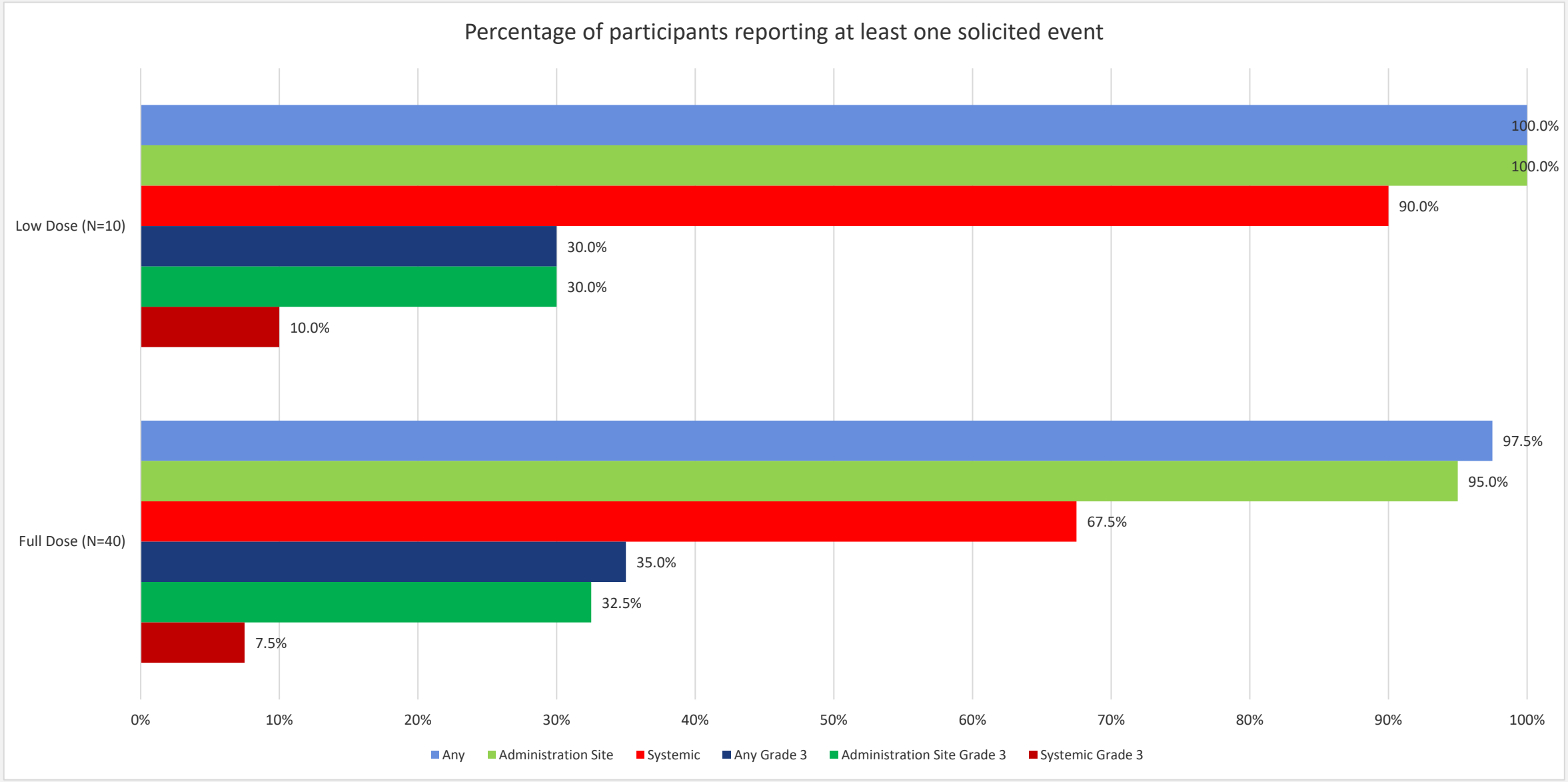
This presentation covers initial data from stage 1 of the study ongoing in Belgium, where 50 participants have been recruited (i.e. data up to 28 days after 2nd administration in the full dose group).



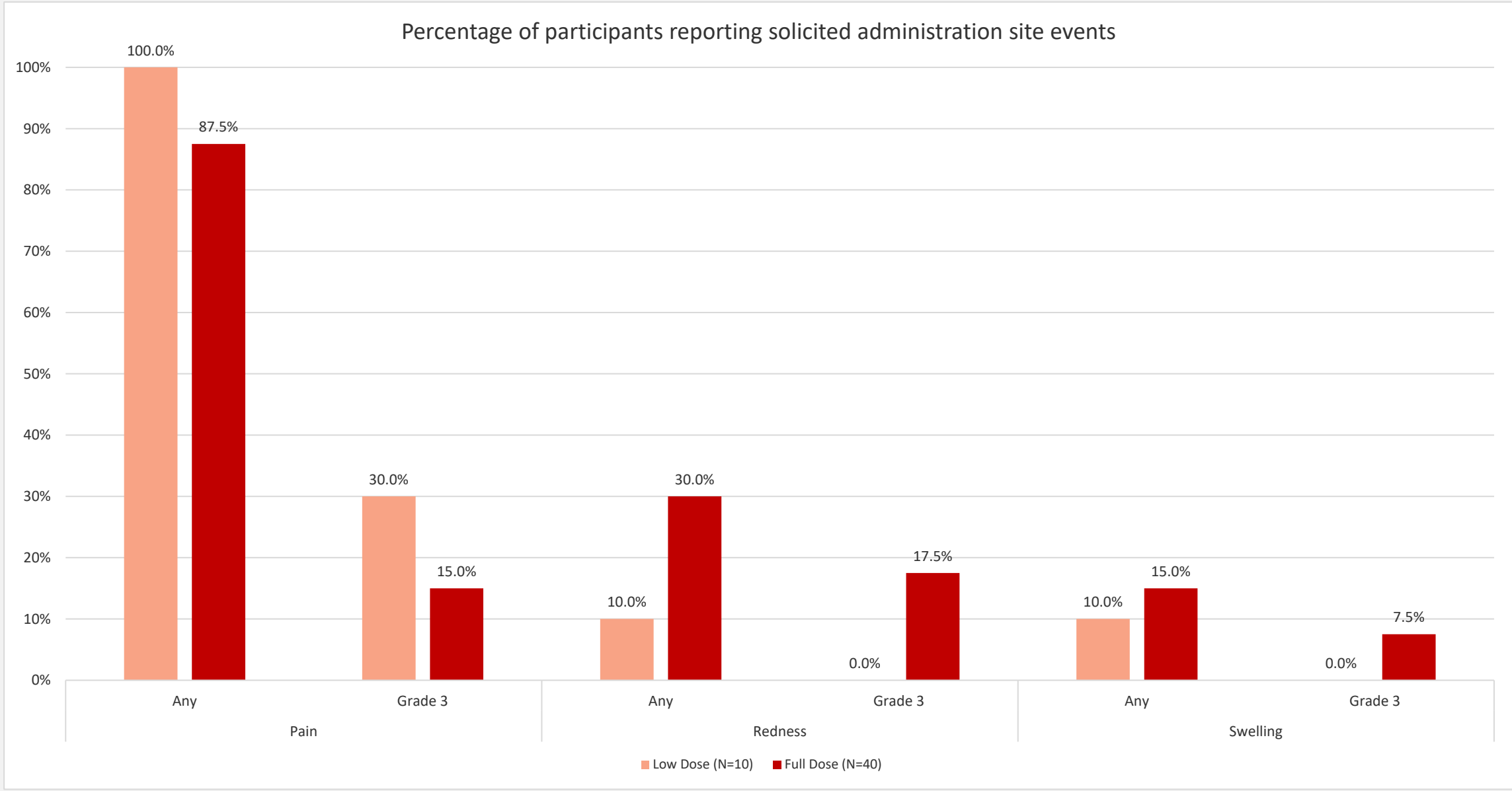
Demographic characteristics of Exposed Population

Summary of Demographic Characteristics (Exposed Set) - Blinded			
Characteristics	**Parameter or Categories**	**Low Dose (N=10) Value or n(%)**	**Full Dose (N=40) Value or n(%)**
Sex	Female	7 (70.0)	29 (72.5)
	Male	3 (30.0)	11 (27.5)
Race	Other	-	2 (5.0)
	White	10 (100.0)	38 (95.0)
Age (years)	n	10	40
	Mean	30.7	34.7
	SD	10.93	10.86
	Minimum	19	19
	Median	28.5	36.0
	Maximum	48	50

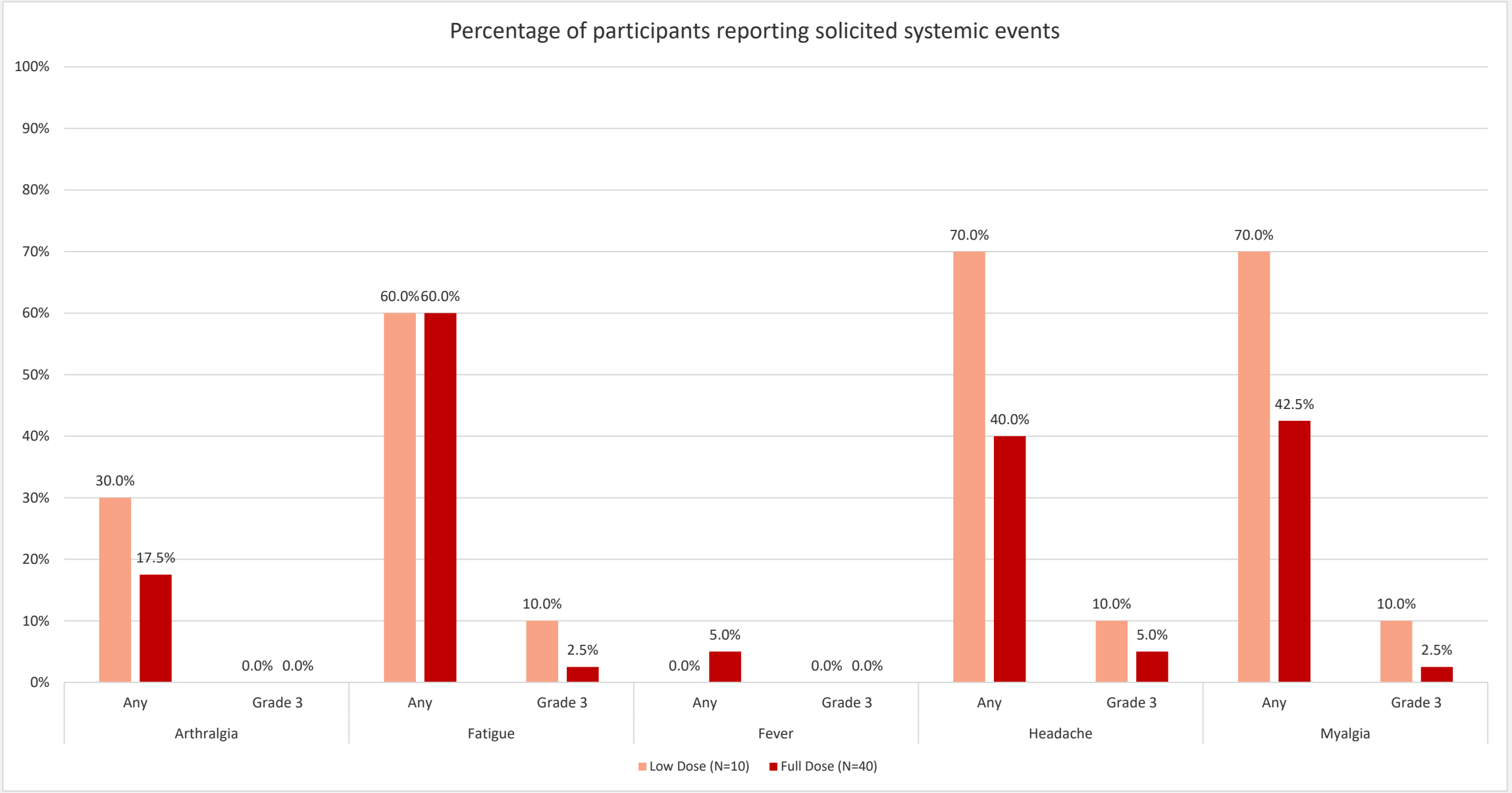
Solicited Events analysis - Blinded



Solicited Administrative Site Events -Blinded



Systemic Solicited Events - Blinded



Unsolicited Adverse Events -Blinded

After all participants received at least 2 doses of study interventions_ comparators

Low Dose group (N=10):

- At least one event reported by 80% of subjects participants.
- 60% reported at least one event considered related to vaccination by the INV
- No Grade 3 reported.
- Overall, most frequent SOC (system organ class) affected were «Infections and infestations» (50% of participants) and « Musculoskeletal and connective tissue disorders" (40% of participants).

Full Dose group (N=40):

- At least one event reported by 90% of subjects participants.
- 50% of subjects reported at least one event considered related to vaccination by the INV
- Overall, most frequent SOC were «Infections and infestations» (42.5% of participants) and «General disorders and administration site Conditions" (37.5% of participants).
- GR3 events were reported in 12.5% of subjects participants.

Conclusions

- After at least two administrations with the low or full doses or controls, the majority of adverse events (AEs) observed are of mild to moderate intensity.
- No safety concerns are currently identified from the analysis of **solicited, unsolicited AE events and Safety lab test results**
  - No SAE considered related to vaccination reported
  - No AE leading to withdrawal
  - Injection site pain is the most frequent event reported in both steps, consistent with other GMMA studies.
  - Myalgia, fatigue and headache are the most frequent systemic solicited AEs
  - Severe unsolicited AEs considered related to vaccination were reported in 2 subjects overall.
  - Safety lab test results: most laboratory results were within normal reference ranges and there were no clinically significant changes from normal

Based on available safety data, clinical development has progressed into healthy adults in an endemic African country, to further assess safety and immunogenicity of the iNTS-TCV vaccine.

Acknowledgements

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- All study participants and their families

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iNTS-TCV

CARB-X
Combating Antibiotic-Resistant Bacteria

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Declaration and conflicts

KW has nothing to disclose. YSI, ALDP, ASB, GLC, OR, BG, CC, RLG, VC, UNN, RC and AKA are GSK employees. GLC, OR, RLG, VC, UNN, RCA, and AKA hold GSK shares or stock options.

Thank you

GSK