



Workshop On Refining The Regulatory Context Of Controlled Human Infection Models

Results from the Inno4Vac RSV B CHIM

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A new RSV CHIM

After recent successes, the RSV vaccine pipeline remains filled

RSV CHIMs are mainly conducted using the RSV A/Memphis/37 strain (since 2010)

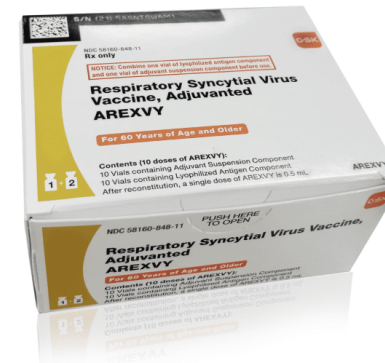
Need increases for a new CHIM using a more recent challenge strain

A contemporary RSV B challenge strain was developed by ST2

2022 – 2024 Strain isolation & selection

2024 – 2025 GMP manufacturing of RSV B strain

Apr – Sep 2025 Clinical evaluation at CHDR



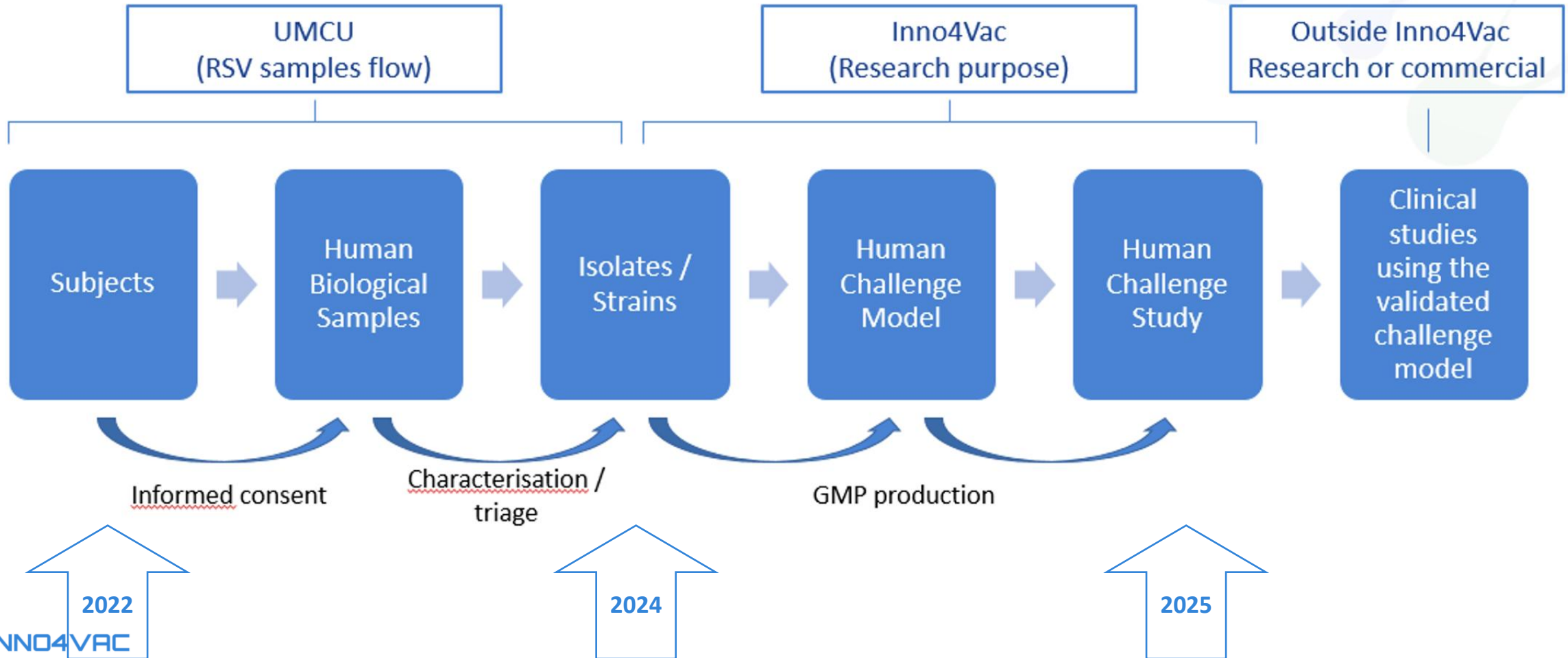
A new RSV CHIM



Prof. Ab Osterhaus



Dr. Martin Ludlow



RSV B strain – dose titration study

First-in-human, outpatient CHIM in 30 healthy participants (18-55 years)

- Dose-escalation scheme with pilot groups (n=3) and confirmatory groups (n=7)
- Three doses: 10^4 / 10^5 / 10^6 TCID₅₀

Clinical objectives

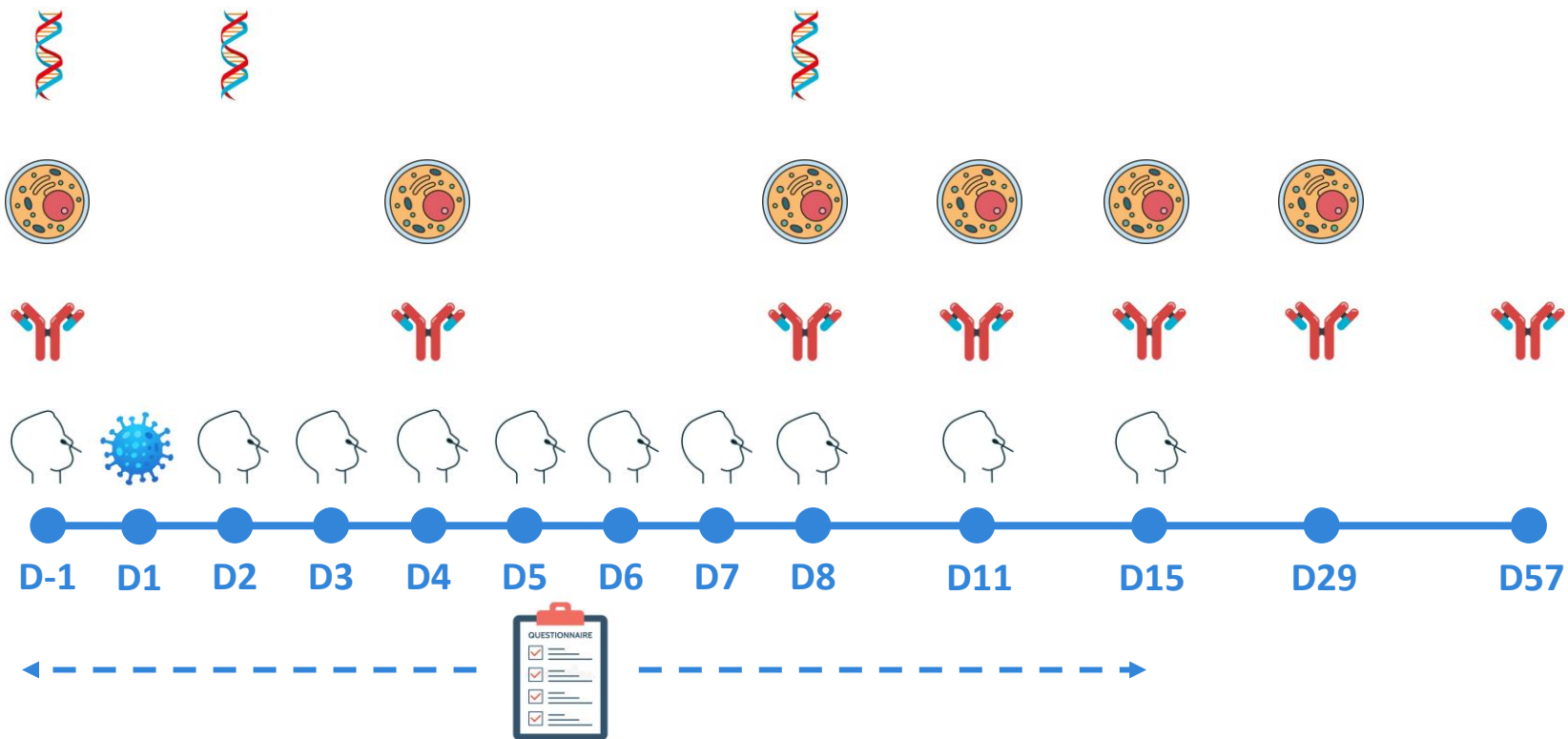
1. Find the dose required to induce a PCR-confirmed infection rate of 70%
2. Assess safety and tolerability of novel challenge strain
3. Characterize symptomatology & viral kinetics
4. Evaluate local & systemic immune responses



Dr. Natalie Mazur



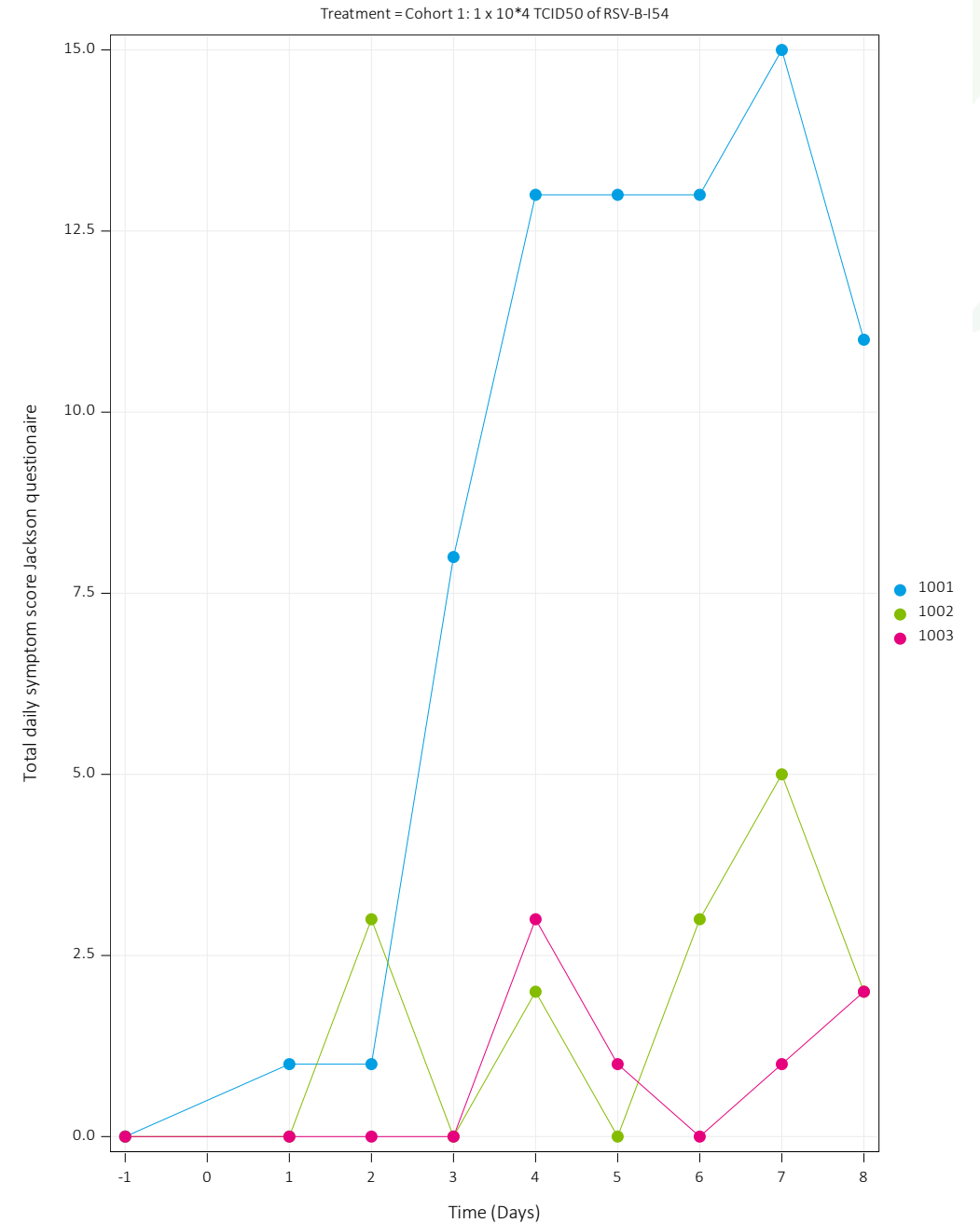
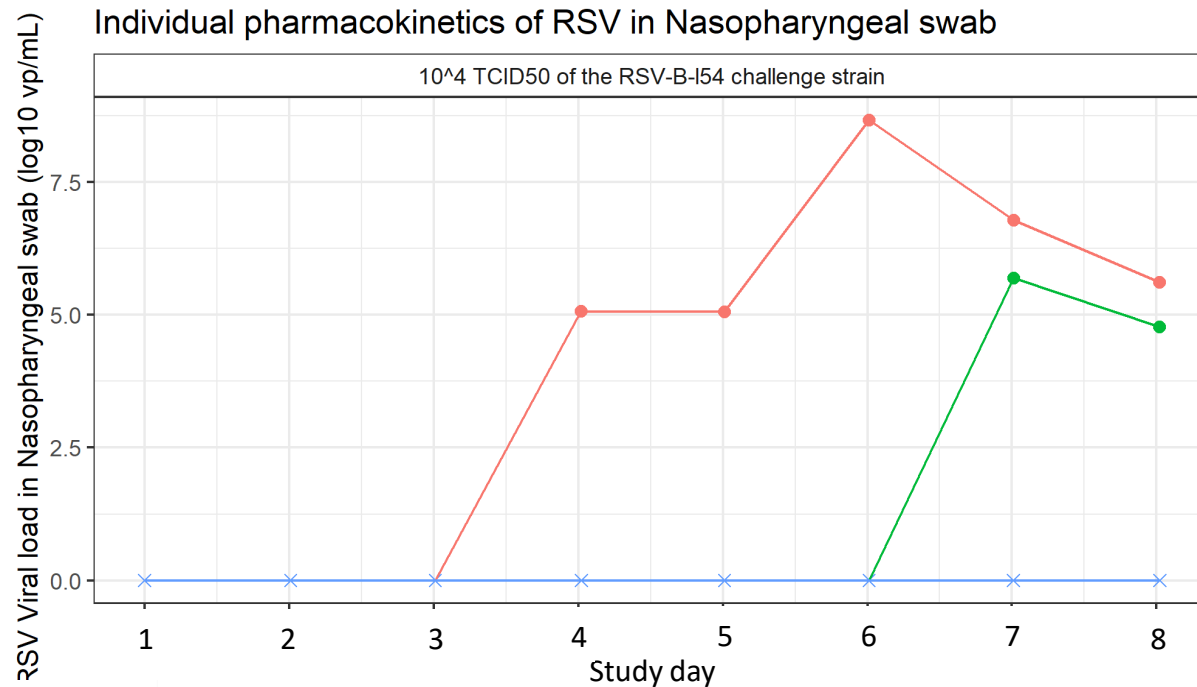
RSV B strain – dose titration study



RSV B CHIM – Results

First sentinel cohort (n=3) – low dose (1×10^4 TCID₅₀)

1. No safety issues
2. 2/3 participants with positive PCRs
3. 2/3 participants with RSV disease



RSV B CHIM – Results



RSV B CHIM – Results



First confirmation cohort (n=7) – low dose (1×10^4 TCID₅₀)

1. No safety issues
2. 1/7 participants with positive PCRs
3. 0/7 participants with RSV disease

RSV B CHIM – Results



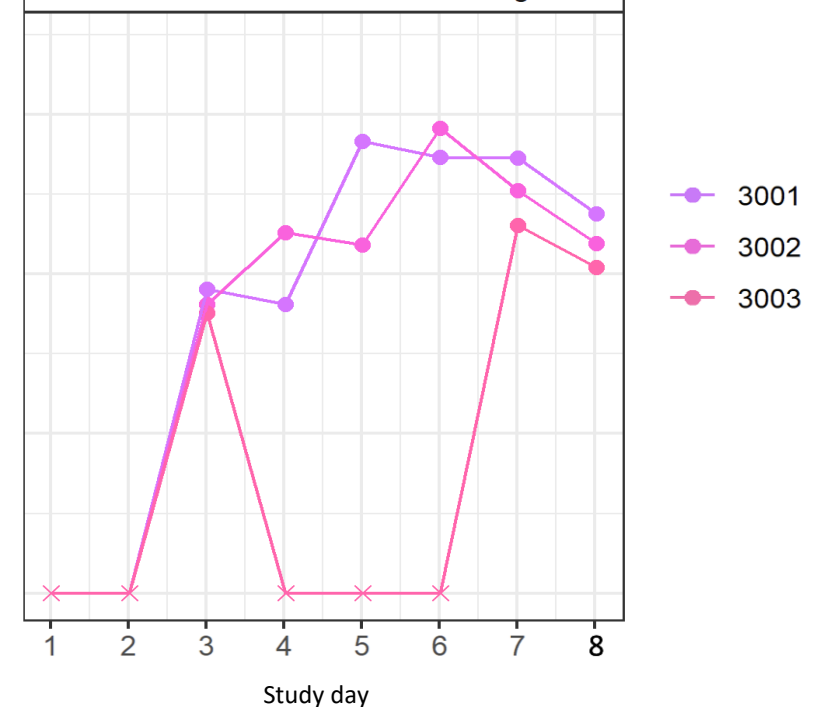
First confirmation cohort (n=7) – low dose (1×10^4 TCID₅₀)

1. No safety issues
2. 1/7 participants with positive PCRs
3. 0/7 participants with RSV disease

Second sentinel cohort (n=3) – medium dose (1×10^5 TCID₅₀)

1. No safety issues
2. 3/3 participants with positive PCRs
3. 2/3 participants with RSV disease

10^5 TCID₅₀ of the RSV-B-I54 challenge strain



RSV B CHIM – Results

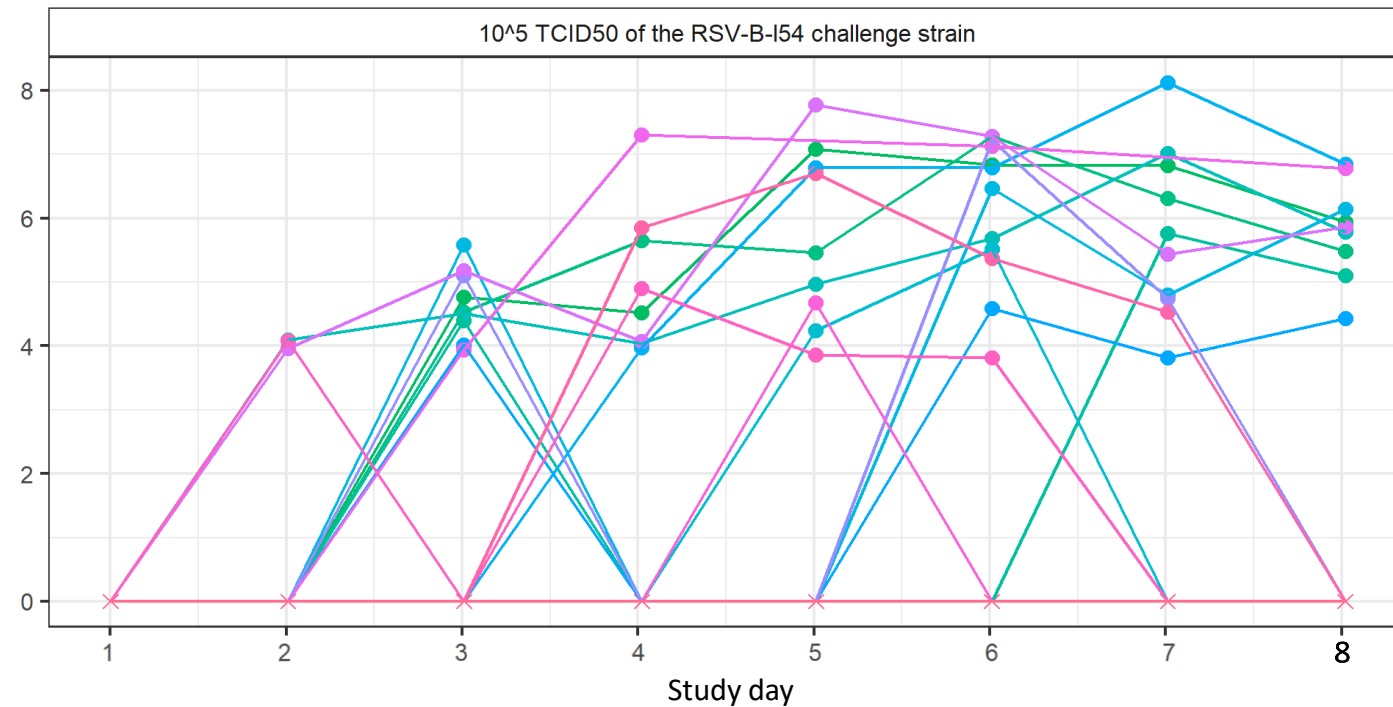
19 individuals inoculated with medium dose of 1×10^5 TCID₅₀

No SAEs or other safety issues

Infection rate: 14/19 (74%)

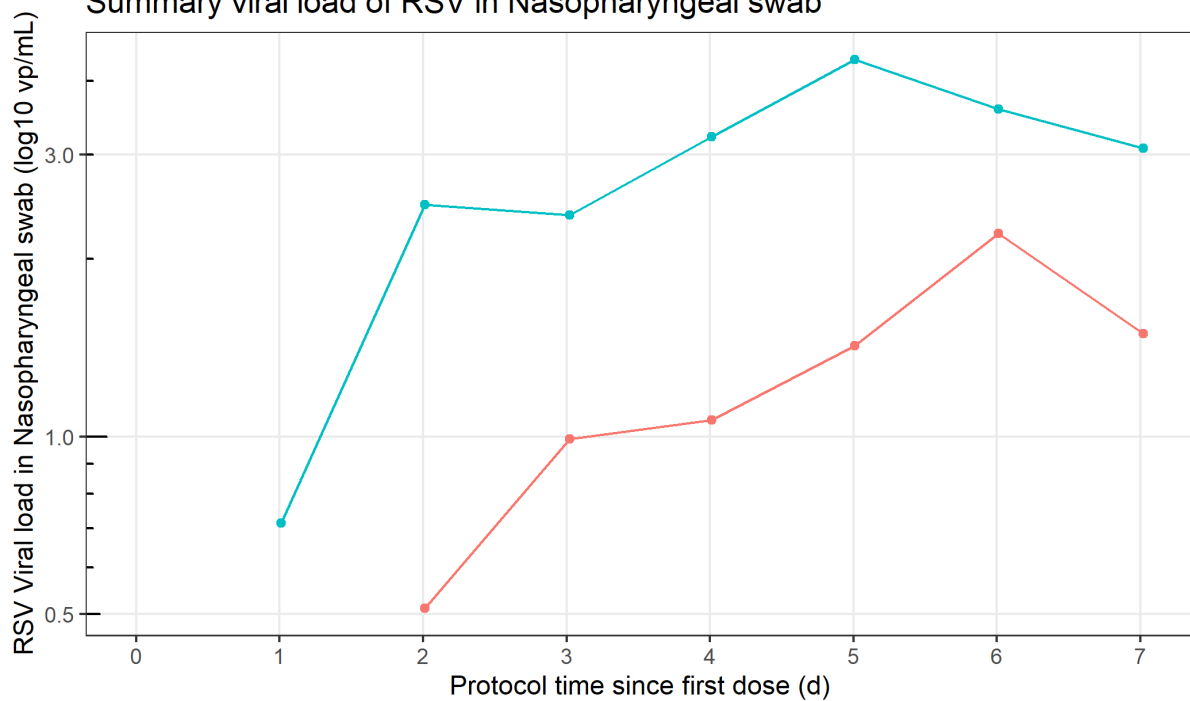
Disease rate: 12/19 (63%)

Study	Virus strain	Infection rate	Disease rate
Jordan	A/Memphis/37b – 10^6	52%	42%
Ascough	A/Memphis/37b – 10^6	38%	50%
Sadoff	A/Memphis/37b – 10^6	65%	46-62%
Kelly	A/Memphis/37b – 10^6	68%	?
Bagga	A/Memphis/37b – 10^6	77%	?
Habibi	A/Memphis/37b – 10^6	56%	38%

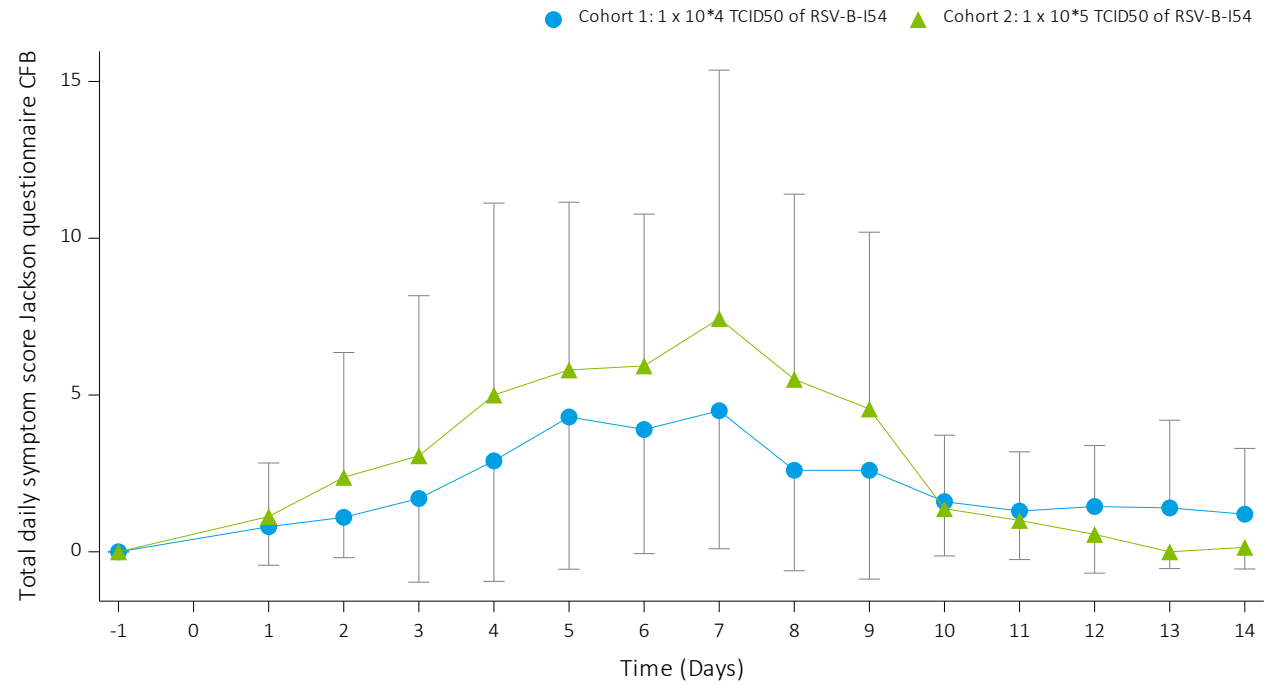


The Inno4Vac RSV B virus as a challenge strain

Summary viral load of RSV in Nasopharyngeal swab

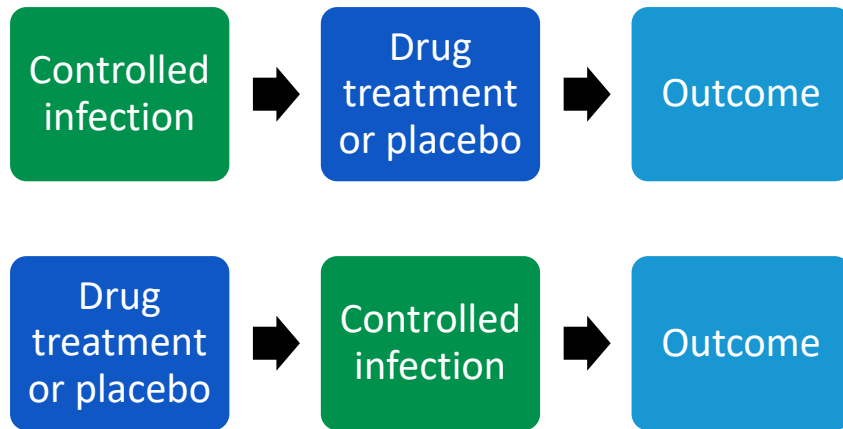
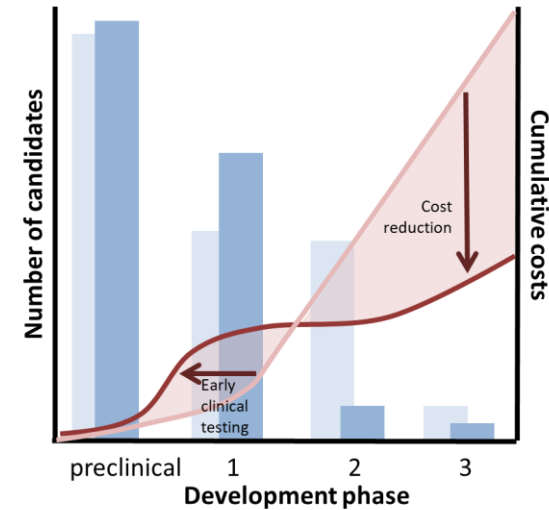


—●— 10⁴ TCID50 of the RSV-B-I54 challenge strain —●— 10⁵ TCID50 of the RSV-B-I54 challenge strain

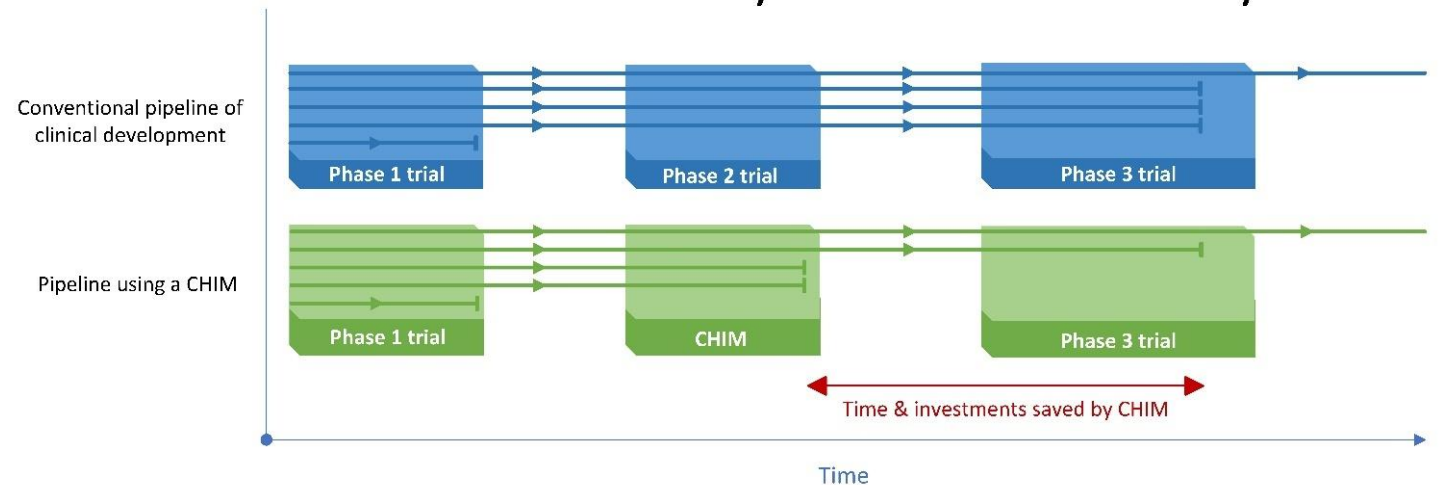


Establishment of a novel RSV B CHIM

- ✓ Outpatient CHIM is accessible and cost-effective
- ✓ No screening for pre-existing immunity
- ✓ Harmonized clinical protocols
- ✓ >700 GMP vials available for clinical use



CHIMs allow for early assessment of vaccine efficacy



The Inno4Vac RSV B virus as a challenge strain



- ✓ In-use stability for 2 hours on room temperature
(All inoculations performed $<\pm 30$ minutes after thawing)
- ✓ A dose of 1×10^5 TCID₅₀ is sufficient for robust clinical endpoints
(Current A/Memphis/37b strain requires 10-fold higher dose)
- ✓ Low rate of asymptomatic infection
(Only 2 of 14 infections)
- ✓ GMP production resulted in 750 vials for clinical use
($1 \times 10^{6.3}$ TCID₅₀/mL → sufficient for >7,000 inoculations)

ST2 Ambitions

Plans for 2026

- Extensive immune analyses on FIH samples
- Older adult CHIM at Imperial College London
 - Including lower airway sampling
 - Harmonized clinical protocols

Influenza

2023-2025	Strain isolation, selection & characterization
2025 (Sep)	Start of challenge strain manufacturing
2026	First-in-human dose titration study @ CHDR



Regulatory workshop on standardisation of clinical procedures, endpoints and data robustness of human challenge studies – A stakeholder meeting report

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