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Modeling the kinetics and durability of the humoral response to a chikungunya virus-like particle vaccine

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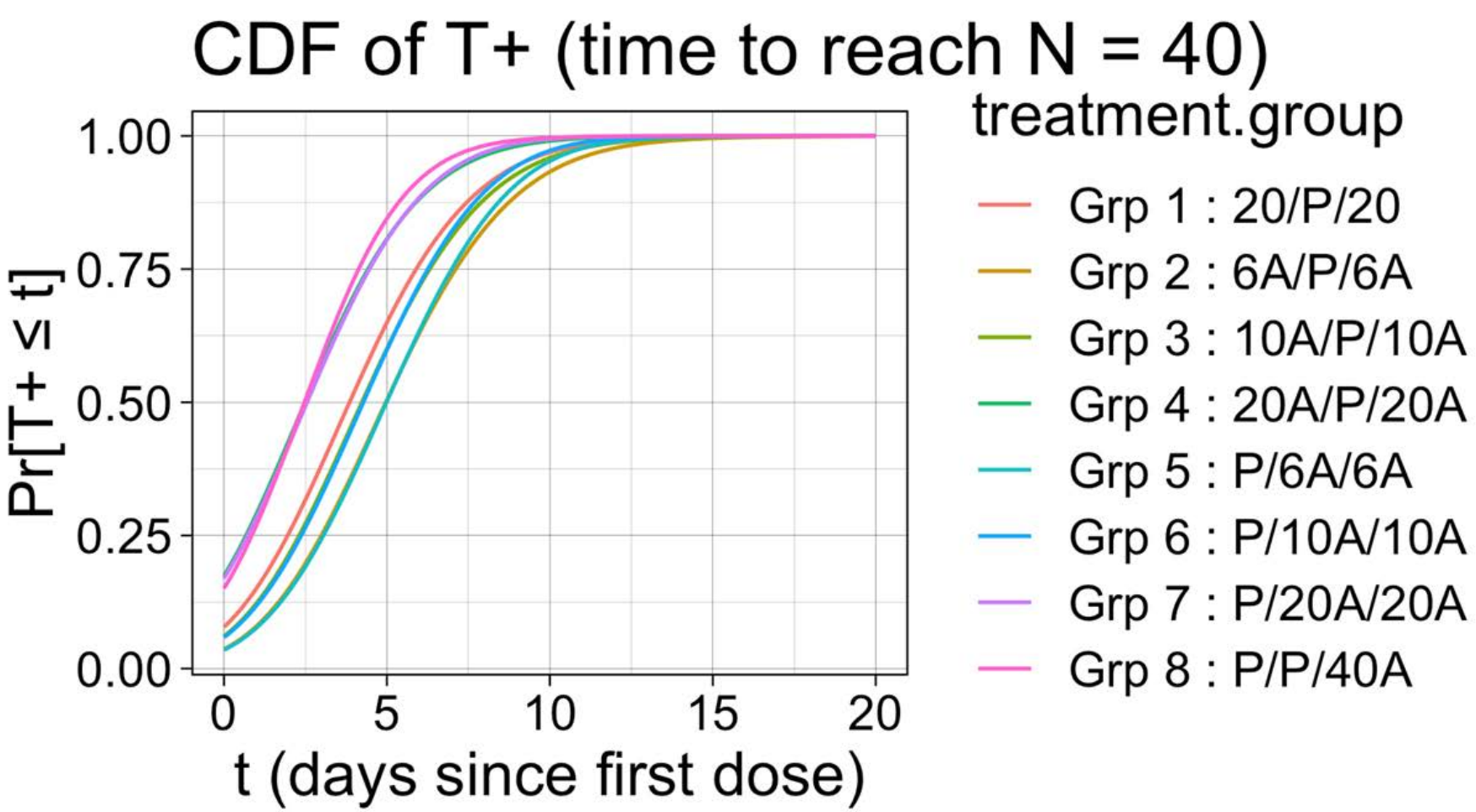
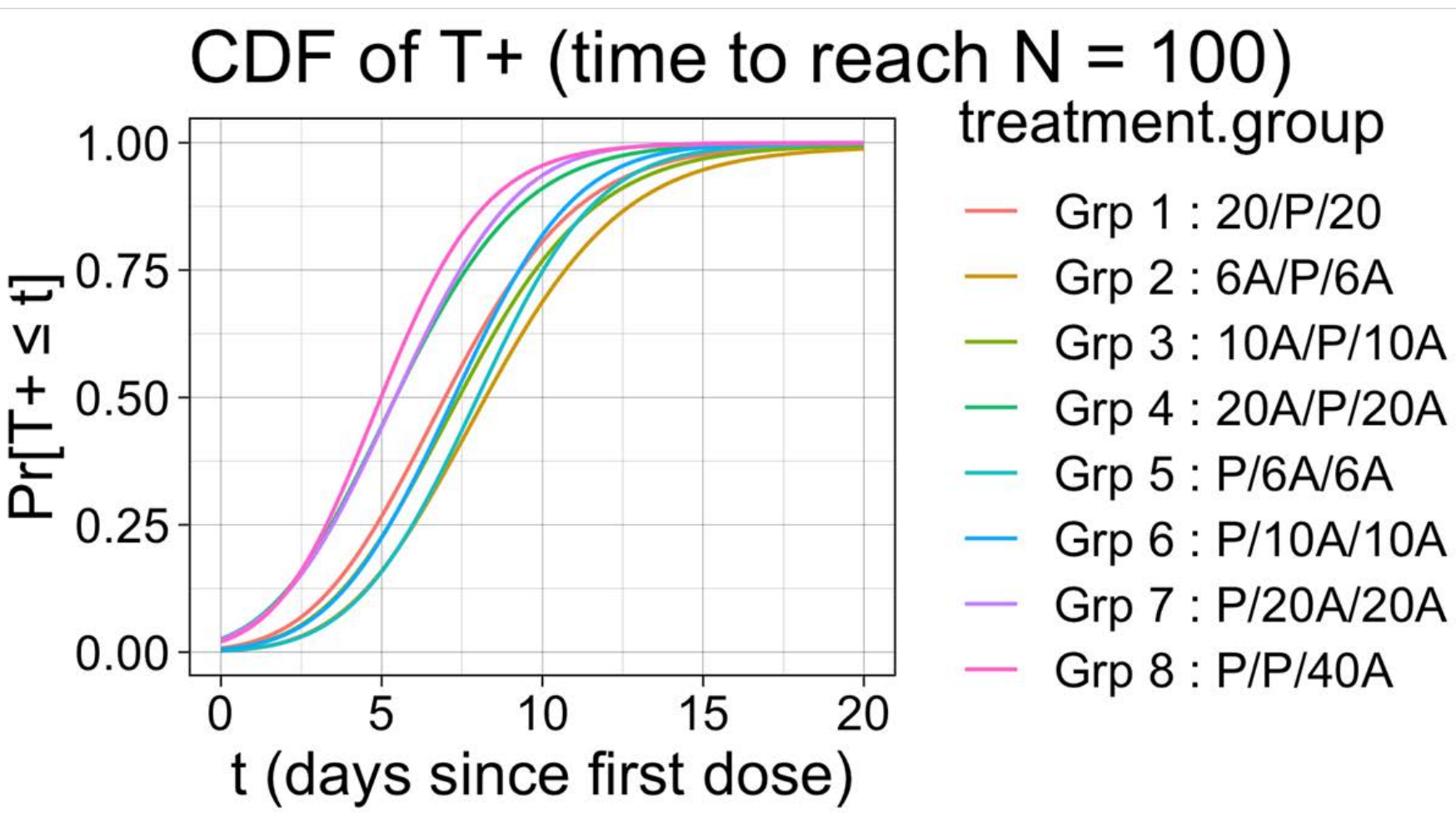
Chikungunya disease causes disruptive epidemics of febrile illness. Using data from a Phase 2 dose-finding study, we model antibody levels after immunization with a chikungunya virus-like particle (VLP) vaccine to characterize the kinetics and durability of the humoral immune response.

The analysis included blood samples taken at roughly weekly intervals through Week 8 and at additional timepoints up to one-year post-immunization. Neutralizing antibody titers were determined using a neutralization assay and measured with 80% cutoff (NT80). We used Generalized Additive Mixed Effects Models (GAMM) to estimate the effect of vaccine formulation (dose, schedule, adjuvant) on the kinetics of the response.

A GAMM with a simple concave-down smooth function and a random effect for study participant fit the data well (R-sq – 80.7%). All effects – presence of adjuvant, VLP dose, and dosing schedule – significantly affected the magnitude and dynamics of the neutralizing antibody response. A single dose with adjuvant elicited the highest titer at 8 days post-immunization (dpi) and at 365 dpi, while 2 doses administered 14 days apart elicited the highest titers at 22 dpi. At titer thresholds of 40 and 100, >75% of participants seroconverted by day 8 and 10, respectively, and the single-dose group was quickest to seroconvert. At 365 dpi, the probability of titers falling below a threshold of 100 was lowest for the single-dose group (<0.05).

The rapid, durable immune response after a single dose of the VLP vaccine would support its utility for travelers to chikungunya affected regions.


CDF of T+ (time to reach N = 40)
Pr[T+ ≤ t]
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
t (days since first dose)
treatment.group
Grp 1 : 20/P/20
Grp 2 : 6A/P/6A
Grp 3 : 10A/P/10A
Grp 4 : 20A/P/20A
Grp 5 : P/6A/6A
Grp 6 : P/10A/10A
Grp 7 : P/20A/20A
Grp 8 : P/P/40A


CDF of T+ (time to reach N = 100)
Pr[T+ ≤ t]
1.00
0.75
0.50
0.25
0.00
0
5
10
15
20
t (days since first dose)
treatment.group
Grp 1 : 20/P/20
Grp 2 : 6A/P/6A
Grp 3 : 10A/P/10A
Grp 4 : 20A/P/20A
Grp 5 : P/6A/6A
Grp 6 : P/10A/10A
Grp 7 : P/20A/20A
Grp 8 : P/P/40A