Supplementary Material

# Supplementary Tables

**Supplementary** **Table S1** – Summary statistics of individual fits of viral load data. c: viral clearance, δ: infected cell clearance, p: viral production rate, Emax,immunity: maximum acquired immunity effect on viral clearance, SD: standard deviation, %CV: coefficient of variation (100\*mean/SD).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **c** | ***δ*** | **p** | **Emax,immunity** |
| **mean** | 5.07 | 0.54 | 10.2 | 57.0 |
| **SD** | 2.18 | 0.16 | 4.3 | 23.4 |
| **%CV** | 43% | 30% | 42% | 41% |

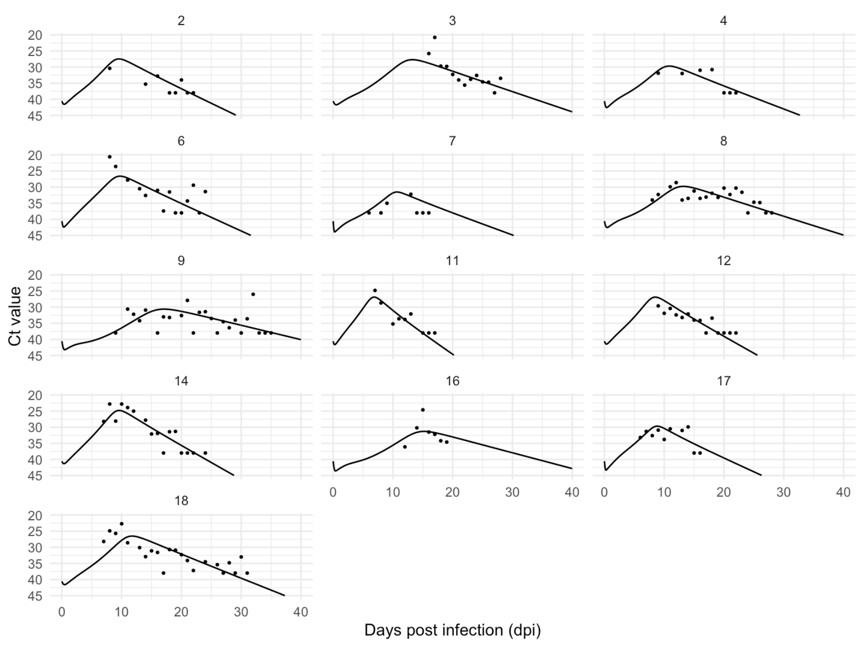
**Supplementary** **Table S2** - Viral kinetics model parameters. EC50: half maximal effective concentration; IC50: half maximal inhibitory concentration; HCQ: hydroxychloroquine; IVM: ivermectin; NTZ: nitazoxanide; ART: artemisinin; LPV: lopinavir

| **Parameter** | **Definition** | **Value** | **Reference** |
| --- | --- | --- | --- |
| *β* | Cellular infection rate |  | Calculated |
| *δ* | Infected cell death rate | 0.54 | Estimated |
| *p* | Viral production rate | 10.2 | Estimated |
| *c* | Viral clearance | 5.07 | Estimated |
| *R0* | Within-host reproduction number | 3.79 | (Li et al., 2020) |
| *T0* | Initial target cells | 105 | Fixed by authors |
| *V0* | Initial virus load (inoculum) | 100 | Fixed by authors |
| *EC50, immunity* | EC50 for immune response | 10.2 | Estimated from (Long et al., 2020) |
| *Hill immunity* | Slope of dose-response curve | 3.4 | Estimated from (Long et al., 2020) |
| *Emax, immunity* | Maximum effect on viral clearance | 57.0 | Estimated |
| HCQ | EC50 viral entry | 8.51 µM | (Liu et al., 2020) (averaged) |
| Protein binding | 50% | (Furst, 1996) |
| IVM | IC50 helicase | 0.1 µM | Fixed by authors |
| IC50 nAChR | 0.156 µM | (Degani-Katzav et al., 2017) |
| Protein binding | 93% | (Klotz et al., 1990) |
| Lung accumulation | 2.6 | (Lifschitz et al., 2000) |
| NTZ | EC50 | 2.12 µM | (Wang et al., 2020) |
| Protein binding | 99% | (FDA, 2005) |
| Lung accumulation | 0.7 | (Rajoli et al., 2020) |
| ART | EC50 | 70 µM | (Nair et al., 2021) |
| Protein binding | 88% | (Jagdev S. Sidhu, 1997) |
| LPV | IC50 protease | 26.63 µM | (Choy et al., 2020) |
| Protein binding | 99% | (Boffito et al., 2004) |
| Lung accumulation | 1.78 | (Atzori et al., 2003) |

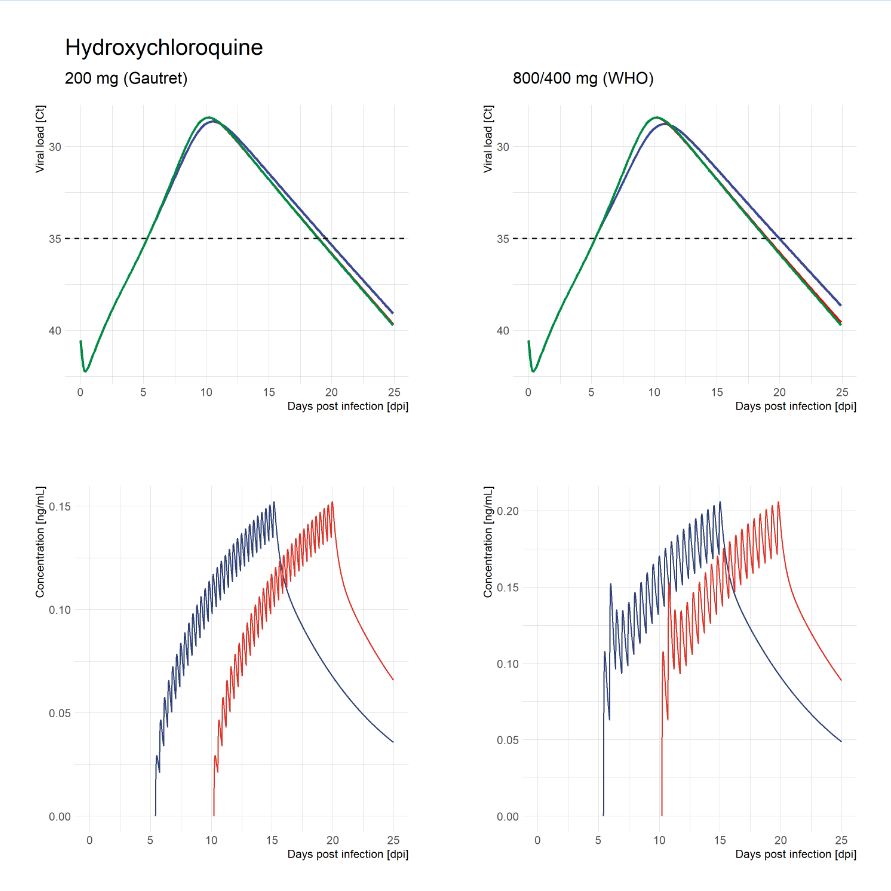
**Supplementary Table S3** - Summary results of viral load simulations. dpi: days post infection; d: day; min Ct: minimum serial cycle threshold values; tmax: time to peak concentration; ΔAUC%: percentage difference in area under the curve; HCQ: hydroxychloroquine; ART: artemisinin; IVM: ivermectin; LPV/r: lopinavir/ritonavir; NTZ: nitazoxanide. Treatments were initiated either on positivity (5.4 dpi) or on peak (10.2 dpi). Dosing of different modeled treatment regimens: HCQ 200 mg every 8h for 10 days; HCQ 800 mg every 12h for 1 day, then 400 mg every 12h for 9 days; IVM 300 µg/kg every 24h for 3 days; IVM 600 µg/kg every day for 3 days; NTZ 1200 mg every 6h for 5 days; NTZ 2900 mg every 12h for 5 days; ART 500 mg once a day for 5 days; LPV/r 400/100 mg every 12h for 14 days.

| **Treatment** | **Timing** | **Dosage** | **Start positivity** | **Duration** | **Ctmin** | **Tmax** | **ΔAUC%** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| ART 500 | on positivity | 500 mg qd 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| ART 500 | on peak | 500 mg qd 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| HCQ 200 | on positivity | 200 mg q8h 10d | 5.4 | 14.1 | 28.6 | 10.5 | -4.6 |
| HCQ 200 | on peak | 200 mg q8h 10d | 5.4 | 13.5 | 28.4 | 10.2 | -0.3 |
| HCQ 800 | on positivity | 800 mg q12h 1d,  400 mg q12h 9d | 5.4 | 14.5 | 28.8 | 10.9 | -8.2 |
| HCQ 800 | on peak | 800 mg q12h 1d,  400 mg q12h 9d | 5.4 | 13.6 | 28.4 | 10.2 | -0.6 |
| IVM 300 | on positivity | 300 µg/kg q24h 3d | 5.4 | 14.2 | 28.7 | 10.9 | -8.8 |
| IVM 300 | on peak | 300 µg/kg q24h 3d | 5.4 | 13.6 | 28.4 | 10.2 | -3.4 |
| IVM 600 | on positivity | 600 µg/kg q24h 3d | 5.4 | 15.6 | 29.0 | 12.3 | -22.3 |
| IVM 600 | on peak | 600 µg/kg q24h 3d | 5.4 | 14.0 | 28.4 | 10.2 | -13.2 |
| LPV/r 400/100 | on positivity | 400/100 mg q12h 14d | 5.4 | 13.5 | 28.4 | 10.2 | -0.4 |
| LPV/r 400/100 | on peak | 400/100 mg q12h 14d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| NTZ 1200 | on positivity | 1200 mg q6h 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| NTZ 1200 | on peak | 1200 mg q6h 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| NTZ 2900 | on positivity | 2900 mg q12h 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| NTZ 2900 | on peak | 2900 mg q12h 5d | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |
| No treatment | NA | - | 5.4 | 13.5 | 28.4 | 10.2 | 0.0 |

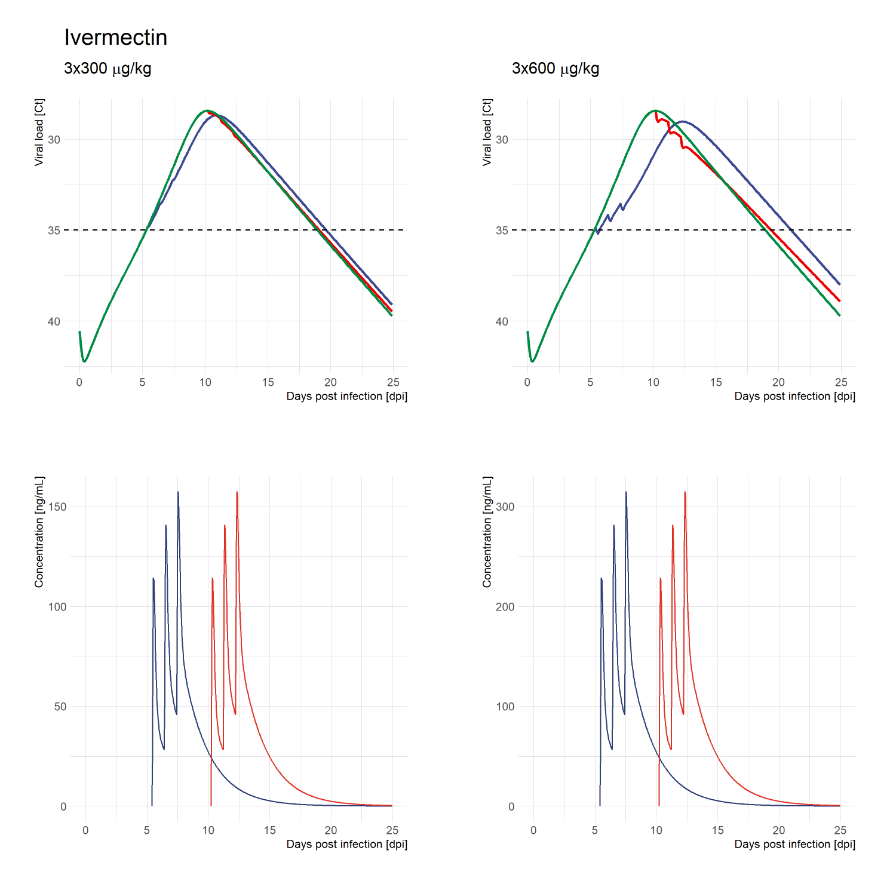
# Supplementary Figures



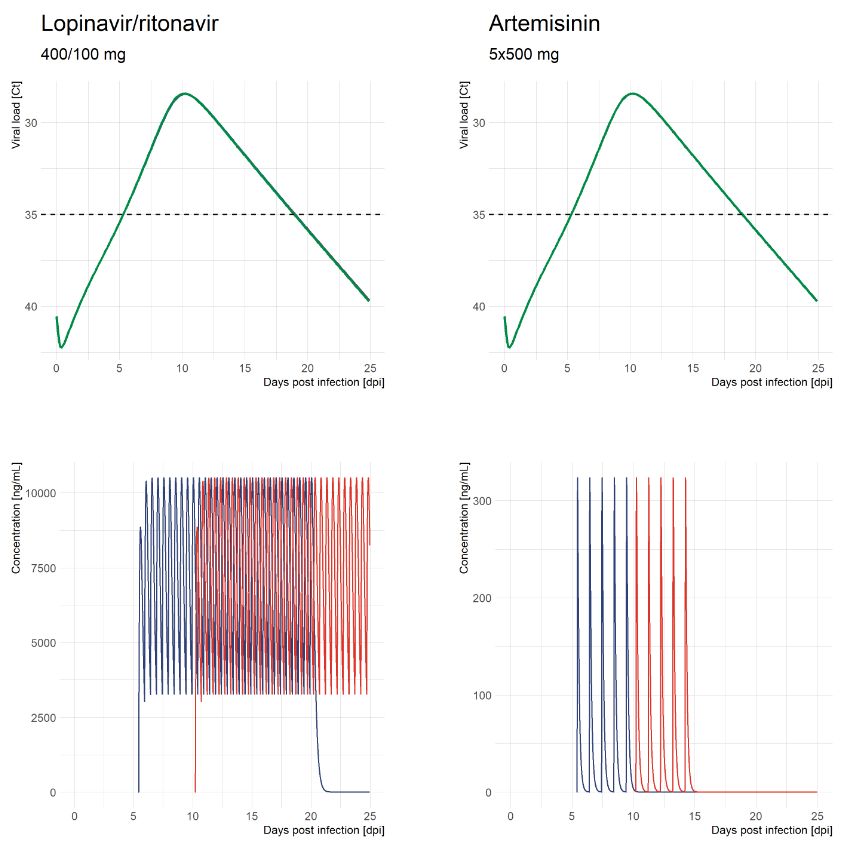
**Supplementary Figure S1** - Individual plots of serial cycle threshold (Ct) values by days post infection in SARS-CoV-2 of patients included in the analysis (n=13, dots) and model fit (line).



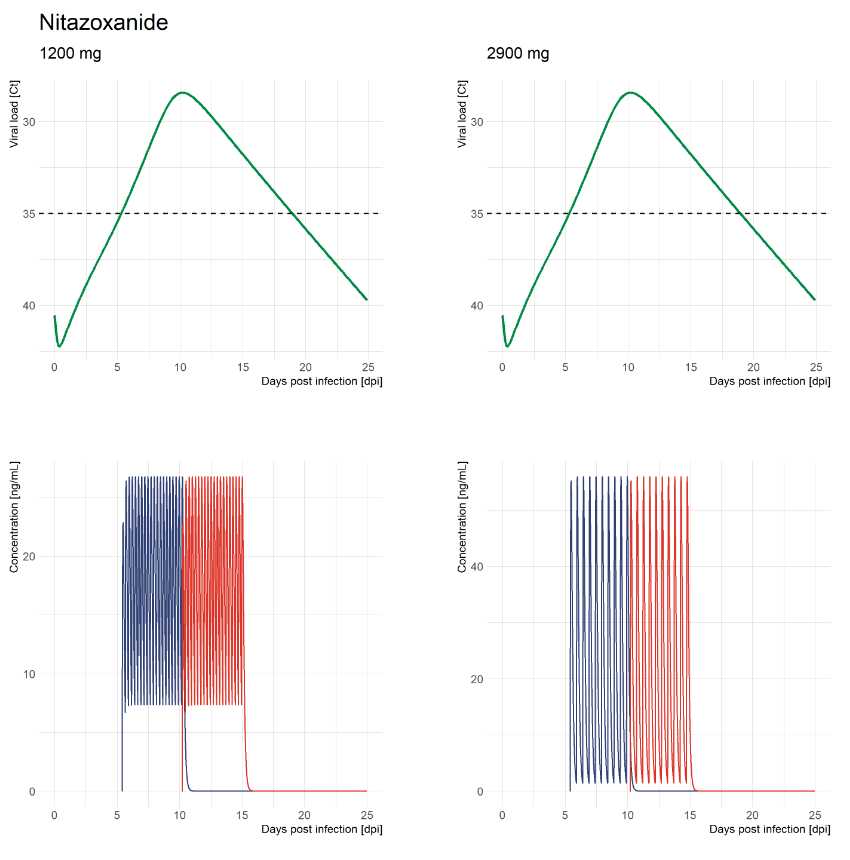
**Supplementary Figure S2** – Effect of Hydroxychloroquine pharmacokinetic on SARS-CoV-2 viral kinetics (blue: treatment on positivity, red: treatment on peak, green: untreated)



**Supplementary Figure S3** – Effect of ivermectin pharmacokinetic on SARS-CoV-2 viral kinetics (blue: treatment on positivity, red: treatment on peak, green: untreated)



**Supplementary Figure S4** – Effect of lopinavir/ritonavir and Artemisinin pharmacokinetic on SARS-CoV-2 viral kinetics (blue: treatment on positivity, red: treatment on peak, green: untreated)



**Supplementary Figure S5** – Effect of nitazoxanide pharmacokinetic on SARS-CoV-2 viral kinetics (blue: treatment on positivity, red: treatment on peak, green: untreated)

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