**Table**

**Table 1.** Model validation

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| --- | --- | --- | --- | --- |
| Clinical study | PK parameter | Predicted value | Observed value | Predicted value /Observed value |
| Chloroquine | | | | |
| A single dose of 600 mg administration in healthy subjects9 | AUC0-7days (µM\*h) | 88.79 (69.31-118.78) | 90.0 (48.90-212.3) | 0.98 |
| Cmax (μM) | 2.84 (2.15-3.48) | 1.80 (1.30-5.20) | 1.58 |
| Vd/F (L) | 7,825 (4,898-10,057) | 8672 (2,593-32,503) | 0.90 |
| CL/F (L/h) | 10.56 (6.11-17.48) | 11.30 (5.70-20.30) | 0.93 |
| T1/2 (days) | 22.21 (8.83-43.98) | 23.30 (10.2-54.60) | 0.95 |
| AAFEs | NA | NA | 1.15 |
| Loading dose of 600 mg administration on day 1, followed by 600 mg on day 2, and followed by 300 mg on day 3 in healthy volunteers 9 | AUC0–28days (μM\*h) | 488.26 (251.11-992.98) | 636.3 (394.2-1010.9) | 0.77 |
| Cmax (μM) | 4.09 (2.44-7.70) | 3.4 (1.4-5.6) | 1.20 |
| Vd/F (L) | 5,876 (1,770-12,260) | 3,721 (1,248-20,516) | 1.58 |
| CL/F (L/h) | 9.8 (4.7-19.2) | 9.5 (5.4-20.6) | 1.03 |
| T1/2 (days) | 16.47 (4.76-57) | 13.2 (4-44) | 1.25 |
|  | AAFEs | NA | NA | 1.26 |
| Multiple doses of 600 mg administration on day 1, followed by 600 mg on day 2, and followed by 300 mg on day 3 in Thai healthy subjects 10 | AUC0–28days (μg\*h/mL) | 112.32 (58.50-163.07) | 122 (103-182) | 0.92 |
| Cmax (ng/mL) | 1,220 (830-1,550) | 838 (658-1,587) | 1.45 |
| T1/2 (hours) | 144.76 | 150 | 0.96 |
| AAFEs | NA | NA | 1.26 |
| Chloroquine | AAFE | NA | NA | 1.21 |
| Ritonavir | | | | |
| Multiple doses of 200 mg of ritonavir given every 12 hours for 2 weeks 8 | AUC24h,day16 (μg\*h/mL) | 64.11 | 43.80 | 1.46 |
| Cmax (μg/mL) | 5.02 | 4.5 | 1.11 |
| Cmin (μg/mL) | 0.64 | 0.60 | 1.06 |
| AAFEs | NA | NA | 1.20 |
| Multiple doses of 300 mg of ritonavir given every 12 hours for 2 weeks 8 | AUC24h,day16 (μg\*h/mL) | 107.04 | 60.70 | 1.76 |
| Cmax (μg/mL) | 7.99 | 6.50 | 1.23 |
| Cmin (μg/mL) | 1.30 | 0.70 | 1.86 |
| AAFEs | NA | NA | 1.59 |
| Multiple doses of 400 mg of ritonavir given every 12 hours for 2 weeks 8 | AUC24h,day16 (μg\*h/mL) | 139.71 | 114.20 | 1.22 |
| Cmax (μg/mL) | 10.39 | 11.70 | 0.88 |
| Cmin (μg/mL) | 1.74 | 1.10 | 1.58 |
| AAFEs | NA | NA | 1.30 |
| Multiple doses of 500 mg of ritonavir given every 12 hours for 2 weeks8 | AUC24h,day16 (μg\*h/mL) | 191.25 | 170.30 | 1.12 |
| Cmax (μg/mL) | 13.22 | 14.20 | 0.93 |
| Cmin (μg/mL) | 3.13 | 2.30 | 1.36 |
| AAFEs | NA | NA | 1.18 |
| Ritonavir | AAFEs | NA | NA | 1.30 |
| Lopinavir | | | | |
| Multiple doses of lopinavir/ritonavir (400/100 mg) given twice daily for 3 weeks7 | AUC24h,day21 (μg\*h/mL) | 217.97 | 185.2 | 1.17 |
| Cmax (μg/mL) | 10.52 | 9.81 | 1.07 |
| Ctrough (μg/mL) | 7.08 | 7.13 | 0.99 |
| AAFEs | NA | NA | 1.08 |
| Multiple doses of lopinavir/ritonavir (800/200 mg) given once daily for 3 weeks 7 | AUC24h,day21 (μg\*h/mL) | 221.09 | 164.90 | 1.34 |
| Cmax (μg/mL) | 12.14 | 10.94 | 1.11 |
| Ctrough (μg/mL) | 5.05 | 3.62 | 1.39 |
| AAFEs | NA | NA | 1.27 |
| Multiple doses of lopinavir/ritonavir (400/100 mg) given twice daily 6 | Plasma-concentration (μg/mL) | 7.95 | 8.10 | 0.98 |
| Epithelial lining fluid concentration (μg/mL) | 17.47 | 14.4 | 1.21 |
| AAFEs | NA | NA | 1.11 |
| Lopinavir | AAFEs | NA | NA | 1.17 |
| Rifampicin | | | | |
| Single dose of 450 mg 11 | AUC0-24h (μg\*h/mL) | 62.33 | 44 | 1.42 |
| Cmax (μg/mL) | 5.70 | 6.60 | 0.86 |
| Clearance (L/hours) | 8.62 | 8.70 | 0.99 |
| AAFEs | NA | NA | 1.18 |
| Single dose of 600 mg 12 | AUC0-24h (μg\*h/mL) | 85.92 | 76.95 | 1.12 |
| Cmax (μg/mL) | 7.95 | 9.85 | 0.81 |
| Clearance (L/hours) | 8.67 | 8.25 | 1.05 |
| AAFEs | NA | NA | 1.13 |
| Single dose of 600 mg 13 | Bronchial mucosa concentration (μg/mL) | 9.29 | 7.90 | 1.17 |
| Epithelial lining fluid concentration ((μg/mL) | 4.71 | 5.5 | 0.86 |
| AAFEs | NA | NA | 1.17 |
| Rifampicin | AAFEs | NA | NA | 1.16 |
| All drugs | AAFEs | NA | NA | 1.20 |