**Table 1.** Simulated change in rivaroxaban PK parameters in the presence of ketoconazole

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Simulated (n=200) | | | | | | Observed (n=20) | | | | | |
| Rivaroxaban 10 mg and Ketoconazole  CYP and P-gp Inhibition  (Mueck et al., 2013) | **AUC**  **(µg.h/L)** | **Cmax (µg/L)** | | **CLH**  **(L/h)** | | **CLR**  **(L/h)** | **AUC**  **(µg.h/L)** | **Cmax (µg/L)** | | **CLH**e  **(L/h)** | | **CLR**  **(L/h)** |
| Mean | 1800 | 197 | | 2.92 | | 3.46 | 2298 | 237 | | 2.75 | | 1.60 |
| CV (%) | 39 | 23 | | 38 | | 54 | 26 | 20 | | 26 | | 33 |
| Ratio of simulated/observed | ***0.73*** | ***0.80*** | | 1.06 | | ***2.16*** |  |  | |  | |  |
| Success criteria for ratio of simulated/observed | 0.78-1.28 | 0.83-1.21 | | 0.78-1.28 | | 0.74-1.36 |  |  | |  | |  |
| Fold Change vs Healthya | **AUC Fold Change (90% CI)** | | **CLH Fold Change (90% CI)** | | **CLR Fold Change (90% CI)** | | **AUC Fold Change**b | | **CLH Fold Change**c | | **CLR Fold Change**c | |
|  | 1.56  (1.47, 1.67) | | 0.45  (0.42, 0.49) | | 1.00  (0.92, 1.09) | | 2.58 | | 0.32 | | 0.64 | |
| Success Criteria for Fold Change | 1.48-4.50 | | 0.17-0.58 | | 0.38–1.07 | |  | |  | |  | |
|  | **Simulated (n=200)** | | | | | | **Observed (n=20)** | | | | | |
| Rivaroxaban 10 mg and Ketoconazole  CYP, P-gp and OAT3 Inhibition  (Mueck et al., 2013) | **AUC**  **(µg.h/L)** | **Cmax (µg/L)** | | **CLH**  **(L/h)** | | **CLR (L/h)** | **AUC**  **(µg.h/L)** | **Cmax (µg/L)** | | **CLH**e  **(L/h)** | | **CLR (L/h)** |
| Mean | 2738 | 241 | | 2.87 | | 1.21 | 2298 | 237 | | 2.75 | | 1.60 |
| CV (%) | 34 | 21 | | 36 | | 30 | 26 | 20 | | 26 | | 33 |
| Ratio of simulated/observed | 1.19 | 1.02 | | 1.04 | | 0.76 |  |  | |  | |  |
| Success criteria for ratio of simulated/observed | 0.78-1.28 | 0.83-1.21 | | 0.78-1.28 | | 0.74-1.36 |  |  | |  | |  |
| Fold Change vs Healthya | **AUC Fold Change (90% CI)** | | **CLH Fold Change (90% CI)** | | **CLR Fold Change (90% CI)** | | **AUC Fold Change**b | | **CLH Fold Change**c | | **CLR Fold Change**c | |
|  | 2.41  (2.27, 2.56) | | 0.44  (0.41, 0.48) | | ***0.37***  ***(0.35, 0.40)*** | | 2.58 | | 0.32 | | 0.64 | |
| Success Criteria for Fold Change | 1.48-4.50 | | 0.17-0.58 | | 0.38–1.07 | |  | |  | |  | |