

Analysis Plan: Pharmacokinetics of Advantage Arrest

NCT04184271

Document Date: 07/30/2020

For the pharmacokinetic analysis, baseline serum fluoride and silver concentrations will be assessed and when appropriate, subtracted from other timed serum concentrations to adjust for baseline levels.

Pharmacokinetic analysis will be performed using Phoenix WinNonlin (Certara).

- The time to peak concentration (T_{max}), observed and baseline-corrected peak concentrations (C_{max}), and observed 24-h concentration ($C_{24\text{ h}}$) will be reported.
- The elimination rate constant (k_{elim}) will be determined by nonlinear regression with a minimum of 3 time points with decreasing concentrations over time observed after the peak concentration.
- Half-life ($t_{1/2}$) will be calculated as $\ln(2)/k_{elim}$.
- Area under the curve (AUC): The 24-hour AUC ($AUC_{0-24\text{ hr}}$) will be calculated using a log-linear trapezoidal rule of baseline-corrected serum concentrations from time = 0 to 24 h. The $AUC_{0-\infty}$ will be calculated using a log-linear trapezoidal rule of baseline-corrected serum concentrations and extrapolated to infinite time by $C_{24\text{ hour}}/k_{elim}$, where $C_{24\text{ hour}}$ is the 24 hour concentration.
- The percent extrapolated AUC will be calculated as $(AUC_{0-\infty} - AUC_{0-24\text{ hr}})/AUC_{0-\infty} \times 100$.
- The total urinary recovery of fluoride and silver will be determined by multiplying the concentration measured in the urine collected over 24 hours by the total volume of urine collected over 24 hours.

Statistical analysis will be performed using Excel to calculate the mean \pm standard deviation for the pharmacokinetic parameters. No statistical comparisons will be made as it is a single arm study.