Is Dilute Russell’s Viper Venom Time a Useful Assay To Monitor Patients Treated By Rivaroxaban Or Dabigatran Eteixilate?
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References


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Objective

To analyse and compare the results obtained with STA®-DRVV Screen and STA®-DRVV Confirm with the plasma drug levels measured by LC-MS/MS.

Methods

60 plasmas from patients treated with rivaroxaban and 48 plasmas from patients treated with dabigatran etexilate were included in the study. Plasma concentrations were measured by LC-MS/MS. STA®-DRVV Screen and Confirm (Diagnostica Stago®) were performed on the 108 plasma samples. All methodologies were performed according to the recommendations of the manufacturer.

Results

The dabigatran plasma concentration ranged from 0 to 413 ng/mL and the rivaroxaban plasma concentration ranged from 0 to 426 ng/mL.

Correlation between STA®-DRVV Screen and LC-MS/MS measurements

Calibrated STA®-DRVV Screen and dabigatran or rivaroxaban plasma concentrations correlate well (Figures 1 C). The Spearman correlation is 0.84 (95% CI: 0.72 – 0.91; p<0.0001) and 0.88 (95% CI: 0.82 – 0.93) for dabigatran and rivaroxaban, respectively. When expressed in seconds as or ratios the relation is not linear and is best fit by a second order relation (Figures 1 A & B). Results of the Bland-Altman analysis reveal a mean difference of ~37 ng/mL and ~21 ng/mL for dabigatran and rivaroxaban, respectively, with large confidence intervals. This implies that STA®-DRVV Screen tends to overestimate the concentration of dabigatran and rivaroxaban in plasma samples. Therefore STA®-DRVV Screen should not be used to estimate plasma concentrations of both dabigatran and rivaroxaban. However, specific cut-off associated with supra-therapeutic concentrations at C trough (i.e. 200 ng/mL which represent the 90th percentile of plasma concentrations at C trough) could be defined. Thus, a ratio of 2.5 or 3.0 could exclude plasma concentration above 200 ng/mL for dabigatran and rivaroxaban, respectively.

Correlation between STA®-DRVV Confirm and LC-MS/MS measurements

Calibrated STA®-DRVV Confirm and dabigatran or rivaroxaban plasma concentrations correlate well (Figures 2 C). The Spearman correlation is 0.94 (95% CI: 0.89 – 0.97; p<0.0001) and 0.89 (95% CI: 0.82 – 0.94; p<0.0001) for dabigatran and rivaroxaban, respectively. When expressed in seconds or as ratios the relation is not linear and is best fit by a second order relation (Figures 2 A & B). Results of the Bland-Altman analysis reveal a mean difference of ~40 ng/mL and ~16 ng/mL with large confidence interval for dabigatran and rivaroxaban, respectively. This implies that STA®-DRVV Confirm tends to overestimate the concentration of dabigatran and rivaroxaban in plasma samples. Therefore STA®-DRVV Confirm should not be used to estimate plasma concentrations of both dabigatran and rivaroxaban. As for STA®-DRVV Screen, specific cut-off could be proposed and a ratio of 1.8 or 2.5 at C trough with STA®-DRVV Confirm could exclude supra-therapeutic levels of dabigatran and rivaroxaban, respectively.

Discussion

The dabigatran plasma concentration ranged from 0 to 413 ng/mL and the rivaroxaban plasma concentration ranged from 0 to 426 ng/mL.

The DRVV cannot be used to accurately estimate dabigatran and rivaroxaban plasma concentrations.

- Specific cut-off could however be proposed to rule out excessive concentrations (i.e. concentrations > 200 ng/mL at C trough)
- However, these cut-offs are specific for dabigatran and rivaroxaban due to difference in sensitivities and also depend on the quantity of phospholipid in the test.