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

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Published in:
Blood 2013 122:3634; published ahead of print December 6, 2013

Publication date:
2013

Document Version
Peer reviewed version

Link to publication
Citation for published version (HARVARD):

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Download date: 03. Aug. 2019
Disclosure

The authors have no relevant conflicts of interest to disclose.

References


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Discussion

The dabigatran plasma concentration ranged from 0 to 413ng/mL and the rivaroxaban plasma concentration ranged from 0 to 426ng/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 or as 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 -37ng/mL and -21ng/mL for dabigatran and rivaroxaban, respectively, with large confidence interval. 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.

Specific cut-off associated with supra-therapeutic concentrations at Ctrough (i.e. concentrations > 200ng/mL at Ctrough) could be defined. Thus, a ratio of 2.5 or 3.0 could exclude plasma concentration above 200ng/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 -40ng/mL and -16ng/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 Ctrough with STA-DRVV Confirm could exclude supra-therapeutic levels of dabigatran and rivaroxaban, respectively.

Conclusions

- 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 > 200ng/mL at Ctrough).
- 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.