



Evaluation of Antiphospholipid Lupus Panel tested on Yumizen G1500 (HORIBA)

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INTRODUCTION

The laboratory classification of lupus anticoagulant (LA) is via prolongation of phospholipid-dependent clotting tests. Guidelines currently recommend the use of two screening assays. The first test should be dilute Russell's viper venom time (dRVVT) and the second should be a LA-sensitive APTT^{1,2}. Xa-DOAC interference in DRVVT is a growing issue. Different reagents have varying sensitivity to Xa-DOAC with risk of false positive or negative depending on reagents³.

AIM

To evaluate the performance of LA screening tests tested on the Yumizen G1500 (HORIBA, France) against predicate LA screening tests tested on the Sysmex CN6000 (Sysmex, UK)

- APTT -Yumizen G APTT & Yumizen G APTT Liq (HORIBA, France)
- DRVVT - DVVtest and DVVconfirm (BioMedica Diagnostics, Canada)
- APTT - Actin FS & Actin FSL (Siemens, UK)
- DRVVT - LA1 and LA2 (Siemens, UK)
- Evaluate DVVtest and DVVconfirm reagent sensitivity to XA-DOAC

METHOD

- Anonymised samples previously investigated for LA were selected.
- Samples were classified based on historical LA1/LA2 results.
- Samples previously screened for direct/indirect Xa inhibitors via anti-Xa (LMWH) assay during initial testing
- Siemens LA1 and LA2 Reference Interval (RI) calculated using 99th centile^{1,2}, and results normalised with pooled normal plasma
 - LA negative (n=48) (ratio <1.20) & LA positive (n=41) (ratio >1.20)
- Local RI (+/-2SD)⁴ was established for the 4 APTT reagents and DVVtest/DVVconfirm. The mean of RI used to normalise DVVtest/DVVconfirm⁴.

Xa-DOAC Spiking

- Pooled Normal plasma was spiked with increasing concentration of Rivaroxaban, Apixaban and Edoxaban.
- Xa-DOAC concentration established using Biophen Heparin LRT (Hyphen Biomed, UK) on Sysmex CN6000 (Sysmex UK)
- DVVtest & DVVconfirm performed at each concentration and normalised screen confirm ratio (NSCR) calculated.

RESULTS

Yumizen G APTT, Yumizen G APTT Liq and DVVtest/DVVconfirm demonstrated good repeatability/reproducibility in both normal (CV <2.5% and <8.9%) and abnormal (CV <5.2% and <11.1%) samples (see Table 1).

LA Negative Group: DVVtest/DVVconfirm identified 46/48 samples as LA negative (ratio <1.27). Two samples gave abnormal NSCR (1.41 and 1.47). Prolongation APTT was seen in Yumizen G APTT (n=12), Yumizen G APTT Liq (n=10), Actin FS (n=6) and Actin FSL (n=10).

LA Positive Group. DVVtest/DVVconfirm identified 25/41 samples as LA positive (ratio >1.27). Prolongation APTT was seen in Yumizen G APTT (n=24), Yumizen G APTT Liq (n=18), Actin FS (n=5) and Actin FSL (n=21).

DVV test/DVV confirm showed different sensitivity to Xa-DOAC. For all Xa-DOAC spiking, NSCR remained below positivity cut off as concentration increased (Figure 1).

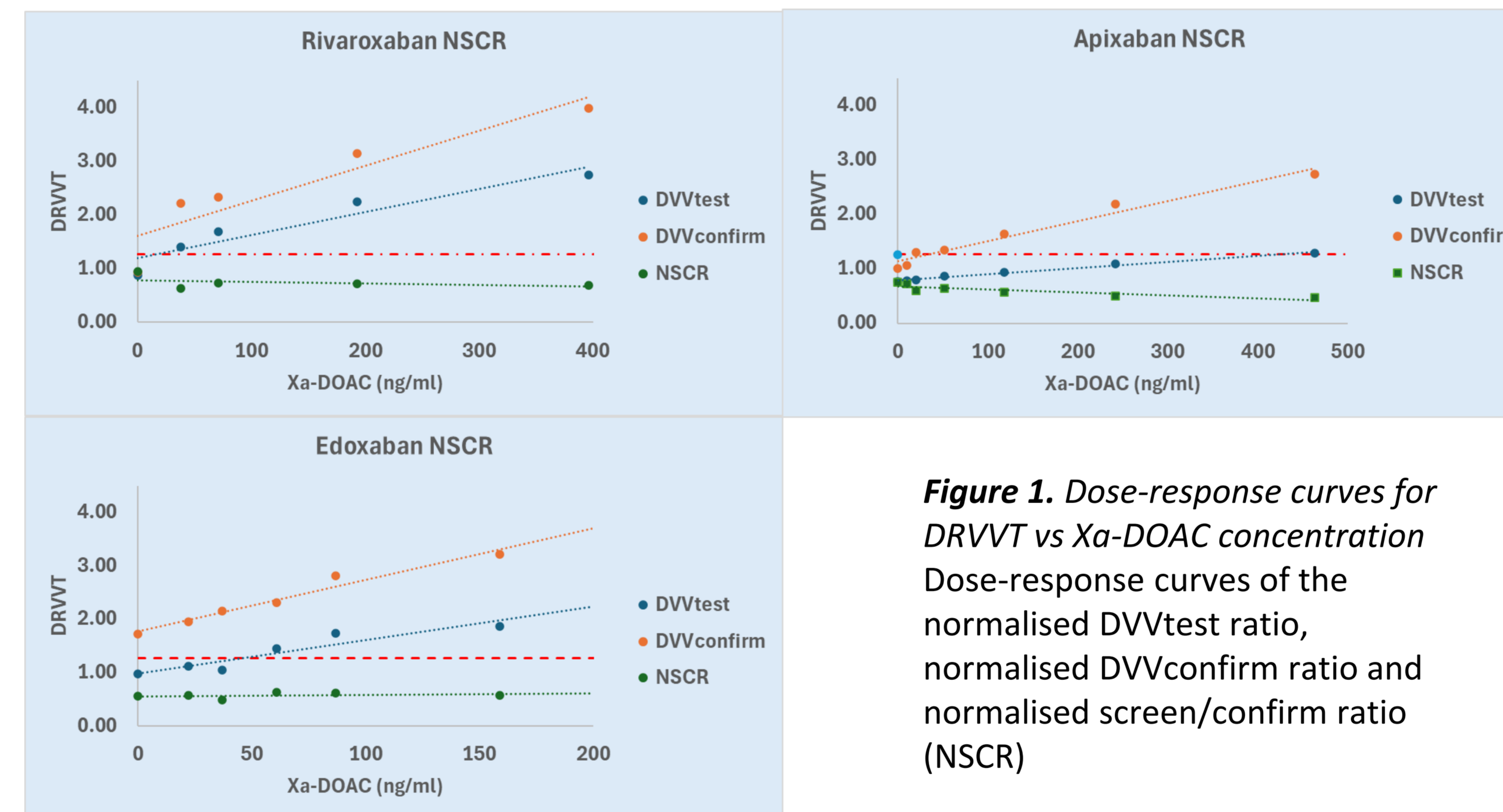


Figure 1. Dose-response curves for DRVVT vs Xa-DOAC concentration. Dose-response curves of the normalised DVVtest ratio, normalised DVVconfirm ratio and normalised screen/confirm ratio (NSCR)

Test	Sample type	Repeatability			Reproducibility		
		n	Mean (sec)	CV (%)	n	Mean (sec)	CV (%)
APTT	Normal	10	33.1	1.7	20	37.3	8.9
APTT	Abnormal	10	64.3	2.4	17	71.3	9.9
APTT Liq	Normal	10	29.9	2.5	23	35	7.2
APTT Liq	Abnormal	10	66.6	3.7	19	67	11.1
DVVtest	Normal	10	37.3	1.1	21	39.1	8.1
DVVtest	Abnormal	10	60.1	1.2	22	81.1	9.1
DVVconfirm	Normal	10	28.2	2.2	20	32.5	8.5
DVVconfirm	Abnormal	10	32.7	5.2	19	37.9	9.6

Table 1. Performance Characteristics of Yumizen G APTT, Yumizen G APTT Liq DVVtest and DVVconfirm

CONCLUSIONS

- Yumizen G APTT, Yumizen G APTT Liq, DVVtest/DVVconfirm are reliable and easy-to-use reagents.
- Good agreement seen in LA negative samples and discordance in LA positive samples. With the heterogeneous nature of LA antibodies, this is not an unexpected finding when comparing dRVVT reagents as no single test can detect every LA.
- DVVtest and DVVconfirm NSCR can potentially generate false negative results in patients on Xa DOAC.
- DOAC interference can be mitigated via use of activated charcoal after local verification^{1,2}

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CONTACT INFORMATION

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