A Digital Microfluidic Approach to Accurate Heparin Monitoring in DOAC-Treated Patients

V Pamula[1], L Nichols[1], A Ullal[1], A Winners[2], K Simmerman[2], D Arroyo Lugo[2], C Davis[1], C Graham[1], R Sista[1], M Reyes Gil[2]

[1]Baebies, Inc., Durham, NC, USA; [2]Cleveland Clinic, Cleveland, OH, USA

BACKGROUND

- Patients on direct oral anticoagulants (DOACs) may need to transition to heparin during surgery or when rapid reversal of anticoagulation is necessary.
- The presence of residual DOACs is known to interfere with anti-Factor Xa (aFXa) tests.
- We previously developed a rapid (< 15 minute) test on a point-of-care digital microfluidic (DMF) platform to test aFXa. Here, we present interference or lack thereof with apixaban and rivaroxaban.

METHODS

- Remnant citrated whole blood samples were obtained from patients (IRB-approved), who had aFXa ordered as part of their clinical care. Four samples came from patients with remnant apixaban, and 56 samples were confirmed as without DOAC exposure.
- To test analytical interference, pooled normal whole blood was spiked with unfractionated heparin at 0.5 IU/mL and apixaban or rivaroxaban at 0, 100, and 200 ng/mL.
- Clinical samples were tested on both the DMF platform and Stago® (comparator - chromogenic assay on plasma from centrifugation).
- For the DMF aFXa test, 50 µL of whole blood was separated into plasma within the cartridge and a fully automated novel fluorogenic assay was performed. Results were analyzed using correlation and simple regression to assess equivalence and interference.
- To deplete samples of DOACs, citrated whole blood was centrifuged to separate plasma, and a DOAC Remove™ tablet was added. The DOAC-depleted plasma sample was tested on the comparator and compared to whole blood samples containing DOACs run on the DMF platform.

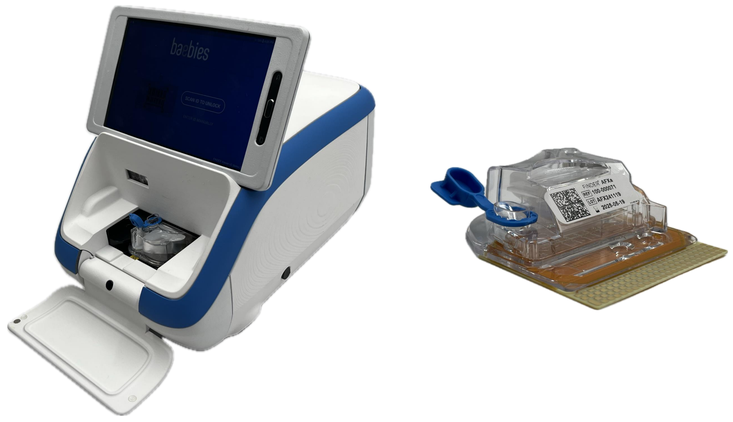

Figure 1: Baebies' point-of-care instrument and cartridge for aFXa testing.

RESULTS

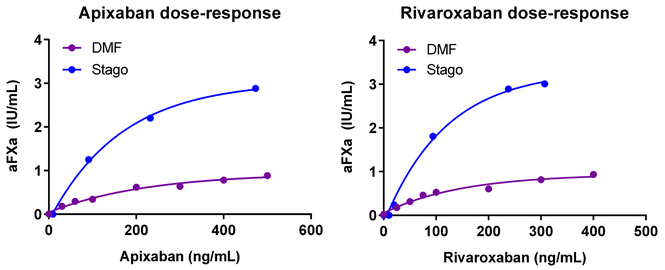

Figure 2: Apixaban and rivaroxaban showed steeper dose-response curves on the comparator than on DMF.

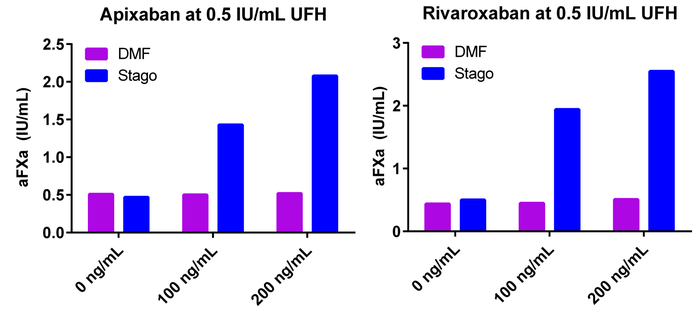

Figure 3: aFXa measurements remained essentially unchanged with apixaban (0.50-0.52 IU/mL) or with rivaroxaban (0.44-0.51 IU/mL) spiked at 0–200 ng/mL, while the comparator assay values increased 3-5x from baseline.

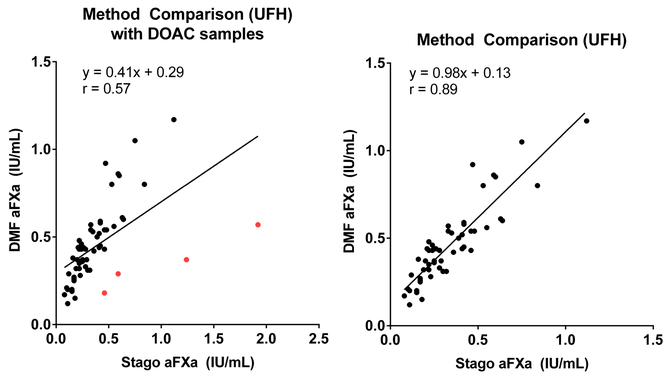

Figure 4: Four clinical samples from patients with residual apixaban showed significantly higher values on comparator (0.46–1.92 IU/mL) than DMF (0.14–0.45 IU/mL). In contrast, in 56 patient samples without any DOAC exposure, DMF correlated strongly with the comparator (R = 0.89; slope = 0.98), confirming assay equivalence in the absence of DOAC interference.

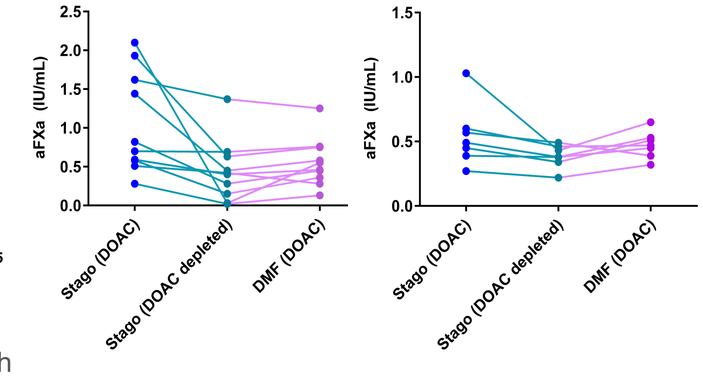

Figure 5: DOAC-depleted citrate whole blood on Stago compared to whole blood samples with DOACs on Stago and the DMF platform. aFXa results from the DMF platform correlate better with the DOAC-depleted samples.

CONCLUSIONS

- **The digital microfluidic aFXa test remained remarkably tolerant to the presence of DOACs.**
- **This novel approach could enhance anticoagulation management in patients transitioning from DOACs to unfractionated heparin.**
- **Further clinical studies are underway to establish clinical performance.**

Research reported here was supported by the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health under awards R44HL169045 and R44HL140662. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

For investigational use only. Not yet available for sale or use. Performance not yet established.