Patient Plasma BIVV001 [efanesoctocog] Assays

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The experience I have in Sydney measuring BIVV001 is for the nine patients we have in the clinical trial and as a participant in the recently published Pipe field study of BIVV001 measurement. We tested one chromogenic and two APTT reagents, FS and FSL, all on a Sysmex analyser and got results within expectation based on provisional information given to us by the drug manufacturer when we first started measuring sample.

Our routine assay is FSL on the Sysmex with SHP calibrator, and results are generally within 10% of trial central laboratory results on several samples we had comparative data for, so all good so far. The product potency is assigned with Actin FSL APTT reagent. As far as I am aware our site is the only one measuring BIVV001. The product is not currently licenced in Australia but should that occur then validation across different analyser types and reagent types will be required.

For sites that are required to measure BIVV001 but require validation of their result accuracy the situation can be challenging.

A product specific calibrator has been used successfully for other product so potentially is the solution here, but as far as I am aware it is not available. Another avenue would be to request samples set of spiked plasma samples containing BIVV001 from the manufacturer to allow local sites to check assay accuracy as part of their test validation process.

The field study by Pipe et al shows that FVIII assays with two commonly used reagents, Synthasil on the ACLTOP, and Actin FS on the Sysmex/Atellica cause significant underestimation and overestimation, respectively.

In the Pipe study all but perhaps one data set were run on affiliated analysers. There is a lack of data on APTT reagent on non-related analysers. A starting point would be to look at the data and choose an APTT reagent for the analyser type in your laboratory that gave satisfactory recoveries. For Sysmex/Atellica this would be Actin FSL. For Stago analysers CK Prest (4 users) and PTT-A (2 users) were reasonable. For ACLTOP users only Synthafax (1 user) was reasonable, but with only one study participant more data are needed for confirmation. Most reagent had linearity issues, with the lowest assay levels being higher than target. In general, there was a linearity issue with most reagents, an area where a product-specific calibrator may be useful in rectifying.

Choosing to use Actin FSL on a non-affiliated analyser is an option but there is no guarantee results would be the same as on an affiliated analyser. Test protocols, dilutions, buffers and clot end-point detection methods all play a role determining final results. When I did a pilot study on the ACLTOP with FSL there appears to be underestimation, so more investigation is necessary. At present, it seems choosing affiliated reagent analyser combinations based on field study data is the only option for laboratories that do not have access to a reference method. All this point to the need for samples sets with known spiked values to assist laboratories in test validation.

As for using correctors, it is less than ideal due the chance of a transcription error. Most FVIII products can be measured by chromogenic methods but BIVV001 overestimates by ~2-3x, depending on the kit being used, with variation between kits. I agree a corrector is less than ideal. Within the chromogenic group there was a large spread of results, so no single corrector would work for all. I could be possible work in a single centre that has validated their own reagent and can tightly monitor results.