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[O26-1] O26-1: Immunosuppressive drugs: assey and genotyping

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[O26-1-2] Long-term performance of laboratory developed LC-MS/MS tests and an FDA- approved immunoassay for the therapeutic drug monitoring of Everolimus

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Background

Laboratory developed tests (LDTs) are analytical tests developed and validated “in-house” for clinical diagnostic purposes. Regulatory agencies, such as the United States Food and Drug Administration (FDA), are encouraging the use of regulatory approved assays rather than LDTs.
Our ongoing Zortracker everolimus study provides validation samples each month to participating clinical laboratories that perform therapeutic drug monitoring (TDM) of everolimus. This allowed for the long-term comparison of the performance of LC-MS/MS assays, most of which are LDTs, versus the FDA-approved everolimus Quantitative Microsphere System (QMS, Thermo Fisher) over 4 years.

Methods

During the study period, each participating laboratory received a set of the same 3 different, blinded samples every month. LC-MS/MS and QMS assays were compared using Passing Bablok regression. To detect trends over time, data was analyzed in 1-year periods. Data was analyzed with and without exclusion of outliers as identified using the maximum normed residual (Grubbs) test.

Results

The slopes of the Passing Bablok regressions remained unchanged in 2013 and 2014 (reference LC-MS/MS; test QMS: slope=0.947 and 0.983). No significant increase was observed in 2015 (slope=1.087). In 2016, however, the slope had increased significantly to 1.388, suggesting a substantial positive bias of the QMS compared to LC-MS/MS. Inclusion of outliers did not affect these results. The inter-laboratory variability of the LC-MS/MS and QMS assays remained unchanged from 2013 to 2015, with coefficients of variance (CV%, with outliers excluded) for LC-MS of 14.6%, 18.0%, 17.1%, and for QMS of 11.5%, 11.6% and 13.4%, respectively. In 2016, the average CV% for the LC-MS/MS laboratories dropped to 14.3%, while for the QMS laboratories it had increased to 16.8%.

Conclusions

Initially, everolimus concentrations in patient samples measured by QMS laboratories were in good agreement with LC-MS/MS laboratories. While the CV% of the LC-MS/MS LDT assays remained unchanged, inter-laboratory variability of the QMS assay seemed to trend higher and was worse than LC-MS/MS in 2016. Importantly, the QMS assay had drifted towards a significant positive concentration bias in 2016, emphasizing the need for long-term, independent performance tracking of TDM assays, including FDA-approved assays.