Analytical evaluation of the Abbott Architect™ transplant parameters: cyclosporin, tacrolimus and sirolimus

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Cyclosporin, tacrolimus and sirolimus are potent immunosuppressant drugs, used to prevent graft rejection after organ transplantation. Because of narrow therapeutic ranges and variable bioavailability, drug monitoring is necessary. We evaluated the analytical performance of the Abbott Architect™ assays for monitoring these drugs. All parameters are measured in whole blood and require a manual pretreatment step.

Accuracy and between-run precision were evaluated based on at least 10 measurements of Abbott Immunoassay-MCC liquid controls (3 levels). For evaluation of within-run precision, control material was analysed 6 times in one run after separate pretreatment. For tacrolimus a functional sensitivity assay (20% CV) was performed to determine the limit of quantification (LOQ), measuring 5 low concentration samples (0.2-3 ng/mL), during 4 days in triplicate.

A method comparison with the currently used routine method was performed: Siemens Dimension-Xpand™ for cyclosporin and tacrolimus, LC/MS/MS for sirolimus.

Since the sirolimus assay shows good cross-reactivity with everolimus (another immunosuppressant) a method comparison with LC/MS/MS was conducted.

At 90.3-955 ng/mL cyclosporin, bias (n=11) varied between -0.6 and -2.6%; between (n=11) and within-run CV ranges 7.7-12.3% and 7.5-9.9% respectively. At 4.3-16.7 ng/mL tacrolimus, bias (n=18) varied between -0.5% and -2.9%; between (n=18) and within-run CV ranges 5.6 -10.9% and 2.46-5.73% respectively. Functional sensitivity of the tacrolimus assay was 0.67 ng/mL. At 4.8-20 ng/mL sirolimus, bias (n=16) varied between 0.9 and 3.6%; between (n=16) and within-run CV ranges 2.8 -5.7% and 2.5-3.8% respectively.

Method comparison for cyclosporin (n=33) showed that a 14.6% lower result could be expected compared to Dimension-Xpand™. For tacrolimus (n=100) a 20.6% higher result was obtained compared to Dimension-Xpand™. For sirolimus (n=89) a 43.4% higher result was observed compared to LC/MS/MS. Everolimus can be determined with the sirolimus assay, results (n=26) are 45.9% higher compared to LC/MS/MS.

Overall analytical performance of the Abbott Architect™ immunosuppressant assays is satisfactory. Both accuracy and precision are comparable to or better then those of currently used methods. Functional sensitivity of tacrolimus is similar to values previously reported. Method comparison showed higher results for tacrolimus, sirolimus and everolimus, this is probably due to enhanced cross-reactivity with metabolites compared to Dimension-Xpand™ and LC/MS/MS respectively. Lower results for cyclosporin might be caused by less

interference of degradation products. Abbott Architect™ assays for cyclosporin and tacrolimus require sample pretreatment whereas Dimension-Xpand™ does not.