Fresh Whole Blood Immunosuppressants Program Review

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Introduction

The RCPAQAP has offered a lyophilised whole blood immunosuppressant program since 2010. The material in the lyophilised program is made from an immunosuppressant free whole blood base spiked with parent drugs. In addition, in 2013, 2015 and 2018, three fresh whole blood immunosuppressant patient samples were distributed to participants enrolled in the lyophilised program as part of an ongoing method comparison. The advantage of whole blood patient samples is that they are routine patient samples (including metabolites) so by definition are commutable provided collection and handling does not cause any unexpected effects. Data from the 2018 whole blood patient immunosuppressant survey was compared with similar spiked levels in the lyophilised samples in the 2018 immunosuppressant program to assess potential metabolite cross-reactivity.

Method

Fresh, trough level samples were collected from three consenting transplant patients. One was on Cyclosporine, one on Sirolimus+Tacrolimus and one on Everolimus+Tacrolimus therapy. The samples were subsequently delivered within 4 working days from the July 2018 dispatch date (both locally and internationally). Analysis was completed within 2 weeks of collection. A total of 56 laboratories participated in the program. Results with similar levels in the 2018 lyophilised program were compared to the whole blood samples except for Everolimus which is not currently available in the lyophilised material.

Results

The Analytical Performance Specifications (APS – set by the Special Therapeutic Drugs Advisory Committee) are the same for both programs. The majority of participants were able to achieve results within the APS for all measurands across both surveys (Table 1).

Summary data (including the spread of results and performance limits) for the patient and lyophilised surveys are shown in Figures 1a–4. The medians, means and CV's are based on all result data.

Discussion

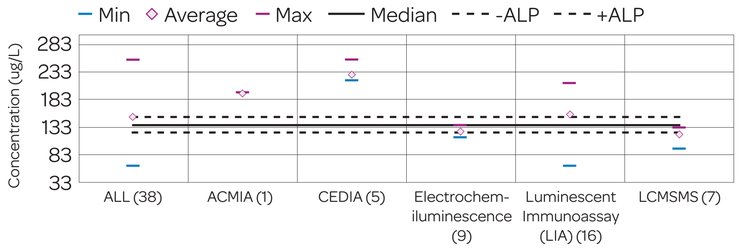
Overall, between lab performance was similar across methods for patient and lyophilised samples with the exception of CEDIA cyclosporine immunoassay methods in the patient samples which showed a positive bias compared to LCMSMS and other methods. This is likely due to metabolite cross-reactivity in the patient samples when compared with the lyophilised samples (which only contain the parent drug). Overall cross-reactivity with metabolites (some of which may be therapeutic) complicates interpretation of patient results, and could be an issue if clinicians are trying to interpret results from different laboratories using different methods.

Conclusion

This study (while limited) demonstrates the value of comparing patient samples with spiked/lyophilised EQA material where a metabolite cross-reactivity may otherwise not be evident. It is suggested that patients on immunosuppressant therapy are monitored using the same methodology ideally from the same laboratory. If clinicians or labs are transitioning from one methodology to a different methodology or to an alternate laboratory, it may be beneficial to assay at least one sample (ideally three in succession) from each individual patient in parallel. For some cyclosporine assays, consideration should also be given to the use of method-specific therapeutic intervals.

Immunosuppresants Whole Blood Program
2018 Cyclosporine Summary Report

Analytical Performance Specifications: ± 10 up to 100, then ± 10% > 100 ug/L
Sample 3-01 Median: 137



Comments: This sample was from a 26 year old male who received a stem cell transplant in May 2018. The patient has CML and has been on Cyclosporin since May 2018.

Figure 1a. Immunosuppressants Whole Blood Program, 2018 Cyclosporine Summary Report

Immunosuppresants Lyophilised Program
2018 Cyclosporine Summary Report

Analytical Performance Specifications: ± 10 up to 100, then ± 10% > 100 ug/L
Sample 68-03 Median: 65.5

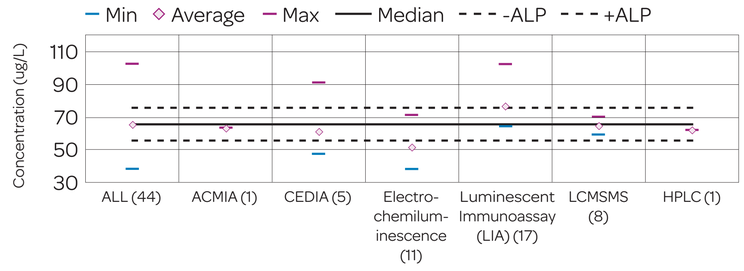
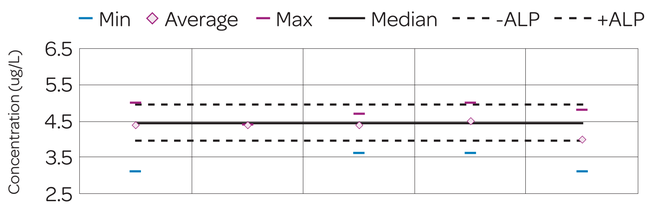


Figure 1b. Immunosuppressants Lyophilised Program, 2018 Cyclosporine Summary Report

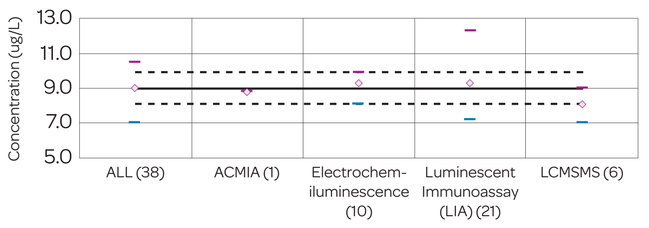
Immunosuppresants Whole Blood Program
2018 Tacrolimus Summary Report

Analytical Performance Specifications: ± 0.5 up to 5.0, then ± 10% > 5.0 ug/L
Sample 3-02 Median: 4.5



Comments: 3–02 This sample was from a 19 year old female who received a renal transplant in January 2017. The patient has been on Tacrolimus and Sirolimus since that time and was at steady state.

Sample 3-03 Median: 9.0

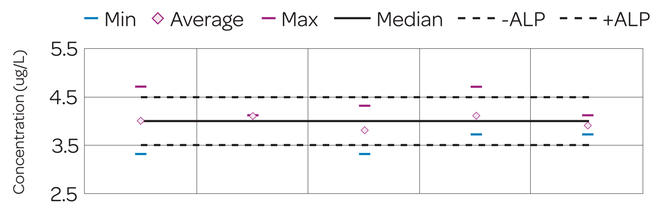


Comments: 3–03 This sample was from a 47 year old male who received a renal transplant in September 2017. The patient has been on Tacrolimus and Everolimus since January 2018 and was at steady state.

Figure 2a. Immunosuppressants Whole Blood Program, 2018 Tacrolimus Summary Report

Immunosuppresants Lyophilised Program
2018 Tacrolimus Summary Report

Analytical Performance Specifications: ± 0.5 up to 5.0, then ± 10% > 5.0 ug/L
Sample 68-03 Median: 4.0



Sample 68-07 Median: 8.0

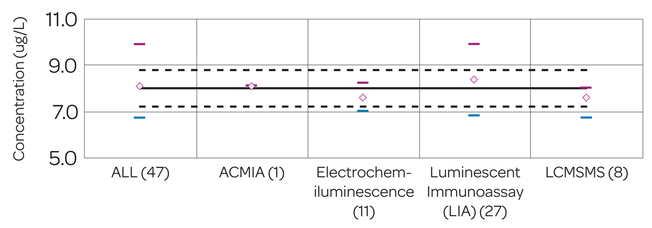
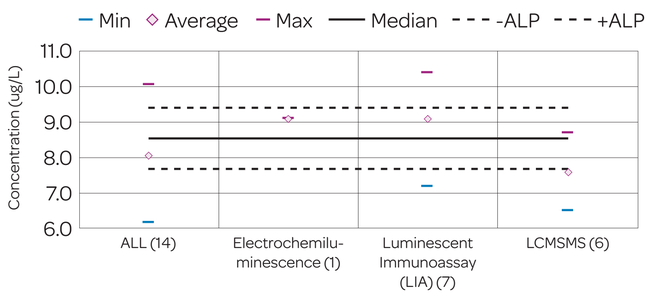


Figure 2b. Immunosuppressants Lyophilised Program, 2018 Tacrolimus Summary Report

Immunosuppresants Whole Blood Program
2018 Sirolimus Summary Report

Analytical Performance Specifications: ± 0.5 up to 5, then ± 10% > 5 ug/L
Sample 3-02 Median: 8.6



Comments: This sample was from a 19 year old female who received a renal transplant in January 2017. The patient has been on Tacrolimus and Sirolimus since that time and was at steady state.

Figure 3a. Immunosuppressants Whole Blood Program, 2018 Sirolimus Summary Report

Immunosuppresants Lyophilised Program
2018 Sirolimus Summary Report

Analytical Performance Specifications: ± 0.5 up to 5, then ± 10% > 5 ug/L
Sample 68-07 Median: 10.9

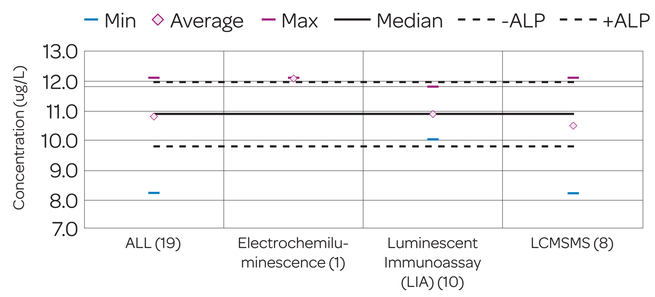
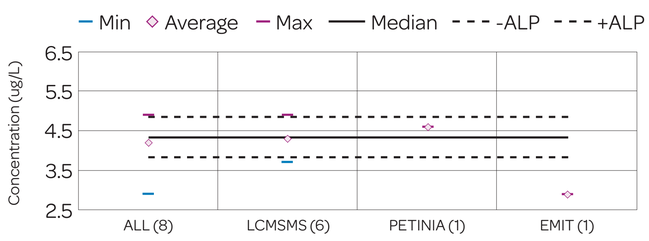


Figure 3b. Immunosuppressants Lyophilised Program, 2018 Sirolimus Summary Report

Immunosuppresants Whole Blood Program
2018 Everolimus Summary Report

Analytical Performance Specifications: ± 0.5 up to 5.0, then ± 10% > 5 ug/L
Sample 3-03 Median: 4.4



Comments: This sample was from a 47 year old male who received a renal transplant in September 2017. The patient has been on Tacrolimus and Everolimus since January 2018 and was at steady state.

Figure 4. Immunosuppressants Whole Blood Program, 2018 Everolimus Summary Report

Table 1. Percentage of the labs within their method group APS

% Within method group APS				
Immuno-suppressant Program	Cyclosporine (%)	Tacrolimus (%)	Sirolimus (%)	Everolimus (%)
Whole Blood	71	83	57	88
Lyophilised	86	94	89	N/A

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