

# Amikacin Concentrations and Target Ranges for Mycobacterial Infection

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## Introduction

- Amikacin is increasingly being used in the management of multi-drug resistant mycobacterial infection.
- Current dosing guidelines recommend 15 mg/kg once daily (OD) or 25 mg/kg thrice weekly (TW).<sup>1</sup>
- Target concentrations for amikacin are end of infusion peaks of 35-45 mg/L (OD) or 65-80 mg/L (TW) and troughs <5 mg/L.<sup>1</sup>
- It is not clear whether the recommended amikacin dosage guidelines achieve these target concentrations.

## Aim

- To determine whether amikacin dosage guidelines for multi-drug resistant mycobacterial infections achieve peaks of 35-45 mg/L (OD) or 65-80 mg/L (TW) and troughs <5 mg/L.

## Methods

- Patients >18 years old with a mycobacterial infection and at least one recorded amikacin dose and peak concentration were included in the audit.
- The following data were extracted from drug monitoring forms: age; weight; height; creatinine concentration; amikacin doses, concentrations and times.
- Individual estimates of amikacin volume of distribution (V) and clearance (CL) were determined by MAP Bayesian pharmacokinetic analysis.<sup>2</sup>
- Individual CL and V estimates were used to predict the following amikacin concentrations
  - 15 mg/kg daily 1 h and 24 h after the start of a 1 h infusion
  - 25 mg/kg thrice weekly 1 h and 48 h after the start of a 1 h infusion
- The percentages of patients who achieve amikacin concentrations below, within and above the target peak and trough ranges were determined for each regimen.

## Results

- Data were collected from 83 patients (Table 1), of which 33% (OD) and 35% (TW) had predicted peaks within the relevant target amikacin range (Table 2).
- Concentrations were more likely to be above than below the upper concentration target range (Table 2, Figure 1 and Figure 2).
- 34% of patients achieved peaks >50 mg/L with the OD regimen and 11% of patients achieved peaks of >100 mg/L on the TW regimen.
- Patients with estimated creatinine clearance <30 mL/min had troughs >5 mg/L at the end of the dosage interval.

Table 1 Patient demographic and clinical data

| Clinical characteristics                      | Number/Median (Range) |
|---|-----------------------|
| Patients (Male/Female)                        | 83 (49/34)            |
| Age   | 45 (19 – 79)          |
| Weight  | 60 (36 – 94)          |
| Estimated Creatinine Clearance (mL/min)       | 69 (60 – 193)         |
| Estimated Amikacin Clearance (L/h)            | 4.0 (0.49 – 10.4)     |
| Estimated Amikacin Volume of Distribution (L) | 17.9 (8.6 – 44.4)     |

Table 2 Percentages of amikacin peaks and troughs within ranges

| Regimen                | Amikacin Concentration (mg/L) | Percentage of Patients |
|------------------------|-------------------------------|------------------------|
| 15 mg/kg once daily    | Peak <35                      | 14%                    |
|                        | Peak 35 – 45                  | 33%                    |
|                        | Peak >45                      | 53%                    |
|                        | Trough <5                     | 94%                    |
| 25 mg/kg thrice weekly | Peak <65                      | 25%                    |
|                        | Peak 65 – 80                  | 35%                    |
|                        | Peak >80                      | 40%                    |
|                        | Trough <5                     | 95%                    |

Figure 1 Predicted steady state peak and trough amikacin concentrations ONCE DAILY regimen

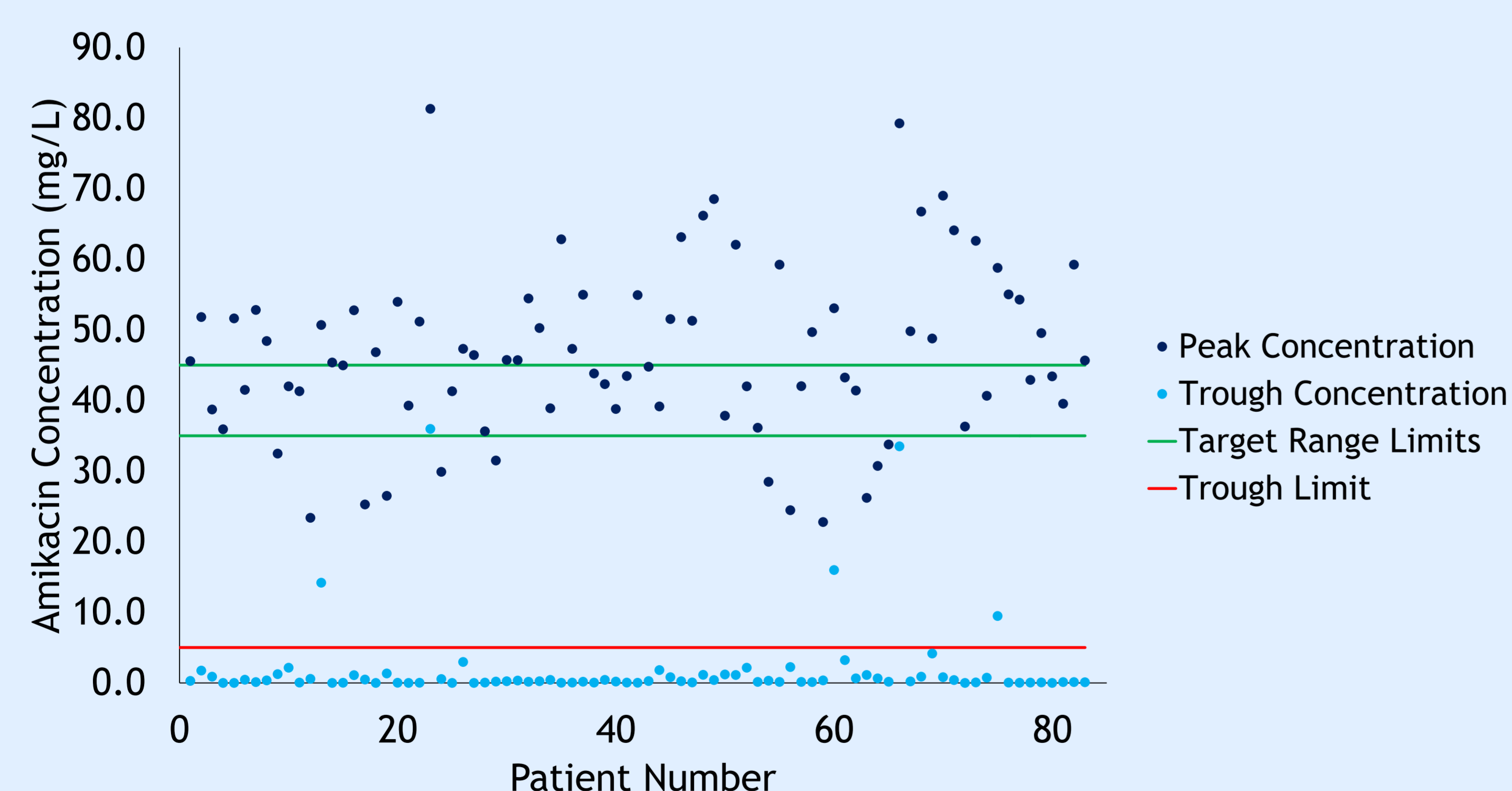
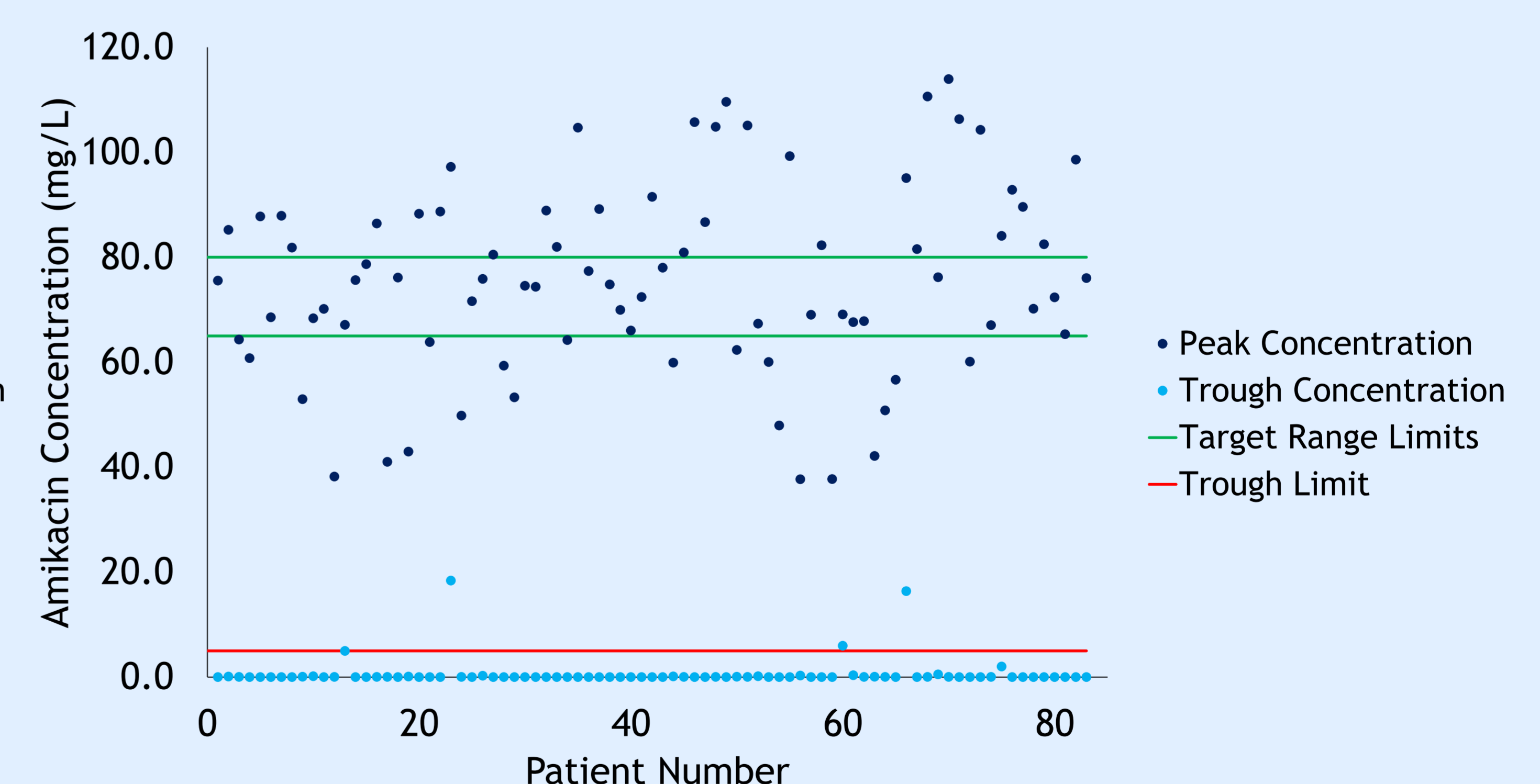


Figure 2 Predicted steady state peak and trough amikacin concentrations THRICE WEEKLY regimen



## Summary and Conclusions

- Amikacin guidelines for mycobacterial infections achieve peak concentrations that are typically within or above the stated target range.
- Trough concentrations are excessive for patients with renal impairment (CrCl <30 mL/min).
- Guidelines should be modified to allow greater flexibility in peak concentrations and to provide guidance for patients with renal impairment.

## References

1. Peloquin CA, et al. Aminoglycoside Toxicity: Daily versus thrice-weekly dosing for treatment of mycobacterial diseases. *Clin Inf Dis* 2004;38:1538–1544.
2. Kelman AW, et al. OPT: a package of computer programs for parameter optimisation in clinical pharmacokinetics. *Br J Clin Pharmacol* 1982;14:247–256.