



This prospective study quantifies vancomycin pharmacokinetics in morbidly obese and non-obese individuals, in order to guide vancomycin dosing in the obese” Smit et al (2019).

Abstract:

**AIMS:** For vancomycin treatment in obese patients, there is no consensus on the optimal dose that will lead to the pharmacodynamic target ( $AUC\ 400-700\ mg\cdot h\ L^{-1}$ ). This prospective study quantifies vancomycin pharmacokinetics in morbidly obese and non-obese individuals, in order to guide vancomycin dosing in the obese.

**METHODS:** Morbidly obese individuals ( $n=20$ ) undergoing bariatric surgery and non-obese healthy volunteers ( $n=8$ ) (total body weight (TBW) 60.0-234.6 kg) received a single vancomycin dose (obese:  $12.5\ mg\ kg^{-1}$ , maximum 2500 mg; non-obese: 1000 mg) with plasma concentrations measured over 48 hours (11-13 samples per individual). Modelling, internal validation, external validation using previously published data and simulations ( $n=9950$  individuals, TBW 60-230 kg) were performed using NONMEM.

**RESULTS:** In a three-compartment model, peripheral volume and clearance increased with TBW (both  $p<0.001$ ), which was confirmed in the external validation. A dose of  $35\ mg\ kg^{-1}$  per day (maximum 5500 mg/day) resulted in a  $>90\%$  target attainment ( $AUC>400\ mg\cdot h\ L^{-1}$ ) in individuals up to 200 kg, with corresponding trough concentrations of 5.7-14.6  $mg\ L^{-1}$  (twice daily dosing). For continuous infusion, a loading dose of 1500 mg is required for steady

state on day 1.

**CONCLUSIONS:** In this prospective, rich sampling pharmacokinetic study, vancomycin clearance was well predicted using TBW. We recommend that in obese individuals without renal impairment, vancomycin should be dosed as 35 mg kg<sup>-1</sup> per day (maximized at 5500 mg/day). When given over two daily doses, trough concentrations between 5.7-14.6 mg L<sup>-1</sup> correspond to the target exposure in obese individuals.

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### Reference:

Smit, C., Wasman, R.E., Gouloze, S.C., Wiezer, M.J., van Dongen, E.P.A., Mouton, J.W., Brüggemann, R.J.M. and Knibbe, C.A.J. (2019) Population pharmacokinetics of vancomycin in obesity: finding the optimal dose for (morbidly) obese individuals. *British Journal of Clinical Pharmacology*. October 29th. doi: 10.1111/bcp.14144. .

