Single dose Linezolid Pharmacokinetics in ill Patienys with Impaired Renal Function Epecially Chronic Hemodialysis Patients

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Abstract

ABSTRACT: Background and Objective: Renal failure patients were treated with linezolid (LZD)
for proven or suspected infections by multi-resistant Gram-positive cocci. The aim of this study
was to determine if dose adjustment of LZD is needed as a function of renal impairment or
not, especially that a significant component of LZD is eliminated unchanged in urine. Methods:
The single dose pharmacokinetics of LZD was investigated. Eighteen non-infected male
subjects with various degrees of renal impairment ranged from normal to severe chronic
impairment were enrolled, including end-stage renal disease (ESRD) patients maintained on
hemodialysis (HD). LZD was administered as a single oral 600mg dose, and blood samples
were drawn at different times and analysed by a validated HPLC assay method. Plasma
profiles were evaluated by non-compartmental and compartmental approaches. Results and
Discussion: A similar rate and extent of LZD absorption and elimination and comparable body
exposure was observed in both healthy subjects and acute renal failure patients. The extent of
LZD exposure was significantly increased by 3-fold in ESRD patients in their off-dialysis day.
Furthermore, the t1/2 and MRT values were significantly increased by ~5- and 3-fold, respectively.
The Vd/F values of LZD did not change with renal function. A significant decrease in
CL/F by ~3-fold was observed in ESRD patients in their off-dialysis day however, CL/F was
significantly increased by ~4-fold during HD. Approximately half of the administered LZD
dose was removed during the HD session in these selected cohorts of ESRD patients. LZD
was generally well tolerated. Conclusions: The dose of LZD did not need to be

adjusted for
patients with acute renal dysfunction or ESRD on HD. One of the twice-daily doses should
be administered after the dialysis session because almost half of the LZD dose was substantially
removed by HD. During the first three dialysis sessions of the treatment course, to avoid
potentially ineffective therapy, a supplemental dose of LZD might be given if necessary or the
dose of LZD should be administered 4 h before the beginning of the HD session. This was to
keep LZD levels above the MIC for the organism causing the infection being treated.

International 2014, January