

Abstract

NNZ-2566 is a novel, small molecule being developed as a treatment for cognitive impairment in different CNS conditions, including Rett and Fragile-X syndrome, both of which are associated with moderate to severe neurodevelopmental disorder. In current study we characterise the population pharmacokinetics of NNZ-2566 after administration of single and repeated ascending doses to healthy subjects. A meta-analytical approach was used to analyse pharmacokinetic data from 3 different studies, in which a total of 61 healthy subjects (median age 23 years, range 19 to 38) were treated with NNZ-2566. Doses of NNZ-2566 ranged from 6.0 to 100 mg/kg after oral administration and from 0.1 to 30 mg/kg after intravenous administration. A two-compartment model with first order absorption and elimination was found to best describe the pharmacokinetics of NNZ-2566. Inter-individual variability was identified in clearance, absorption rate, central volume of distribution, peripheral volume of distribution and inter-compartmental clearance. Population predicted clearance and central volume of distribution were 10.35 L/h and 20.23 L, respectively. No accumulation, metabolic inhibition or induction was observed during the course of treatment. Dose proportionality was observed across the dose range evaluated in healthy subjects. In addition, oral bioavailability appeared to vary with food intake. The relatively short half-life of 1.4 h suggests the need for a twice or three times daily regimen to maintain relevant systemic levels of NNZ-2566 in plasma.