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A new pegylated recombinant *E.coli* L-asparaginase preparation (MC0609): Comparative pharmacokinetic/pharmacodynamic characterisation in Beagle dog and influence of anti-PEG IgM antibodies on the pharmacokinetics in B6D2F1 mice

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A new pegylated recombinant *E. coli* L-asparaginase (PEG-rASNase MC0609) was designed by medac GmbH (Germany) to improve pharmacokinetic (PK) characteristics of pegylated L-asparaginase in comparison to pegaspargase (Oncaspar®) used as first-line treatment in patients with acute lymphoblastic leukaemia (ALL). Comparative PK, pharmacodynamic (PD) and immunogenicity studies were performed in Beagle dogs after single-dose intravenous (i.v.) administration of MC0609 or pegaspargase. Striking differences in PK and PD properties between both pegylated preparations were observed. The different PK characteristics were confirmed by a population pharmacokinetic (PopPK) analysis. PK parameters of pegaspargase in Beagle dog were in the same range than the parameters determined in paediatric ALL patients. Therefore, the Beagle dog was considered a clinically relevant model for PK evaluation of pegaspargase. In addition, the potential impact of pre-existing anti-PEG antibodies on the ASNase activity of PEG-rASNase MC0609 and pegaspargase was investigated in immune competent B6D2F1-hybrid mice. Anti-PEG IgM antibodies were successfully induced in mice after repeated i.v. administration of 40 kDa PEG-Diol without being conjugated to a carrier. All animals detected "positive" for anti-PEG IgM antibodies and control animals (without prior PEG-Diol pre-sensitisation) were treated once i.v. with PEG-rASNase MC0609 or pegaspargase. ASNase activity profiles were obviously not influenced by the IgM positivity of animals. No accelerated decrease of ASNase activity was observed irrespective of successful PEG-Diol pre-sensitisation and presence of acquired anti-drug-IgG and/or anti-PEG IgM antibodies.

Biography

Poppenborg Sabine M has completed her PhD from University of Bielefeld, Germany, University of Montpellier, France and Post-doctoral studies from MRC Medical Research Council, Cambridge, UK. Since 2007, she is a Scientist in the Pharmacology/Toxicology unit of medac Gesellschaft für klinische Spezialpräparate mbH, Germany, a pharmaceutical company specialised on products for oncology, autoimmune diseases and urology.

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