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Meeting abstract

Influence of the Duffy genotype on pharmacokinetics and pharmacodynamics of recombinant monocyte chemoattractant protein (MCP-1) in vivo

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Monocyte chemoattractant protein-1 (MCP-1) binds to the Duffy antigen (Fy) on erythrocytes, which may act as a sink for several chemokines including MCP-1. We hypothesized that infusion of MCP-1 could result in different pharmacokinetics of MCP and possibly altered pharmacodynamics between Duffy positive and negative individuals. The primary aim of this trial was to compare pharmacokinetics of MCP-1 between Duffy positive and Duffy negative individuals under infusion of recombinant human MCP-1. This was a randomized, double-blinded, placebo-controlled dose escalation trial in 36 healthy volunteers. Subjects received infusions of 0.02–2.0 μg/kg MCP-1 or placebo for one hour. MCP-1 displayed linear pharmacokinetics. Duffy negative individuals reached maximal plasma levels earlier, but plasma concentration profiles were not altered. MCP-1 markedly increased monocyte counts, and estimated EC_{50} values were 10-fold higher in Duffy positive than Duffy negative subjects. Increased monocyte counts were associated with decreased surface expression of intercellular adhesion molecule 1 (ICAM-1, CD54). In contrast, MCP-1 neither altered CCR-2 or CD11b surface expression nor markers of platelet or endothelial activation, inflammation and coagulation. MCP-1 acts as a highly selective chemoattractant for monocytes in humans. The Duffy antigen had minimal effects on pharmacokinetics of MCP-1, but may affect EC_{50} values.