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Title: The absorption, distribution, metabolism and excretion (ADME) of single oral doses of AZD5069, a novel CXCR2 antagonist, in healthy male volunteers

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Body: BACKGROUND: AZD5069 is a CXC chemokine receptor-2 (CXCR2) antagonist with potential as a novel COPD treatment. Initial studies have indicated an acceptable safety profile for AZD5069. This study characterised the ADME of a single oral dose of AZD5069. METHODS: In this phase I, open-label, non-comparative, single centre study, healthy male volunteers received a single oral dose of 120 mg [^{14}C]AZD5069. Blood and urine samples (for radioactivity analysis, metabolite profiling, identification and bioanalysis of AZD5069) and faeces samples (for radioactivity analysis and metabolite profiling) were collected. Safety and tolerability were also assessed. RESULTS: Subjects (n=6) were white males (aged 50–65 years, mean BMI 25.6 kg/m^2). The mean recovery of radioactivity in urine and faeces was 100% (range 98–103% [65% in urine, 35% in faeces]). 6.7% of the AZD5069 dose was recovered unmetabolised in urine. AZD5069 was rapidly absorbed and the apparent terminal elimination half-life was 10 hours. There were no deaths, serious adverse events (AEs) or withdrawals due to AEs. Four subjects reported 6 AEs, with headache the most commonly observed event. There were no clinically significant safety and tolerability findings, other than the expected reversible reduction in circulating neutrophil numbers. CONCLUSION: Absorption of AZD5069 was rapid. Complete recovery of radioactivity was attained, with the majority being excreted in the urine. Only a small fraction was renally excreted as parent drug, suggesting that metabolism is the primary route of elimination. No safety concerns were identified.