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Quantification of the time course of CYP3A inhibition, activation, and induction using a population pharmacokinetic model of microdosed midazolam continuous infusion

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Reported adverse events for the different study arms in the clinical trial

In the course of the study, a total of 26 adverse events occurred in 16 of the 24 subjects (66.6%).
The most common side effect was headache. About 21% of the subjects suffered from cephalgia during the study days. Headache occurred in 42% of the female subjects during the study days, in two of them more than once. None of the male subjects reported headache.
Two of the subjects with cephalgia had received placebo in addition to midazolam infusion, and a third experienced pain with midazolam infusion.
In both the rifampicin group and the voriconazole oral group, one subject had a headache. The first was 9.5 h after voriconazole administration and the second was 4.5 h after rifampicin administration.
One subject on placebo complained of headache, nausea and vomiting about 7 h after starting the midazolam infusion. One subject with a history of migraine suffered from severe headache, nausea and vomiting several times about 3 h after efavirenz administration which was treated after the end of the midazolam infusion.
One subject noticed dizziness when going to the toilet about 1 h after efavirenz administration.
Three of the four subjects (75.0%) who received oral voriconazole noticed an altered visual perception in the first 2 h after ingestion.
Laboratory changes in the final examination occurred in 33%. An increase in creatine kinase was seen in 12.5%, followed by an increase in aspartate aminotransferase and anaemia in 8.3%. The two subjects with aspartate aminotransferase elevation (also with creatine kinase increase) had both received voriconazole, one orally and one intravenously.