Interleukin-2 treatment effect on imatinib pharmacokinetic, P-gp and BCRP expression in mice:

Titre	Interleukin-2 treatment effect on imatinib pharmacokinetic, P-gp and BCRP expression in mice:
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Résumé en anglais	The aim of this study was to investigate the effect that recombinant interleukin-2 (rIL-2) (0.16 MUI/injection) had on the pharmacokinetics of imatinib (IM) in plasma. In this study, IM was given orally to mice at a dose of 150 mg/kg once a day for 11 days (from day 1 to 11) either alone or in combination with intraperitoneal injections of rIL-2 twice a day from day 8 to 11. Pharmacokinetic parameters were determined using WinNonLin software. Areas under the curve were compared using Bailer's method. The repeated administration of the rIL-2+IM combination was shown to have two pharmacokinetic advantages compared with repeated IM doses alone. In addition to the pharmacodynamic interest of this treatment, we found that the combined treatment significantly increased the IM Cmax ($P<0.05$) and significantly increased the IM trough concentration (C24 h) ($P<0.01$), which was always above the minimum therapeutic IM concentration (1 µmol/l) in plasma. Those pharmacokinetic modifications may be explained, in part, by a decrease in the P-glycoprotein expression in the three intestinal segments of the mice (duodenum, $P<0.01$; jejunum, $P<0.05$; and ileum, $P<0.05$) and a decrease in BCRP expression in the duodenum segment ($P<0.05$) due to rIL-2. In another experiment, we found a significant induction of intestinal P-glycoprotein expression in mice that had been given IM orally (150 mg/kg) twice a day for 11 days. It would be interesting to further investigate the IM disposition associated with rIL-2 treatment for clinical applications.
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