Elimination of [14C]-LY3023414 by Aldehyde Oxidase and CYP Enzymes in Humans Following Oral Administration

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ABSTRACT

All adverse events (AEs) reported in the study were mild and resolved without treatment. Dysgeusia and diarrhea were the most frequent AEs. No serious AEs were considered related to the study drug. In conclusion, LY3023414 was absorbed rapidly and eliminated completely from the body following oral administration. LY3023414 was cleared primarily by metabolism through aldehyde oxidase and cytochrome P450 (CYP)–mediated pathways.

RESULTS

Figure 1. Mean Concentration of LY3023414 in Plasma and DBS and Total Radioactivity in Plasma and Whole Blood Following Oral Administration of Single 150-mg Dose of [14C]-LY3023414

Table 1. LY3023414 PK Parameters in Plasma and DBS and Total Radioactivity in Plasma and Whole Blood Following Single 150-mg Dose of [14C]-LY3023414

Table 2. Distribution of LY3023414 and Its Metabolites in Plasma, Urine, and Feces

Table 3. Enzyme Kinetics of AO- and CYP-Mediated LY3023414 Metabolism

CONCLUSIONS

In AUC0–12, pooled plasma, parent drug accounted for a mean of 62% of the total radioactivity, whereas metabolites M2 and M12 accounted for 23% and 9% of the radioactivity, respectively.

Metabolites M2 and M12 were the predominant drug-related components observed in urine and feces, accounting for 9% and 6% of the radioactivity in urine and 32% in feces, respectively.

In general, similar to plasma LY3023414 was absorbed rapidly and eliminated completely from the body following an oral dose. LY3023414 was cleared primarily by metabolism through aldehyde oxidase and cytochrome P450 (CYP)–mediated pathways.

Adverse Events

All adverse events (AEs) reported in the study were mild and resolved without treatment, except for non-drug-related myalgias, which were treated with ibuprofen.

Reference: