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A Phase 1 Study to Evaluate the Absorption, Metabolism, and Disposition of Dordaviprone in Healthy Adult Participants

Yohannes Teffera [1], Tim Tippin [1], Angela Bartkus [1], Francine A de Castro [2], Shamia L Faison [2], Marion Morrison [1], Mark J Mullin [1], Odin Naderer [1]

Affiliations

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Abstract

Dordaviprone (ONC201) is a novel, small-molecule imipridone with antitumor activity in patients with a glioma. Six healthy male participants received a single 625-mg (100-µCi) oral dose of [^{14}C]-dordaviprone. Blood, plasma, urine, and feces were collected up to 288 hours after dosing and analyzed by liquid scintillation counting. Metabolite profiles were evaluated using liquid chromatography-radiometric detection, and metabolite identification was accomplished by liquid chromatography with tandem mass spectrometry. Concentrations of drug-derived radioactivity in blood and plasma peaked at 1 hour after dosing and were below the limit of quantitation by 72 hours (whole blood) to 96 hours (plasma) after dosing. Seventy-one percent of the administered radioactivity was recovered in urine and 20% in feces. In plasma, the major circulating compounds were dordaviprone and the inactive metabolite ONC207, each contributing approximately one third of the total radioactivity area under the curve. Of the 19 metabolites identified in plasma, no other single metabolite contributed more than 10% to the total radioactivity area under the curve. Unchanged dordaviprone was a minor component in excreta (less than 0.3%), with multiple metabolites identified in urine and feces. Given the lack of dordaviprone in excreta and the metabolites formed, the primary route for dordaviprone elimination was through urinary excretion of oxidative metabolites.

Keywords: ONC201; dordaviprone; excretion; mass balance; metabolism.