YM-58483, 4-methyl-4’-[3,5-bis(trifluoromethyl)-1H-pyrazol-1-yl]-1,2,3-thiadiazole-5-carboxanilide, potently inhibits store-operated sustained Ca\(^{2+}\) influx and IL-2 production in T lymphocytes, and is under development as a drug for the treatment of autoimmune diseases and chronic inflammation. When YM-58483 was intravenously and orally administered to eight dogs, four dogs showed higher plasma concentrations and slower elimination of the unchanged drug than the other four dogs; the former was categorized as poor metabolizers (PM) and the latter was as extensive metabolizers (EM). In the intravenous administration study, total clearance was 61 ± 14 mL/h/kg for PM dogs and 564 ± 85 mL/h/kg for EM dogs, and elimination half-lives were 71 ± 22 h for PM dogs and 20 ± 10 h for EM dogs. Both parameters were significantly different between two groups. In contrast, absolute bioavailability between two groups was comparable (58 ± 18% for PM dogs and 56 ± 11% for EM dogs). Total clearance in both PM and EM was lower than hepatic blood flow rate in dogs, suggesting that the elimination of YM-58483 is limited by hepatic intrinsic clearance. Subsequently, to elucidate the difference in the in vivo pharmacokinetics of YM-58483 in EM and PM dogs, in vitro metabolism studies were performed using liver microsomes prepared from phenotyped dogs. YM-58483 was metabolized at a higher rate in EM dog microsomes than in PM dog microsomes. In addition, in the incubation mixture, two oxidative metabolites, M1 and M2, were observed in EM dogs while only M2 was observed in PM dogs. Findings in the in vitro metabolism studies support that the in vivo polymorphic pharmacokinetics of YM-58483 in dogs are attributed to the difference in metabolic clearance of this compound.