As part of a research program to develop 3rd generation antitumor platinum complexes, a series of platinum complexes which have 4,5-bis-(aminomethyl)-1,3-dioxolane derivatives as bidentate amine ligands, represented by the general structural formula was prepared.

The $R_1$ and/or $R_2$ substituents in this series of platinum complexes can be hydrogen, alkyl, or jointly formed cyclohexane. Two $X$s can be a bidentate leaving ligand such as 1,1-cyclobutanedicarboxylate, malonate, dimethylmalonate, ethylmalonate, glycolate, L-lactate, or N-methyliminodiacetate. From based on the pharmacological and toxicological studies, we have chosen SKI 2053R, cis-malonato[(4R,5R)-4,5-bis(aminomethyl)-2-isopropyl-1,3-dioxolane] platinum(II) complex (NSC D644591) as a candidate for clinical evaluation.

The antitumor activity of a new antitumor platinum complex, cis-malonato [(4R,5R)-4,5-bis(aminomethyl)-2-isopropyl-1,3-dioxolane]platinum(II) (SKI 2053R, NSC D644591), was compared with those of cisplatin and carboplatin using murine tumors. We evaluated three platinum complexes against L1210/CPR, a subline of L1210 leukemia sensitive to cisplatin for their abilities to overcome tumor resistance to cisplatin. The in vitro cytotoxicity of SKI 2053R to L1210 cell line was 2.5-fold less potent than that of cisplatin, and was 10-fold more cytotoxic than that of carboplatin. SKI 2053R retained similar cytotoxic effect and antitumor activity to L1210/CPR cell line, like the cytotoxicity of SKI 2053R to L1210 cell line, while either cisplatin or carboplatin had not property to overcome the acquired cisplatin-resistance. SKI 2053R exhibited greater or comparable antitumor activity than cisplatin or carboplatin in murine tumor models.