**Antitumor Activity of MPC-2130 in Human Hematopoietic Cell Lines and Ovarian and Prostate Tumor Xenografts in Athymic Nude Mice**

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**ABSTRACT**

MPC-2130 was discovered at Myriad Pharmaceuticals, Inc. as a result of an extensive medicinal chemistry effort. The original lead compound, from which MPC-2130 was derived, was discovered in a yeast–based high throughput screen. Targeted chemical modifications and additional medicinal chemistry efforts yielded MPC-2130, a highly active, orally available, small molecule that selectively inhibits the expression of the Bcl-2 family member, MCL-1. This compound is a novel, potent agent that induces apoptosis in a broad range of tumor cell lines, including hematopoietic, ovarian, and prostate cancers.

**RESULTS**

MPC-2130 was evaluated in a series of in vitro and in vivo assays designed to establish its antitumor activity in human tumors. These studies were designed to assess the ability of MPC-2130 to inhibit the growth of OVCAR-3 and RAMOS cell lines through an apoptotic mechanism. These studies also evaluated the pharmacokinetic parameters of the compound in mice. The preclinical data suggest that MPC-2130 may be an effective therapy against multiple tumor types in humans.

**MATERIALS AND METHODS**

**Cytotoxicity of MPC2130 in hematopoietic and solid tumor systems.**

MPC-2130 was tested in a series of in vitro and in vivo assays designed to establish its antitumor activity in human tumors. These studies were designed to assess the ability of MPC-2130 to inhibit the growth of OVCAR-3 and RAMOS cell lines through an apoptotic mechanism. These studies also evaluated the pharmacokinetic parameters of the compound in mice. The preclinical data suggest that MPC-2130 may be an effective therapy against multiple tumor types in humans.

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**CONCLUSIONS**

- MPC-2130 is a highly potent and selective Bcl-2 family inhibitor that induces apoptosis in a broad range of tumor cell lines, including hematopoietic, ovarian, and prostate cancers.
- The preclinical data suggest that MPC-2130 may be an effective therapy against multiple tumor types in humans.
- MPC-2130 shows good pharmacokinetic parameters with high brain penetration.
- MPC-2130 significantly inhibits OVCAR-3 xenograft growth.
- MPC-2130 shows a trend toward inhibition of LNCaP xenograft growth.
- Animals dosed on a QD x 5 regimen do not lose significant body weight.