Repeat-Dose Toxicity and Metabolism of Topical E/Z-Endoxifen Gel in Minipigs

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Abstract

There is growing interest in developing breast cancer prevention agents, but few have been tested for efficacy and bioavailability. Topical estrogen receptor modulators (SERMs) are promising agents for breast cancer prevention, but such treatments may also result in systemic bioavailability and toxicity. In this study, we investigated the repeat-dose toxicity and metabolism of topical E/Z-endoxifen gel, a SERM that is currently in clinical trials for breast cancer prevention. Minipigs were exposed to topical administration of E/Z-endoxifen gel for 28 days, and plasma and mammary gland tissue levels were measured. Our results suggest that topical E/Z-endoxifen is well tolerated by female Göttingen minipigs. Daily administration of E/Z-endoxifen doses of 2 mg or less was very well tolerated by female Göttingen minipigs. Daily administration of E/Z-endoxifen doses of 2 mg or less was very well tolerated by female Göttingen minipigs. 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