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Accelerating Medicines, Together

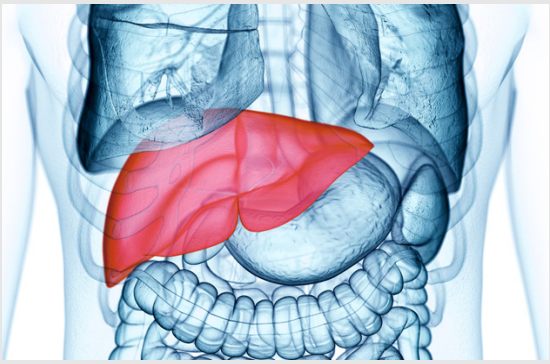
CASE STUDY

PK MODELING SUPPORTS DOSING STRATEGY FOR PATIENTS WITH HEPATIC IMPAIRMENT

Primary biliary cholangitis (PBC) is a chronic disease that impedes bile flow from the liver, resulting in increased bile acid concentration, which causes cell damage. Untreated PBC can lead to liver failure and death. At the start of this project, the only approved treatment for PBC was not effective for all patients.

Intercept Pharmaceuticals was developing obeticholic acid (OCA) as an alternative treatment for PBC. OCA activates farnesoid X receptors (FXR) in the liver to decrease bile acid concentration.

As liver damage occurs as PBC progresses, Intercept needed to develop an OCA dosing strategy for patients both with and without hepatic impairment. A clinical hepatic impairment study revealed that while systemic OCA concentrations increased as hepatic impairment worsened, the level of FXR activation in the liver remained similar across all groups. Plasma OCA concentration proved to be a poor surrogate for liver OCA concentration.



Therefore, Phoenix NLME was used to create a physiologic PK model to explore the relationship further. The model was validated by comparing its predicted OCA-plasma exposures to those observed in both the patients and volunteers.

Both the Phoenix model and clinical data demonstrated a significant increase in systemic exposure to OCA in patients with hepatic impairment. But liver exposure to OCA increased only modestly in patients with hepatic impairment compared to healthy volunteers. These results supported the safety and efficacy of OCA and the need to reduce dosing only for PBC patients with moderate and severe hepatic impairment.

When the FDA approved Ocaliva (OCA) in May 2016, it was the first new drug approved for PBC in almost 20 years.

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Headquartered in New York, Intercept Pharmaceuticals is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, including PBC and nonalcoholic steatohepatitis (NASH). Founded in 2002, Intercept has operations in the United States, Europe, and Canada.

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