Letter to Editor

The Treatment of Primary Biliary Cholangitis [PBC] a New Dawn?

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PBC has undergone 5 name changes since the original description. These include Hanot's Cirrhosis, Xanthomatos Biliary Cirrhosis, Chronic Non Suppurative Destructive Cholangitis, Primary Biliary Cirrhosis and Currently Primary Biliary Cholangitis. The etiology and pathogenesis remain obscure however there have been a number of agents that have been evaluated without success these include, steroids, methotrexate, penicillamine, vitamin E mycophenylate and a variety of other immuno-suppressive agents.

About 30 years ago ursodeoxycholic acid was approved by the FDA in a weight based dosage of 13 to 15 mg/Kg in divided daily doses. Nearly 2 years ago obeticholic, a Farnesoid X Receptor [FXR] [Ocaliva, Intercept Pharmaceuticals] was approved in select patients who were intolerant to ursodeoxycholic acid [2%] or who failed to adequately respond to this therapy [30%].

Recently a number of novel diverse have began evaluation. Peroxisome Proliferative Activated Receptors [PPAR] agonists are all in focus. These agents have 3 different receptors alpha, gamma and delta. Bezafibrate a pan PPAR receptor agonist has been shown to be effective in normalizing the Alkaline Phosphatase [ALP] in 66% of studies. It also improved fatigue [a cardinal debilitating feature of PBC and lessened pruritus another frequent symptom] and it lessened liver stiffness. It has yet to be approved by the FDA. Seladelpar [MBX 8025, CymaBay Therapeutics] is a delta agonist, however adverse effects namely an autoimmune hepatitis has limited further evaluation. Finally elafibranor [GFT 505, Genfit] an alpha and delta agonist was effective in reducing ALP in a dosage of 120 mg daily, it also improved pruritus.

Another FXR agonist [EDP-305, Enanta] has shown considerable activity against a raised ALP and it did not aggravate any other symptoms. Combination therapy of obeticholic acid and bezafibrate is now ongoing.

The NOX-14 inhibitor GKT 831, Genkyotex is another focus of evaluation.

It is estimated that there are about 30,000 patients in the USA with PBC. A number of unexplained questions remain unanswered, why there is a 90% female predominance, why patients with histology showing evidence of granulomas fare better than those without granulomas a puzzling aspect.

We appear to be on the cusp of major advances in the treatment of this vexing condition. Encouraging results offer great promise. Perhaps we are approaching the dawn of new effective therapies and a more successful outcome for a disease that has baffled scientists for decades.

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