

Present and Emerging Pharmacotherapies for Non-alcoholic Steatohepatitis

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Abstract—The hallmark of non-alcoholic fatty liver disease (NAFLD) is excessive fatty accumulation in the hepatocytes, which leads to inflammation and cell injury with or without fibrosis (non-alcoholic steatohepatitis, NASH). NASH is the main cause of chronic liver disease in the western world which affects up to a one-third of the population in many developed countries and a major health problem, owing to its close association with obesity, diabetes, and the metabolic syndrome. In coming decade, NASH will overtake hepatitis C virus infection as the leading cause of liver transplantation in the USA. However, the understanding of the pathogenesis and progression of NASH has evolved and several promising novel therapies to target and possibly reverse fibrosis are being evaluated but there are no current FDA-approved therapies that eradicate this disease. Innovative NASH therapies include four main pathways: targeting hepatic fat accumulation (Farnesoid X receptor), targeting oxidative stress, inflammation and apoptosis pathway (Apoptosis signalling kinase 1 (ASK 1) inhibitor), targeting intestinal microbiomes and metabolic endotoxemia (TLR4 antagonist) and the final target is hepatic fibrosis. These targets are currently being evaluated in an international phase 3 trial for treatment of NASH and within next few years these therapeutic options for NASH will curb the rising trend of NASH related diseases. Here, our study mainly focuses on the anti-inflammatory agents such as apoptosis signal regulating kinase 1 inhibitors that shows promising therapy for NASH.

Keywords: Non-alcoholic fatty liver disease(NAFLD), Non-alcoholic steatohepatitis(NASH), Farnesoid X Receptor(FXR) Apoptosis Signal Regulating Kinase-1(ASK-1).