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LETTER

Saroglitazar – A Potential Therapeutic Option in Treating NASH? [Letter]

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Dear editor

We read the extremely informative study "Non-Alcoholic Steatohepatitis (NASH) – A Review of a Crowded Clinical Landscape, Driven by a Complex Disease" published by Fraile et al[1] in the prestigious journal "Drug Design, Development and Therapy". We would like to appreciate the remarkable work done by the authors on this thorough review, congratulate them on its successful publication, and make further contributions.

This review discussed the potential mono-therapeutic options for Non-alcoholic steatohepatitis (NASH) including drugs such as Saroglitazar (Zydus Cadila), Obeticholic acid (Intercept Pharmaceuticals), Cenicriviroc (Allergan), Aramchol (Galmed Pharmaceuticals), Resmetirom (Madrigal Pharmaceuticals), Dapagliflozin, and Semaglutide (Novo Nordisk). The review further discusses the role of anti-diabetic drugs, co-therapies, and antibodies in the treatment of NASH.[1]

Even though this review provided exhaustive details in terms of the potential therapeutic options for NASH, we believe that the review provides incomplete vital details in regards to the clinical trial conducted in the United States to demonstrate the efficacy of Saroglitazar.[2]

Fraile et al[1] in this review explained Saroglitazar Magnesium (Lipaglyn) has been approved in India for the treatment of type 2 diabetes (T2D) and dyslipidemia. Furthermore, in 2020 Saroglitazar qualified for NASH treatment in India as a result of the promising results of the Phase 3 clinical trial, EVIDENCES II, conducted on Indian NASH patients. In this trial, the histologic improvements of NASH were assessed by liver biopsy, a gold standard in assessing the prognosis of chronic liver diseases. However, a Phase 2 trial conducted in the United States[2] included NASH patients on the basis of elevated ALT levels, although no definitive ALT levels can be used to predict NASH[3] and normal ALT levels are found in approximately 25% of these patients.[4] Hence, saroglitazar cannot be recommended only on the basis of a particular subset of patients with elevated ALT without histological endpoints.

Moreover, in the study conducted by Gawrieh et al, the efficacy of Saroglitazar was demonstrated by reporting a significant decrease in ALT levels after 16 weeks. But, this reduction in ALT was not associated with a proportional decrease in Liver Fat Content or improvement in insulin resistance (as assessed by the HOMA-IR index).[4]

To help understand its role better it is important to adopt additional ingenious placebo-controlled trials in biopsy-proven NASH with histological endpoints.

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