LETTER TO THE EDITOR

Olezarsen in Severe Hypertriglyceridemia: A Bangladesh Perspective on Cost and Liver Safety

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Dear Editor,

The recent trial by Marston et al.[1] showed that olezarsen substantially lowers triglycerides and reduces acute pancreatitis events in patients with severe hypertriglyceridemia. However, from a Bangladesh perspective, two critical barriers stand out: prohibitive cost and a concerning liver-fat signal. Olezarsen is an antisense oligonucleotide that degrades apolipoprotein C-III messenger RNA, lowering apoC-III and thereby enhancing lipoprotein-lipase–mediated clearance of triglyceride-rich lipoproteins. The therapy is priced at tens of thousands of US dollars per year, recently reduced from a launch price of over half a million.[2] In Bangladesh, an average person's total health spending was only 53.46 US dollars annually in 2023.[3] Most families pay for medicines out of pocket,[4] and even cheap fibrates are a burden for many. The proposed therapy is expensive and unreachable for over 99% of the population. The reduction in pancreatitis, indicated by a number needed to treat (NNT) of 4 in the highest-risk group (those with triglycerides ≥880 mg/dL and a history of pancreatitis), is indeed a scientific accomplishment but holds no practical significance in the context of Bangladesh based on the observation regarding its practical limitations in the country's healthcare landscape that holds true for several systemic and socioeconomic reasons.[5]

The hepatic safety signal compounds the problem. At 12 months, liver fat measured by MRI (normal <5%) rose by 2.28 percentage points with the 50 mg dose and 4.18 points with the 80 mg dose, compared to 0.14 points with placebo. A clinically meaningful jump of ≥5 percentage points occurred in 27.5% of patients on 50 mg and in 40.2% on 80 mg, against 12.5% on placebo. These increases happened on top of a baseline median liver fat of 13.9%, meaning many participants already had fatty liver. This is especially worrisome for Bangladesh. Non-alcoholic fatty liver disease is extremely common in Bangladesh, driven largely by obesity and diabetes-related insulin resistance.[5] A large proportion of our patients with severe hypertriglyceridemia likely already have hepatic steatosis. The investigators themselves note that the clinical significance of the hepatic fat increase is unclear, and that it was not correlated with the elevations in liver enzymes seen with olezarsen. Even so, a sustained, dose-dependent rise in hepatic fat is difficult to dismiss in such a population, and the one-year trial duration cannot exclude longer-term progression to steatohepatitis or fibrosis. With advanced imaging to monitor liver fat not widely available here, such a change could go undetected until it is too late.

The pancreatitis benefit is real, but the combination of an unaffordable price and a concerning hepatic safety signal in a population already shouldering a heavy burden of fatty liver disease makes olezarsen unsuitable for widespread use in Bangladesh. Long-term safety data and drastic price reductions are needed before this therapy can even be considered in resource-limited settings. Olezarsen is a genuine step forward, yet the question remains whether

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steps forward in clinical science can be made to walk in the same direction as steps forward in equity. For populations like Bangladesh, which are burdened by the disease, vulnerable in their livers, and priced out of the cure, that question is not rhetorical.

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