LBP-024

Performance of AASLD, AGA, AACE guidelines to identify patients for resmetirom treatment: pooled dataset including more than 4,000 patients with liver biopsy

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Background and Aims: Resmetirom, a THR-β agonist, is the first and only treatment approved for metabolic dysfunction-associated steatohepatitis (MASH) as of March 2024. Resmetirom label indicates to treat patients with MASH and moderate to advanced fibrosis consistent with F2/F3. There is no requirement for liver biopsy. We aimed to describe the accuracy of AASLD, AGA and AACE guidelines and of non-invasive biomarkers to identify patients for resmetirom treatment.

Method: We combined screening data from 10 industry-funded MASH phase 2 trials. The target population for resmetirom treatment was defined as patients with MASH (at least 1 point in each component) and moderate (F2) to advanced (F3) fibrosis. We described the proportion of patients meeting those criteria according to existing guideline thresholds. We also explored additional biomarkers to further identify patients for resmetirom treatment.

Results: 4,025 patients with centrally assessed liver biopsy were included in this analysis. Among them, 1,490 (37%) met the criteria for resmetirom treatment, 441 (11%) had cirrhosis, 1,787 (44%) had F0-F1, and 307 (8%) had F2-F3 without MASH. Among the patients considered as low risk who would not have an indication for resmetirom treatment according to existing guidelines, 31% met the criteria for resmetirom treatment, 4% had cirrhosis, 58% had F0-F1, and 7% had F2-F3 without MASH. Among the patients considered as intermediate or high risk who would have an indication for resmetirom treatment according to guidelines, 46% met the criteria for resmetirom treatment, 20% had cirrhosis, 27% had F0-F1, and 7% had F2-F3 without MASH. Among the group of patients with AST ≥ 40 (if HbA1c < 6.5%) or AST ≥ 30 (if HbA1c ≥ 6.5%), 53% met the criteria for resmetirom treatment, 13% had cirrhosis, 28% had F0-F1, and 6% had F2-F3 without MASH. In the patients who do not meet these AST/HbA1c thresholds, 25% met the criteria for resmetirom treatment, 9% had cirrhosis, 58% had F0-F1, and 8% had F2-F3 without MASH. Among the group of patients with FAST ≥ 0.67 (if HbA1c < 6.5%) or FAST ≥ 0.50 (if HbA1c ≥ 6.5%), 60% met the criteria for resmetirom treatment, 19% had cirrhosis, 17% had F0-F1, and 4% had F2-F3 without MASH.

Conclusion: The current guidelines support the appropriate selection of patients for resmetirom treatment. However, there is a significant proportion of patients requiring treatment that will not be identified and a non-negligible proportion of patients who do not require treatment that will be treated. Alternative simple biomarkers increase accurate selection of patients. This highlights the need for a refined approach to identify patients for resmetirom treatment using combinations of NITs and their correlation to outcomes.