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Institute for Clinical and Economic Review
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VIA Electronic Delivery

RE: Draft Scope: Obeticholic Acid for the Treatment of Nonalcoholic Steatohepatitis with Fibrosis: Effectiveness and Value

Request for Comments

Dear Sir or Madam:

The undersigned organizations appreciate the opportunity to comment on the Institute for Clinical and Economic Review (ICER) draft scope entitled "Obeticholic Acid for the Treatment of Nonalcoholic Steatohepatitis with Fibrosis: Effectiveness and Value."

Central to understanding the impact of NASH are 8 core issues that must be considered and addressed equally within the draft scoping document:

1. Lack of public and clinician awareness of NASH
2. The intrinsic link to other diseases
3. NASH impact on quality of life
4. Unique issues at each stage of the disease
5. Challenges in diagnosing NASH
6. Risks of adverse outcomes, including liver cancer
7. Lack of treatment options
8. Liver transplantation and complications

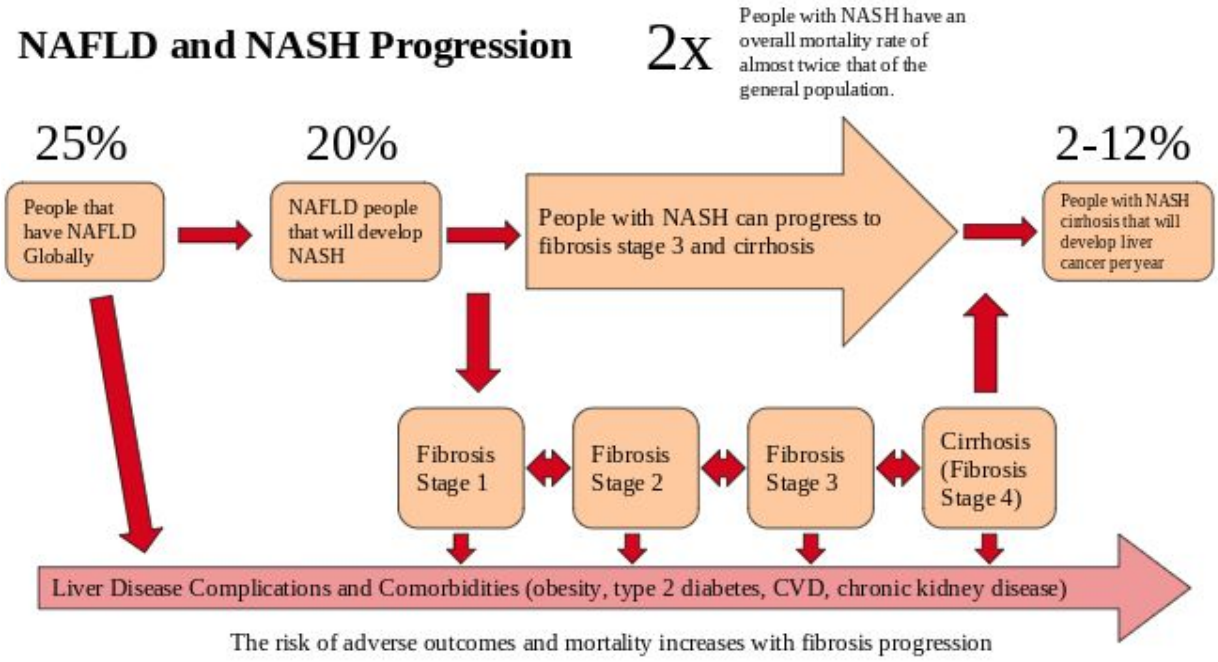
With the required length limitation we will focus this letter on 3 of the topics above.

First, there is a lack of public and clinician awareness of NASH, leading to underreported and varying prevalence.[1 2 3] Symptoms of NASH are non-specific and often misinterpreted.[2 4] NASH is typically only detected once it has progressed to cirrhosis or liver cancer,[4] therefore most people live for years unaware of the damage. Existing data is derived from

people with NAFLD selected for biopsy. Given that liver biopsy is rarely performed outside of a specialist setting, this is not truly representative of the scope of the NAFLD population, and plays a role in the under-reporting of NASH in primary care settings.[5]

Second, there are major concerns with the "gold standard" for NASH diagnosis, liver biopsy. The risky, invasive, and expensive procedure can also be subject to sampling variability and should be a diagnostic test of last resort.[2 6] Biopsy also plays a role in the high costs associated with NAFLD care, independent of metabolic comorbidities. The largest increases in health care utilization and costs in NAFLD are represented by liver biopsies and hospitalizations.[7] Currently, acceptable and relatively accurate non-invasive tests (NIT) exist are being developed to assess liver fibrosis.[8 9 10 11]

Third, the risk of adverse outcomes and mortality increases with fibrosis progression. NASH patients have a seven year mortality rate of 7.9%, almost twice that of the general population.[12 13 14 17] Presence and degree of fibrosis are main factors in determining disease outcome of NASH.[12 13 14] The rate of disease progression is not uniform; some patients experience fast fibrosis progression while others follow a slower, or regressive, course.[16] CVD is the most common cause of death, followed by cancer outside the liver and liver related complications (due to cirrhosis and liver cancer).[12 13 15] Approximately 2–12% of NASH patients develop liver cancer annually.[18] For people with end-stage liver disease and/or NASH-related liver cancer liver transplantation is the only option.[19]



The rise of NASH, its complications and comorbidities carry significant economic costs for health systems and society. The efficacy and side effects of OCA or any other pharmacologic intervention should be evaluated against the cost of disease progression and cost as well as efficacy of current standard of care (weight loss). Existing analyses show increasing costs with increasing severity of disease.[17 20] Including inpatient,

outpatient, professional services, emergency department, and drug costs, the lifetime direct costs of the total U.S. NASH population is $222.6 billion.[21] Advanced NASH patients are estimated to be 20% of the total NASH population, but account for almost half of the cost total ($95.4 billion).[21 22]

Each critical point highlighted in this letter must be considered across each stage of NASH, and when looking at potential other benefits offered by the intervention not considered as part of the evidence on comparative clinical effectiveness.

We look forward to continuing to work together on a report that correctly captures the costs associated with this life threatening disease.

With appreciation and respect,

American Gastroenterological Association
Global Liver Institute

Endnotes

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