EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA Reflection Paper on NASH

March 2024 Liver Forum

Disclaimer

The views expressed here are my personal views, and may not be understood or quoted as being made on behalf of the EMA or reflecting the position of the European Medicines Agency

Keypoints

1. **Stakeholders are expected to have the term «NASH» being consecutively replaced with «MASH»**
    1. Positive diagnostic criteria vs. Diagnosis of exclusion only
2. **Composite (intermediate) Endpoint based on histology maintained with both parts to independently demonstrate significance to placebo**
    1. Histology state of the art for diagnosis and follow up in clinical trials
    2. Call for further validation of non-invasive methods
    3. For compensated cirrhotic patients non-invasive diagnosis for inclusion would need to be justified.
    4. Intermediate endpoint (reversal of cirrhosis) for cirrhotic population maintained

Keypoints

CMA based on intermediate endpoint strategy as possibility (case by case review)

Positive BR balance:

Please refer to the intermediate endpoint (reasonable assumption for the prediction of long-term outcomes)

Likely that the applicant will provide comprehensive data post-authorization

Mind obstacles for continuation of confirmatory trials post approval (dropouts, trial integrity, availability of other drugs)

The medicine fulfills an unmet medical need

Currently unmet medical need

The benefit of immediate availability outweighs the risk that additional data are required

Keypoints

Combination treatment

Exploration of the properties of the single substances during the development of the combination treatment. Reiteration on the need for a sound justification of the principles for the justification of combination treatments and the expectations that **at least a "reduced factorial study"** is conducted in phase 2, and that demonstration of the contribution of the effects of each of the components should be based at least on the given intermediate endpoints

In clinical practise liver biopsies are often not done to assure the diagnosis.

- The generation of data in a population with assured diagnosis (based on biopsy) may have influence of the indication wording.
- For an unrestricted indication consistency of results with non-biopsied patients may be needed.
- Developments in completely non-invasive diagnosed patient population are outside the scope of this reflection paper. Scientific advise should be sought.

Any questions?

Further information

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