Liver Forum 13

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Proposal for setting up an

AI/ML Digital Liver Histology Working Group

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Why Using Digital Pathology with Artificial Intelligence (AI-DP) in Assessment of Fibrosis?

- AI-DP provides precise, standardized and reproducible **quantification** of liver fibrosis on a continuous scale
- Identifies more granularity of collagen fibers and changes in response to treatment;
- Avoids the inter- and intra-observer variations in the current subjective assessment and the limitations of categorical assessment in conventional scorings;
- Allows asking specific questions and obtaining details than can not be seen by the human eye and conventional microscopy.
- Allows assessment of fibrosis dynamics and treatment response by combining the AI-DP outputs with imaging, non-invasive tests and clinical parameters.

NB! AI digital pathology is not a replacement of the diagnostic assessment of liver histology

Recommendations

- In phase 2B and subpart H:
  - replace conventional diagnosis of NASH resolution by digitally assisted measures of disease activity
  - Histological pattern of improvement should be viewed in the context of the MOA of the therapeutic agent
  - Conventional stage fibrosis regression should be replaced by a more holistic approach taking into consideration changes in fibrosis related parameters in different regions of liver sections

RESEARCH AGENDA:

- Link short term changes in histological activity to fibrosis progression
- Validate short term changes in fibrosis patterns for future risk of progression to cirrhosis and outcomes
- Generate algorithms with NITs and short-term histological changes for disease and response monitoring COU
- Use comprehensive fibrosis radar plots to define best combinations for Precision Medicine

Why is such a group necessary?

- There is a major need to evaluate digital histology measurements and link the short-term changes in fibrosis patterns and other NASH features (ballooning, inflammation) with long-term clinical outcomes.
- Need for broad collaborative investigations across clinical trials (different sponsors and MoAs), as well as clinical cohorts with long-term follow-up and hard end-points.
- Validate the quantitative changes in fibrosis parameters and patterns in relation to future risk of progression to cirrhosis, as well as for reversal of cirrhosis.
- Given that liver fibrosis is a common pathway for disease progression and a key prognostic determinant for clinical outcomes, the working group will not be limited to NASH but could also evaluate other diseases – alcohol-related, HBV, etc.
- Work with the regulatory authorities to optimise the place of AI digital liver histology for clinical trial end-points and regulatory approvals.

Digital Pathology with AI analyses of tissue slides is already used in clinical practice and trials: recent examples

➢ **Prostate Cancer diagnosis**	- Paige Prostate AI software - Paige (FDA approved) - Galen Prostate AI software – Ibex (approved in EU)
➢ **Breast Cancer diagnosis**	- Galen Breast Solution AI model – Ibex (approved in EU)
➢ **Detection of Breast Cancer metastases in lymph nodes**	- Paige Breast Lymph Node, AI digital tool *Paige - Press Release 2022*
➢ **PD-L1 tumour expression**	- Digital quantification with AI tool, BMS/PathAI, *AACR June 22-24 2020, Poster 2017*
➢ **Cardiac Allograft rejection**	- Diagnosis and grading in of endomyocardial biopsies *J Lipkova, T Chen et al. Nature Medicine 2022:28;575–582*

What are the goals and deliverables

- To develop recommendations (and/or position papers), with input from all key stakeholders, how to incorporate AI digital assessment of liver histology in clinical trials and for liver research

- To facilitate the acceptance of AI digital assessment of liver histology by the regulatory authorities and inform regulatory guidance for drug development in liver diseases

Why is an AI/ML Digital Liver Histology Working Group a good fit for the Liver Forum ?

THE FORUM
For Collaborative Research℠

Mission	***Facilitating Collaborative Research in Drug Development and Health Policy***
Unique structure	*Brings together all relevant stakeholders - patients/patient advocates, academia, governmental agencies, pharma and diagnostic companies and professional societies, which all together co-own the Forum collectively.*
Track record	*In collaborative liver research and contributions to drug development*