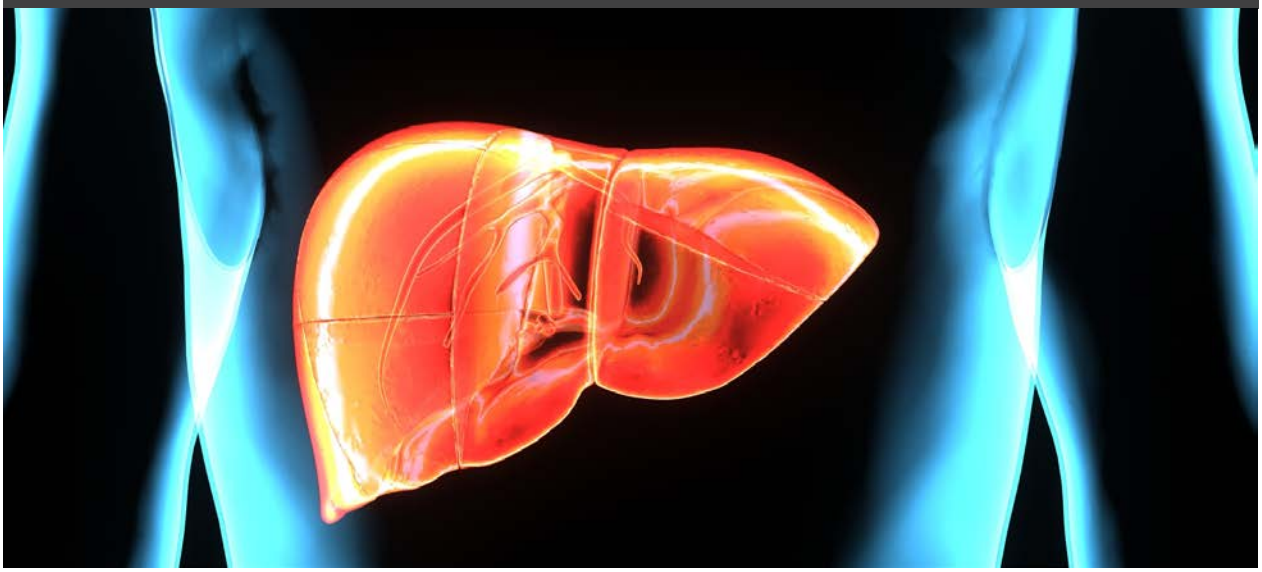
EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

29 October 2018
EMA/269375/2017
Human Medicines Evaluation Division

EMA stakeholder interaction on the development of medicinal products for chronic non-infectious liver diseases (PBC, PSC, NASH)

Programme

3 December 2018
European Medicines Agency, Canary Wharf, London, United Kingdom



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Background

There is an unmet medical need of pharmaceutical treatment options in the indications Primary Sclerosing Cholangitis (PSC) and Non-alcoholic steatohepatitis (NASH) and also the repertoire of effective and safe drugs for the treatment for Primary Biliary Cholangitis (PBC; previously termed “Primary Biliary Cirrhosis”) remains limited.

The main feature of chronic liver diseases, including PSC, PBC, and NASH is their slow progression which constitutes a major challenge for drug development essentially with regard to a balanced choice of patient populations, clinically relevant endpoints and duration of observation periods.

In all three diseases, symptoms are usually unspecific or at least non-predictive for the long-term outcome of the disease, and the use of hard clinical outcome parameters as endpoint, similar for all three entities, such as liver transplantation and death is struggling with feasibility issues. In addition, the consequent, necessary use of repeated liver biopsies with its inherent risks of complications and deterrence of patients from recruitment points to the need for the validation of surrogate outcome parameters to replace histology.

There is also a need for the identification of the most suitable patient population, balancing unmet medical needs, the mechanism of action of drug candidates, and the disease severity with regard to grade of inflammation and stage of fibrosis development.

The requirement for long-term observation also raises questions on the balance between timely availability of new compounds, the choice of appropriate licensing strategies and the conduct or continuation of clinical studies post-approval with the associated problems of patient adherence and ethics as well as the regulatory need for (repeated) re-assessment.

In addition, whereas NASH is a frequent disease with increasing prevalence and must be regarded to be a consequences of the “obesity epidemic”, two of the three disease entities (PBC and PSC) are rare diseases, and drug candidates in the field usually have orphan drug designation. The most efficient use of a restricted patient population is therefore an additional top level requirement for the conduct of clinical trials.

Objectives of the Meeting

- Discuss the difficulties and opportunities for drug development in the field of chronic liver disease (PBC, PSC, NASH), which should include:
  - Identification of appropriate endpoints including validation of adequate surrogate endpoints/biomarkers
  - Suitable study populations
  - Potentially adequate trial designs.
- Discuss similarities and differences of the disease entities and their impact on regulatory requirements.
- Specify needs and anticipated problems of Paediatric drug development (especially for NASH)

Scientific Organising Committee

Elmer Schabel	Federal Institute for Drugs and Medical Devices (BfArM), Germany Gastroenterology Drafting Group (GDG)
Mark Ainsworth	University of Copenhagen, Denmark Gastroenterology Drafting Group (GDG)
Peter Szitányi	First Faculty of Medicine and General University Hospital, Charles University in Prague, Czech Republic Gastroenterology Drafting Group (GDG)
Johannes Taminiau	Universitair Ziekenhuis Antwerpen, Belgium Gastroenterology Drafting Group (GDG)
Joachim Musaus	European Medicines Agency (EMA)
Chrissi Pallidis	European Medicines Agency (EMA)
Richard Vesely	European Medicines Agency (EMA)

Programme details

Room *3A*

08:00 **Arrival and registration**

Reception, ground floor (45')

08:45 **Welcome and introduction**

Zaide Frias, Head of Human Medicines Evaluation Division, EMA **(10')**

09:00 **Session 1: Primary Biliary Cholangitis (PBC)**

Chair: Elmer Schabel, Bundesinstitut für Arzneimittel und Medizinprodukte, *DE*
Co-Chair: Mari Thoern, Läkemedelsverket, *SE*

PBC – The patient perspective
Robert Mitchell-Thain, PBC Foundation, *UK* **(10')**

Authorisation of Ocaliva for PBC in the EU and the remaining open issues
Joachim Musaus, EMA **(10')**

Definition, natural history and current therapeutic interventions
Gideon Hirschfield, Toronto General Hospital, *Canada* **(15')**

Historical outcome parameters used in PBC and the search for potential alternatives
Bettina E Hansen, ERASMUS MC, *NL* **(15')**

Potential trial designs and suitable study populations
Bettina E Hansen, ERASMUS MC, *NL* **(15')**

Discussion (60')

11:05 **Coffee Break**

11.20 **Session 2: Primary Sclerosing Cholangitis (PSC)**

Chair: Michael Trauner, Vienna University of Medicines, *AT*
Co-Chair: Peter Szitányi, First Faculty of Medicine and General University Hospital, Charles University in Prague, *CZ*

PSC – The patient perspective
Martine Walmsley, PSC Support, *UK* **(10')**

Definition, natural history and the lack of approved therapeutic interventions
Douglas Thorburn, Royal Free London NHS Foundation Trust, *UK* **(15')**

Currently proposed endpoints in PSC: the search for reliable surrogate outcome parameters
Cyriel Ponsioen, Academic Medical Center, *NL* **(15')**

Potential trial designs and suitable study populations
Michael Trauner, Vienna University of Medicines, *AT* **(15')**

The need for paediatric developments in PSC, trial duration and endpoints
Henkjan Verkade, University Medical Center Groningen, *NL* **(15')**

Discussion (60')

13:20 Lunch break

14:00 Session 3: Non-alcoholic steatohepatitis (NASH)

Chair: Deirdre Kelly, Birmingham Children's Hospital, *UK*
Co-Chair: Peter Mol, Medicines Evaluation Board, *NL*

NASH - The patient perspective
Yvonne Gray, *UK,* **(10')**

Overview on current paediatric investigation plans
Chrissi Pallidis, EMA **(10')**

Definition, natural history and current therapeutic interventions
***Frank Tacke*,** Uniklinikum Aachen, *DE* **(15')**

Outcomes in NASH trials: From histology combined with "hard outcomes" to less invasive reliable surrogates (including biomarkers)?
Laurent Castera, Hôpital Beaujon, *FR* **(15')**

Potential trial designs and suitable study populations
Quentin Anstee, Newcastle University, *UK* **(15')**

Paediatrics: Population in need, clinical trial duration and endpoints
Piotr Socha, The Children's Memorial Health Institute, *PL* **(15')**

Discussion (60')

Wrap up (30')

16:50 End of meeting

Conference venue and Secretariat

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Travel and Accommodation

Participants must possess valid travel documents and, where relevant, a visa for entry into the United Kingdom. Should you require an official letter of invitation, please contact CNILD_workshop@ema.europa.eu

Recording and Photography

The Agency records or broadcasts a number of its meetings, including some virtual meetings. This is part of the Agency's commitment to the principle of transparency as enshrined in the Treaty on the European Union. The conference will be recorded. By attending these events you consent to any photographing, recording, broadcast and publication of presentations on the EMA website.

WiFi access

WiFi is available throughout the EMA. Login details can be found on the back of your EMA access pass.

Restaurant facilities

Restaurant, deli bar and coffee bar are available (located on 4th floor) - please note you will need to have either £10.00 or €10.00 minimum cash in order to purchase a pre-paid canteen card

There are also many cafes and restaurants in the Canary Wharf area. More information can be found in the Canary Wharf area guide (restaurants, shops, etc.):

www.allinlondon.co.uk/regions/canary-wharf

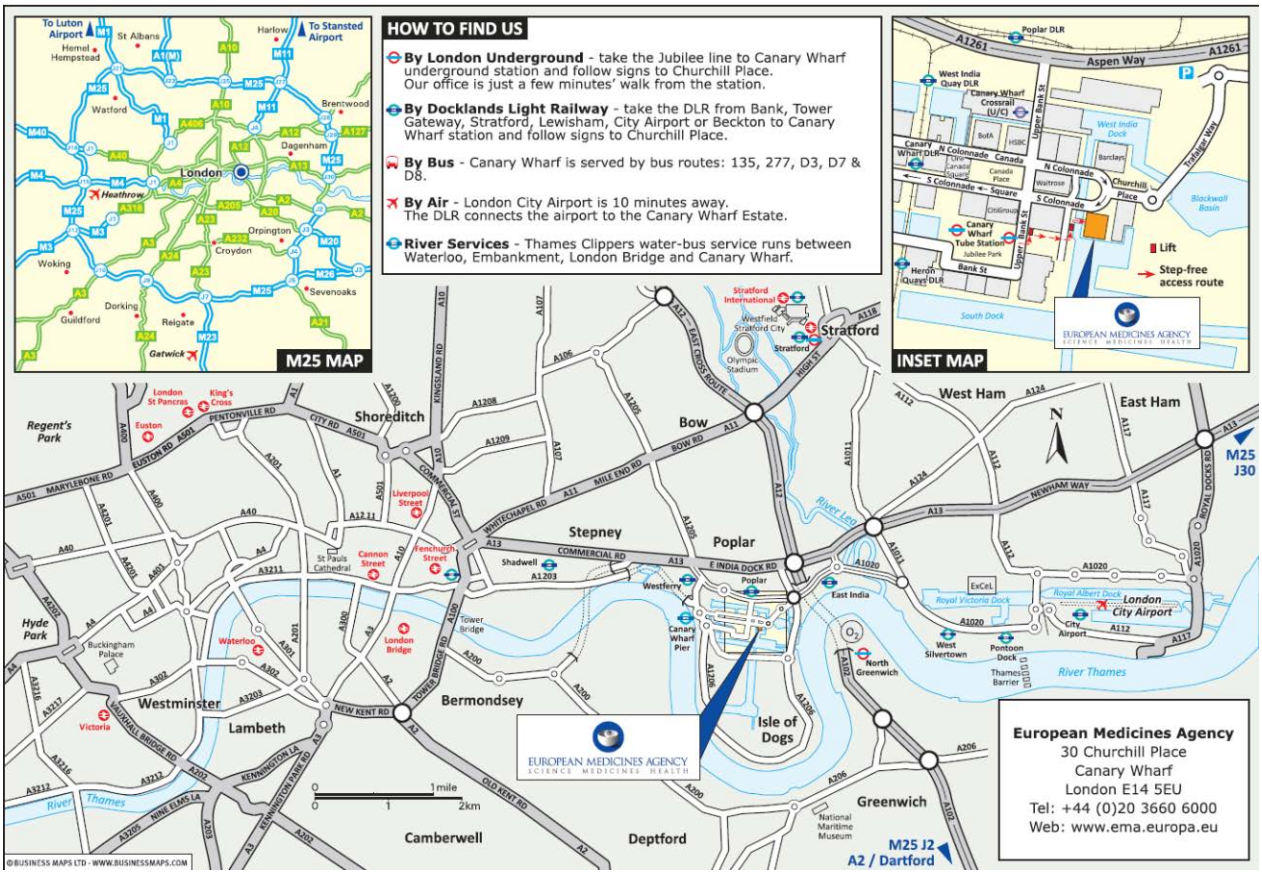
http://www.canarywharf.com/workwithus/The-Estate/Estate-Map/

Getting to Canary Wharf

The EMA is located in Canary Wharf, a business district in the east of London.

Please find below the public transport options for travelling to Canary Wharf together with the approximate journey times and the map of the area.

Directions to European Medicines Agency and map of the area



By Docklands Light Railway (DLR)

Both venues are a short walk from Canary Wharf or Heron Quays station on the DLR. Services run from Bank, Tower Gateway, Lewisham, Stratford, King George V and Beckton.

By Underground

The nearest stop for both venues is Canary Wharf station on the Jubilee Line. From East exit (NB. This is the closest exit to 30 Churchill Place): exit the station and turn left into Upper Bank Street, turn right at Canada Square and continue straight into Churchill Place.

By Bus

Canary Wharf is serviced by local bus numbers D3, D7, D8, 135 and 277.

River services

River services run between Embankment, London Bridge and Canary Wharf throughout the day. Canary Wharf pier is roughly a 15-minute walk from the European Medicines Agency.

From London City Airport

Take DLR City Airport to Canary Wharf (journey time is around 20 minutes).

From Gatwick Airport

Take a mainline train to London Bridge, then the Jubilee Line to Canary Wharf (journey time around 50 minutes).

From Heathrow Airport

Take the London underground Piccadilly Line to Green Park, change to the Jubilee Line to Canary Wharf (journey time around 1hr 20 minutes).

Alternatively, take the Heathrow Express train to Paddington, then the Circle or Bakerloo line to Baker Street, then the Jubilee Line to Canary Wharf (journey time around 1hr 20 minutes).

Alternatively, you can take the Heathrow Express train to Paddington, then the District or Circle Line to Tower Hill then the Docklands Light Railway (DLR) to Canary Wharf (journey time around 1hr 30 minutes).

From Stansted Airport

Take the Stansted Express to London Liverpool Street then the Circle Line to Tower Hill and change onto the DLR to Canary Wharf (journey time around 70 minutes).

From Luton Airport

Take a first Capital Connect train to London Bridge then the Jubilee Line to Canary Wharf (journey time around 60 minutes).

From St Pancras International train station

Take the Northern Line to London Bridge then the Jubilee Line to Canary Wharf (journey time around 45 minutes).

Contact

Should you have any questions, please contact Monica Simeoni or Joachim Musaus via GastroenterologyDG@ema.europa.eu

Useful links

http://www.tfl.gov.uk/

National Rail

Gatwick Express

Heathrow Express

Stansted Express

Eurostar

Heathrow airport

Gatwick airport

London City

London Stansted

Hillgate travel