Berkeley School of Public Health

EASL European Association for the Study of the Liver

Forum for Collaborative HIV Research

LITMUS
Liver Investigation: Testing Marker Utility in Steatohepatitis

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Liver Investigation: Testing Marker Utility in Steatohepatitis

Professor Quentin M. Anstee PhD, FRCP

Institute of Cellular Medicine,

Newcastle University, UK

imi innovative medicines initiative

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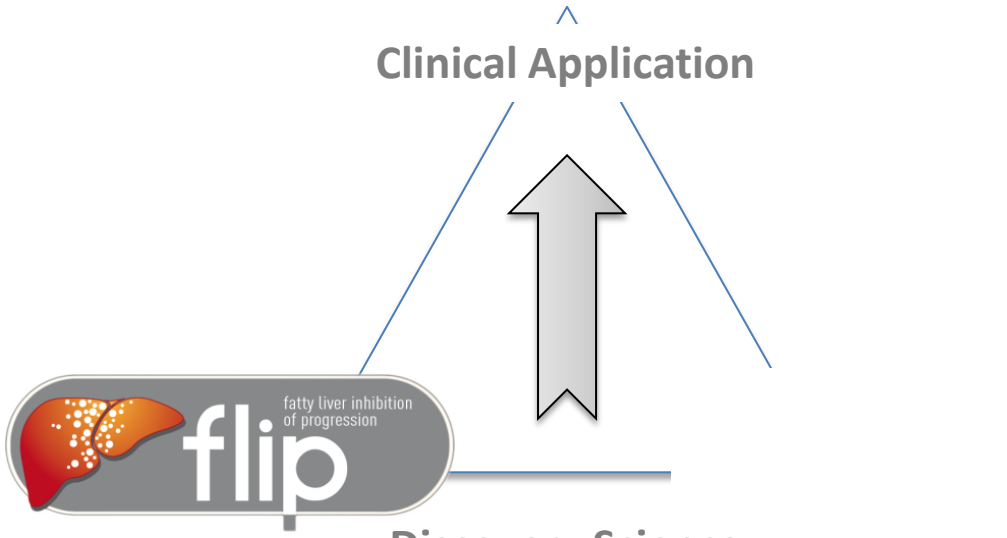

EU FP7 (2010-2013)

EU H2020 (2015-2019)

European Commission

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Aims of the LITMUS Consortium

1. **To leverage existing cross-sectional and longitudinal patient cohorts and bioresources into a single unified resource for biomarker validation.**
2. **To expand the prospective recruitment of patients with histologically characterised NAFLD to further support validation of candidate biomarkers.**
3. **To establish a robust technological and methodological platform and use it for the definitive validation of candidate biomarkers.**
   - An impartial, technology-unbiased platform for biomarker discovery, assessment and validation.
   - Address all 3 FDA BEST biomarker domains (diagnostic, prognostic and monitoring)
   - Clear line of sight to FDA and EMA regulatory qualification.
4. **To define the most accurate and tractable biomarkers relevant to NAFLD.**
   - LITMUS will provide validation data of the requisite standard to support regulatory qualification of biomarkers for trial use against both histological/biochemical indices and clinically relevant long-term outcome measures.
5. **To develop consensus and qualify preclinical models of NAFLD/NASH and then back-translate biomarkers for validation in these models**
   - Supporting pre-clinical drug development and translational drug development.

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Biomarker Needs to Address

- **Diagnostic (BIPED 'Burden/Severity of disease' and 'Diagnostic')**
  - Degree of steatosis,
  - Grade of steatohepatitis,
  - Stage of fibrosis,
  - Discriminating Steatosis (NAFL) vs. Steatohepatitis (NASH)
- **Prognostic (BIPED 'Prognostic').**
  - Stratify individuals by fibrosis progression risk,
  - Discriminate fast vs. slow progressors,
  - Predicting long-term outcomes and hard endpoints
- **Dynamic (BIPED 'Efficacy of Intervention')**
  - Track progression and/or regression of disease severity
  - Efficacy of intervention

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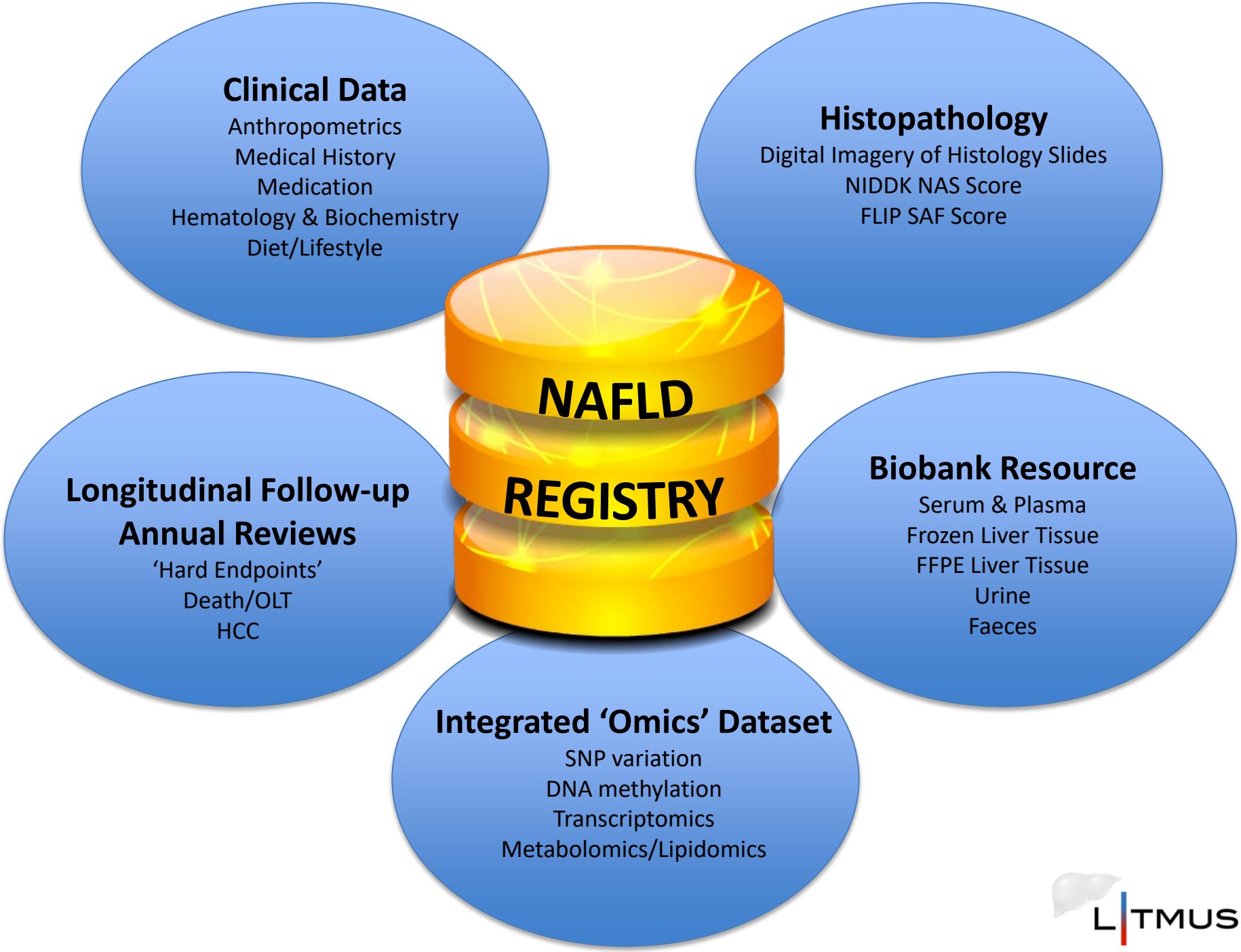
Clinical Data
Anthropometrics
Medical History
Medication
Hematology & Biochemistry
Diet/Lifestyle
Histopathology
Digital Imagery of Histology Slides
NIDDK NAS Score
FLIP SAF Score
NAFLD
REGISTRY
Longitudinal Follow-up
Annual Reviews
'Hard Endpoints'
Death/OLT
HCC
Biobank Resource
Serum & Plasma
Frozen Liver Tissue
FFPE Liver Tissue
Urine
Faeces
Integrated 'Omics' Dataset
SNP variation
DNA methylation
Transcriptomics
Metabolomics/Lipidomics
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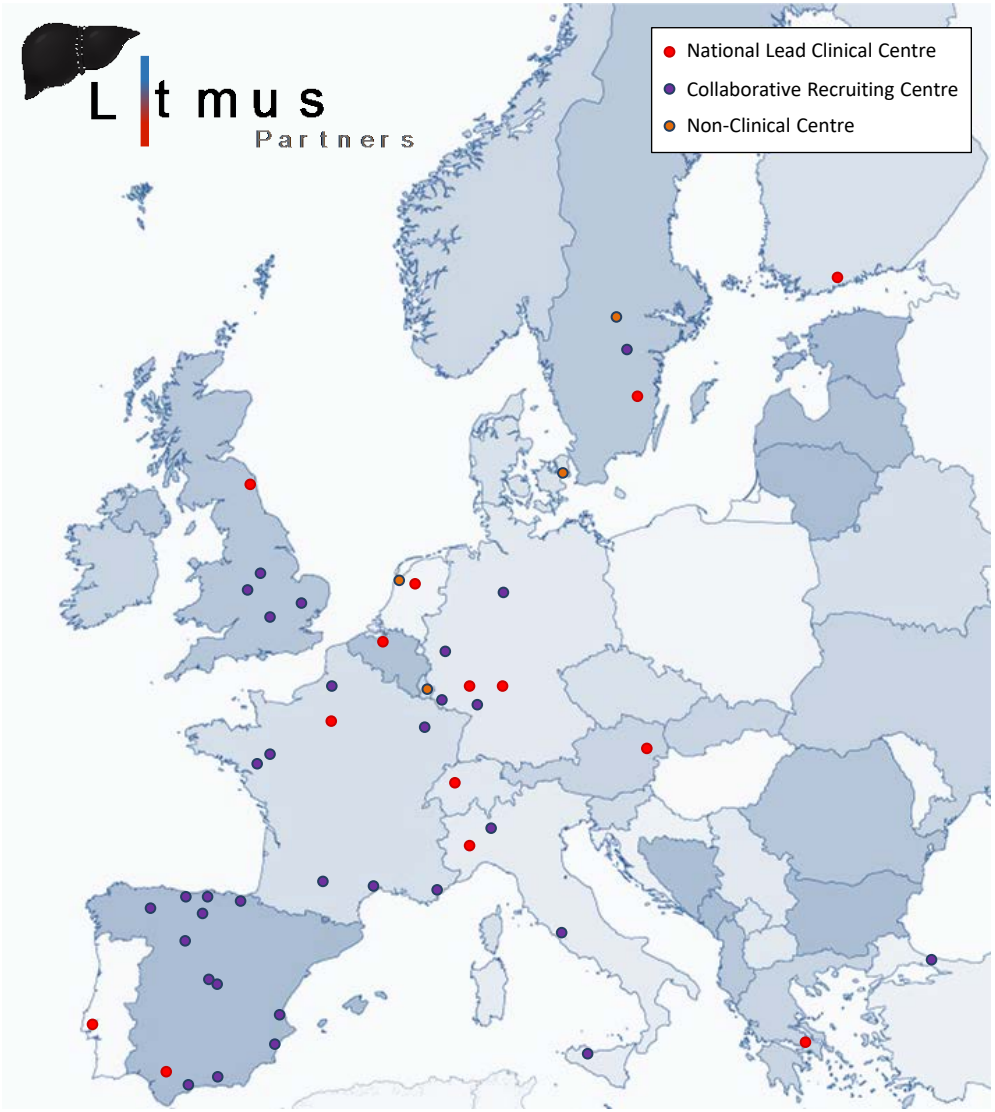
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Partners
National Lead Clinical Centre
Collaborative Recruiting Centre
Non-Clinical Centre

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Work Package Leaders & Key Partners

- **WP1: Project Coordination**
  - Anstee (UNEW) & Wenn (IXS)
- **WP2: Analysis, Evaluation & Evidence Synthesis**
  - Bossuyt (AMC), Boussier (UA)
- **WP3: Patient Cohorts & Bioresources**
  - Ratziu (ICAN), Anstee (UNEW), Bedossa (APHP), Betsou (IBBL), Francque (UZA)
- **WP4: Central laboratory**
  - Karsdal (NB), Leeming (NB), Schuppan (UMC), Daly (UNEW), Hyotylainen (OU), Orsec (OU), Mato (CIC bioGUNE), Clement (ICAN), Geier (UKW)
- **WP5: Imaging**
  - Harrison (UOX), Neubauer (UOX), Banarjee (PERS), Hockings (ANT), Yki-Jarvinen (UHEL), Romero-Gomez (SAS)
- **WP6: Reverse Translation & Pre-Clinical Models**
  - Vidal-Puig (UCAM), Oakly (UNEW), Trautwein (RWTH), Marra (UNIFI), Rodrigues (FML)
- **WP7: 'QED' Qualification, Exploitation & Dissemination**
  - Ratziu (ICAN), Sanyal (UNEW), Bossuyt (AMC), Anstee (UNEW), Day (UNEW), Karsdal (NB), Schuppan (UMC), Dufour (UBER)

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