SYNOPSIS –DISTAL

STUDY TITLE	**Deciphering the self-antigen specific T cell signature of autoimmune liver diseases** **DISTAL**
SPONSOR	Nantes University Hospital
PRINCIPAL INVESTIGATOR **PRINCIPAL INVESTIGATORS**	Dr Jérôme Gournay, Hepatology, Gastroenterology and Gastroenterology, Nantes University Hospital Sophie Conchon, Amédée Renand, UMR 1064 (Transplantation and Immunology Site), University of Nantes
SCIENTIFIC CO-INVESTIGATOR	Amédée Renand, UMR 1064 (Transplantation and Immunology Site), University of Nantes
METHODOLOGY	An observational study based on **the MAI-FOIE biobank**.
MAIN OBJECTIVE	To establish a molecular signature of autoantigen-specific T cells in autoimmune liver diseases
SECONDARY OBJECTIVES	**Grouped into three themes:** **Immunological:** • A new approach to determining the mechanisms of autoimmunity in the liver • To identify autoreactive T cells that could serve as targets for new treatments for autoimmune liver diseases, as alternatives to non-specific immunosuppressants • To identify biomarkers useful in clinical practice: diagnostic tests, tests to assess response to treatment, tests to predict relapse upon discontinuation of treatment, etc. • To understand the molecular mechanisms underlying treatment efficacy and failure **Anatomic pathology and pathophysiology:**

	• To identify new pathophysiological targets associated with the severity of liver lesions, and to assess their prognostic and clinical significance • Identifying and validating new non-invasive markers for diagnosis, severity, prognosis and therapeutic response **Therapeutics:** • Analysis of the long-term therapeutic effects of the treatments used • Analysis of predictors of response to treatment, and of the progression or regression of fibrosis • To facilitate the conduct of ancillary therapeutic studies and clinical trials in this cohort, for which phenotypic data and serum or tissue samples are available. • To issue therapeutic recommendations to improve the management of autoimmune liver diseases • To develop therapeutic trials based on the identified immunological mechanisms
ENDPOINTS	• **clinical:** death, liver transplantation, end-stage liver disease, hepatocellular carcinoma, cirrhotic decompensation, treatment-related adverse events • **immunological:** immunoglobulin levels, autoantibodies, etc. • **pathological and pathophysiological**: fibrosis, cirrhosis, liver biochemistry, associated viral infections, etc. • **socio-economic**: quality of life, costs, perception of toxicity, adherence to treatment, behavioural changes, etc.
PLANNED NUMBER OF PARTICIPANTS	220 patients (100 in Nantes and 120 spread across the other 7 sites)
PARTICIPATING SITES	Angers, Brest, Rennes, Tours, Poitiers, Orléans, La Roche-sur-Yon, Nantes
INCLUSION CRITERIA	**Criterion 1 and one other of the criteria (2a, 2b, 3, 4) are required for inclusion.** **1 – Signing of the consent form** **2a – Treatment-naïve autoimmune hepatitis (AIH): at least 2 of the following criteria:** - ALAt >2N or IgG >1.1N

	- Presence of autoantibodies: ANA (anti-nuclear), ML (anti-smooth muscle), AMA (anti-mitochondrial), SLA (anti-soluble liver antigen), LKM1 (anti-endoplasmic reticulum), LC1 (anti-liver cytosol) - Lesions suggestive of PBH (interface hepatitis, lymphocytic or plasmacytic portal or lobular infiltrate) **2b- Relapse following discontinuation of treatment (patient considered treatment-naïve)** **3- Presence of a specific autoantibody against (SLA, LKM1 or LC1)** **4- Controlled HAI for which treatment is to be discontinued** **In Nantes only:** **Primary Biliary Cholangitis (PBC): at least 2 of the following criteria** - Alkaline phosphatase (ALP) > 1.5N or gamma-GT > 3N - Presence of anti-mitochondrial antibodies ≥ 1/40 - Lesions suggestive of PBC (pericanalicular portal lymphocytic infiltrate, bile duct lesions, ductopenia) **Non-alcoholic steatohepatitis (NASH)**: histologically compatible findings **Primary sclerosing cholangitis (PSC)**: if there is overlap with HAI
EXCLUSION CRITERIA	- Positive HIV serology - HBV infection (presence of HBsAg) - Positive HCV serology and PCR - Isolated PSC
TREATMENT	No specific treatment within this cohort
PROVISIONAL TIMETABLE	The aim is to contribute to the MAI-FOIE biobank at a rate of 6 inclusions per year in each of the planned sites outside Nantes. Enrolment will begin in the first quarter of 2021; the study is planned to run for 3 years of enrolment and 7–10 years of annual patient follow-up.