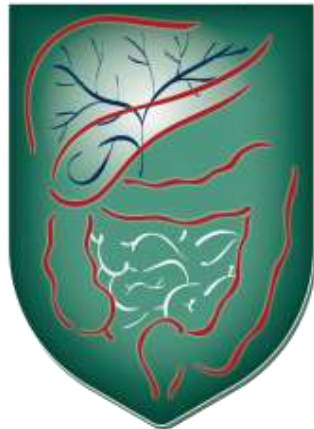


# Studi di autoimmunità in PITER e partecipazione al registro italiano delle malattie autoimmuni del fegato

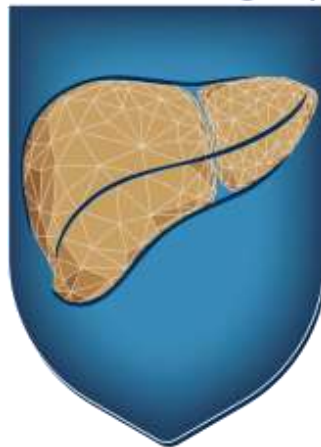
Italian PBC Registry



Italian PSC Registry



Italian AIH Registry

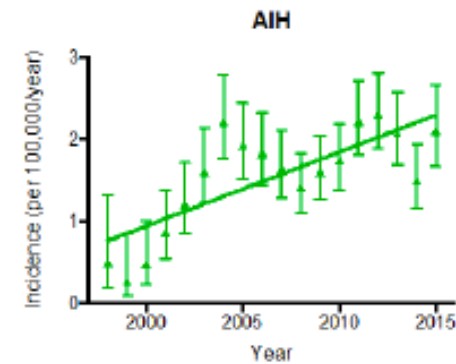
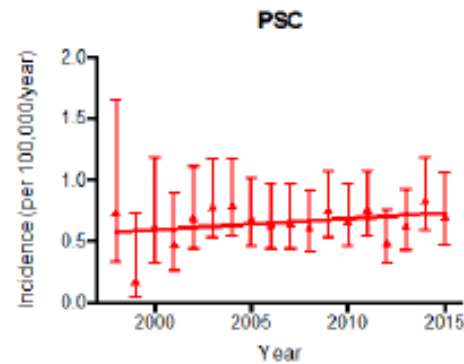
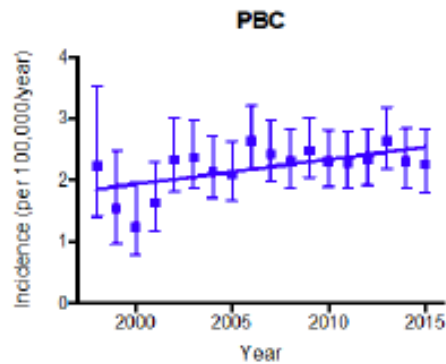


Marco Carbone

Centro delle Malattie Autoimmuni del Fegato, Università di Milano-Bicocca  
Epatologia, ASST GOM Niguarda

# How many patients get AIHD every year?

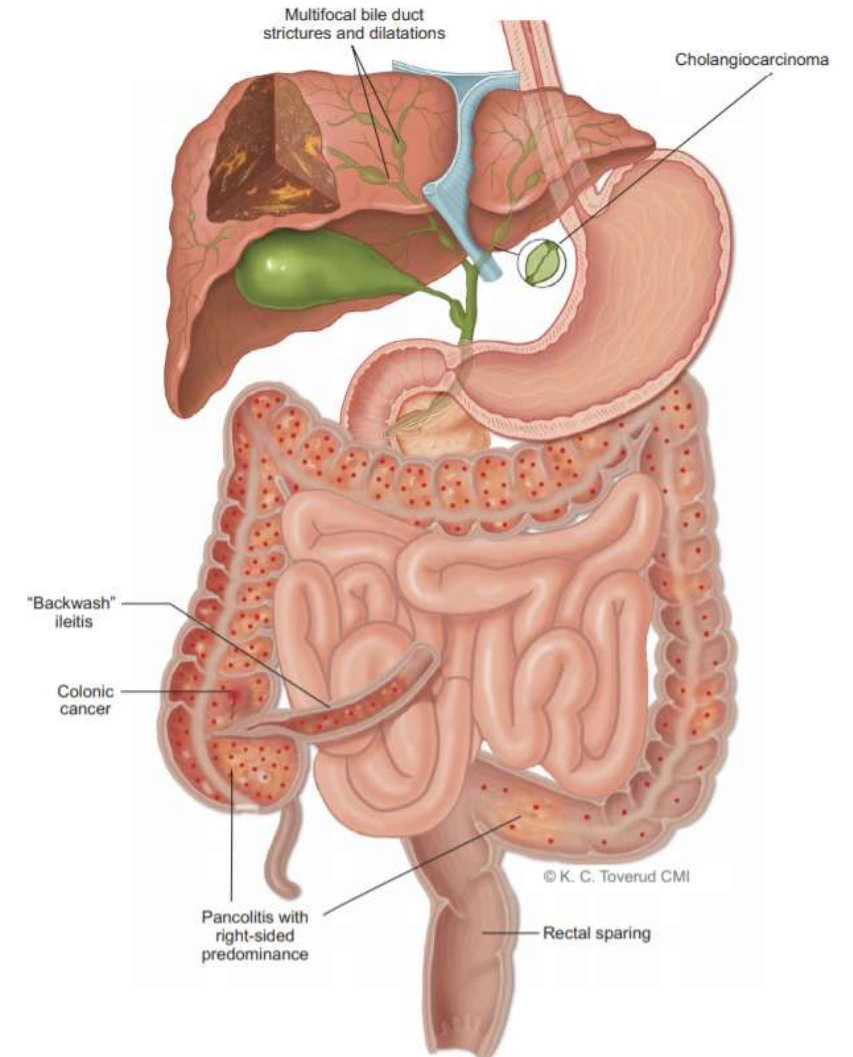
- **PBC** – 2.3 (2.2-2.4) *cf.* 0.3-5.8
- **PSC** – 0.7 (0.6-0.7) *cf.* 0-1.3
- **AIH** – 1.7 (1.6-1.8) *cf.* 1.68 (1.60 to 1.76) Denmark
  - cases/100,000/year from 1998-2015
- *cf.* **Multiple Sclerosis** – 5.5 (5.1-5.9) and **T2DM** – 396 (394-398)



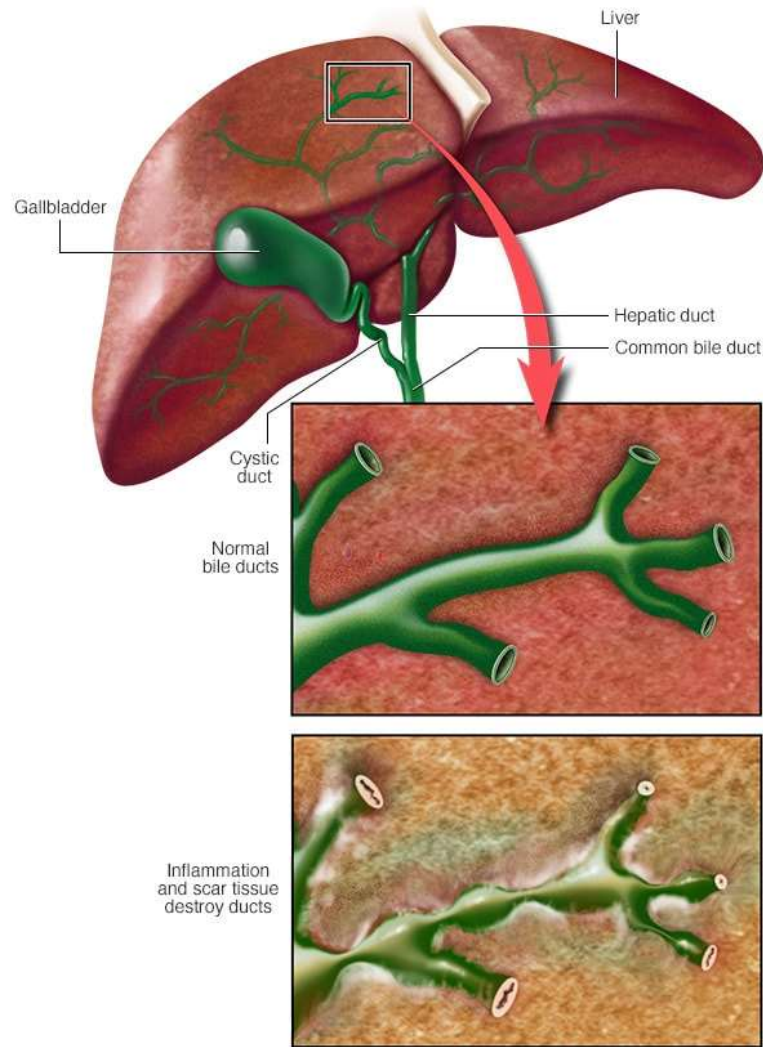
Boonstra, K., et al. (2012). *JHep*, 56(5), 1181–1188; Alonso, A., et al., (2007) *J. Neurology*, 254(12), 1736–1741; Sharma, M., et al., (2017) *BMJ Open*, 6(1), e010210.

# Primary sclerosing cholangitis - PSC

- Rare chronic cholestatic liver disease characterised by inflammation and fibrosis of intra- and extrahepatic BD
- The last «black box» in hepatology
- Associated risk of ESLD, CCA and CRC
- No therapies with proven benefit on survival
- Strong association with IBD



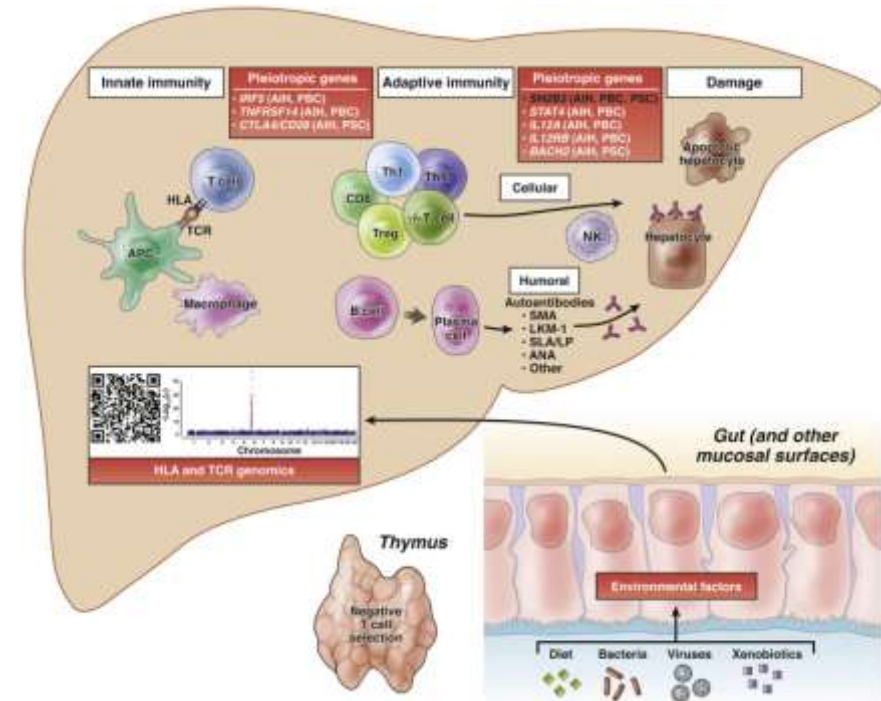
# Primary Biliary Cholangitis - PBC



- Chronic inflammation and destruction of small/medium-sized bile duct (former CNDC)
- Easy to diagnose (AMA and chronic cholestasis)
- 1 in 1000 women > 40yo live with PBC
- Often asymptomatic and at early stage at diagnosis – former “*primary biliary cirrhosis*”
- Itch and fatigue are common
- Other autoimmune conditions (thyroid, celiac, AR, scleroderma)
- Slowly progressive – not always!
- Therapy: backbone is UDCA – 2<sup>nd</sup> line OCA & Fibrates

# Autoimmune Hepatitis - AIH

- Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease which, if untreated, often leads to cirrhosis, liver failure and death
- Prevalence: 10 to 17 per 100 000 in Europe (similar to PBC)
- Women are affected 3-4 times more frequently
- All age groups – bimodal distribution (peaks at puberty and 4<sup>th</sup>-6<sup>th</sup> decade)
- Complex disease - triggers: viruses, drugs?



# Italian Registries of Autoimmune Liver Diseases

- Investigator-initiated project (Pietro Invernizzi, 2017)
- Funded by PAOs, Industry, University of Milano-Bicocca
- >96 liver centres involved
- Aims:
  - Epidemiology
  - Disease course
  - Real-world drug experience (efficacy/safety)

# Team

- Data Manager



- Regulatory Affairs



- Redcap Manager



- PI & Medical team

- Lab Manager



# Steering Committee *PBC Registry*



- Calvaruso Vincenza, **Palermo**
- Carbone Marco, **Milano**
- Cardinale Vincenzo, **Roma**
- Cazzagon Nora, **Padova**
- Marzioni Marco, **Ancona**
- Vespasiani Umberto, **Roma**





# Funders



# CONTRIBUTING SITES

**Monza** – IRCCS San Gerardo dei Tintori

**Bergamo** – ASST Papa Giovanni XXIII

**Milano** – ASST Niguarda - Policlinico di Milano Gastroenterologia & Medicina ad Indirizzo Metabolico – Ospedale S. Giuseppe - IRCCS San Raffaele – ASST Santi Paolo e Carlo – ASST Ovest Milanese di Legnano

**Brescia** – Fondazione Poliambulanza - ASST degli Spedali Civili & Presidio di Gardone VT

**Rozzano** – Istituto Clinico Humanitas

**Gallarate** – ASST Valle Olona

**Como** – Ospedale Valduce

**Cremona** – ASST di Cremona

**Varese** – ASST Sette Laghi

**Treviglio** – ASST di Bergamo Ovest

**Pavia** – Istituto di Cura

**Lecco** – ASST di Lecco

**Aosta** – Azienda USL Valle d'Aosta

**Trento** – Azienda Provinciale per i Servizi Sanitari

**Bolzano** – Azienda sanitaria dell'Alto Adige

**Pordenone** – AO S. Maria degli Angeli

**Trieste** – ASU Integrata di Trieste

**Udine** – ASU Integrata di Udine

**Padova** – AO Gastroenterologia & Medicina Interna

**Verona** – AOU Integrata & Ospedale Borgo Roma

**Treviso** - Ospedale Regionale Ca' Foncello

**Bassano del Grappa** – Ospedale S. Bassiano

**Peschiera del Garda** – Ospedale P. Pederzoli

**Vicenza** - Ospedale San Bortolo

**Torino** – AOU Città della Salute

**Novara** – AOU Maggiore della Carità

**Asti** - Ospedale Cardinal

**Massaia**

**Cuneo** – AO S. Croce e Carle

**Genova** – Ospedale San Martino

**Firenze** – AOU Careggi Clinica Medica & Gastroenterologia

**Pisa** – AOU Pisana Cisanello

**Siena** – AOU Senese

**Ancona** – AOU Ospedali Riuniti

**Modena** – Ospedale Civile di Baggiovara & AOU di Modena

**Parma** – AOU di Parma

**Bologna** – Policlinico S. Orsola Malpighi: Epatologia, Medicina Interna, Malattie epatobiliari e immunoallergologiche, MI per il trattamento delle gravi insufficienze di organo

**Faenza** – Presidio Ospedaliero

**Rimini** – AUSL della Romagna

**Ferrara** – AOU di Ferrara

**Forlì** - Ospedale Pierantoni-Morgagni

**Ravenna** - Ospedale "Santa Maria delle Croci"

**Roma** – Policlinico Umberto I

Policlinico Tor Vergata

Policlinico Gemelli – Med. Int. & CEMAD

Policlinico Campus Bio-Medico

Ospedale Sant'Andrea

S. Camillo Forlanini

**Civitavecchia** – Ospedale S. Paolo

**Latina** – Ospedale Santa Maria Goretti

**Perugia** – AO S. Maria della Misericordia

**Pescara** – Azienda USL

**S. Giovanni Rotondo** – Ospedale Casa Sollievo della Sofferenza: Gastroenterologia & Epatologia

**Bari** – AOU Policlinico Bari

**Foggia** – AOU Ospedali Riuniti

**Castellana Grotte** – IRCCS De Bellis

**Brindisi** – P.O. Perrino

**Barletta** - Ospedale Mons. Dimiccoli

**Cagliari** – AOU Duilio Casula Monserrato, ARNAS G. Brotzu

**Sassari** – AOU di Sassari

**Napoli** – Policlinico Federico II Gastroenterologia – AOU Vanvitelli – Fondazione Evangelica Villa Betania – AO Cardarelli

**Salerno** – AOU Ruggi d'Aragona & Umberto I Nocera Inferiore

**Potenza** – Ospedale San Carlo Borromeo

**Matera** – Azienda Sanitaria locale

**Catanzaro** – AOU Mater Domini A & Geriatria

**Lamezia Terme** - ASP Presidio Ospedaliero

**Cosenza** – AO SS. Annunziata

**Palermo** – AOU Policlinico "Paolo Giaccone" & Ospedale Riuniti Villa Sofia Cervello

**Catania** – ARNAS Garibaldi & Policlinico "G.Rodolico" & P.O. di Acireale

**Messina** – AOU Policlinico Gaetano Martino

**Siracusa** - ASP

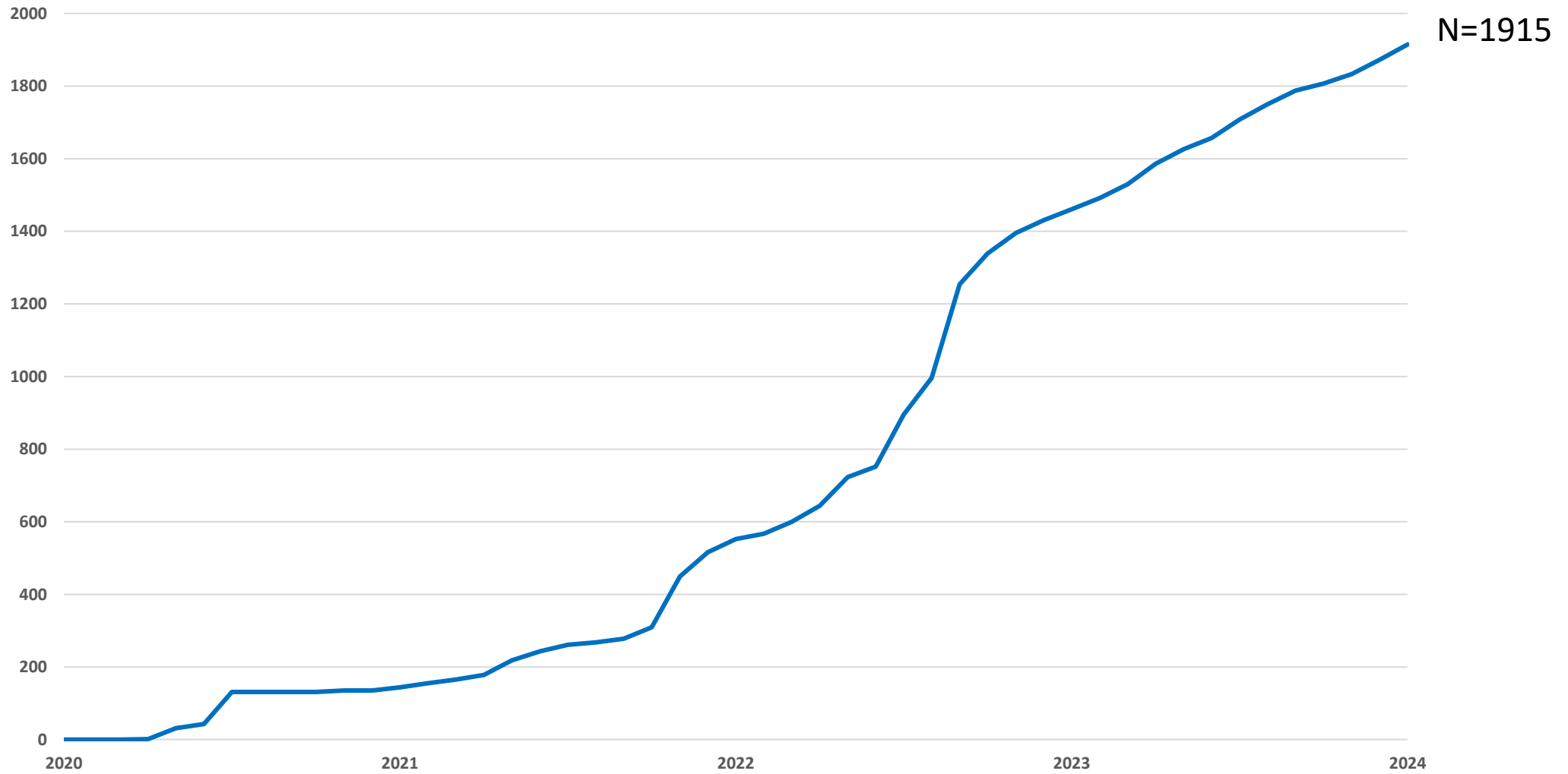
**Activated: 60**

**To be activated: 36**

Italian PBC Registry

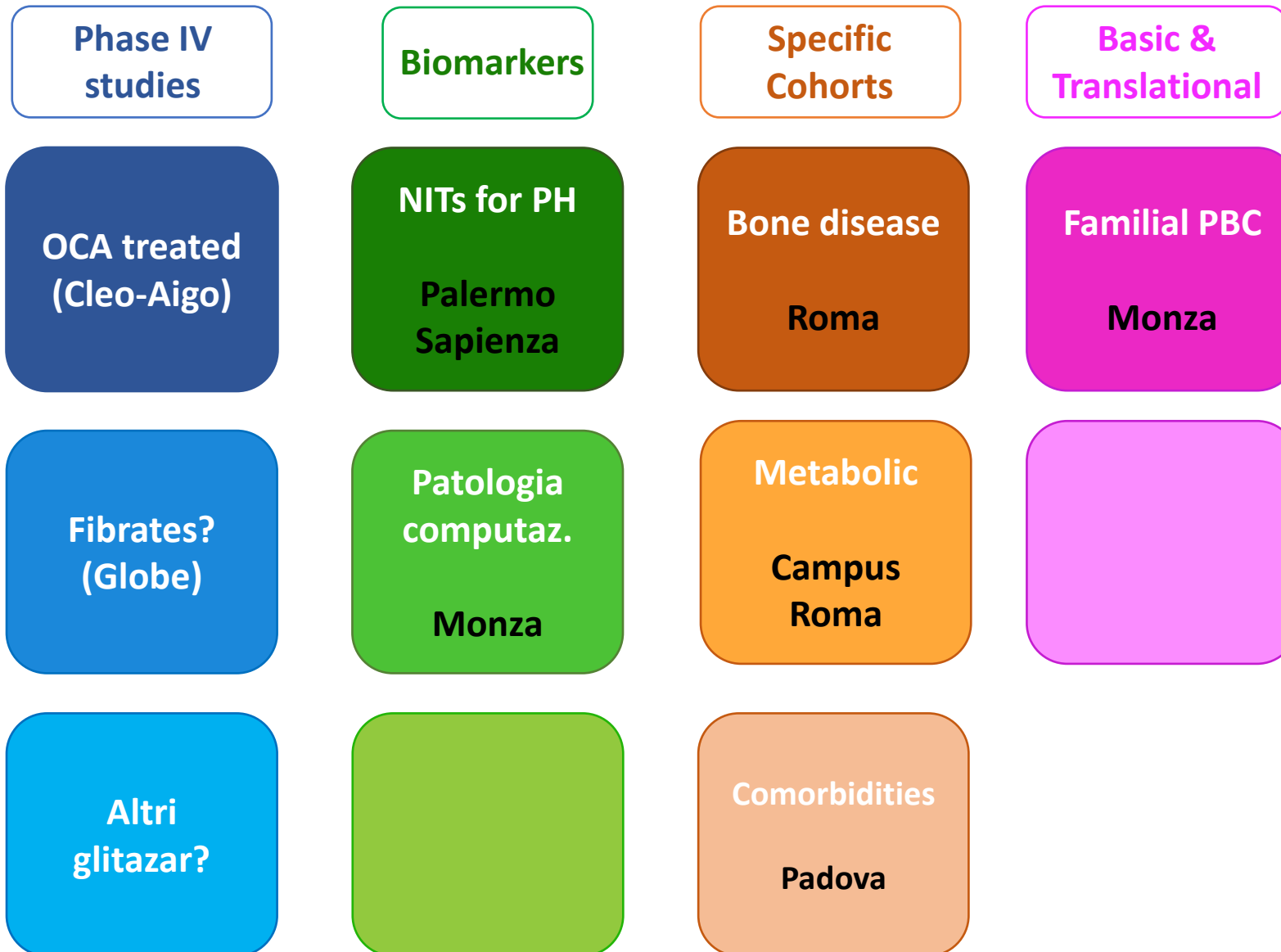


# Recruitment



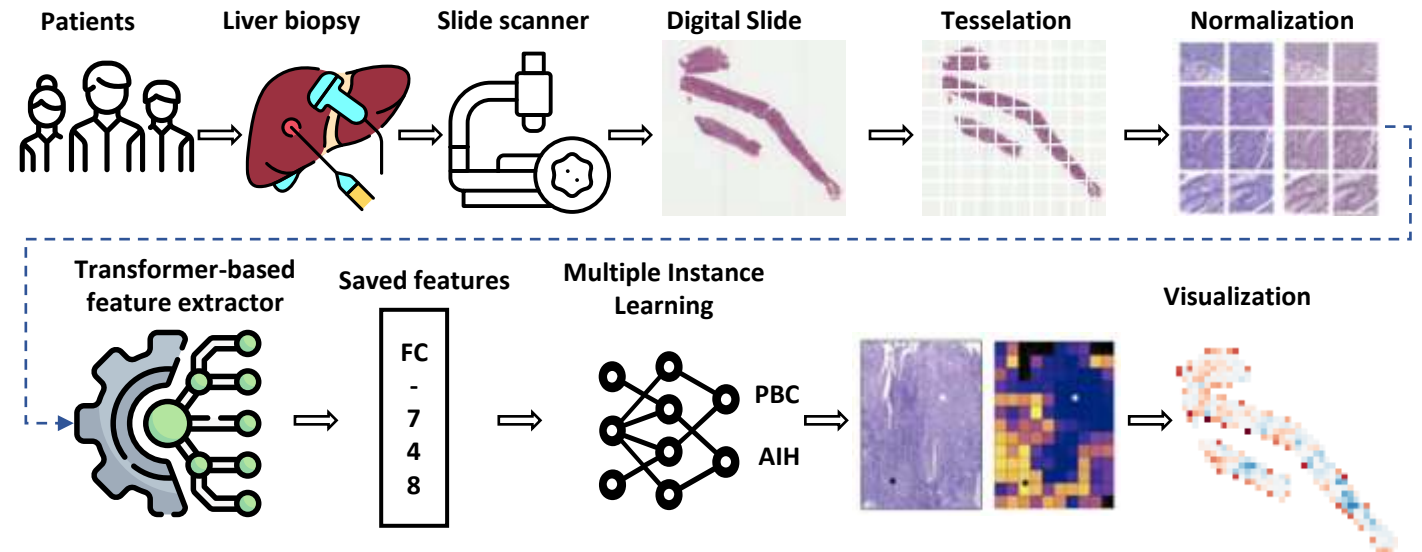
Update at 29.01.2024

# PBC Registry Study Group Overview



# Deep Learning can discriminate AIH from PBC directly from histology without human annotation

- > 400 AIH & > 250 PBC liver biopsies
- Treatment-naive, at diagnosis
- Six centers (ICH, HSG, SG, Novara, Palermo + Hannover)
- DL analysis performed at the Clinical Artificial Intelligence Lab (Prof. Jakob Kather) in Dresden





# Artificial intelligence in MRI

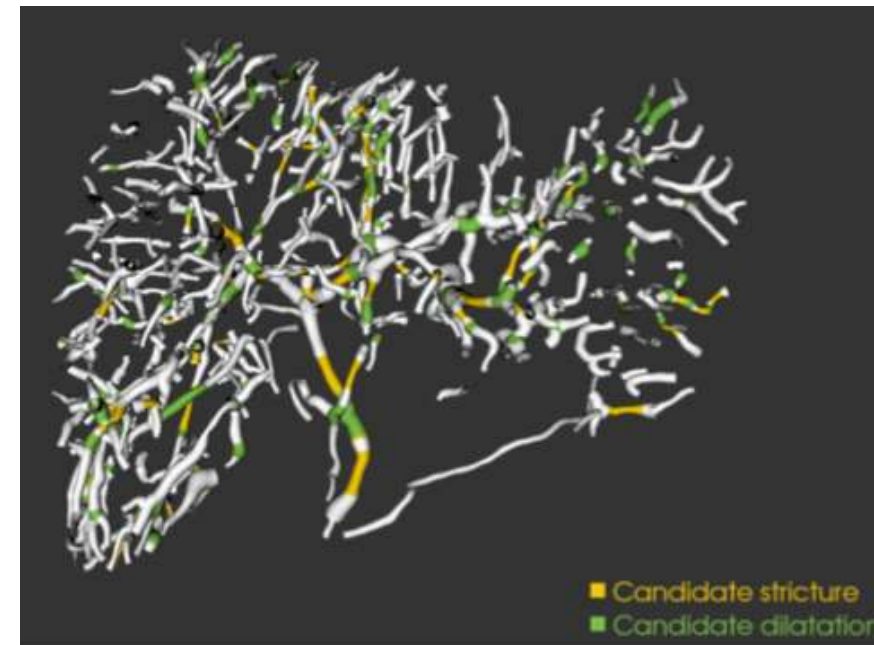
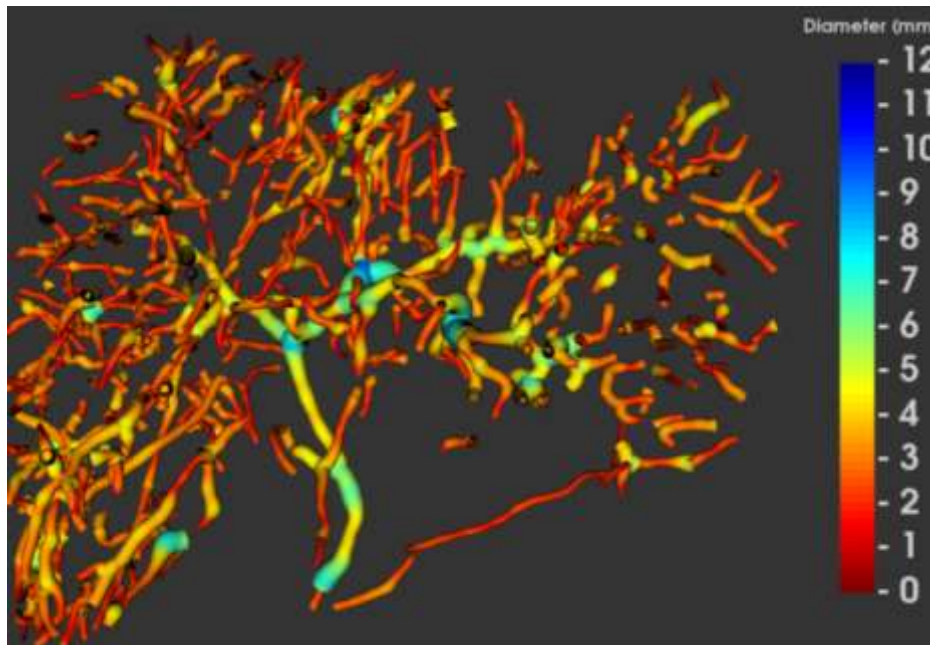


## Biliary system metrics<sup>1,3</sup>

	Measured value
Number of ducts:	491
Number of candidate strictures: <sup>4</sup>	71
Total number of candidate dilatations: <sup>4</sup>	126
Biliary tree volume: <sup>2</sup>	59.5ml
Gallbladder volume: <sup>2</sup>	1.5ml
Total length of ducts:	7096.4mm
Total length of candidate strictures and dilatations: <sup>4</sup>	1096.7mm

## Candidate strictures and dilatations<sup>4</sup>

Number of strictures:	2
Number of dilatations:	1
Minimum stricture diameter:	3.8mm
Maximum dilatation diameter:	6.3mm
Maximum length of stricture:	31.0mm
Maximum length of dilatation:	15.1mm
Maximum stricture severity:	40%
Maximum dilatation severity:	59%



# Publications: Real world data of second-line therapies

Research article



JHEP Reports

## Real-world experience with obeticholic acid in patients with primary biliary cholangitis

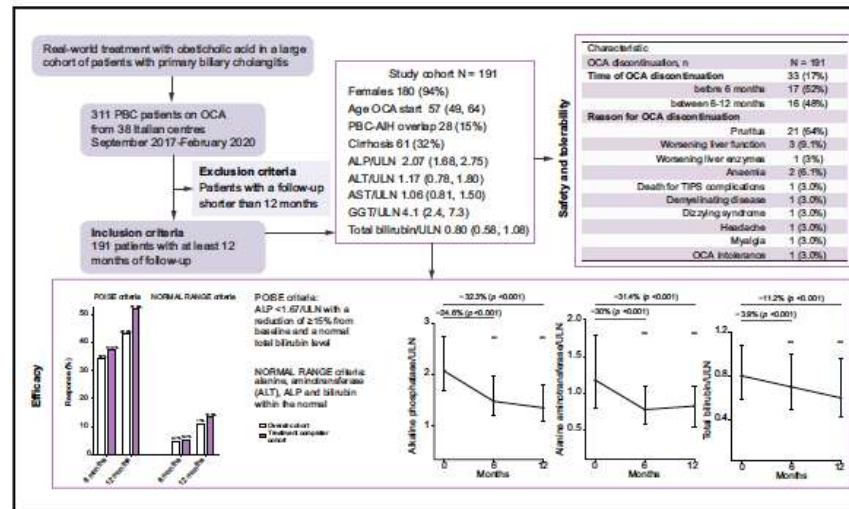
### Authors

Daphne D'Amato, Antonio De Vincentis, Federica Malinverno, Mauro Viganò, Domenico Alvaro, Maurizio Pompili, Antonino Picciotto, Valeria Pace Palitti, Maurizio Russello, Silvia Storato, Marie Graciella Pigozzi, Vincenza Calvaruso, Elisabetta De Gasperi, Ana Lleo, Antonino Castellaneta, Adriano Pellicelli, Nora Cazzagon, Annarosa Floreani, Luigi Muratori, Stefano Fagioli, Grazia Anna Niro, Valentina Feletti, Raffaele Cozzolongo, Natalia Terreni, Marco Marzoni, Rinaldo Pellicano, Pietro Pozzoni, Leonardo Baiocchi, Luchino Chessa, Floriano Rosina, Gaetano Bertino, Maria Vinci, Anna Morgando, Ester Vanni, Gaetano Scifo, Rodolfo Sacco, Maria D'Antò, Valentina Bellia, Roberto Boldizzoni, Silvia Casella, Barbara Omazzi, Guido Poggi, Laura Cristoferi, Alessio Gerussi, Vincenzo Ronca, Rosanna Venere, Francesca Ponziani, Maria Cannavò, Alessandro Mussetto, Rosanna Fontana, Francesco Losito, Evelise Frazzetto, Marco Distefano, Francesca Colapietro, Sara Labanca, Giulia Marconi, Giuseppe Grassi, Giovanni Galati, Sarah Elizabeth O'Donnell, Clara Mancuso, Giacomo Mulinacci, Andrea Palermo, Ernesto Claar, Antonio Izzi, Antonio Picardi, Pietro Invernizzi, Marco Carbone, Umberto Vespasiani-Gentilucci

### Correspondence

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### Graphical abstract



ORIGINAL ARTICLE



## Predictors of serious adverse events and non-response in cirrhotic patients with primary biliary cholangitis treated with obeticholic acid

Antonio De Vincentis<sup>1</sup> | Daphne D'Amato<sup>2</sup> | Laura Cristoferi<sup>3</sup> | Alessio Gerussi<sup>3</sup> | Federica Malinverno<sup>3</sup> | Ana Lleo<sup>4</sup> | Francesca Colapietro<sup>4</sup> | Fabio Marra<sup>5</sup> | Andrea Galli<sup>6</sup> | Cecilia Fiorini<sup>6</sup> | Barbara Coco<sup>7</sup> | Maurizia Brunetto<sup>7</sup> | Grazia Anna Niro<sup>8</sup> | Rosa Cotugno<sup>8</sup> | Carlo Saitta<sup>9</sup> | Raffaele Cozzolongo<sup>10</sup> | Francesco Losito<sup>10</sup> | Edoardo Giovanni Giannini<sup>11</sup> | Sara Labanca<sup>11</sup> | Marco Marzoni<sup>12</sup> | Giulia Marconi<sup>12</sup> | Anna Morgando<sup>2</sup> | Rinaldo Pellicano<sup>2</sup> | Ester Vanni<sup>2</sup> | Nora Cazzagon<sup>13</sup> | Annarosa Floreani<sup>13</sup> | Luchino Chessa<sup>14</sup> | Olivia Morelli<sup>15</sup> | Luigi Muratori<sup>16</sup> | Adriano Pellicelli<sup>17</sup> | Maurizio Pompili<sup>18</sup> | Francesca Ponziani<sup>18</sup> | Annalisa Tortora<sup>18</sup> | Floriano Rosina<sup>19</sup> | Maurizio Russello<sup>20</sup> | Mariarita Cannavò<sup>20</sup> | Loredana Simone<sup>21</sup> | Silvia Storato<sup>22</sup> | Mauro Viganò<sup>23</sup> | Ludovico Abenavoli<sup>24</sup> | Maria D'Antò<sup>25</sup> | Elisabetta De Gasperi<sup>26</sup> | Marco Distefano<sup>27</sup> | Gaetano Scifo<sup>27</sup> | Teresa Zolfino<sup>28</sup> | Vincenza Calvaruso<sup>29</sup> | Giuseppe Cuccorese<sup>30</sup> | Valeria Pace Palitti<sup>31</sup> | Rodolfo Sacco<sup>32</sup> | Gaetano Bertino<sup>33</sup> | Evelise Frazzetto<sup>33</sup> | Domenico Alvaro<sup>34</sup> | Giacomo Mulinacci<sup>3</sup> | Andrea Palermo<sup>3</sup> | Miki Scaravaglio<sup>3</sup> | Francesca Terracciani<sup>1</sup> | Giovanni Galati<sup>1</sup> | Vincenzo Ronca<sup>3</sup> | Massimo Zuin<sup>35,36</sup> | Ernesto Claar<sup>37</sup> | Antonio Izzi<sup>38</sup> | Antonio Picardi<sup>1</sup> | Pietro Invernizzi<sup>3</sup> | Umberto Vespasiani-Gentilucci<sup>1</sup> | Marco Carbone<sup>3</sup> | on behalf of the Club Epatologi Ospedalieri (CLEO)/Associazione Italiana Gastroenterologi ed Endoscopisti Digestivi Ospedalieri (AIGO) PBC Study Group and, the Italian PBC Registry

# Publications: Surrogate endpoints for clinical trial

*Lancet Gastroenterol Hepatol.* Author manuscript; available in PMC 2020 January 15.

Published in final edited form as:

*Lancet Gastroenterol Hepatol.* 2018 September 01; 3(9): 626–634. doi:10.1016/S2468-1253(18)30163-8.

## Pre-treatment prediction of response to ursodeoxycholic acid (UDCA) in primary biliary cholangitis: the UDCA Response Score

M Carbone<sup>1,2,\*</sup>, A Nardi<sup>3,\*</sup>, S Flack<sup>1</sup>, G Carpino<sup>4</sup>, N Varvaropoulou<sup>1</sup>, C Gavrilă<sup>3</sup>, A Spicer<sup>1</sup>, J Badrock<sup>1</sup>, F Bernuzzi<sup>2</sup>, V Cardinale<sup>6</sup>, HF Ainsworth<sup>5</sup>, MA Heneghan<sup>7</sup>, D Thorburn<sup>8</sup>, A Bathgate<sup>9</sup>, R Jones<sup>10</sup>, JM Neuberger<sup>11</sup>, PM Battezzati<sup>12</sup>, M Zuin<sup>12</sup>, S Taylor-Robinson<sup>13</sup>, M Donato<sup>14</sup>, J Kirby<sup>15</sup>, R Mitchell-Thain<sup>16</sup>, A Floreani<sup>17</sup>, F Sampaziotis<sup>18</sup>, L Muratori<sup>19</sup>, D Alvaro<sup>6</sup>, M Marzioni<sup>20</sup>, L Miele<sup>21</sup>, F Marra<sup>22</sup>, E Giannini<sup>23</sup>, E Gaudio<sup>4</sup>, V Ronca<sup>12</sup>, G Bonato<sup>2</sup>, L Cristoferi<sup>2</sup>, F Malinverno<sup>2</sup>, A Gerussi<sup>2</sup>, DD Stocken<sup>5</sup>, HJ Cordell<sup>24</sup>, GM Hirschfield<sup>25</sup>, GJ Alexander<sup>26</sup>, RN Sandford<sup>1</sup>, DE Jones<sup>27</sup>, P Invernizzi<sup>2,†</sup>, GF Mells<sup>1,†</sup> for the Italian PBC Study Group & UK-PBC Consortium.

HEPATOLOGY



AUTOIMMUNE, CHOLESTATIC AND BILIARY DISEASE | HEPATOLOGY, VOL. 74, NO. 3, 2021

## Accuracy of Transient Elastography in Assessing Fibrosis at Diagnosis in Naïve Patients With Primary Biliary Cholangitis: A Dual Cut-Off Approach

Laura Cristoferi<sup>10</sup>,<sup>1,3\*</sup> Vincenza Calvaruso,<sup>4\*</sup> Diletta Overi<sup>10</sup>,<sup>5</sup> Mauro Viganò,<sup>6</sup> Cristina Rigamonti,<sup>7</sup> Elisabetta Degasperis<sup>10</sup>,<sup>8</sup> Vincenzo Cardinale,<sup>9</sup> Sara Labanca,<sup>10</sup> Nicola Zucchini,<sup>11</sup> Anna Fichera,<sup>4</sup> Vito Di Marco,<sup>4</sup> Monica Leutner,<sup>12</sup> Rosanna Venere,<sup>13</sup> Antonino Picciotto,<sup>10</sup> Martina Lucà,<sup>1,2</sup> Giacomo Mulinacci,<sup>1,2</sup> Andrea Palermo<sup>10</sup>,<sup>1,2</sup> Alessio Gerussi<sup>10</sup>,<sup>1,2</sup> Daphne D'Amato,<sup>1,2</sup> Sarah Elisabeth O'Donnell,<sup>1,2</sup> Federica Cerini,<sup>6</sup> Carla De Benedittis,<sup>7</sup> Federica Malinverno,<sup>1,2</sup> Vincenzo Ronca,<sup>1,2</sup> Clara Mancuso,<sup>1,2</sup> Nora Cazzagon,<sup>14</sup> Antonio Ciaccio,<sup>1,2</sup> Donatella Barisani,<sup>1</sup> Marco Marzioni,<sup>15</sup> Annarosa Floreani,<sup>16,17</sup> Domenico Alvaro,<sup>9</sup> Eugenio Gaudio,<sup>5</sup> Pietro Invernizzi,<sup>1,2</sup> Guido Carpino<sup>10</sup>,<sup>18\*\*</sup> Alessandra Nardi,<sup>19\*\*</sup> and Marco Carbone<sup>1,2\*\*</sup>, on the behalf of the Italian PBC Registry

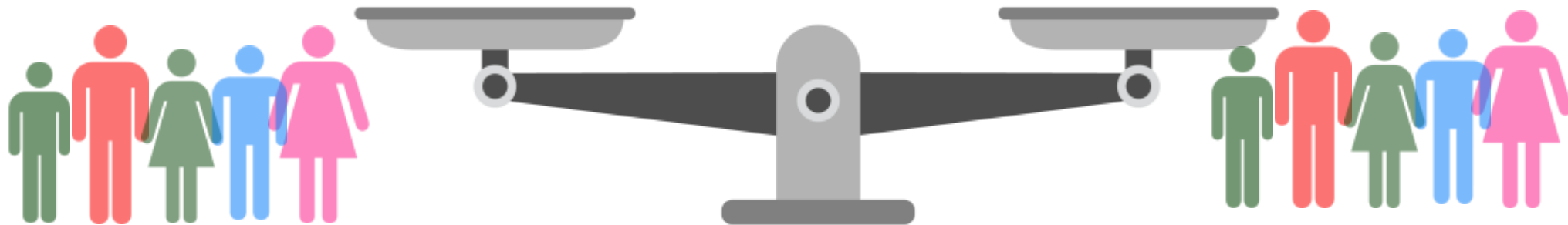




# Future perspective



Crossfertilisation of experiences of data flow and network



## CENTRO MALATTIE AUTOIMMUNI DEL FEGATO



European  
Reference  
Networks



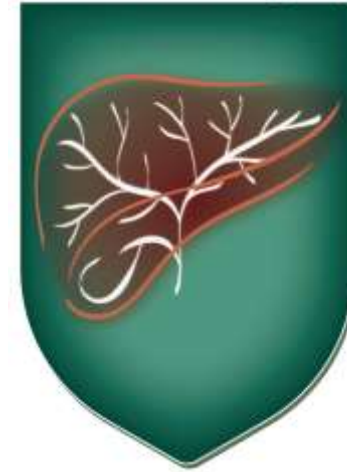
**Pietro INVERNIZZI**  
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Daphne D'AMATO  
Miki SCARAVAGLIO

**LAB MANAGERS:**  
Marco FESTA

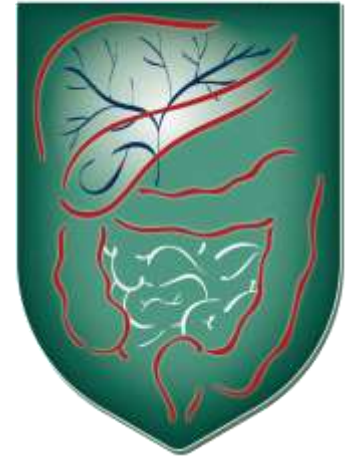
**REGISTRY MANAGER:**  
Eugenia NOFIT  
Emanuela ROSSI

**REGULATORY AFFAIRS:**  
Clara MANCUSO

Italian PBC Registry



Italian PSC Registry



Italian AIH Registry

