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Steatotic Liver Disease (SLD)

Best of EASL Congress 2025

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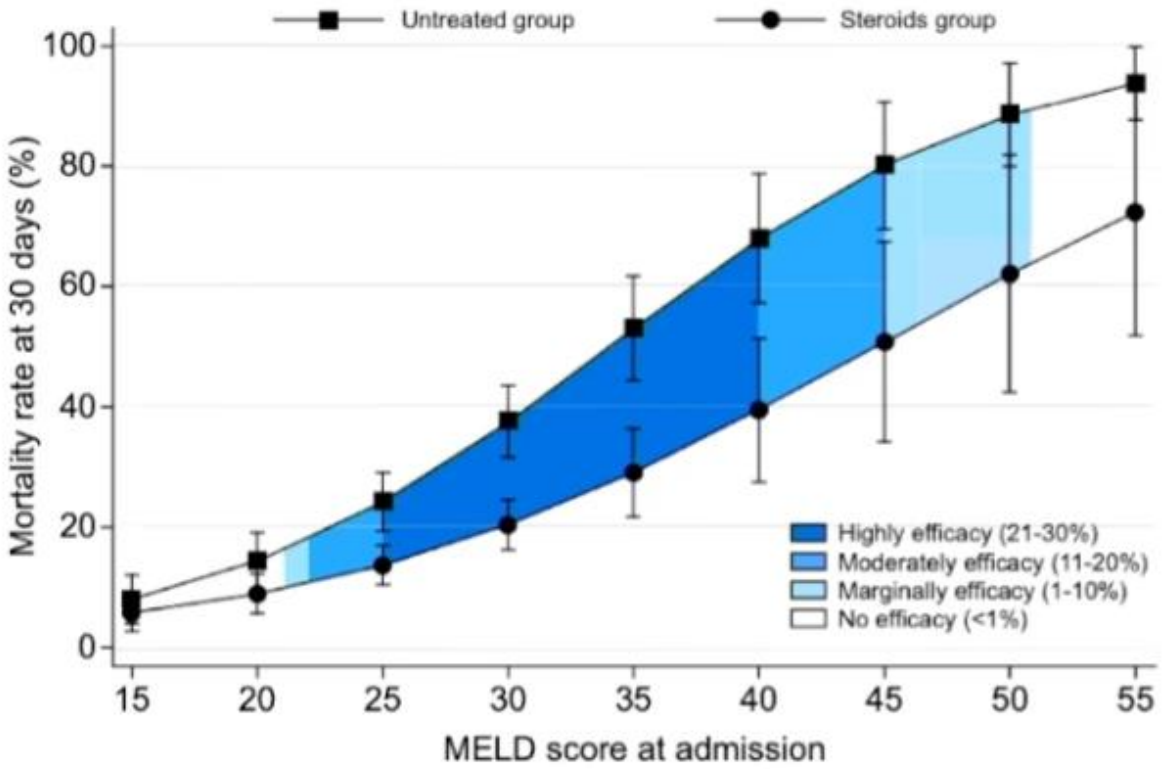
ALD - Therapy

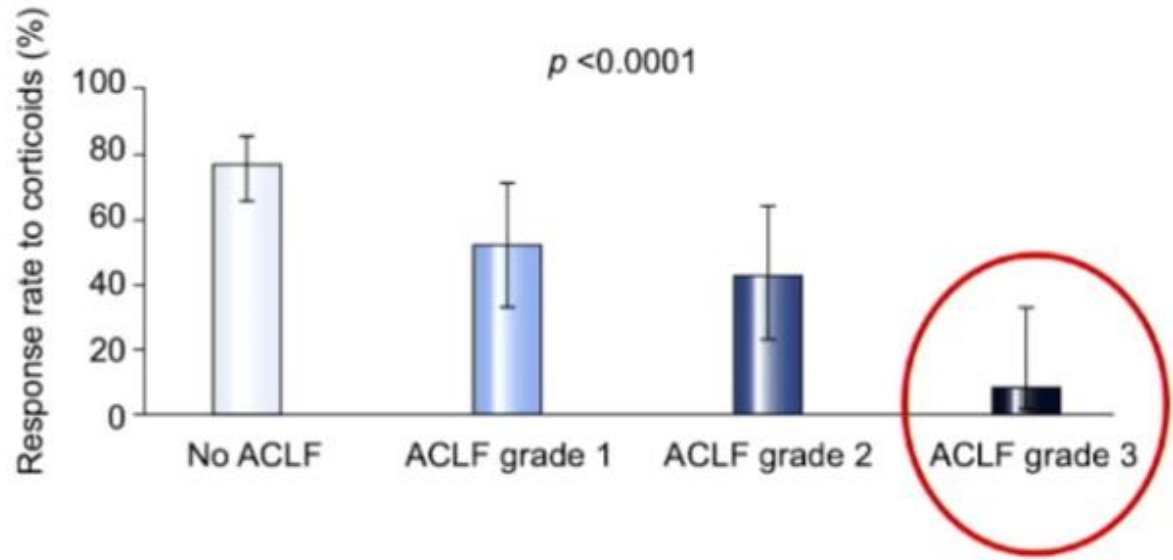
Corticosteroids are ineffective in individuals with severe alcohol-associated hepatitis and early spontaneous improvement: a multicenter randomized controlled trial

Christophe Moreno, Pierre Deltenre, Astrid Marot, Hassane Njimi, Luc Lasser, Delphine Degré, Axel Hittelet, Jean Delwaide, Anja Geerts, Silke François, Boris Bastens, Thierry Gustot, Eric Trepo

Cortisave study investigators

Benefit of steroids not the same for all AAH patients

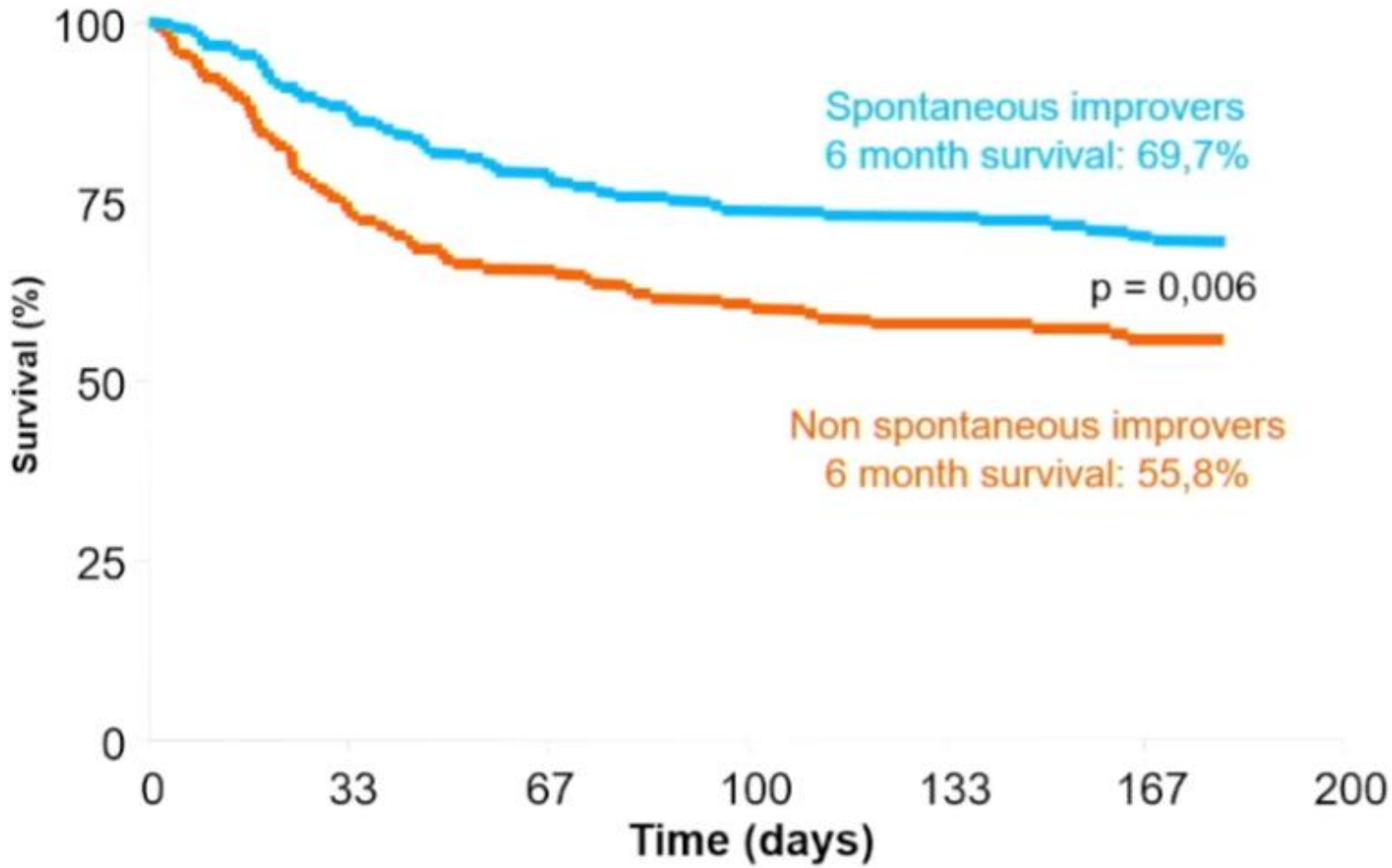




Disease severity

Sersté et al, J Hepatol 2018

Spontaneous serum bilirubin decrease before starting steroids is associated with a better survival



Louvet et al, AASLD 2012

OS-034 Corticosteroids are ineffective in individuals with severe alcohol-associated hepatitis and early spontaneous improvement: a multicenter randomized controlled trial

Background & Aims

- Severe alcohol-associated hepatitis (AH) is a life-threatening disease for which corticosteroid therapy is recommended in the absence of contraindication.
- A significant proportion of patients with severe AH have a spontaneous serum bilirubin decrease early after admission.

Aim: To determine whether corticosteroid therapy is more effective than placebo in individuals with severe AH and early spontaneous improvement.

Methods

Population

- Multicenter, randomised, controlled trial.
- February 2018 and May 2024 in 10 Belgian hospitals .
- 69 patients.
- Age 18 or older, heavy drinkers, recent onset of jaundice, with a biopsy-proven severe AH (mDF ≥ 32 at admission).
- With a spontaneous early improvement (i.e. serum bilirubin level decrease > 10% at day 5-10 after admission).

28-days treatment

- Corticosteroids (CS) (methylprednisolone 32 mg/d).
- Placebo (P).

Endpoints

Primary endpoint was to compare 3-month mortality rate between both groups of treatment.

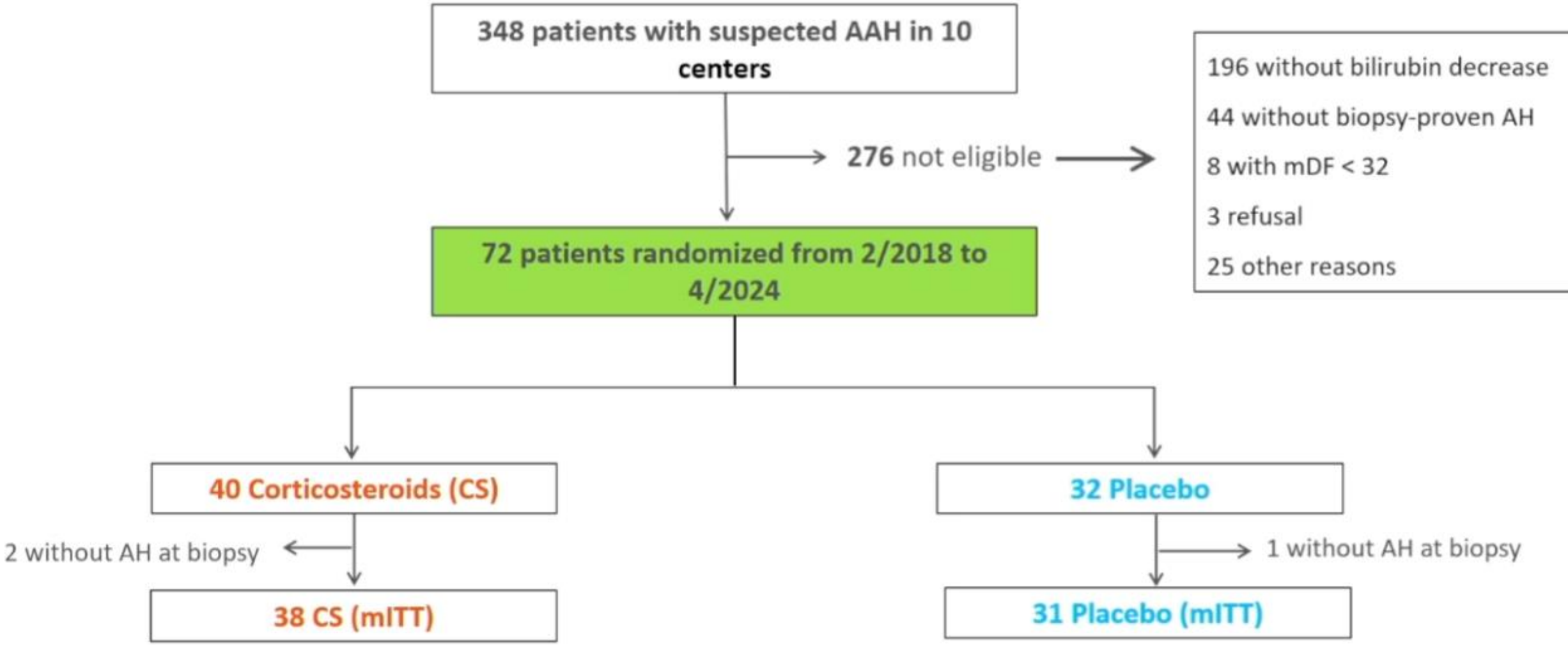
Secondary endpoints were to compare 1-month mortality rate and infection rate during study period between both groups.

Study design

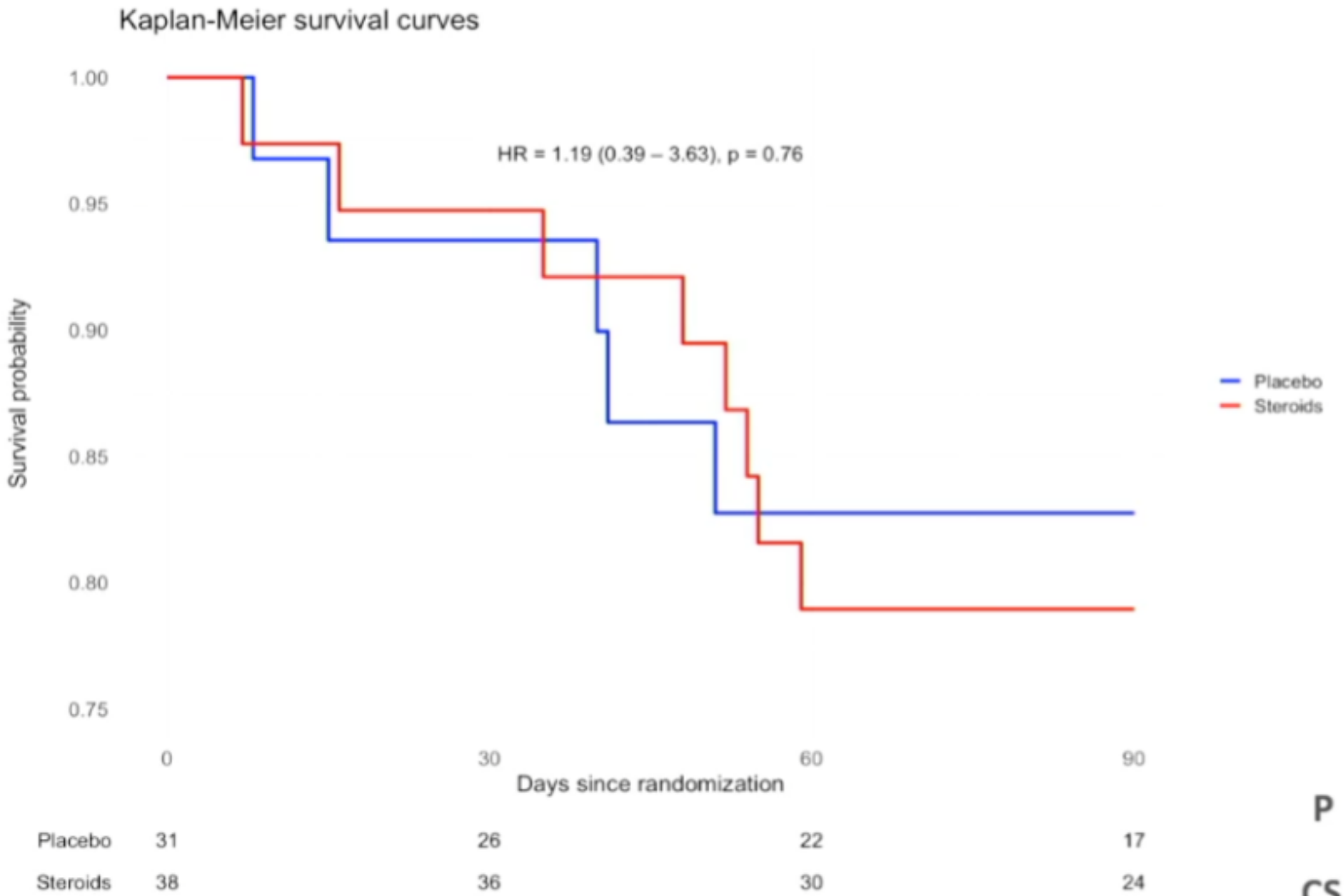
Multicenter, randomized, double blind, placebo-controlled trial

Severe (mDF>32), biopsy-proven AAH

Flow chart


348 patients with suspected AAH in 10 centers
276 not eligible
196 without bilirubin decrease
44 without biopsy-proven AH
8 with mDF < 32
3 refusal
25 other reasons
72 patients randomized from 2/2018 to 4/2024
40 Corticosteroids (CS)
32 Placebo
2 without AH at biopsy
1 without AH at biopsy
38 CS (mITT)
31 Placebo (mITT)

Results: primary endpoint



Survival at 3 Months

	90 Days	p-value[1]	Event N (arm)
		0.76	
P	83% (70%, 98%)		5
CS	79% (67%, 93%)		8

Cox regression (Wald)

Discussion-limitations

- Underpowered study
- Premature study termination
  - Slow recruitement
    - COVID period, decrease in liver biopsy for AH diagnosis, limited number of centers with active recruitment
  - End of insurance cover
- Based on the results observed, a very large number of patients should be recruited to demonstrate a difference in survival between the two groups at 3 months

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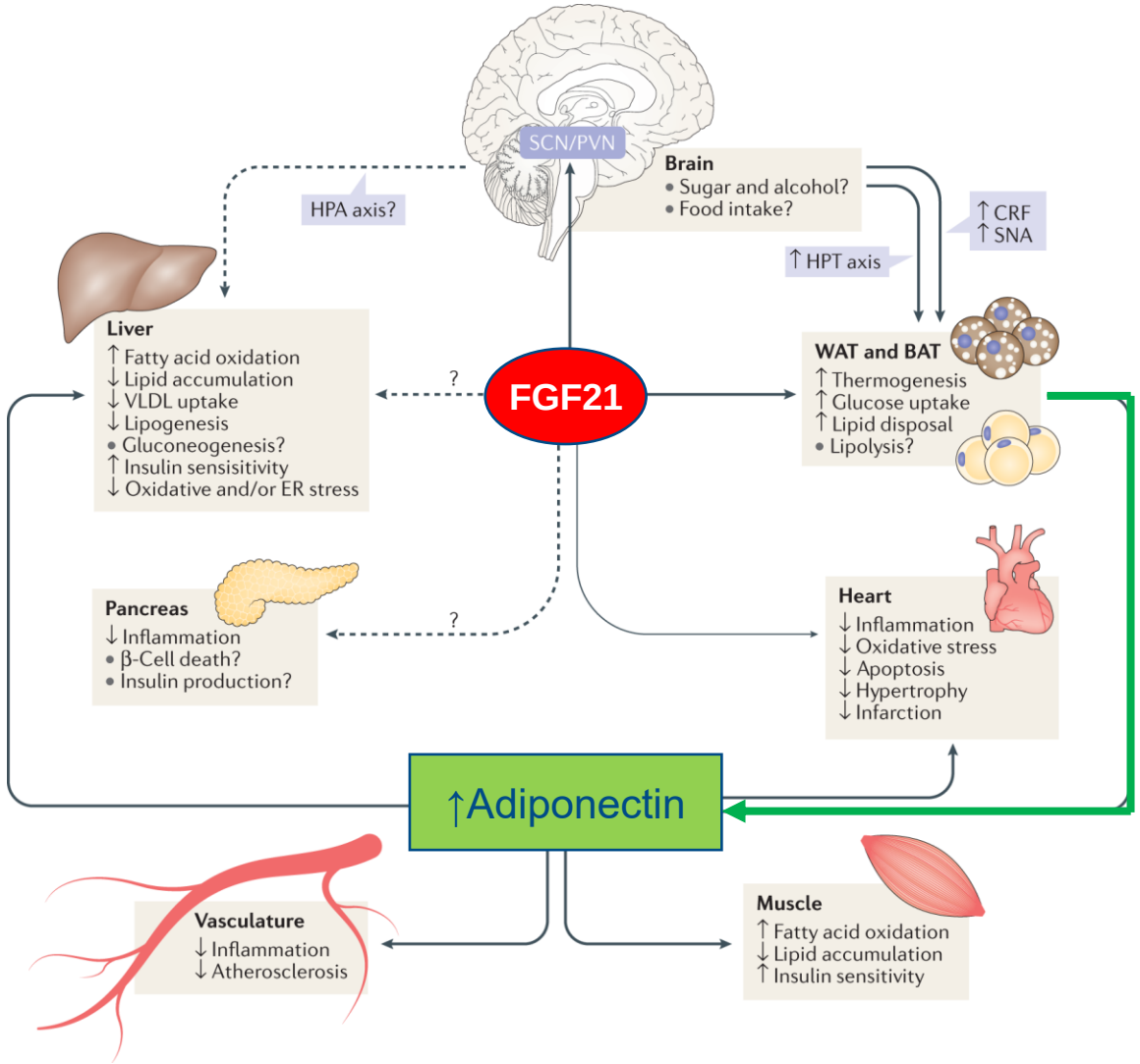
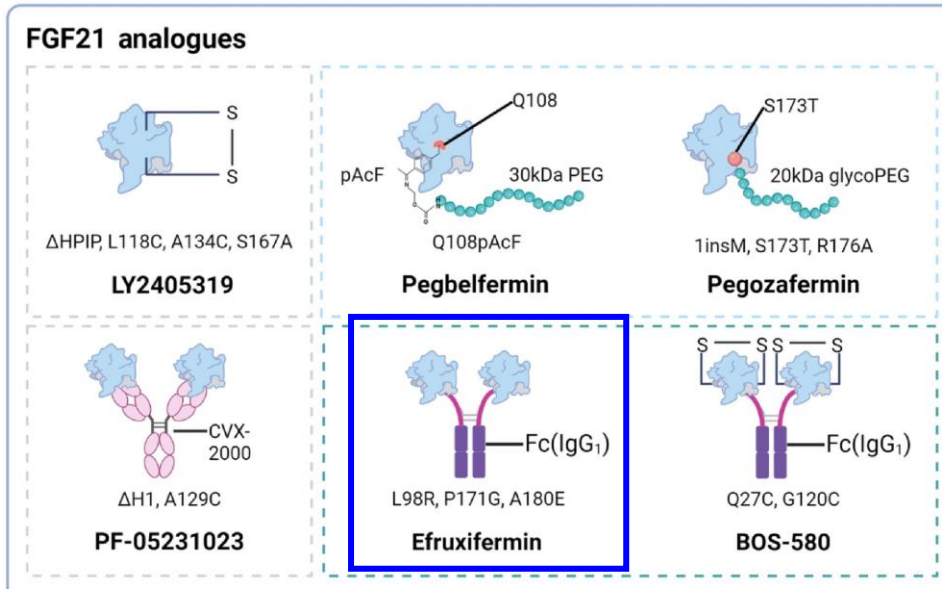
MASLD - Therapy

FGF21 analogues





Increase short half life

→ PEGylating

→ Conjugation with Ig

Chui et al, Trends Endoc Met, 2024

Geng et al, Nat Rev Endoc, 2020

LB25112 Efruxifermin improves fibrosis in participants with compensated cirrhosis due to MASH: results of a 96-week, randomized, double-blind, placebo-controlled, phase 2b trial (SYMMETRY)

Background & Aims

- Metabolic dysfunction-associated steatohepatitis (MASH) is a leading cause of cirrhosis, which can lead to liver failure, hepatocellular cancer, need for transplant, or death.
- There are no approved treatments for cirrhosis due to MASH. Efruxifermin is a bivalent fibroblast growth factor 21 (FGF21) analogue in development for treatment of MASH.

Aim: To assess the efficacy and safety of efruxifermin for 96 weeks in participants with cirrhosis due to MASH.

Methods

➢ Phase 2b, randomised, placebo-controlled, double-blind trial.

Population

181 participants:

- Biopsy-confirmed compensated cirrhosis (F4 fibrosis) due to definitive MASH (78%) or
- Cryptogenic cirrhosis presumed secondary to MASH (22%).

Treatment

- Random assignment (1:1:1).
- Once-weekly subcutaneous efruxifermin (28 or 50 mg) or placebo.

Primary outcome

At least 1-stage fibrosis improvement (cirrhosis reversal) without MASH worsening at Week 36 and at study end (Week 96).

LB25112 Efruxifermin improves fibrosis in participants with compensated cirrhosis due to MASH: results of a 96-week, randomized, double-blind, placebo-controlled, phase 2b trial (SYMMETRY)

Results

Baseline

Age (mean)	61 yrs
Female (%)	67%
BMI (mean)	36 kg/m²
T2D (%)	80%

Efruxifermin treatment in MASH-related cirrhosis

Outcome	Pbo	EFX 28 mg	EFX 50 mg	*p*-value vs placebo
Cirrhosis reversal without MASH worsening				
Week 36 Completer (N = 154)	14%	22%	24%	ns
Week 96 Completer (N = 134)	15%	29%	39%	.131 (28 mg) .009 (50 mg)
Week 96 ITT (N = 181, missing = nonresponse)	11%	21%	29%	.194 (28 mg) .031 (50 mg)
MASH resolution at Week 96 (N = 106)	18%	59%	55%	<.001 (28 mg) .001 (50 mg)

Conclusion

This is the first randomised controlled trial to show pharmacological reversibility of cirrhosis due to MASH. Histology of serial biopsies revealed that longer treatment with 50 mg efruxifermin for 96 weeks resulted in more participants with cirrhosis reversal. These improvements were corroborated by improvements in non-invasive markers of liver fibrosis and injury, as well as metabolic health, suggesting that treatment with efruxifermin may have a positive impact on liver-related outcomes.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efruxifermin in Compensated Liver Cirrhosis Caused by MASH

Mazen Noureddin, M.D.,[1,2] Mary E. Rinella, M.D.,[3] Naga P. Chalasani, M.D.,[4] Guy W. Neff, M.D.,[5] K. Jean Lucas, M.D.,[6] Manuel E. Rodriguez, M.D.,[7] Madhavi Rudraraju, M.D.,[8] Rashmee Patil, M.D.,[8] Cynthia Behling, M.D., Ph.D.,[9] Mark Burch, Ph.D.,[10] Doreen C. Chan, Ph.D.,[10] Erik J. Tillman, Ph.D.,[10] Arian Zari, B.S.,[10] Brittany de Temple, B.S.,[10] Reshma Shringarpure, Ph.D.,[10] Meena Jain, M.B., B.Chir., Ph.D.,[10] Timothy Rolph, D.Phil.,[10] Andrew Cheng, M.D., Ph.D.,[10] and Kitty Yale, B.S.[10]

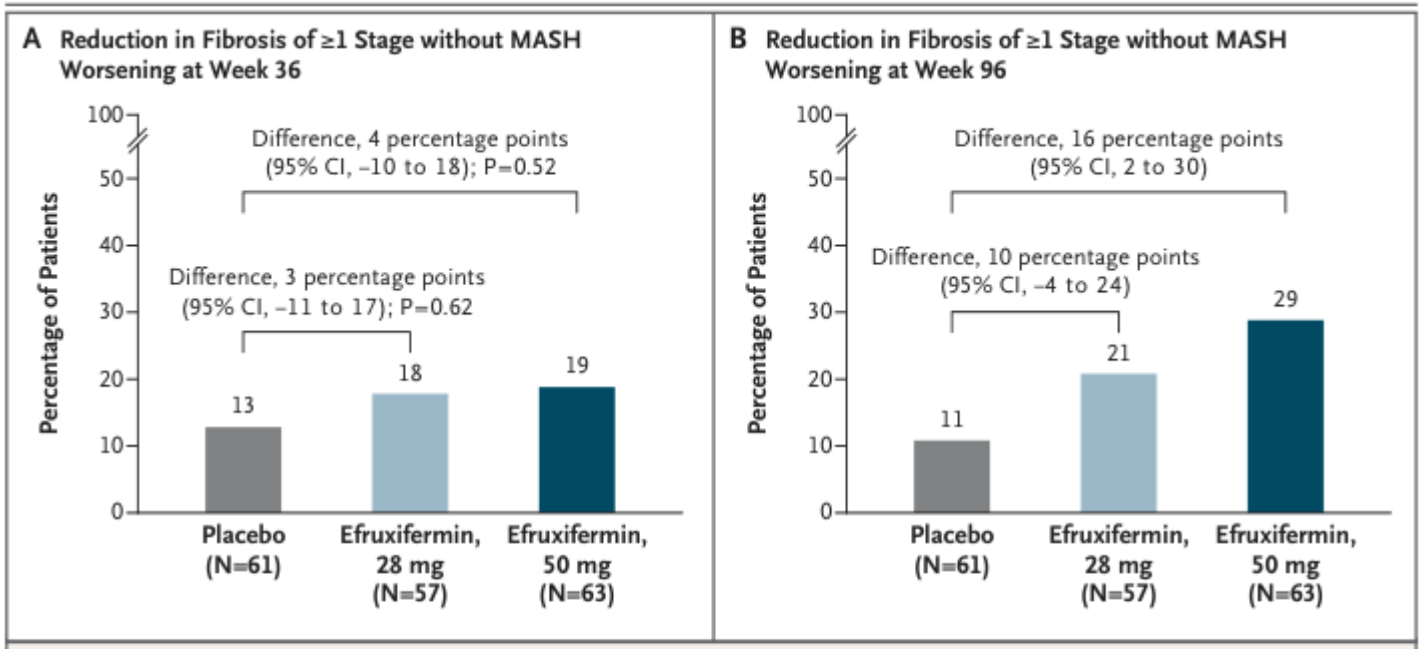


Figure 1. Reduction in Fibrosis without Worsening of MASH.

Shown is the percentage of patients with a reduction in fibrosis without a worsening of metabolic dysfunction–associated steatohepatitis (MASH) at week 36 (primary outcome) (Panel A) and at week 96 (a secondary outcome) (Panel B). MASH worsening was defined as an increase from baseline in any of the subscores of the nonalcoholic fatty liver disease (NAFLD) activity score (NAS): ballooning, inflammation, and steatosis. Data are provided as the mean for the trial group and least-squares-mean difference for the comparison between efruxifermin and placebo with a 95% confidence interval (CI). Confidence intervals have not been adjusted for multiple comparisons and should not be used to infer definitive effects of efruxifermin.

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SLD - Screening

LIVER SCREEN

European Commission

Horizon 2020
European Union funding
for Research & Innovation

High prevalence of undiagnosed liver fibrosis in the adult european population driven by metabolic risk factors and alcohol consumption. Results from the prospective LIVERSCREEN cohort in 30,541 participants

Isabel Graupera*, Maja Thiele*, Laurent Castera, Guillem Pera, Salvatore Piano, Anna Sòria, Núria Fabrellas, Pere Toran, Carla Chacon, Katrine Tholstrup, Helle Lindholm Schnefeld, Marta Tonon, Simone Incicco, Joël Moussy, Vincent Levy, Anita Madir, Sandro Kukic, Daniel Jan Havaj, Svetlana Adamcova-Selcanova, Jesse Pustjens, Laurens van Kleef, Alba Jimenez, Laura Pagès, Mirko Zoncapè, Susanne Weber, Peter Galle, Rebecca Harris, Luis Ibáñez-Samaniego, Alba Diaz, Sönke Detlefsen, Miquel Serra-Burriel, Anita Arslanow, Peter Andersen, Judit Pich, Eva Bonfill, Marco Korenjak, Celine Fournier, Anne Llorca, Marie-Caroline Gourmelon, Harry J de Koning, Jose Lluis Falcó, Adrià Juanola, Elisa Pose, Ingrid Arteaga, Laura Muñoz, Ida Villesen, Johanne Kragh Hansen, Valeria Calvino, Roberta Gagliardi, Bahija Boutouria, Frane Pastrovic, Petra Dinjar Kujundzic, Daniela Zilincanova, Karolina Kristina Sulejova, Diego Rojo, Rob de Knegt, Maykon Diego Melo, Antonio Torrejón, Rosario Hernandez, Jordi Hoyo, Raquel López-Martos, Montserrat Garcia-Retortillo, Rosa M Morillas, Michael Manns, Tom Karlsen, Phil Newsome, Patrick Kamath, Rafael Bañares, Indra N Guha, Jörn M Schattenberg, Frank Lammert, Emmanouil Tsochatzis, Willem P Brouwer, Juan M Pericàs, Lubomir Skladany, Ivica Grgurevic, Dominique Roulot, Paolo Angeli, Aleksander Krag, Llorenç Caballeria, Pere Ginès **for the LiverScreen Consortium investigators.**

LB2553 High prevalence of undiagnosed liver fibrosis in the adult European population driven by metabolic risk factors and alcohol consumption. results from the prospective liverscreen cohort in 30,541 subjects

Background & Aims

- Findings from small-scale, single-country cohorts suggest that undiagnosed liver fibrosis resulting from chronic liver disease is common in the general population.
- However, the exact prevalence and main risk factors remain incompletely understood.

Aim: To investigate the prevalence of undiagnosed liver fibrosis in a prospective large-scale multi-national European cohort and determine the association between liver fibrosis and metabolic risk factors and/or alcohol consumption.

Methods

Population

30,541 participants:
- May 2018 - December 2024
- Older than 40 years
- Without known liver disease
- From the general population in 9 European countries

Data collection
- Demographic data
- Clinical data
- Standard lab parameters

+

Liver fibrosis

Assessed by liver stiffness measurement (LSM) using vibration controlled transient elastography (Fibroscan®).

Subjects' selection

Since LSM < 8kPa rules out significant fibrosis, only subjects with LSM ≥ 8kPa, and/or ALT ≥ 1.5.

Evaluation of liver disease

Primary outcome
- Prevalence of LSM ≥ 8kPa.

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RECRUITMENT

Walking-in

Letter

Phone-call

PRIMARY CARE CENTER

1. **Medical history**
2. **Physical exam**
3. Assessment of **alcohol consumption** (drinks/week & AUDIT-C)
4. **Blood tests** + biobanking
5. **VCTE** to assess liver stiffness measurement (**LSM**) and controlled attenuation parameter (**CAP**).

INCLUSION & EXCLUSION CRITERIA

- Age > 40 years old
- Able to give written informed consent
- Previously known chronic liver disease
- Current malignancy
- Significant extrahepatic disease (impaired short-term prognosis)

Unreliable or failure LSM

LSM ≥ 8kPa and/or ALT ≥1.5 ULN

Complete evaluation for diagnosis and staging of chronic liver disease (CLD)

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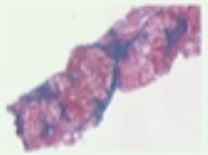
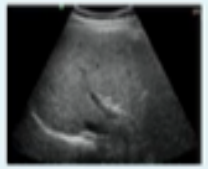
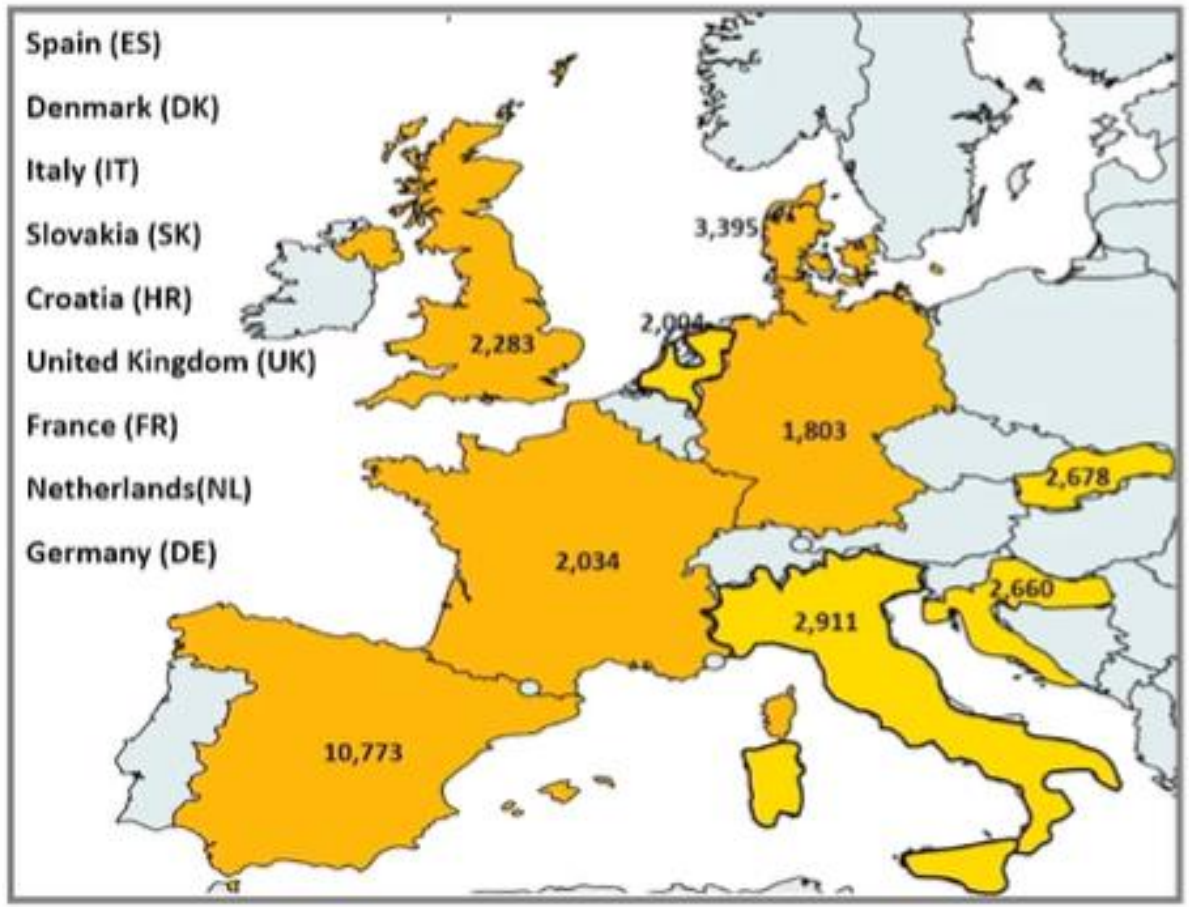
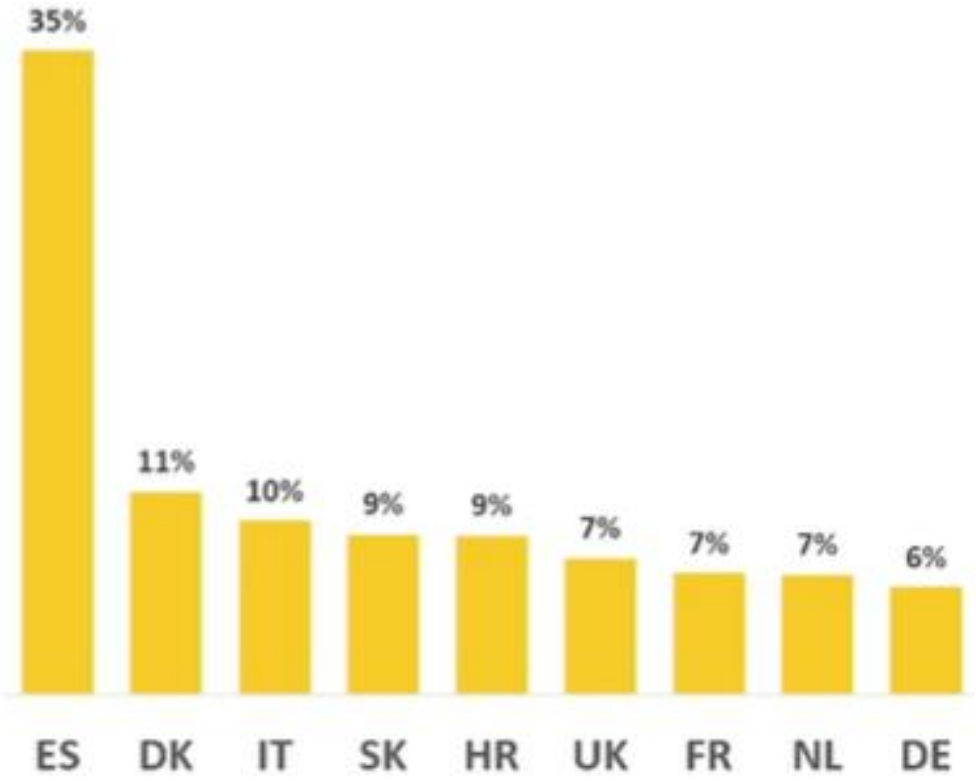
Diagnostic criteria to establish the presence of significant chronic liver disease

	1. **Liver Biopsy** with fibrosis ≥ F1
 	2. In those **without liver biopsy,** at least one of following: a) Radiological signs of chronic liver disease in **abdominal ultrasound* (≥2 criteria)** or b) **LSM ≥ 10 kPa**

*Chronic liver disease criteria on Abd US: heterogeneous parenchyma, enlarged right liver lobe, enlarged left liver lobe including caudate lobe, irregular lobular surface, rounded edges, extrahepatic collaterals, spleen length >13cm, Ascites

Distribution of participants included by country





LB2553 High prevalence of undiagnosed liver fibrosis in the adult European population driven by metabolic risk factors and alcohol consumption. results from the prospective liverscreen cohort in 30,541 subjects

Results

Demographics

Mean age	58 years
Female	57%
Caucasian	89%

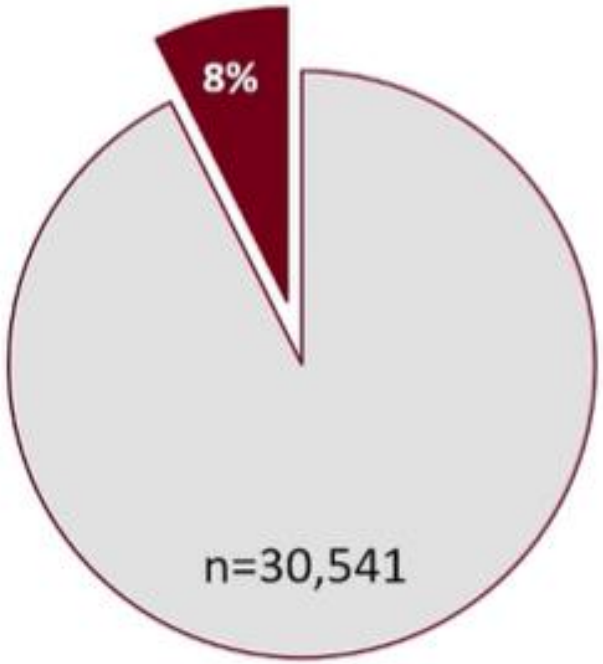
Metabolic risk factors and alcohol use

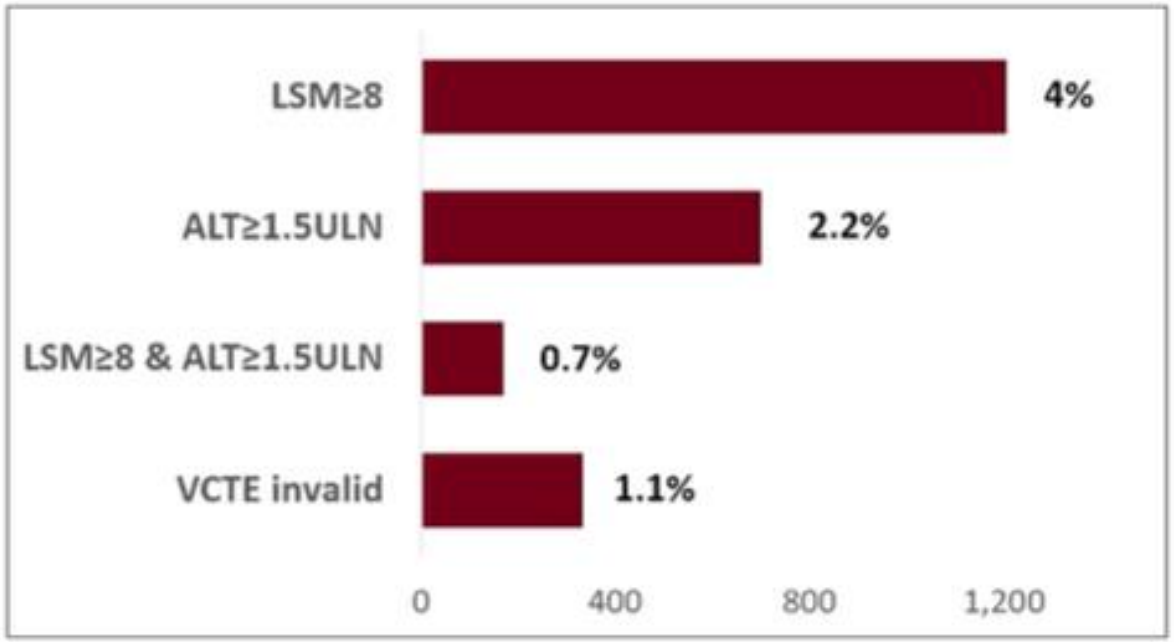
Metabolic risk factors	
Overweight / Obesity	40% / 26%
Dyslipidemia	53%
Arterial hypertension	35%
Type 2 diabetes (T2D)	10%
Alcohol use	
Hazardous consumption (SDU ≥14-21/w or AUDIT-C≥5)	18%
High-risk consumption (SDU≥35-42/w or AUDIT-C≥8)	3.4%

Prevalence and predictors of liver fibrosis

Liver stiffness measurement (LSM)	
Prevalence of LSM ≥ 8kPa	4.6%
Prevalence of LSM ≥ 10 kPa / ≥ 15 kPa	2.5% / 0.8%
Strongest predictors of LSM ≥ 8 kPa	Obesity (OR 3.8), T2D (OR 3.0), high-risk alcohol (OR 2.5)
Steatosis (CAP ≥ 275 dB/m)	32%
LSM ≥ 8 kPa with / without steatosis	8.8% vs 2.6%
Chronic liver disease diagnosis	Confirmed in 31% of referred subjects (67% via biopsy)
Main etiologies	MASLD, ALD, MetALD

Patients referred to the hospital for further evaluation

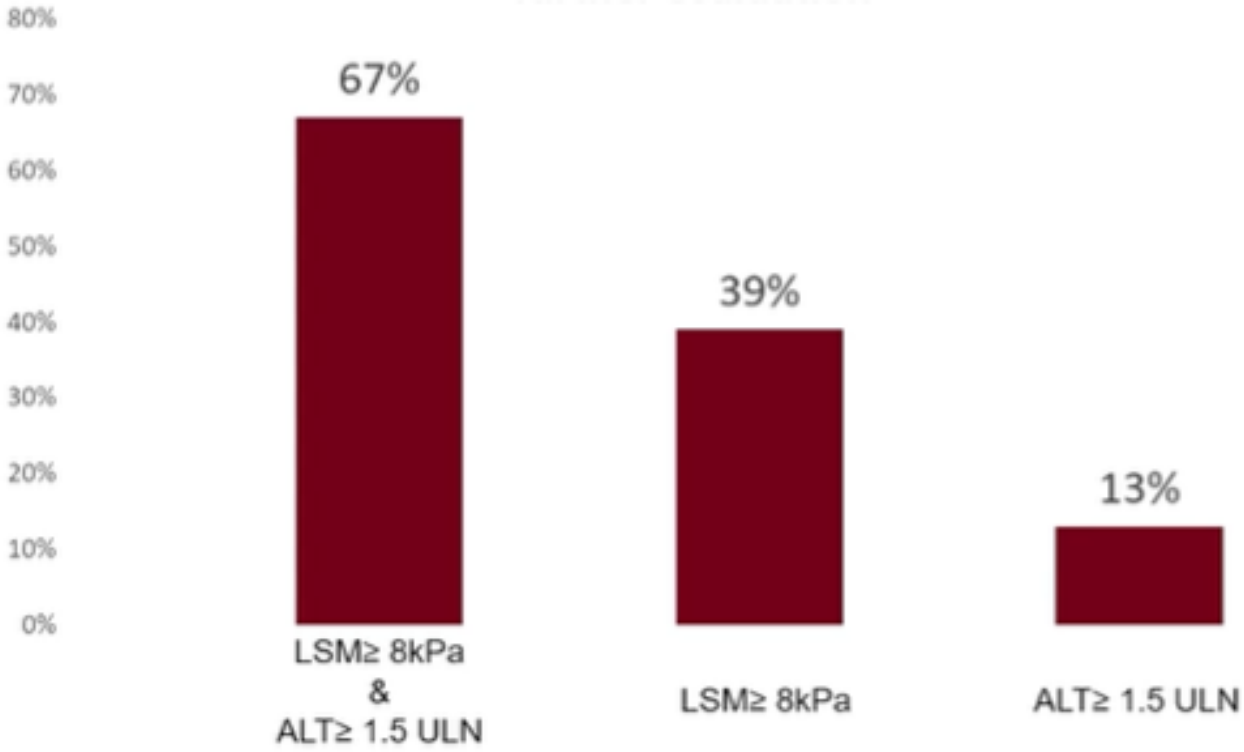




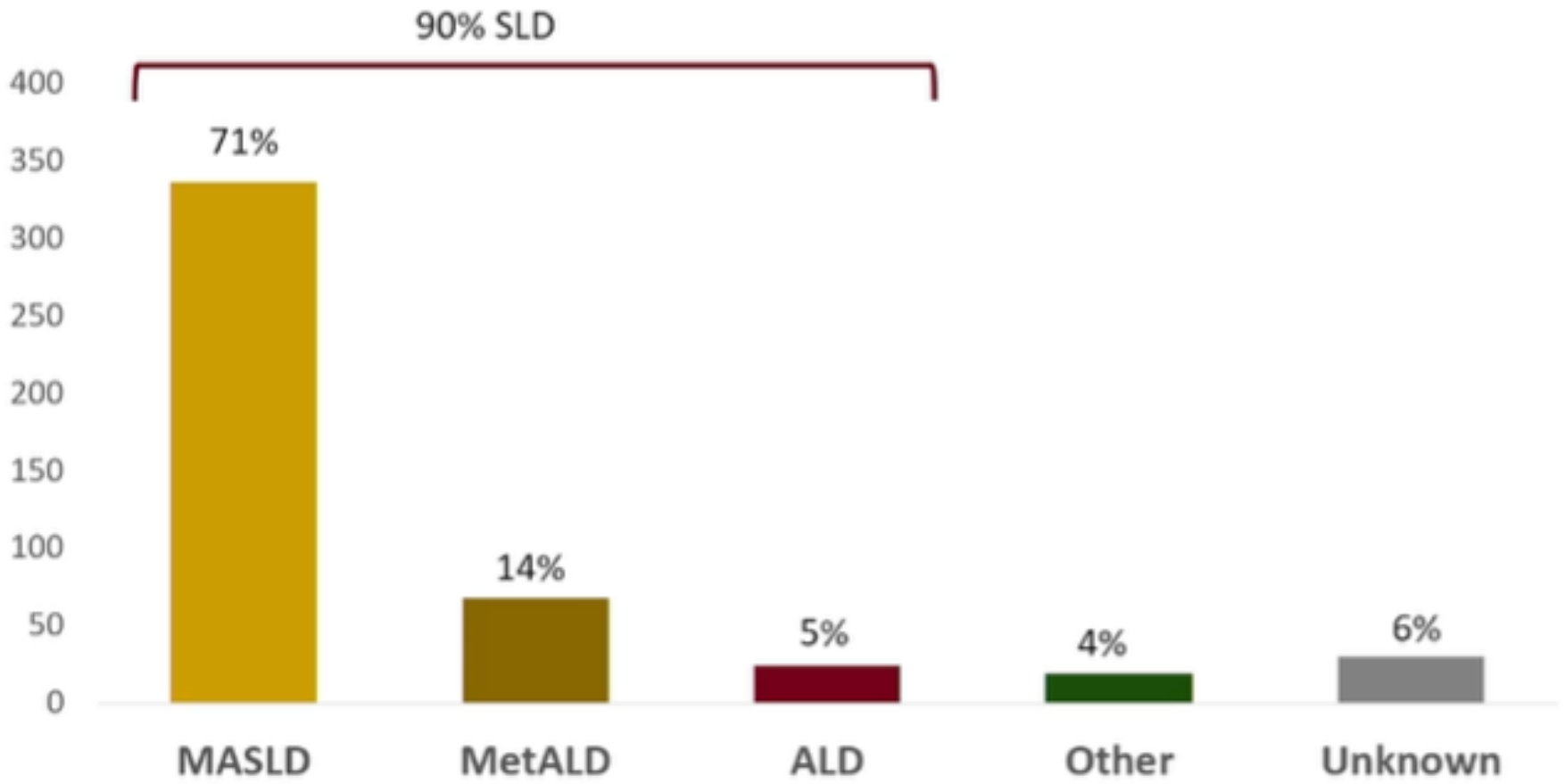
Prevalence of chronic liver disease with liver fibrosis

From patients referred	32%
Overall	1.5%

Prevalence of CLD according to the cause of referral for further evaluation



Distribution of aetiologies in patients with CLD (n= 477)



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Chronic liver disease diagnosis	Confirmed in 31% of referred subjects (67% via biopsy)
Main etiologies	MASLD, ALD, MetALD

Conclusion

In this large-scale European cohort, we found a remarkably high prevalence of undiagnosed liver fibrosis mainly related to steatotic liver disease driven by metabolic risk factors and/or high-risk alcohol consumption. Efforts should be made to identify liver fibrosis early to apply specific therapies that could reverse liver fibrosis.

NL#TIMES TOP STORIES HEALTH CRIME POLITICS BUSINESS
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The Amsterdam RAI Exhibition and Convention Centre, 13 September 2010 - Credit: Adam Kliczek / Wikimedia Commons - License: CC-BY-SA

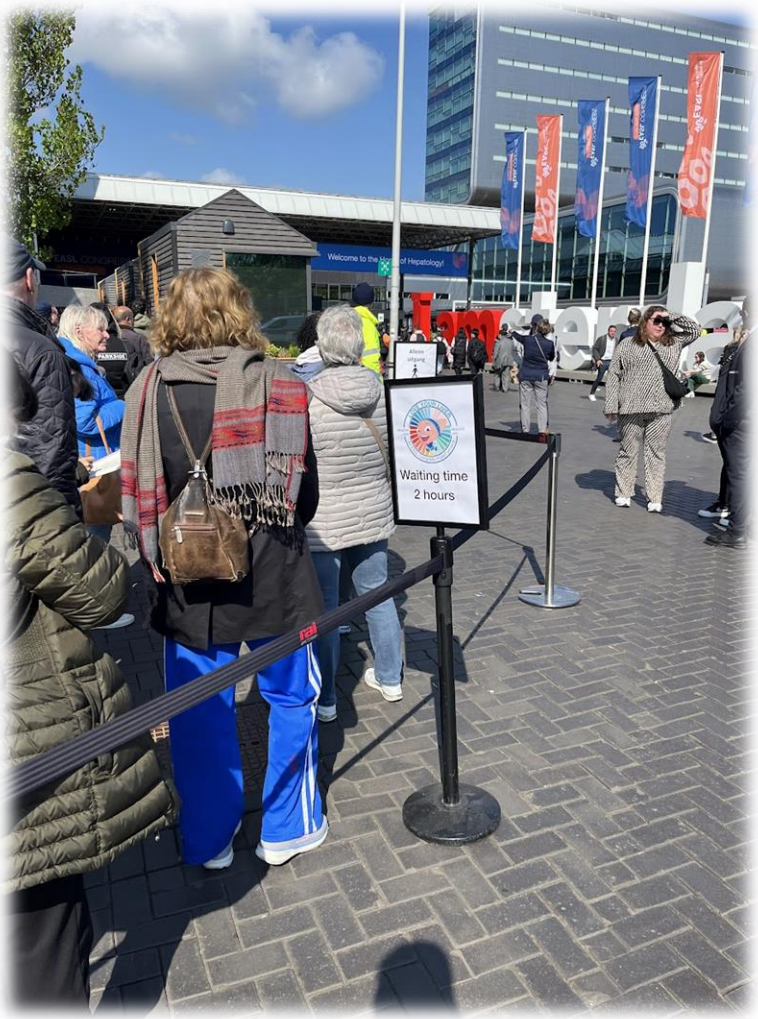
HEALTH BUSINESS RAI AMSTERDAM LIVER DISEASE
LIVER DAMAGE LIVER ABNORMALITIES » MORE TAGS

SUNDAY, 11 MAY 2025 - 13:05

Hundreds get free liver scans in Amsterdam as experts warn of surge in liver disease

Approximately 850 people underwent free liver scans this week at the RAI Amsterdam convention center, where the European Association for the Study of the Liver (EASL) held its annual medical conference through Saturday.

Since Tuesday, visitors could walk in to receive a fibroscan — a non-invasive test that measures liver stiffness and fat content. The free screenings drew long lines, highlighting rising public interest in liver health. Dr. Bart Takkenberg of Amsterdam UMC welcomed the turnout, calling the increased attention to the liver “very positive.”



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