Metabolic Dysfunction–Associated Steatohepatitis (MASH): Du Diagnostic au Traitement

Philippe Mathurin

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Lille

Liens d’intérêt

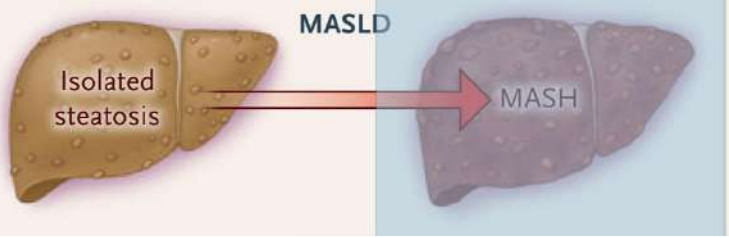
- Abbvie, Astra Zenneca, Boehringer Ingelheim, Gilead Sciences, GSK, Ipsen, Madrigal, Roche

MAFLD: Histoire naturelle

Diagnostic criteria for adult MASLD — hepatic steatosis plus ≥1 trait of metabolic syndrome in the absence of secondary causes of steatosis

Traits of metabolic syndrome:

- BMI ≥25 (≥23 in Asian persons), waist circumference ≥94 cm in men (≥90 cm in Asian men) and ≥80 cm in women
- Fasting glucose level ≥5.6 mmol per liter, glycated hemoglobin level ≥39 mmol per liter, established type 2 diabetes, or treatment with medication
- Blood pressure ≥130/85 mm Hg or medication for hypertension
- Plasma triglyceride level ≥1.70 mmol per liter or triglyceride-lowering medication
- Plasma HDL cholesterol <1.0 mmol per liter for men and <1.3 mmol per liter for women or cholesterol-lowering medication



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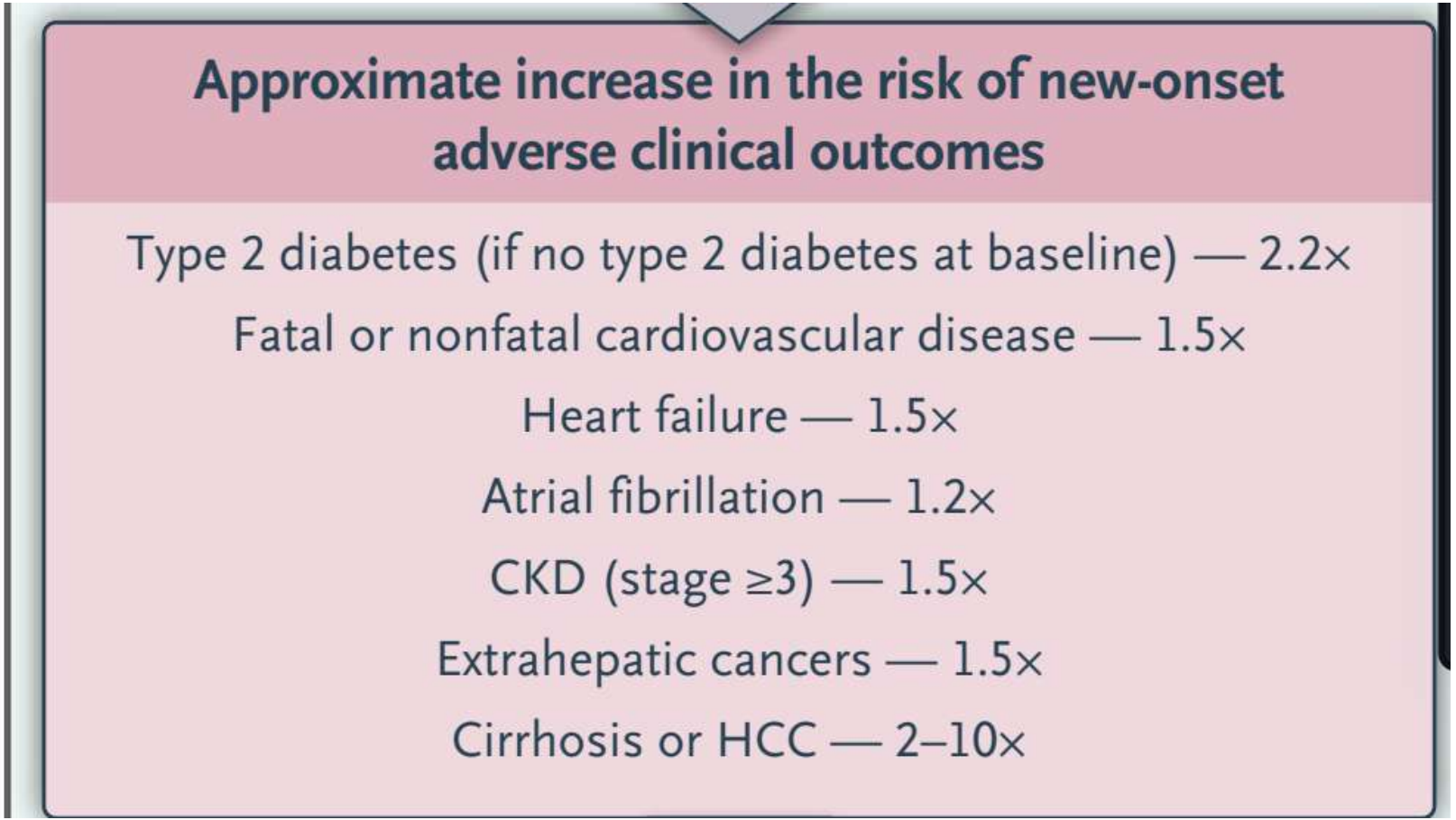
MAFLD: Histoire naturelle



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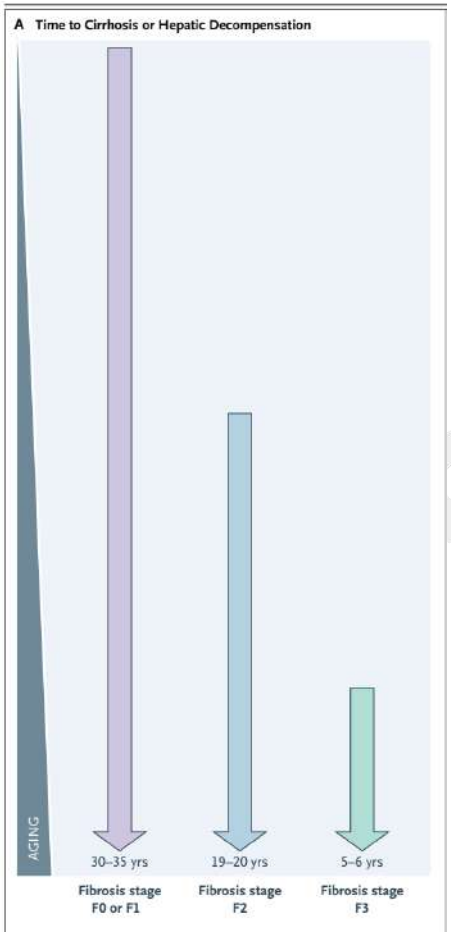

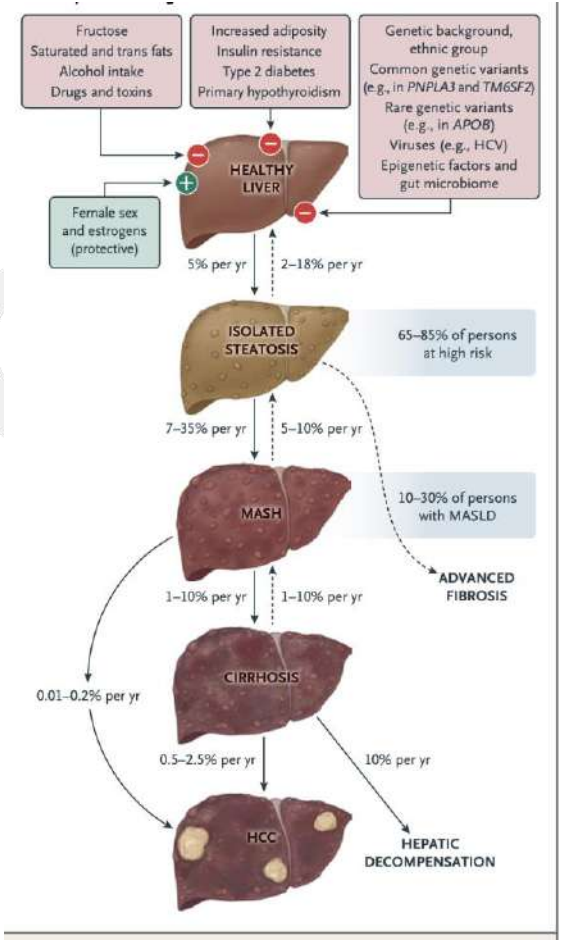

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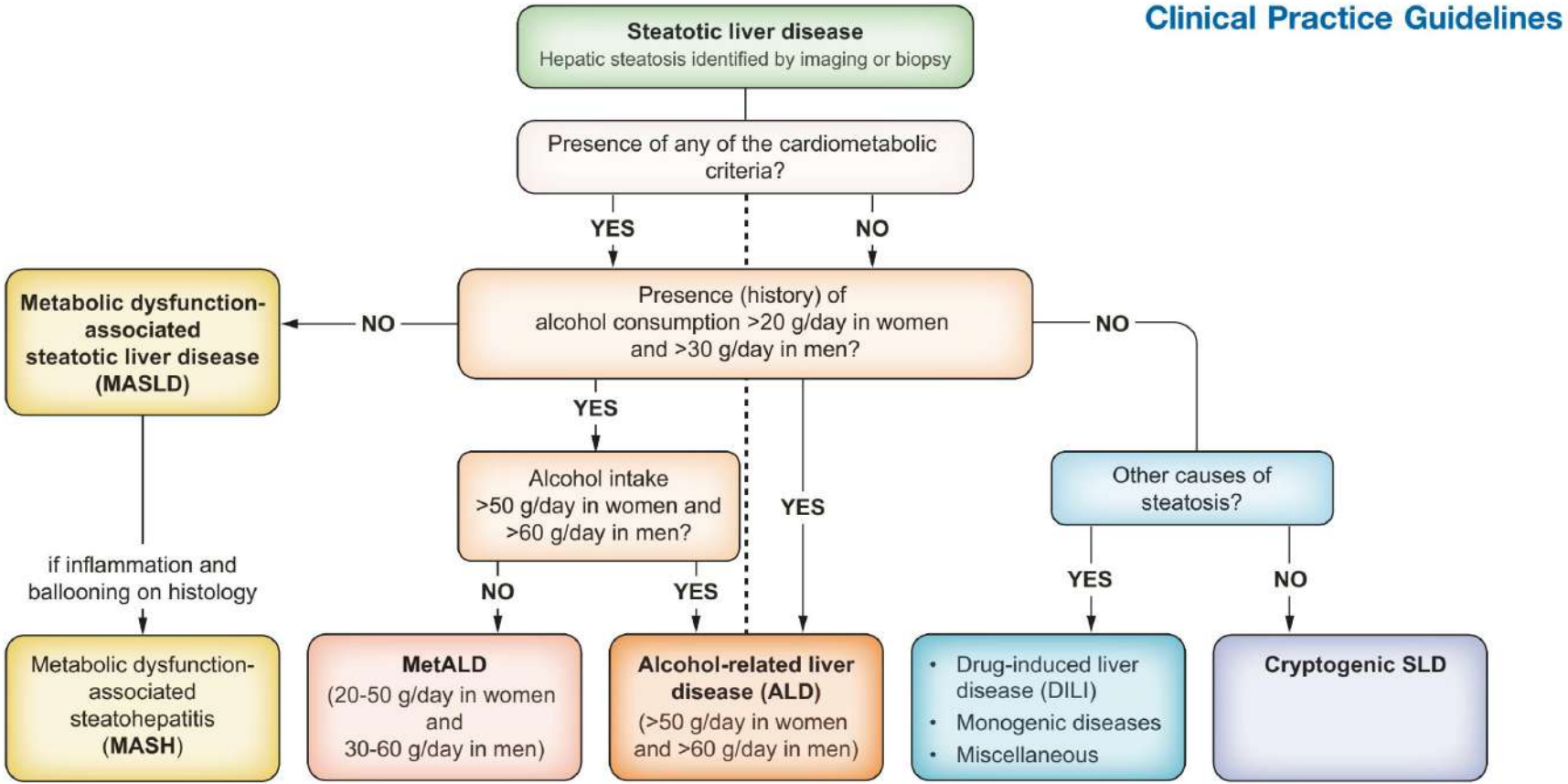
MAFLD: Approche diagnostique

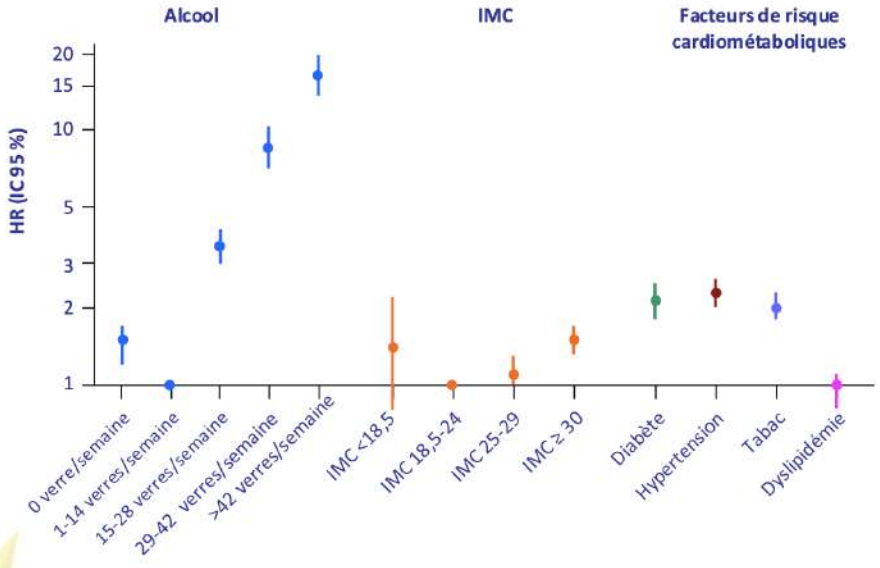


EASL Guidelines J Hepatol 2024

Faut il modifier les seuils de la Met ALD?

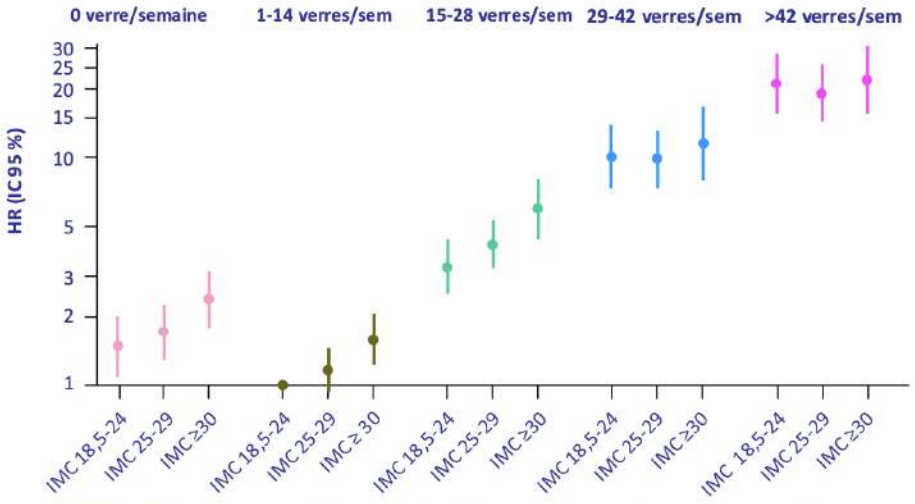
- Etude danoise sur 350 000 individus
  - Suivi de 3,3 millions personne-année de 2010-2017
  - 35 761 décès, 1 211 cas de cirrhose

La consommation d'alcool a un impact majeur sur le risque d'évolution vers la cirrhose



- **Alcool, diabète, HTA, tabac plus importants que l'IMC**

Risque d'évolution vers la cirrhose
L'impact de l'IMC diminue avec l'augmentation de la consommation d'alcool

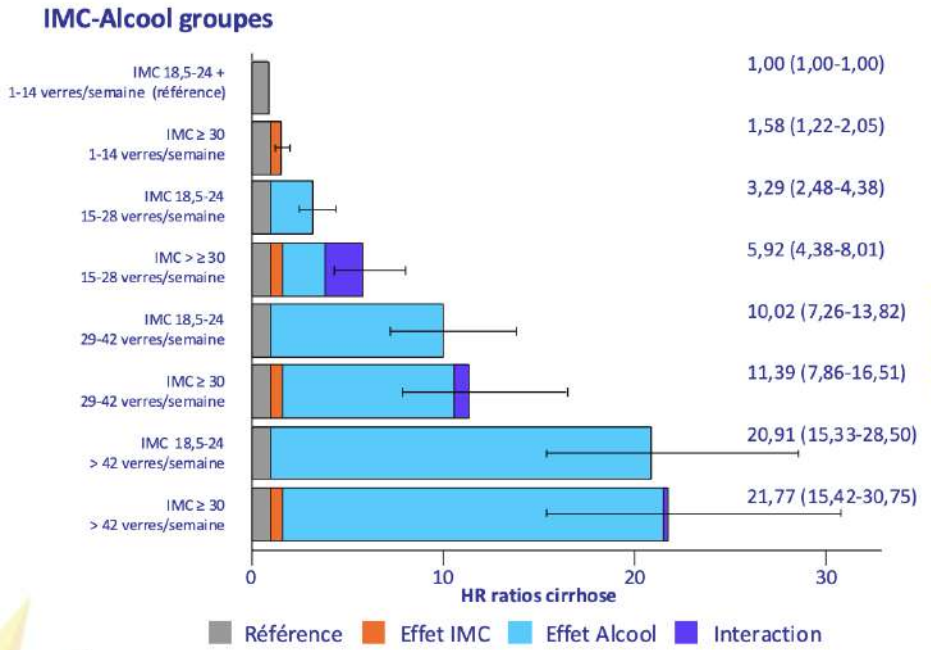


- **L'IMC ≥ 30 augmente le risque de cirrhose en cas de consommation hebdomadaire d'alcool entre 1 et 28 verres**
- **L'IMC ≥ 30 n'augmente pas le risque de cirrhose en cas de consommation hebdomadaire d'alcool ≥ 29 verres**

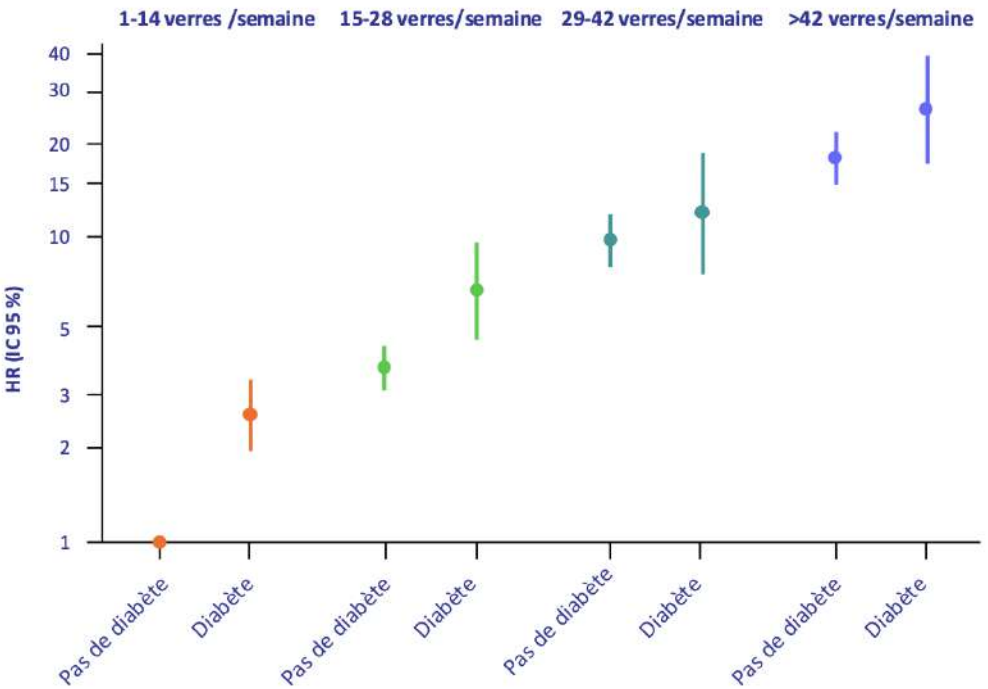
Rønn J, Danemark, AASLD 2025, Abs. 0039 actualisé

Faut il modifier les seuils de la Met ALD?

Risque d'évolution vers la cirrhose
L'interaction IMC-Alcool disparait avec consommation élevée d'alcool



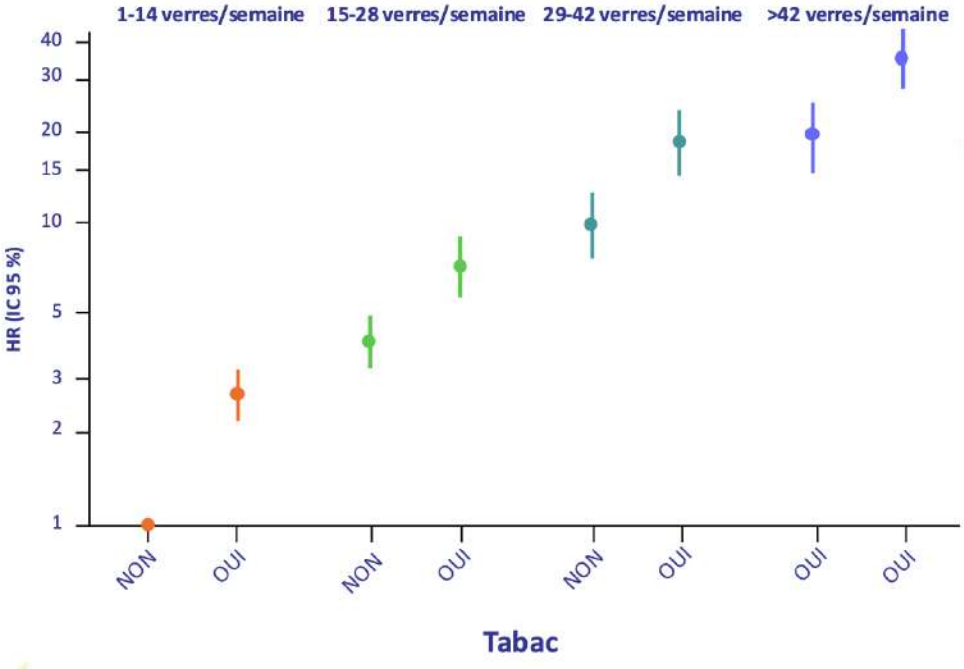
Risque d'évolution vers la cirrhose
L'impact du diabète diminue avec la quantité d'alcool consommé



Rønn J, Danemark, AASLD 2025, Abs. 0039 actualisé

Faut il modifier les seuils de la Met ALD?

Risque d 'évolution vers la cirrhose
L'interaction Tabac-Alcool persiste quelque soit la consommation d'alcool



NB : pas d'effet de la dyslidémie

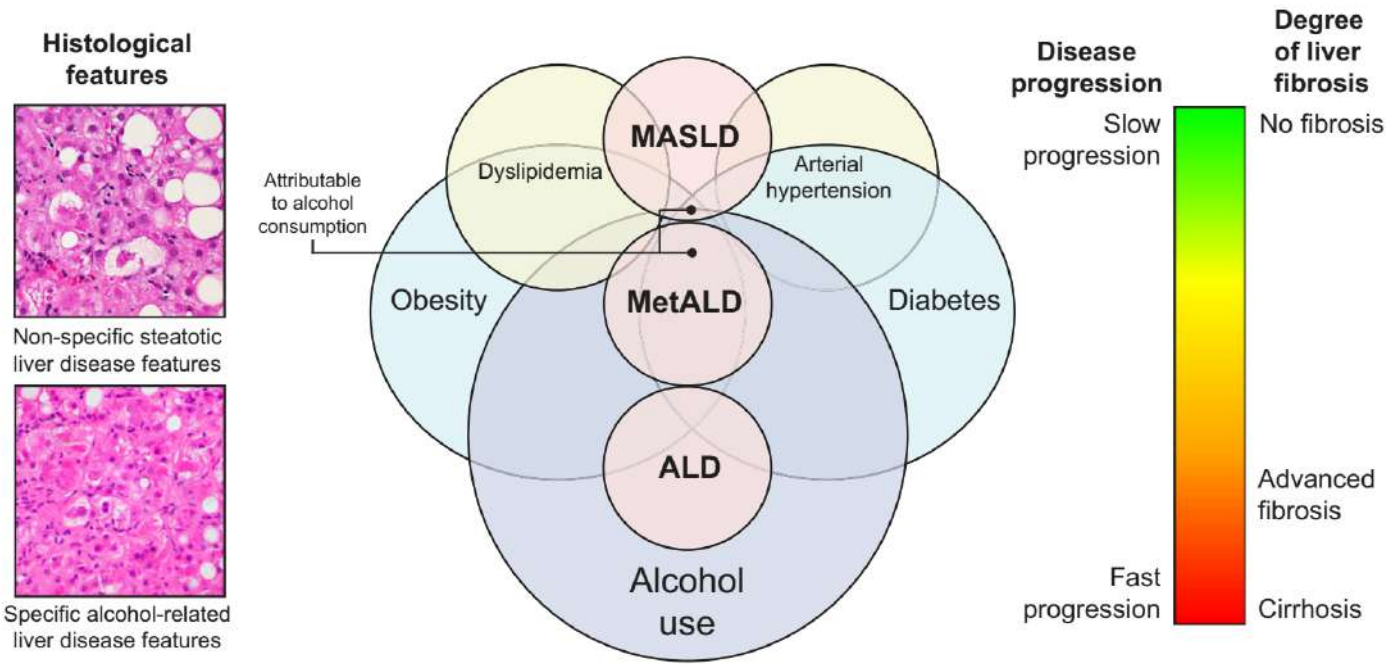
- **Conclusions**
  - L'obésité, le diabète, l'HTA et le tabac augmentent le risque de cirrhose
  - La dyslipidémie n'a pas d'impact sur le risque de cirrhose
  - La fraction attribuable à l'alcool est beaucoup plus importante
  - L'interaction entre le syndrome métabolique et l'alcool augmente jusqu'à 28 verres/semaine puis diminue constamment
  - Seul le tabac conserve un effet synergique indépendamment de la consommation d'alcool

Rønn J, Danemark, AASLD 2025, Abs. 0039 actualisé

Metabolic dysfunction and alcohol-related liver disease (MetALD): Position statement by an expert panel on alcohol-related liver disease

JOURNAL OF HEPATOLOGY

Juan Pablo Arab[1,2,*,†], **Luis Antonio Díaz**[2,3,†], **Jürgen Rehm**[4,†], **Gene Im**[5,†], Marco Arrese[2], Patrick S. Kamath[6], Michael R. Lucey[7], Jessica Mellinger[8], Maja Thiele[9], Mark Thursz[10], Ramon Bataller[11], Robyn Burton[12], Shilpa Chokshi[13], Sven M. Francque[14], Aleksander Krag[9], Carolin Lackner[15], Brian P. Lee[16], Suthat Liangpunsakul[17], Craig MacClain[18], Pranoti Mandrekar[19], Mack C. Mitchell[20], Marsha Y. Morgan[21], Timothy R. Morgan[22], Elisa Pose[11], Vijay H. Shah[6], Debbie Shawcross[23], Nick Sheron[24], Ashwani K. Singal[18], Horia Stefanescu[25], Norah Terrault[16], Eric Trépo[26], Christophe Moreno[26,‡], Alexandre Louvet[27,‡], Philippe Mathurin[27,*,‡]



J Hepatol 2025

MAFLD: Evaluation non Invasive

Non-invasive test	Biological processes reflected	Rule-out cut-off	Rule-in cut-off	Prediction of liver-related outcomes
Primary target: Hepatic steatosis				
US scan – standard	Lipid content	N/A	N/A	+
VCTE: CAP (Controlled attenuation parameter)[166]	Lipid content		S1: 248 dB/m S2: 268 dB/m S3: 280 dB/m	?
MRI – MRI-PDFF[163]	Lipid content		S1: 5% S2: 11-18% S3: 16-23%	+

EASL Guidelines J Hepatol 2024

MAFLD: Evaluation non Invasive

Non-invasive test	Biological processes reflected	Rule-out cut-off	Rule-in cut-off	Prediction of liver-related outcomes
Primary target: Hepatic fibrosis				
FIB-4[140,158,184]	Stress to hepatocytes, hypersplenism	F2: 0.66-0.89 F3: 1.3	F2: 2.67 F3: 2.67	++
VCTE: LSM (liver stiffness)[156,184,259]	Fibrosis, extracellular volume fraction	F3: 8 kPa	F3: 12 kPa	+++
US – 2D-SWE[155]	Fibrosis, extracellular volume fraction	F3: 8 kPa	F3: 10.5 kPa	+++
MRI – MRE[170,358]	Fibrosis, extracellular volume fraction		F2: 3.14 kPa F3: 3.53 kPa F4: 4.45 kPa	+++

EASL Guidelines J Hepatol 2024

MAFLD: Evaluation non Invasive

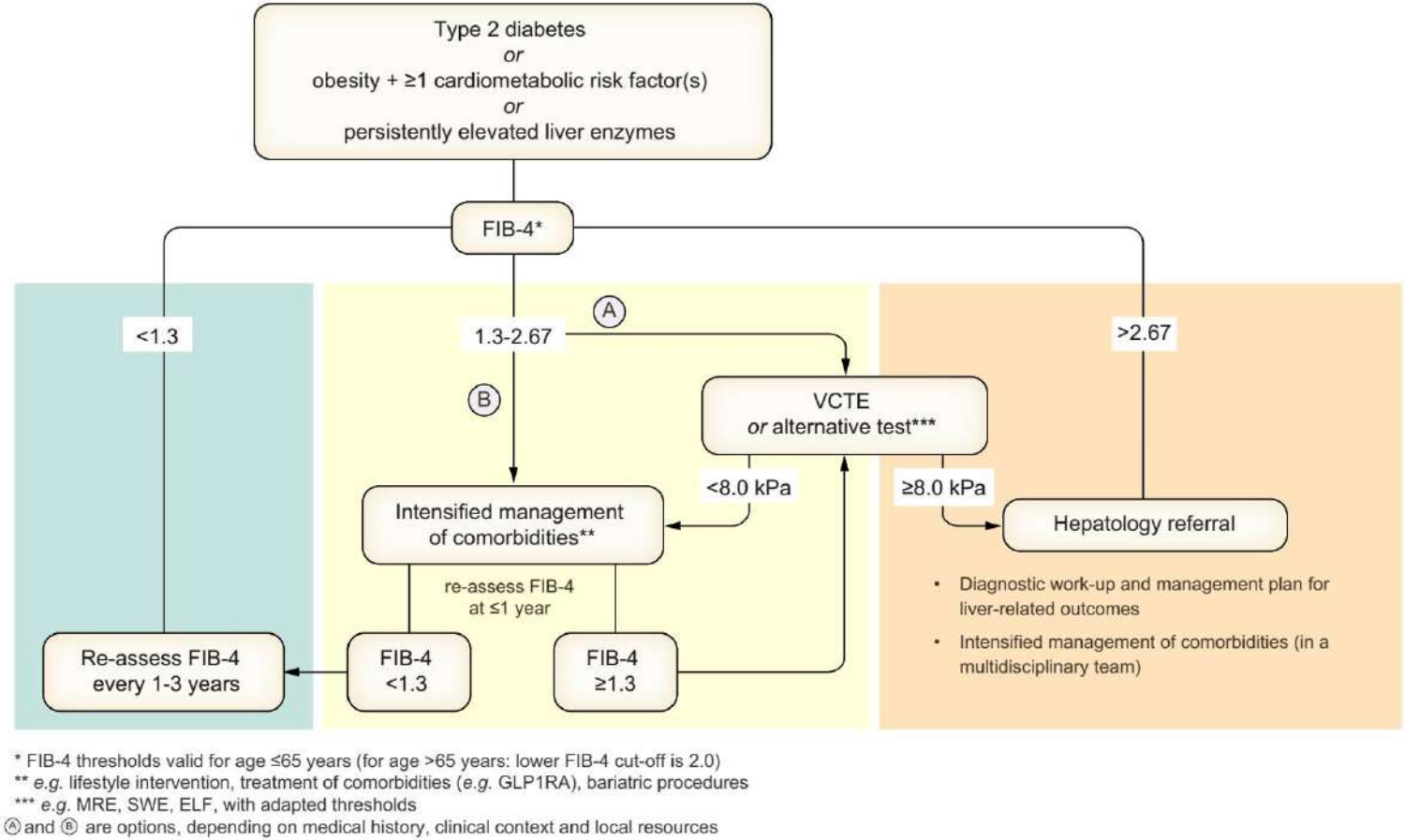
Non-invasive test	Biological processes reflected	Rule-out cut-off	Rule-in cut-off	Prediction of liver-related outcomes
Primary target: "At-risk MASH"				
FAST[168,184]	Stress to hepatocytes, fibrosis, lipid content	0.35	0.67	++
MAST[167]	Stress to hepatocytes, fibrosis, lipid content	0.165	0.242	++
Corrected T1[160]	Extracellular volume fraction, (fibrosis)	825 ms	875 ms	++
NIS2+[352]	Stress to hepatocytes, fibrosis, extracellular matrix remodelling	0.46	0.68	?

Combined scores for fibrosis diagnosis that use blood analyses and imaging results (elastography and steatosis evaluation) have been proposed and tested in recent years:

- MAST = MRE + MRI-PDFF + AST;[167]
- FAST = VCTE (LSM, CAP) + AST;[168]
- MEFIB = MRE + FIB-4.[169,170]

EASL Guidelines J Hepatol 2024

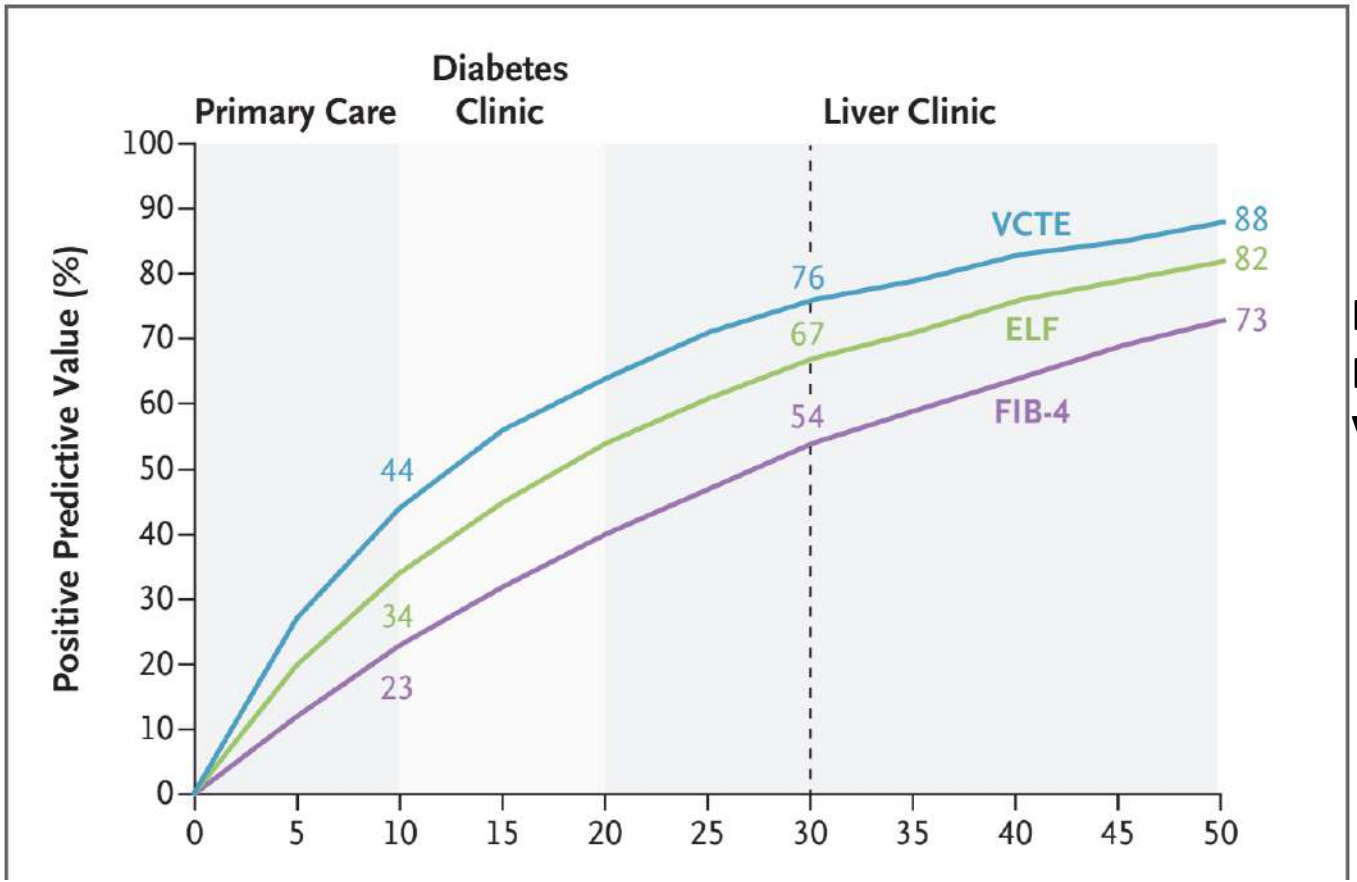
MAFLD: Evaluation non Invasive



* FIB-4 thresholds valid for age ≤65 years (for age >65 years: lower FIB-4 cut-off is 2.0)
** *e.g.* lifestyle intervention, treatment of comorbidities (*e.g.* GLP1RA), bariatric procedures
*** *e.g.* MRE, SWE, ELF, with adapted thresholds
Ⓐ and Ⓑ are options, depending on medical history, clinical context and local resources

EASL Guidelines J Hepatol 2024

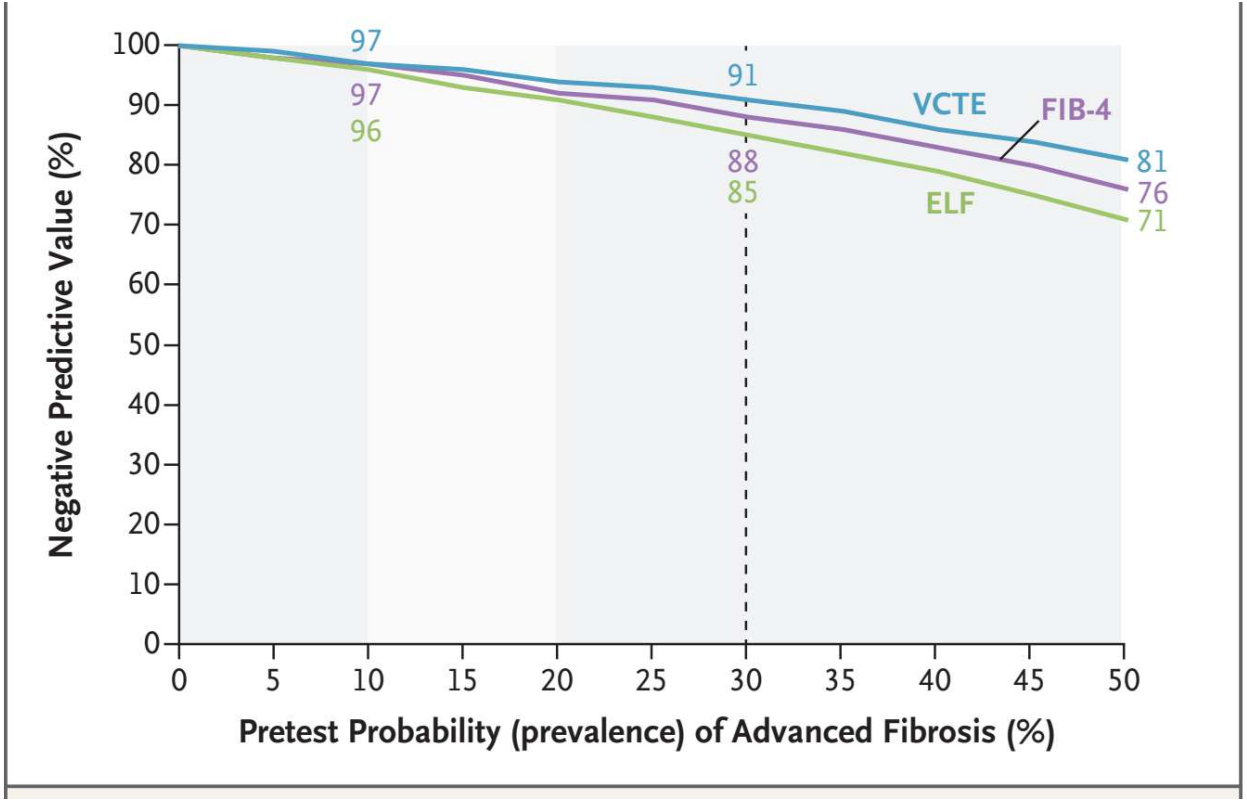
MAFLD: Quels seuils pour approche thérapeutique



FIB-4 (cutoff, 1.3
ELF (cutoff, 9.8)
VCTE (cutoff 9.6 - 11.4 kPa)

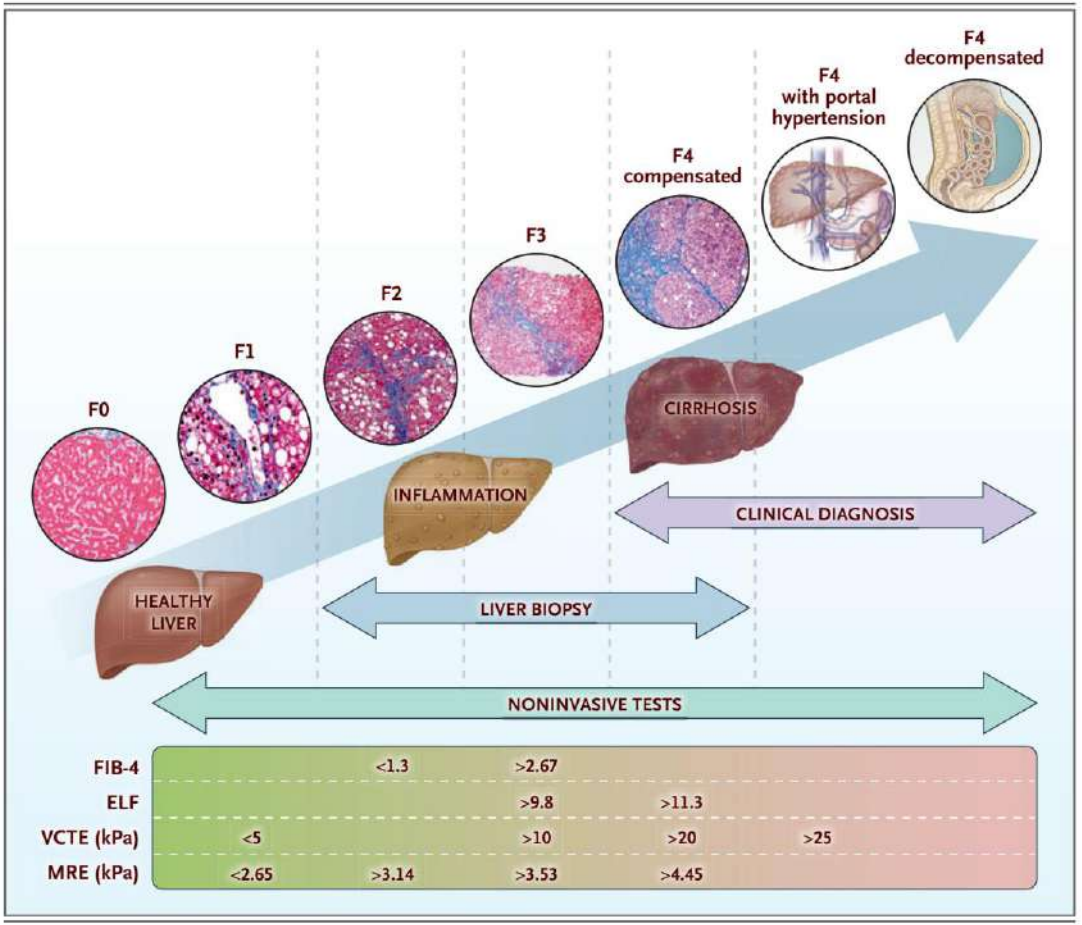
Castera L, NEJM 2025

MAFLD: Quels seuils pour approche thérapeutique



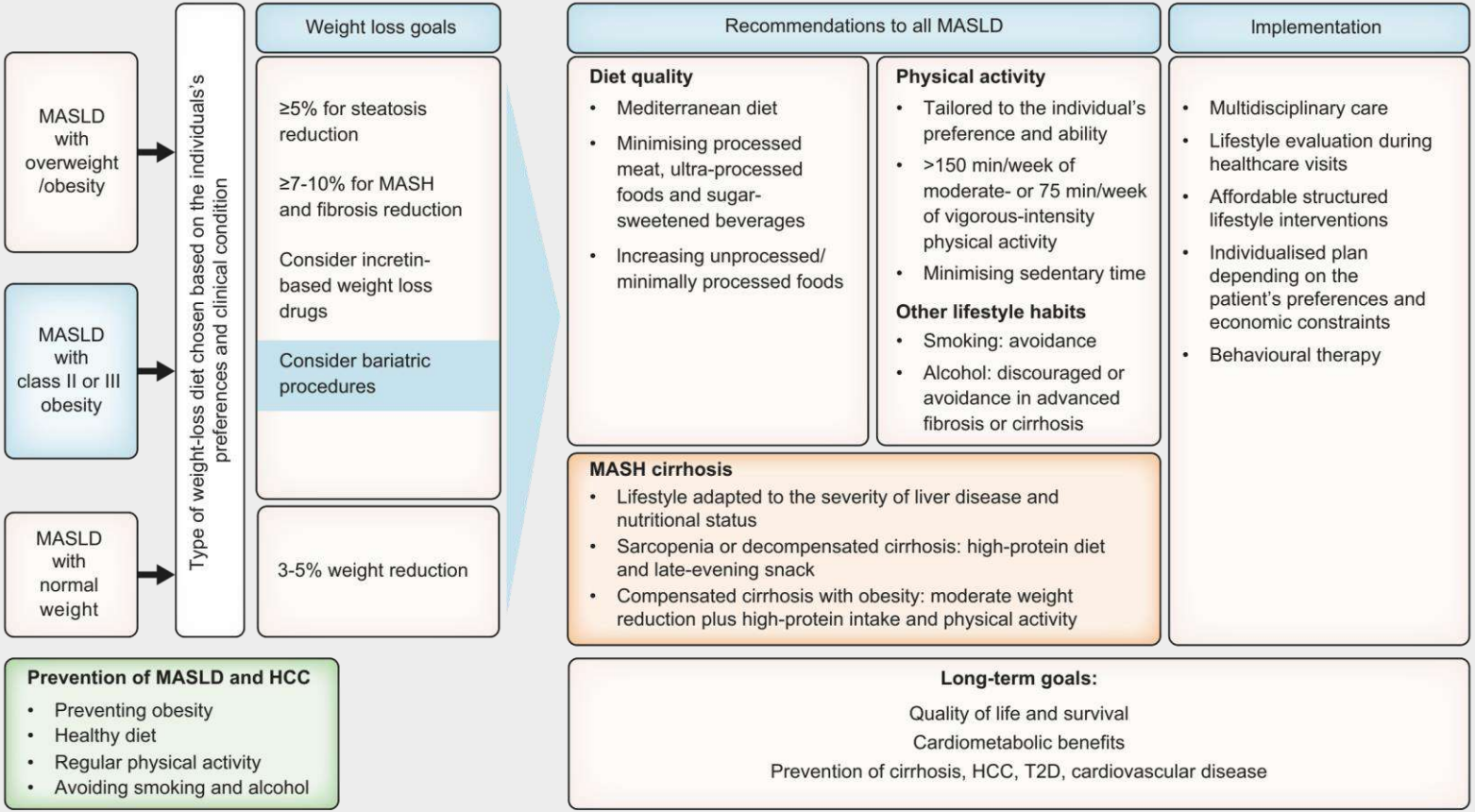
Castera L, NEJM 2025

MAFLD: Quels seuils pour approche thérapeutique



Castera L, NEJM 2025

MAFLD: Stratégie Thérapeutique



Targher G NEJM 2025

MAFLD: Stratégie thérapeutique
Approche progressive

Recommendation

- In adults with MASLD, improving diet quality (similar to the Mediterranean dietary pattern), limiting the consumption of ultra-processed food (rich in sugars and saturated fat) and avoiding sugar-sweetened beverages should be recommended to improve histologically or non-invasively assessed liver injury (**LoE 2, strong recommendation, strong consensus**).

Statement

- There is little evidence that improving diet quality beneficially impacts clinical liver-related outcomes (**LoE 3, consensus**).

EASL Guidelines J Hepatol 2024

MAFLD: Stratégie thérapeutique
Approche progressive

Recommendation

- In adults with MASLD, physical activity and exercise should be recommended to reduce steatosis, tailored to the individual's preference and ability (preferably >150 min/week of moderate or 75 min/week of vigorous-intensity physical activity) (**LoE 1, strong recommendation**, **strong consensus**).

Statement

- In comparison to the well-documented cardiometabolic benefits, there is less robust evidence for benefits of physical activity and exercise on histological outcomes, non-invasively assessed liver damage/fibrosis and liver-related clinical outcomes (**LoE 5**, **strong consensus**).

EASL Guidelines J Hepatol 2024

MAFLD: Stratégie thérapeutique
Approche progressive

Recommendation

- In normal-weight adults with MASLD, diet and exercise interventions should be recommended to reduce liver fat (**LoE 3, strong recommendation**, **strong consensus**).

Statement

- In normal-weight adults with MASLD, there is currently no evidence regarding the beneficial effect of diet and/or exercise on liver histology, fibrosis and liver-related clinical outcomes (**LoE 5, consensus**).

EASL Guidelines J Hepatol 2024

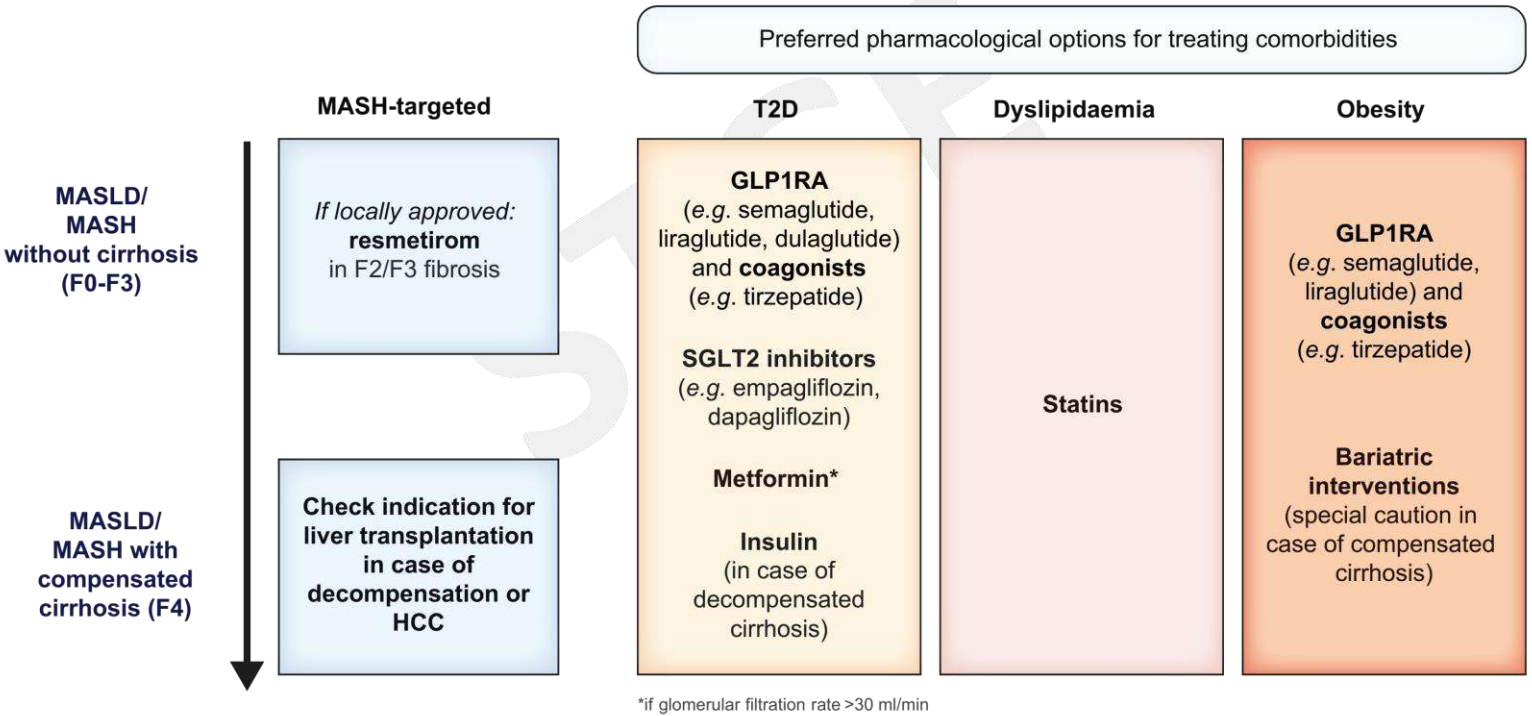
MAFLD: Stratégie thérapeutique
Approche progressive

Statement

- In adults with MASLD, coffee consumption has been associated with improvements in liver damage and reduced liver-related clinical outcomes in observational studies (**LoE 4, strong consensus**).

EASL Guidelines J Hepatol 2024

MAFLD: Stratégie thérapeutique
Approche progressive



EASL Guidelines J Hepatol 2024

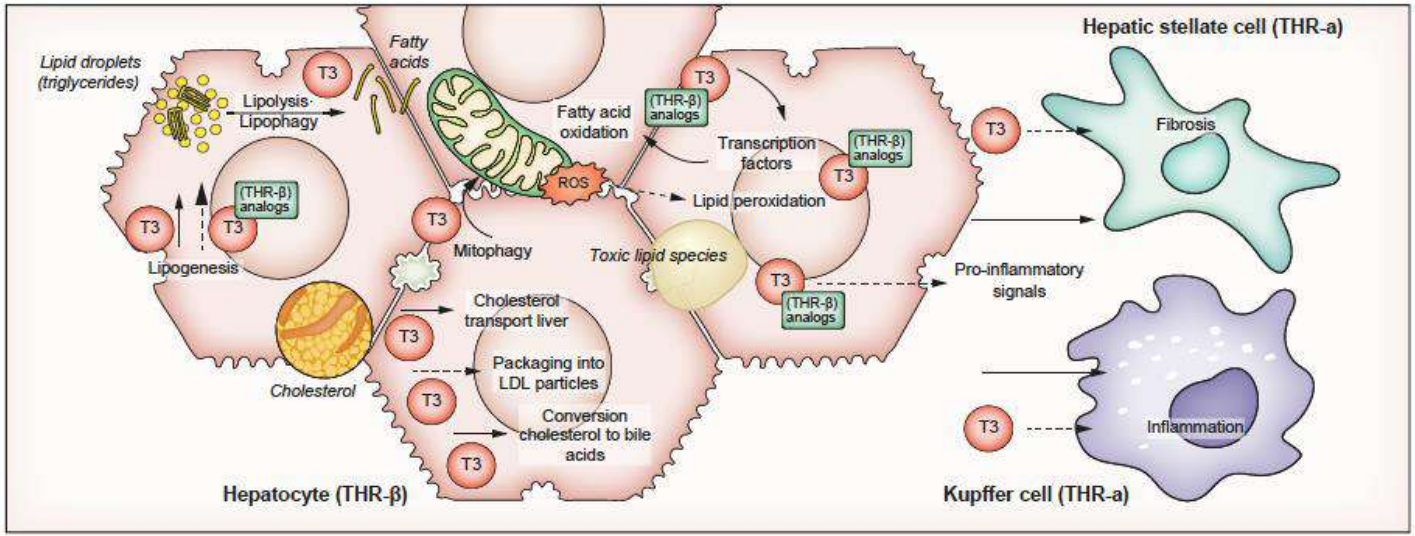
MOLECULES EN EVALUATION THERAPEUTIQUE

MOLECULES EN PHASE III

Resmetiron

Thyroid hormone receptor beta (THR-β) selective agonist

- Resmetirom is an oral, liver-directed THR-β selective agonist in clinical development for the treatment of NASH
- THR-β function in the liver is impaired
- ↓ mitochondrial function and consequently ↑β-oxidation of fatty acids with ↑ in fibrosis



MAESTRO-NASH Trial Design

Resmetirom is an oral, liver-directed, thyroid hormone receptor beta (THR-β)–selective agonist in clinical development for the treatment of NASH

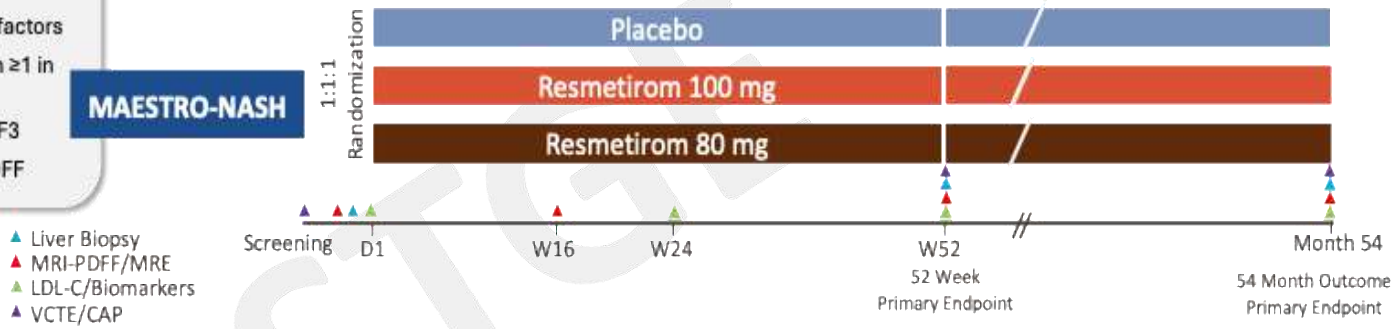
KEY ELIGIBILITY CRITERIA

Presence of ≥3 metabolic risk factors

NASH on biopsy: NAS ≥4 (with ≥1 in each component)

Fibrosis stage F1B, F2, or F3

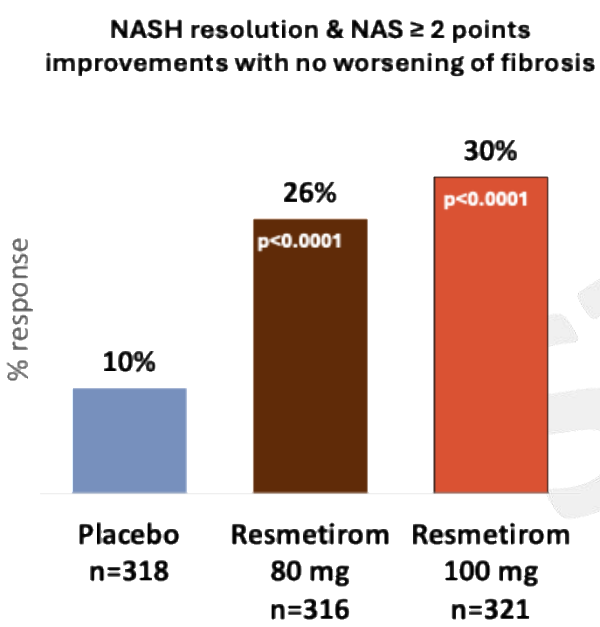
≥8% hepatic fat by MRI-PDFF

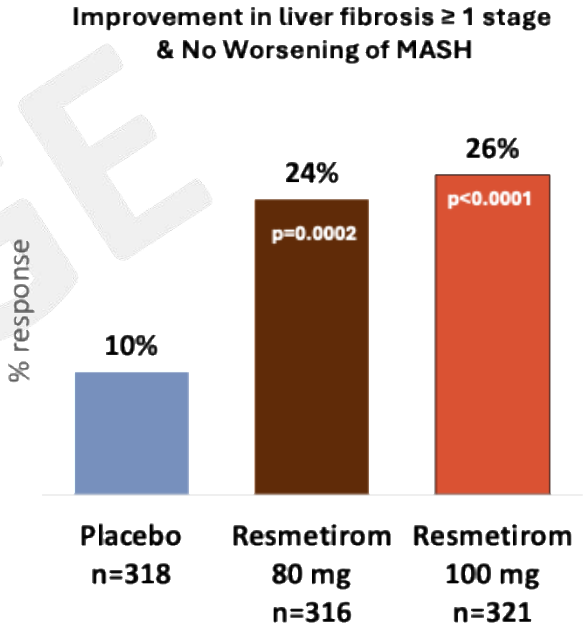


DUAL PRIMARY ENDPOINTS AT WEEK 52

NASH resolution (ballooning score=0, inflammation score=0/1, & ≥2-point reduction in NAS) with no worsening of fibrosis

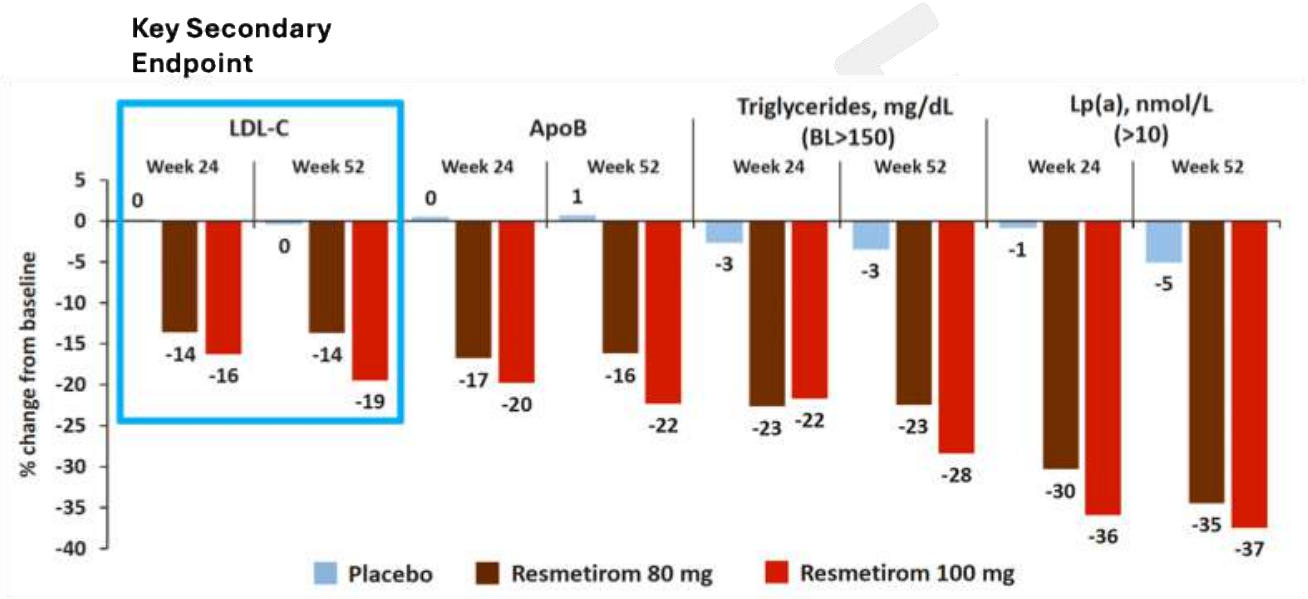
Dual Primary Endpoints - 52-week Sub-Part H





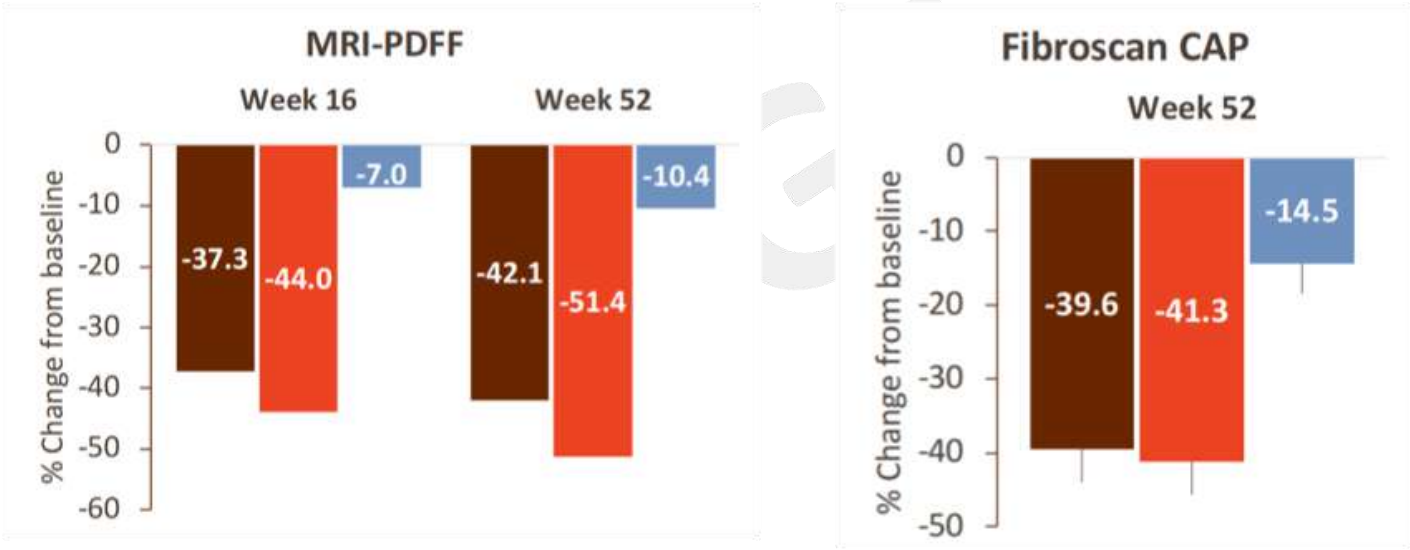
Harrison, NEJM 2024

Secondary Endpoints - Lipids



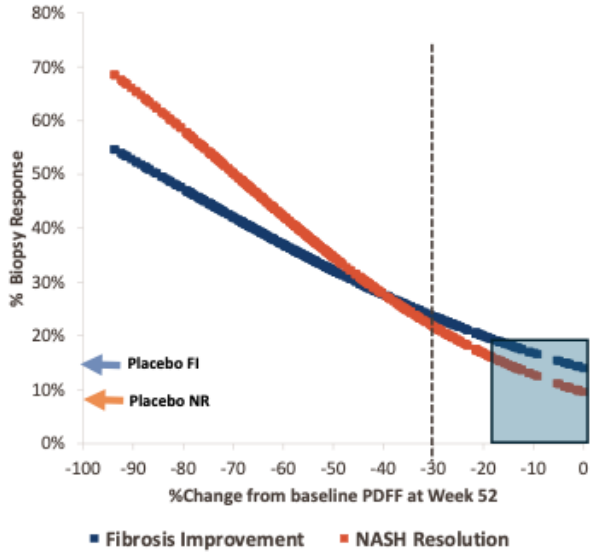
Harrison, NEJM 2024

Changes in hepatic steatosis measured by PDFF and CAP



Harrison, NEJM 2024

PDFF as a Marker of Resmetirom Biopsy Response



- PDFF reduction in resmetirom treated patients was highly associated with both NASH Resolution (NR) and Fibrosis Improvement (FI)
  - **Placebo patients with PDFF reduction of 30% or higher did not associate with improvement in fibrosis**
- A ≥30% PDFF response was observed in 96% and 88% of resmetirom 100 mg responders for NASH resolution and Fibrosis improvement.

Harrison et al. NEJM 2024

Safety Overview

n (%)	Resmetirom 80mg (n=322)	Resmetirom 100mg (n=323)	Placebo (n=321)
≥1 TEAEs	**296 (91.9)**	**296 (91.6)**	**269 (92.2)**
Grade 1 (mild)	71 (22.0)	65 (20.1)	77 (24.0)
Grade 2 (moderate)	180 (55.9)	183 (56.7)	167 (52.0)
≥ Grade 3 (severe)	45 (14.0)	48 (14.9)	52 (16.2)
≥1 drug-related TEAEs	122 (37.9)	134 (41.5)	86 (26.8)
≥1 serious TEAEs	**38 (11.8)**	**41 (12.7)**	**39 (12.1)**
≥1 drug-related serious TEAEs	2 (0.6)	0	1 (0.3)
TEAEs leading to study discontinuation (in 52 Weeks)	**6 (1.9)**	**22 (6.8)**	**8 (2.5)**
Fatal TEAE	1 (0.3)	1 (0.3)	1 (0.3)
3-pt MACE* (adjudicated)	1 (0.3)	1 (0.3)	1 (0.3)
Other cardiovascular events (adjudicated)	0	1 (0.3)	3 (0.9)

Study discontinuations in the 100 mg arm were increased relative to placebo only during the first 12 weeks and were similar in all treatment groups for the remaining period of the first 52 weeks; after 52 weeks, placebo discontinuations were higher than drug treatment arms

Most AE discontinuations in the 100 mg arm were GI-related

No DILI events (adjudicated)

GLP-1 Receptor Agonist Etude Phase III *Semaglutide*

Glucagon Like Peptide-1 (GLP1) Receptor agonists

Mechanisms of action

Mechanisms of action

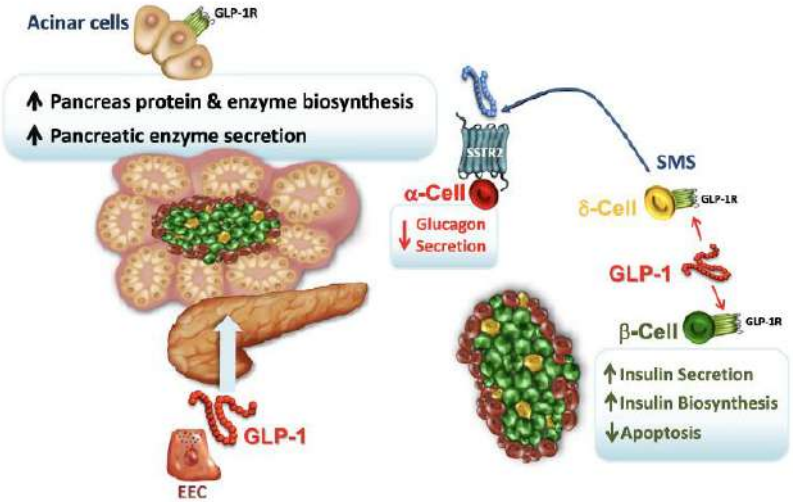
↑insulin secretion in hyperglycemic states,

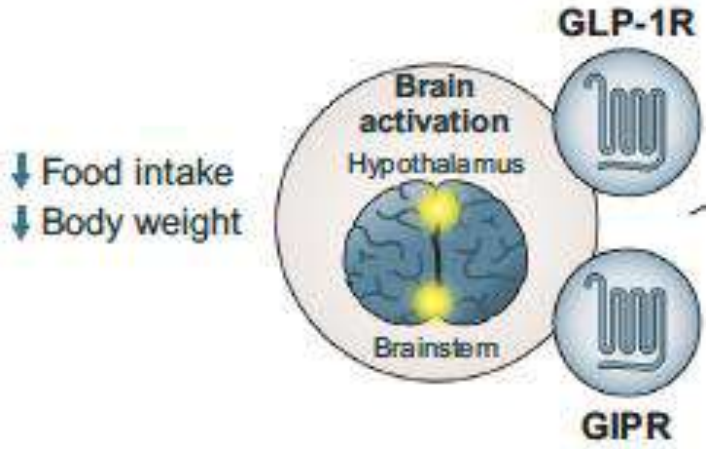
↓ Glucagon secretion in hyperglycemic or euglycemic states,

↓ gastric emptying

↓Appetite

↓ body weight.



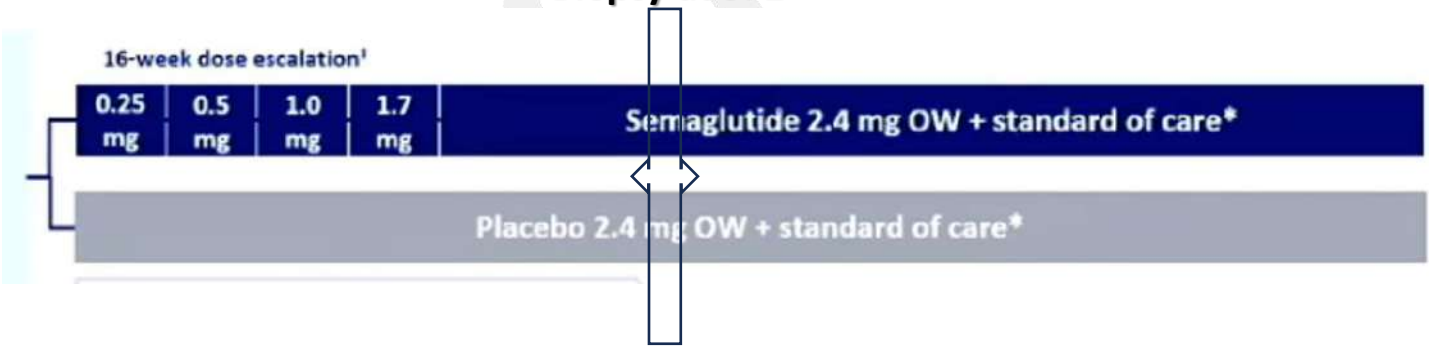


Drucker, Cell Metabolism, 2018

Etude Essence

Essai Phase 3 du Semaglutide dans la MASH

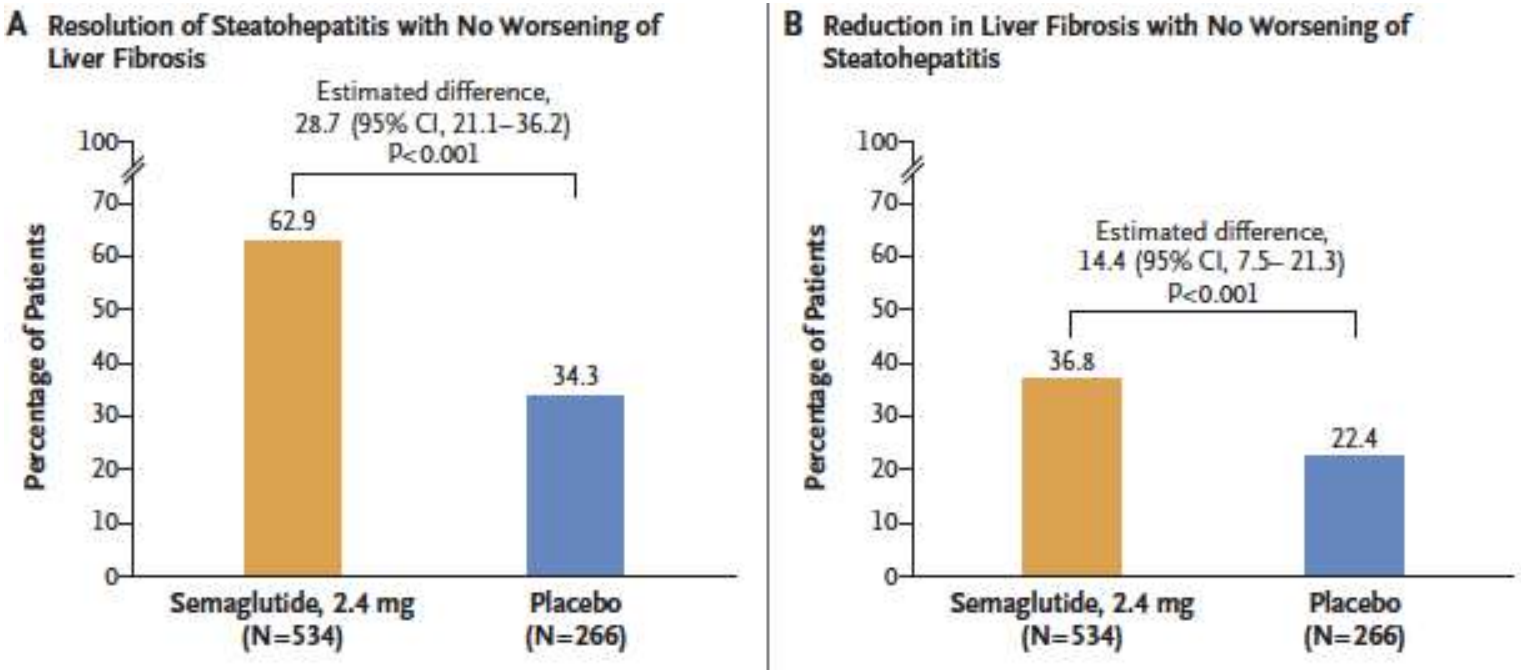
- Histological evidence of MASH
- NAS ≥4
- Histological evidence of fibrosis stage 2 or 3
- Score ≥1 for steatosis, lobular inflammation and hepatocyte ballooning



Sanyal, NEJM, 2025

Essai Phase 3 du Semaglutide dans la MASH

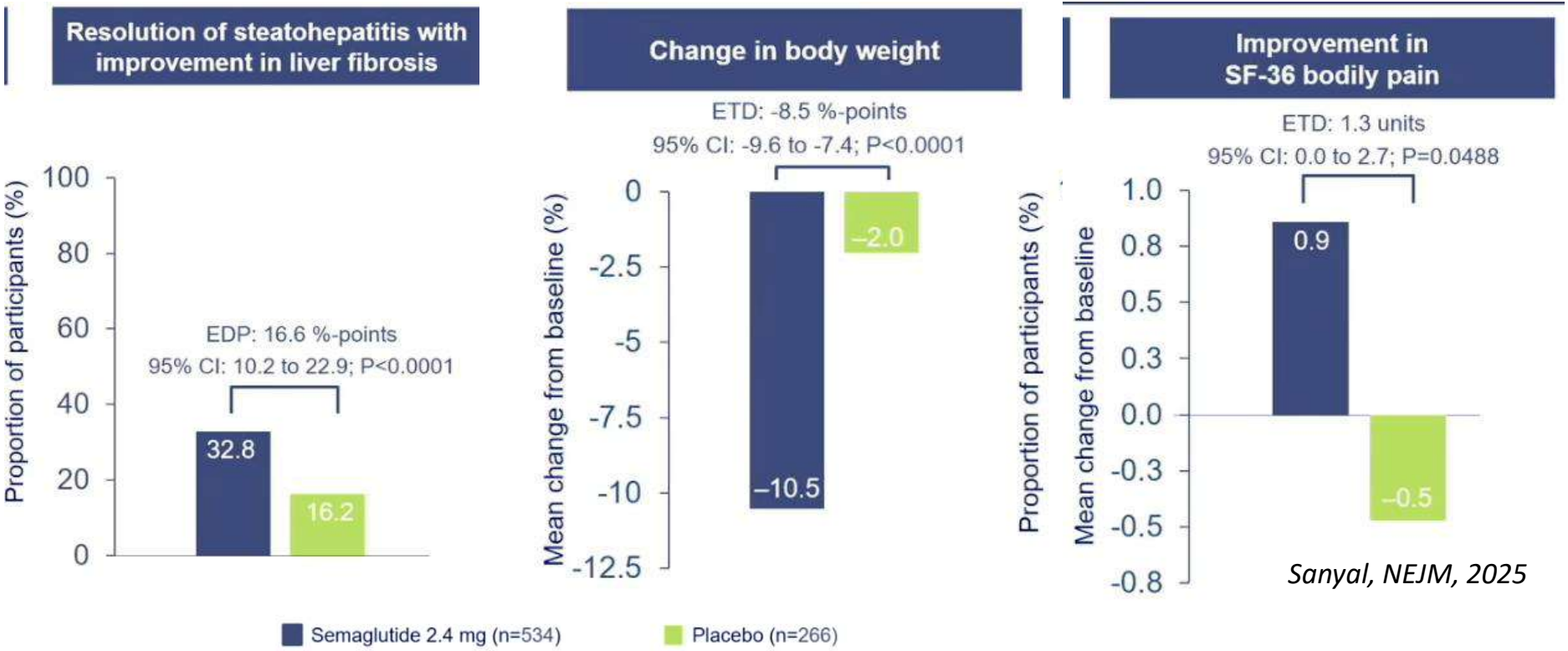
Critère principal de jugement



Sanyal, NEJM, 2025

Essai Phase 3 du Semaglutide dans la MASH

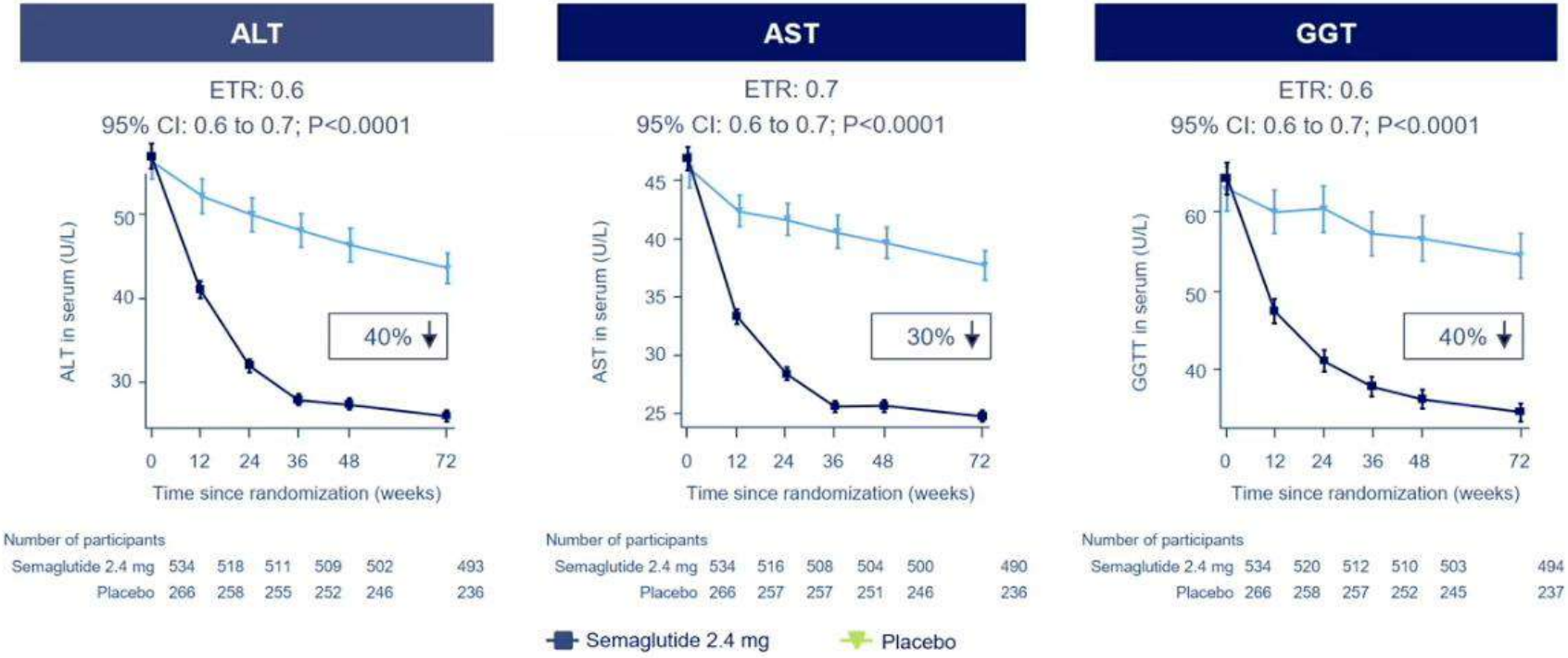
Critères secondaires de jugement



Sanyal, NEJM, 2025

Essai Phase 3 du Semaglutide dans la MASH

Evolution biologie hépatique



Sanyal, NEJM, 2025

Essai Phase 3 du Semaglutide dans la MASH

Changes in cardiometabolic risk parametters

Measure	Semaglutide 2.4 mg (N=534)	Placebo (N=266)	Difference between semaglutide and placebo at week 72 (95% CI)	P value
Absolute change				
Systolic blood pressure, mmHg	-5.39	-1.39	-4.00 (-5.93 to -2.07)	<0.001
Diastolic blood pressure, mmHg	-1.90	0.24	-2.14 (-3.43 to -0.85)	0.001
HbA_{1c}, % [without T2D]	-0.42	0.11	-0.53 (-0.61 to -0.44)	<0.001
HbA_{1c}, % [with T2D]	-1.08	-0.00	-1.08 (-1.27 to -0.89)	<0.001
Relative change				
hsCRP, mg/L	0.46	0.80	0.58 (0.50 to 0.66)	<0.001
Total cholesterol, mg/dL	0.94	0.97	0.97 (0.94 to 1.00)	0.04
Triglycerides, mg/dL	0.83	1.00	0.83 (0.79 to 0.88)	<0.001
LDL cholesterol, mg/dL	0.94	0.96	0.98 (0.94 to 1.02)	0.37
HDL cholesterol, mg/dL	1.03	0.98	1.05 (1.02 to 1.07)	<0.001

Sanyal, NEJM, 2025

Essai Phase 3 du Semaglutide dans la MASH

Safety analysis

	Semaglutide 2.4 mg (N=800)	Placebo (N=395)
	n (%)	n (%)
All AEs	690 (86.3)	315 (79.7)
Fatal AEs	3 (0.4)	6 (1.5)
Serious AEs	107 (13.4)	53 (13.4)
AEs leading to trial discontinuation	21 (2.6)	13 (3.3)
AEs affecting ≥10% of participants		
Nausea	290 (36.3)	52 (13.2)
Diarrhea	215 (26.9)	48 (12.2)
Constipation	178 (22.3)	33 (8.4)
Vomiting	149 (18.6)	22 (5.6)
COVID-19	134 (16.8)	74 (18.7)
Decreased appetite	112 (14.0)	11 (2.8)

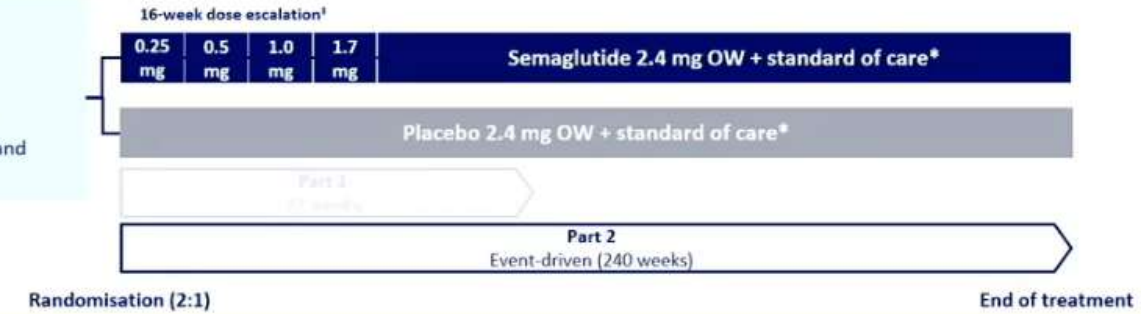
Sanyal, NEJM, 2025

ESSENCE: Semaglutide 2.4 mg in patients with MASH F2–F3

Part 2

Part 2 (full trial): 1200 participants

- Histological evidence of MASH
- NAS ≥4
- Histological evidence of fibrosis stage 2 or 3
- Score ≥1 for steatosis, lobular inflammation and hepatocyte ballooning



Part 2: Key endpoints

- **Cirrhosis-free survival, corresponding to not experiencing one of the following liver-related clinical events:**
  - Histological progression to cirrhosis
  - All-cause mortality
  - Liver-induced MELD score ≥15
  - Liver transplant
  - Hepatic decompensation events‡
- **Supportive secondary endpoint:**
  - Time to first major adverse cardiovascular event (composite)**

MOLECULES EN PHASE II
(PHASE III en cours Agonistes FGF 21)

Dual glucose-dependent insulinotropic polypeptide (GIP)–GLP-1 receptor agonist : **What benefit?**

Mechanisms of action of Glucose-dependent insulinotropic polypeptide:

- the main incretin hormone in healthy persons
- Act centrally to potentiate a GLP-1–induced reduction in food intake

- Unlike GLP-1, GIP is glucagonotropic in a glucose-dependent manner
- Under hyperglycemic conditions
  - ↑ release of insulin thereby lowering glucagon level

- Under euglycemic or hypoglycemic conditions
  - ↑ glucagon levels

- Tirzepatide, a once- weekly glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist

Tirzepatide for MASH with Liver Fibrosis

SINERGY phase 2b trial

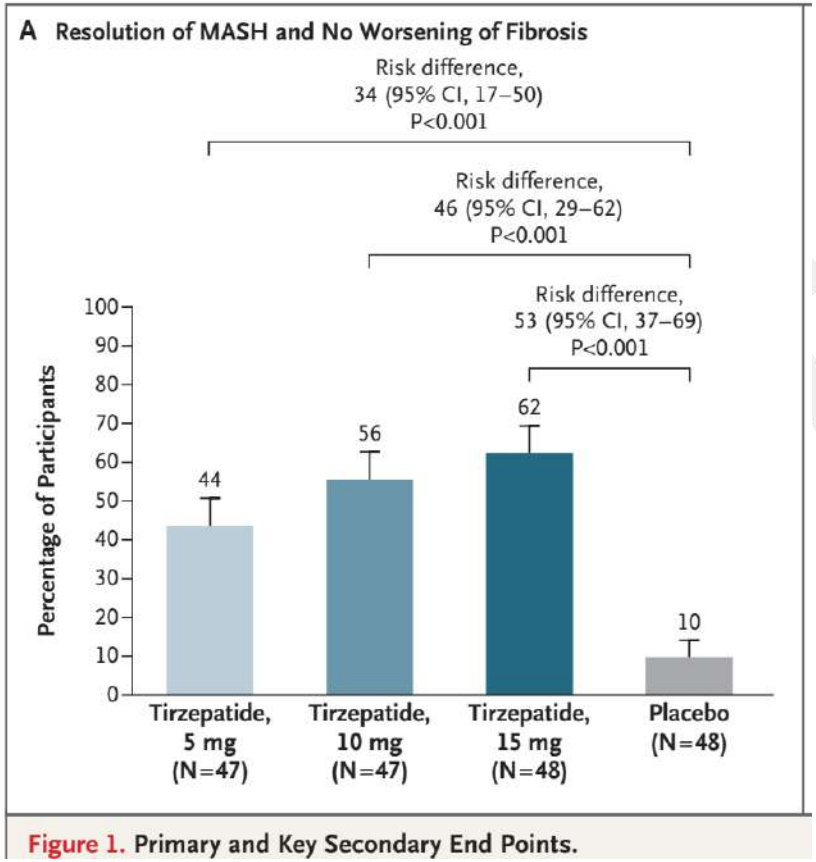
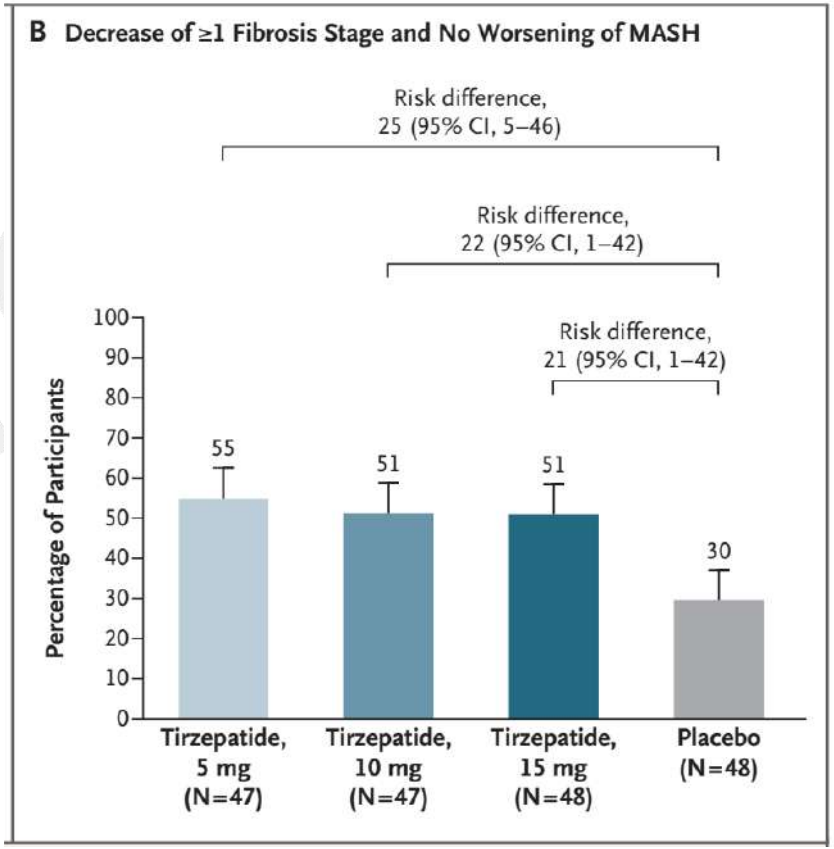


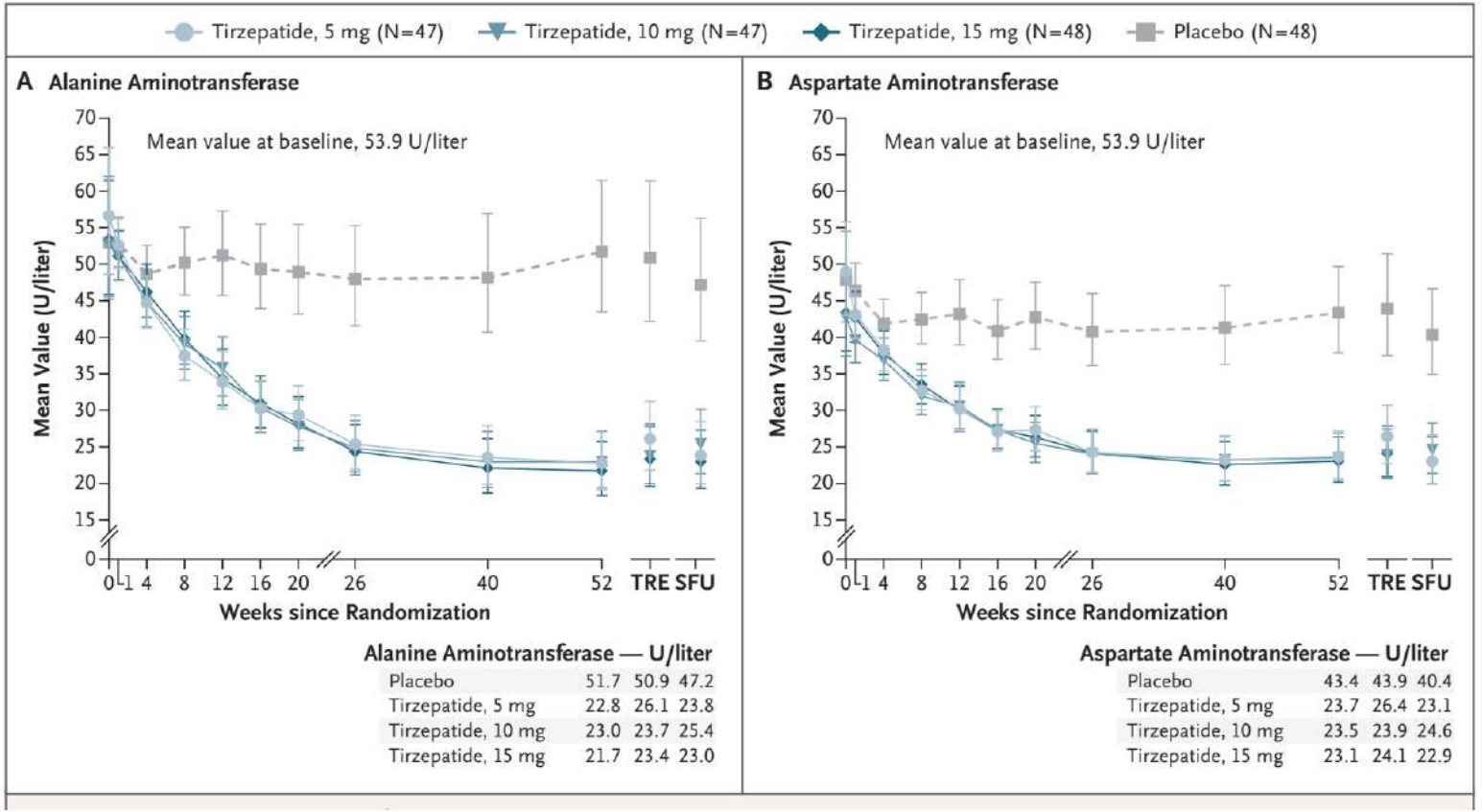
Figure 1. Primary and Key Secondary End Points.



Loomba, NEJM 2024

Tirzepatide for MASH with Liver Fibrosis

SINERGY phase 2b trial

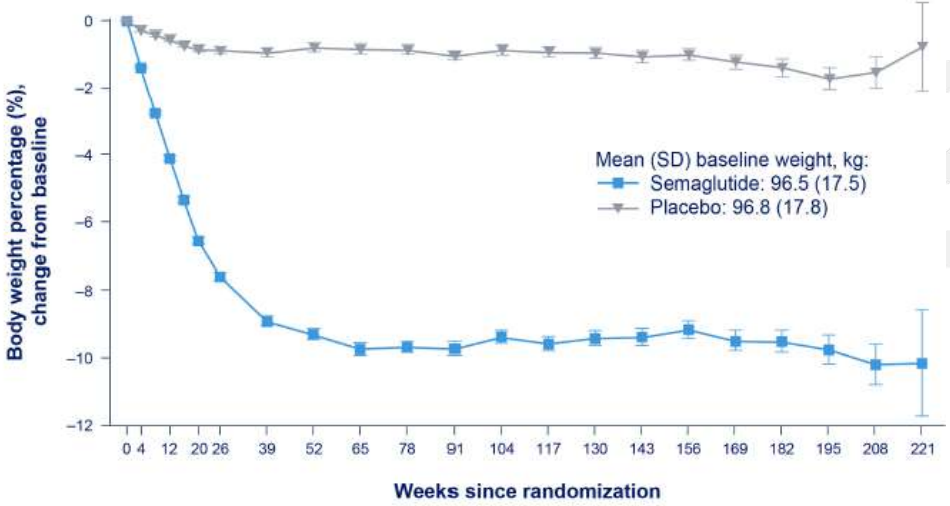


Loomba, NEJM 2024

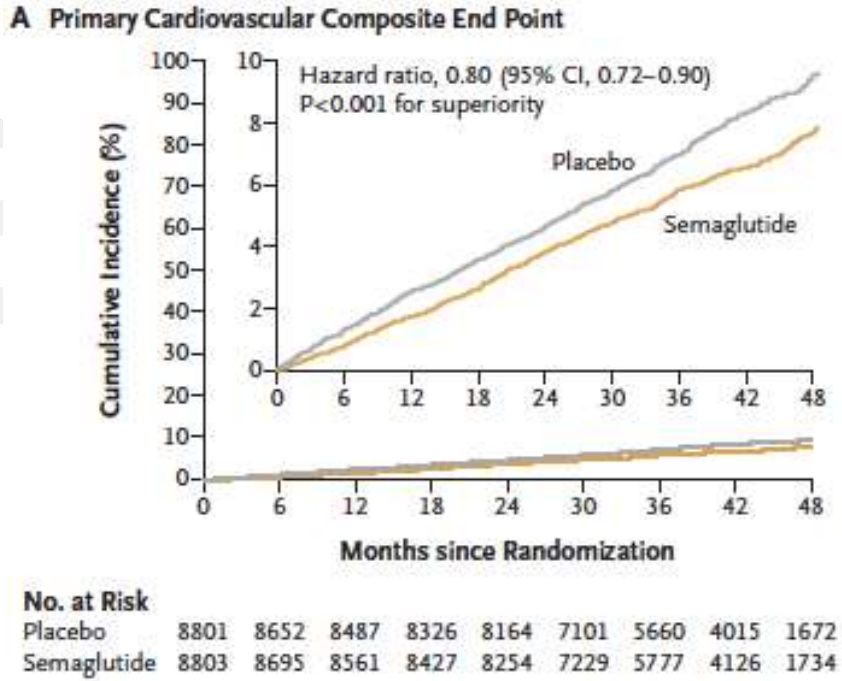
MASLD et Syndrome métabolique

Maladie systémique et risques extra-hépatiques

Semaglutide : ↓ évènements cardiovasculaires
Etude chez patients avec ATCD cardiovasculaire sans DNID



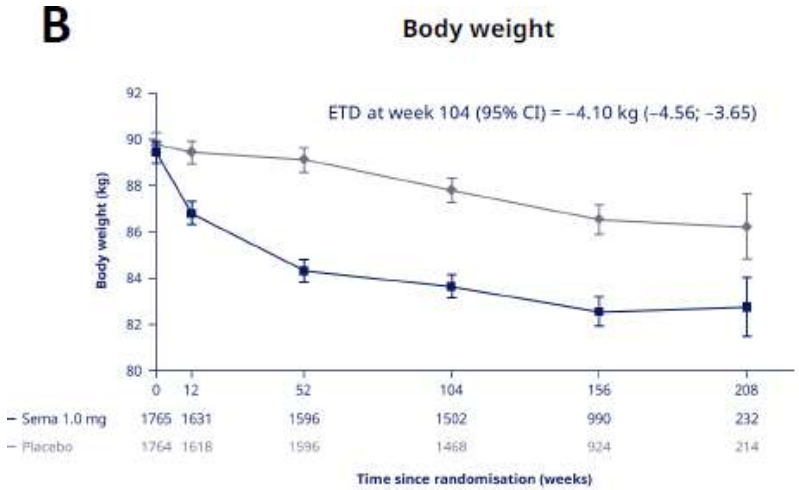
Semaglutide, N	8,803	7,647	7,493	6,690	7,290	6,447	7,282	6,460	7,474	5,991	5,898	4,686	5,085	3,650	2,954	1,737	921	157
Placebo, N	8,801	7,715	7,516	6,704	7,269	6,340	7,272	6,392	7,378	5,871	5,879	4,583	5,014	3,560	2,890	1,698	898	152



Lincoff, NEJM 2023

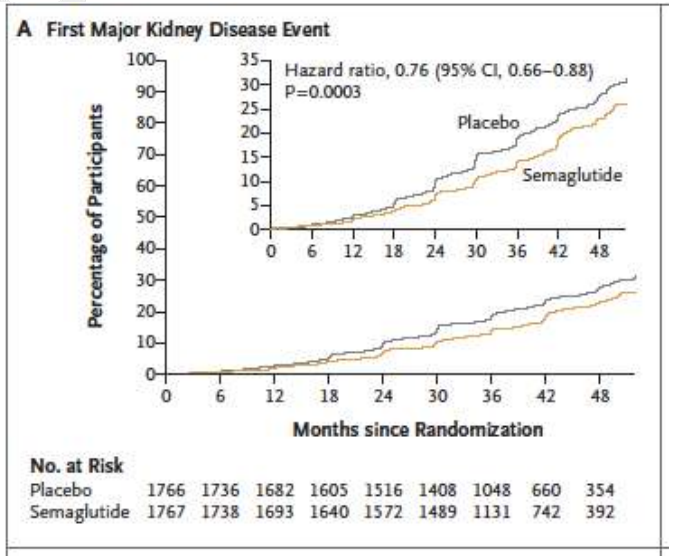
Effect of Semaglutide on Patients with Type 2 Diabetes and CKD*

Change in body weight (kg)



Major kidney disease events (%)

(kidney failure [dialysis, transplantation, eGFR <15 ml/min/1.73 m2] ≥50% eGFR reduction, or death from kidney or CVD causes)



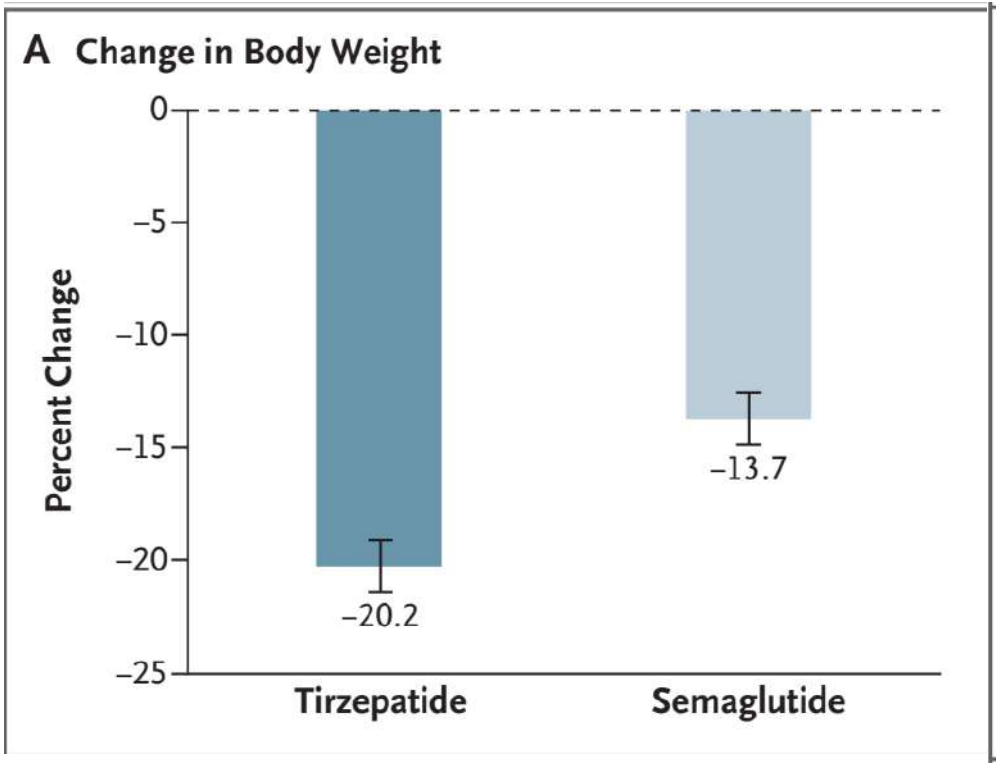
*eGFR 50-75 ml/min/1.73m2 + UalbCr >300 or eGFR 25 to <50 + Ualb/Cr

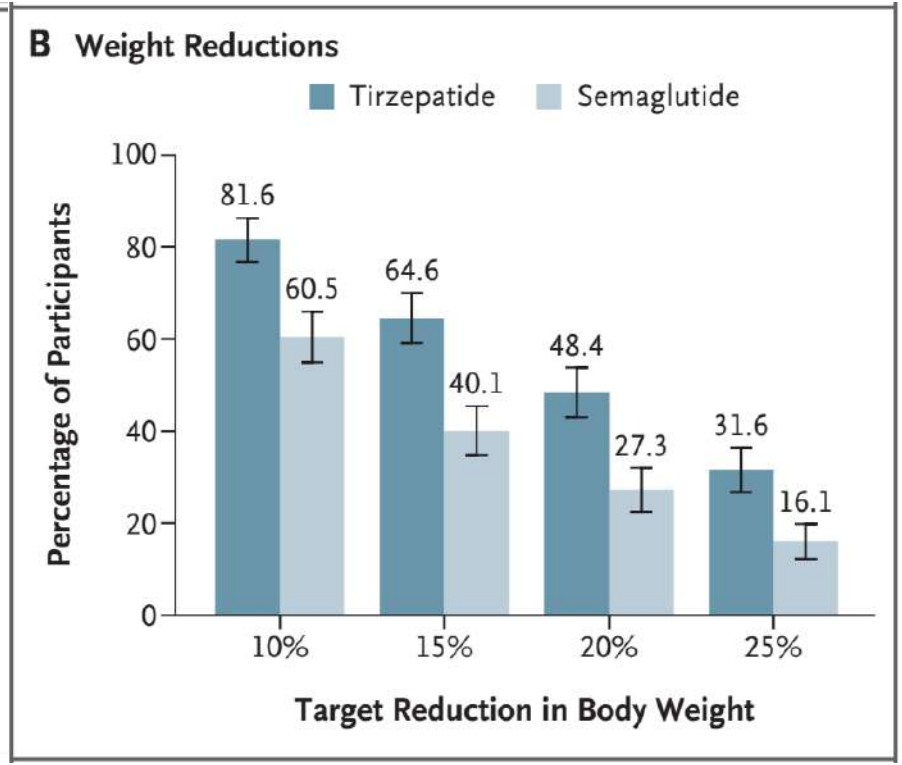
Pekovic, NEJM 2024

COMPARAISON Head to Head

Dual GIP-GLP-1 Receptor Agonist vs GLP-1 Receptor Agonist

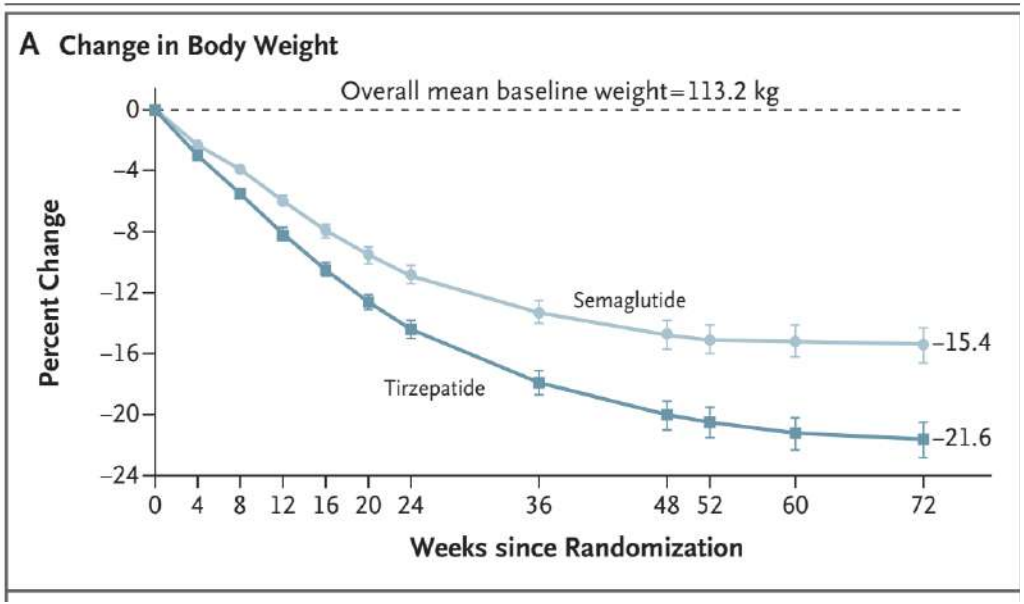
Tirzepatide 10 - 15 mg vs Semaglutide 1,7 - 2,4 mg : *Weight Loss*

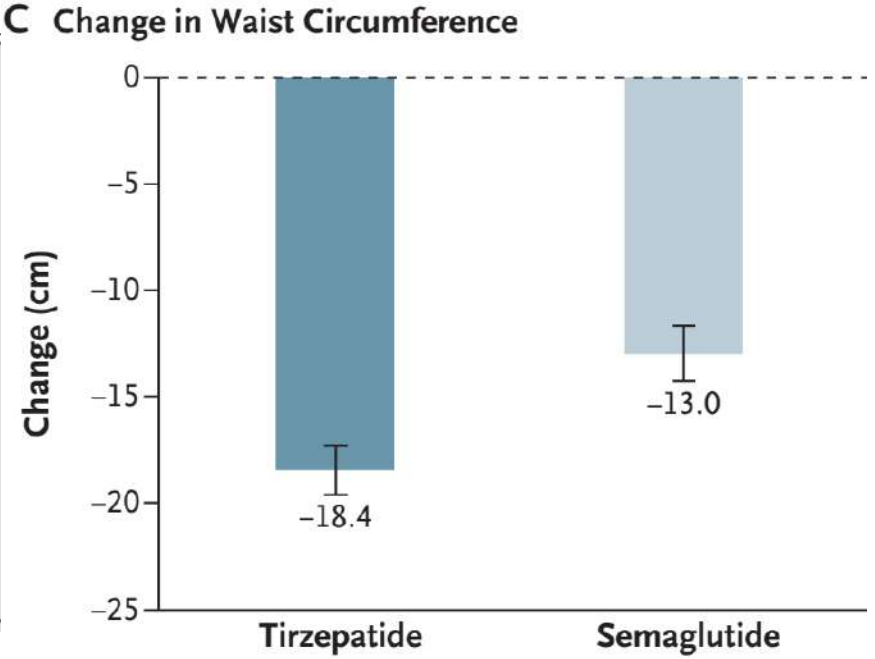




Aronne LJ, NEJM 2025

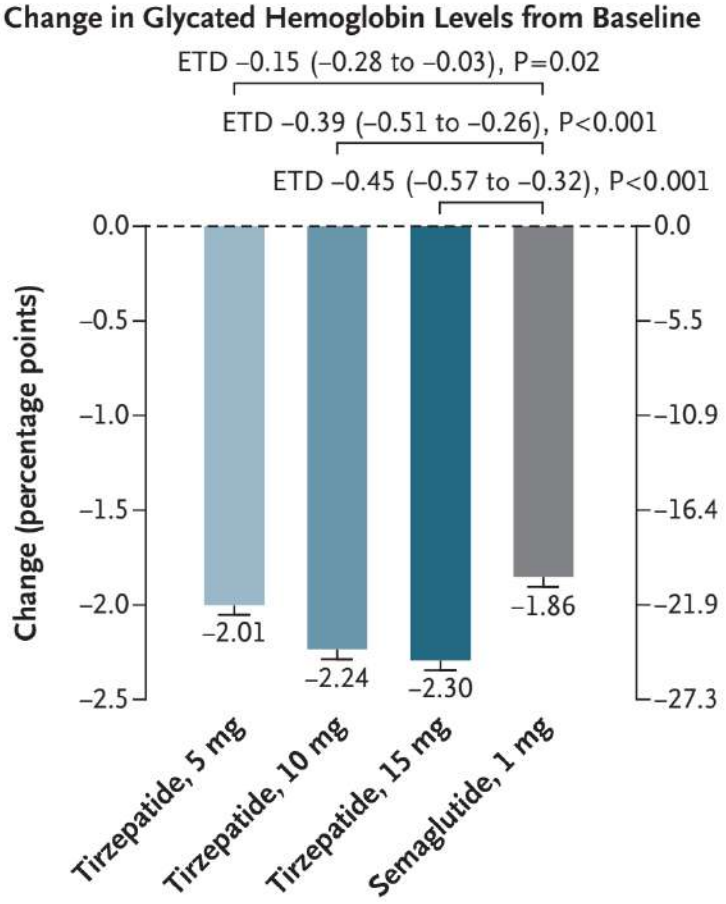
Tirzepatide 10 - 15 mg vs Semaglutide 1,7 - 2,4 mg : *Weight Loss*

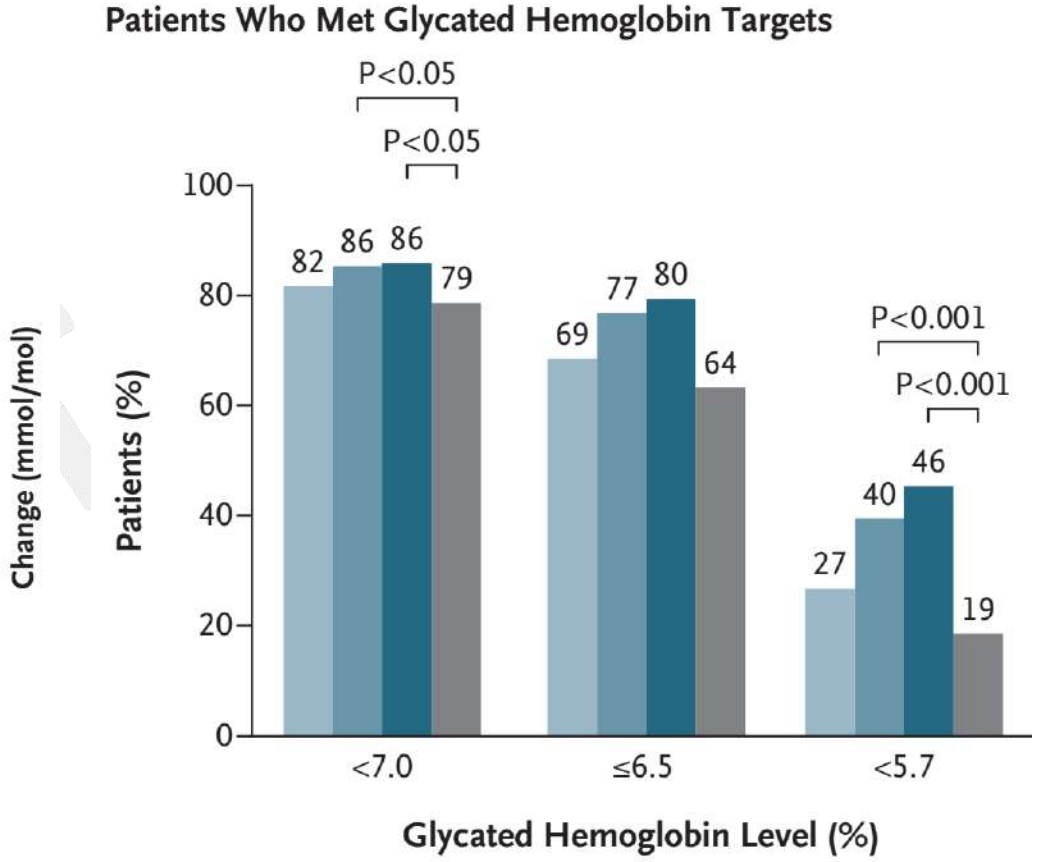




Aronne LJ, NEJM 2025

Tirzepatide 5 - 10 - 15 mg vs Semaglutide 1,7 - 2,4 mg : *Diabète type II*





Frias JP, NEJM 2021

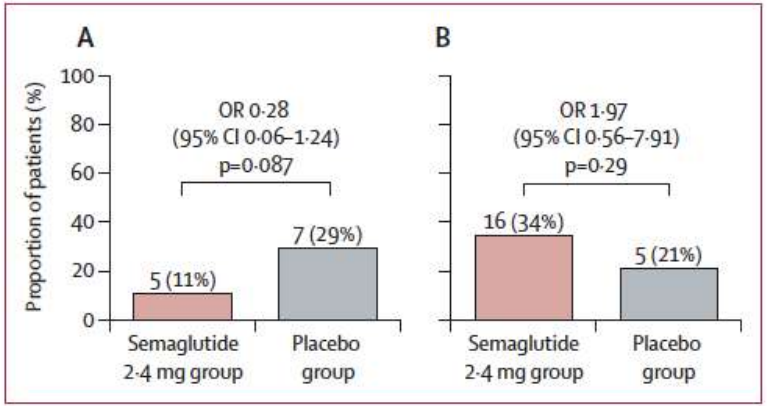
Place de la chirurgie bariatrique chez les patients ayant NAFLD au stade de Cirrhose

Recommendations

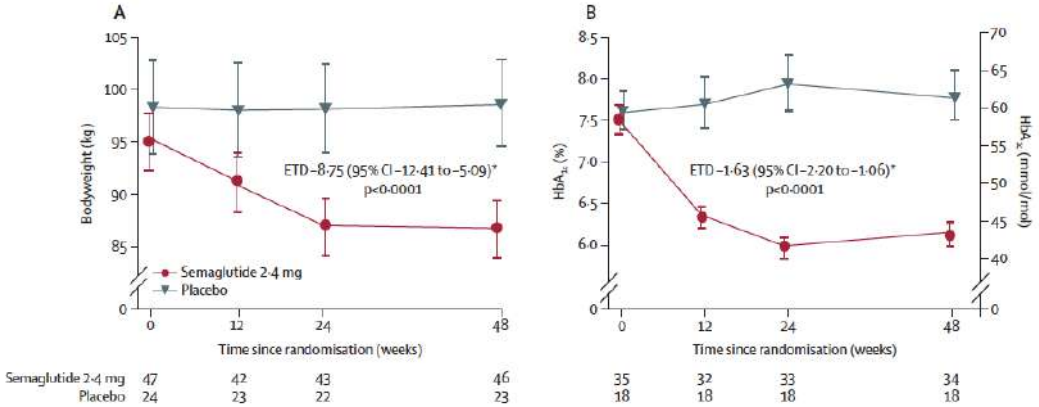
- In adults with non-cirrhotic MASLD who have an approved indication, bariatric surgery should be considered, because it can induce long-term beneficial effects on the liver and is associated with remission of type 2 diabetes and improvement of cardiometabolic risk factors (**LoE 3, strong recommendation, strong consensus**).
- In adults with MASLD-related compensated advanced chronic liver disease/compensated cirrhosis who have an approved indication, bariatric surgery can be considered but careful evaluation (indication, type of surgery, presence of clinically significant portal hypertension) by a multidisciplinary team with experience in bariatric surgery in this particular population is required (**LoE 4, weak recommendation, strong consensus**).

Semaglutide 2.4 mg in patient with MASLD cirrhosis
Essai Phase 2

Histological changes: (A) liver fibrosis and (B) resolution of MASH

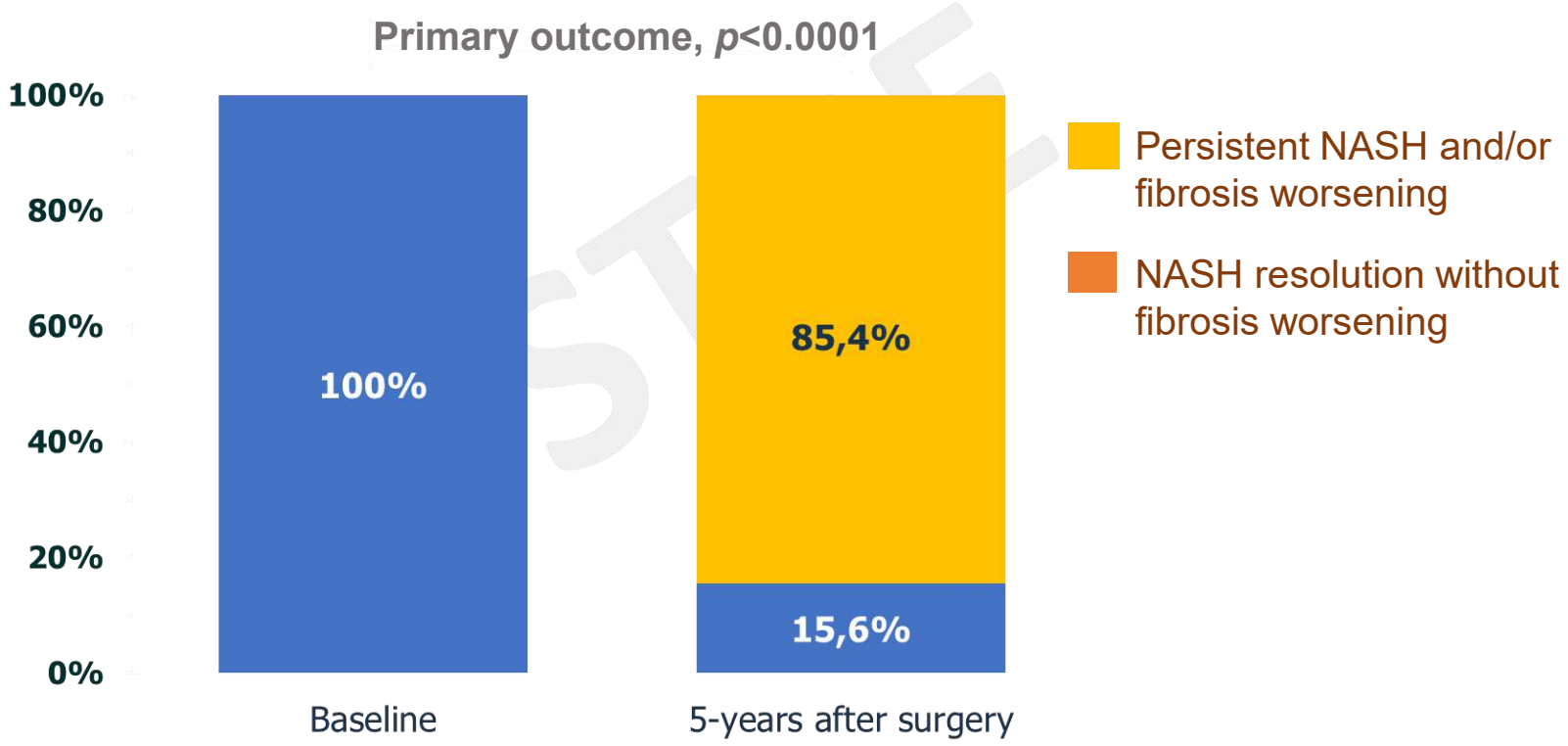


Changes in metabolic body weight (A) and HbA1c (B)



Loomba, The Lancet 2023

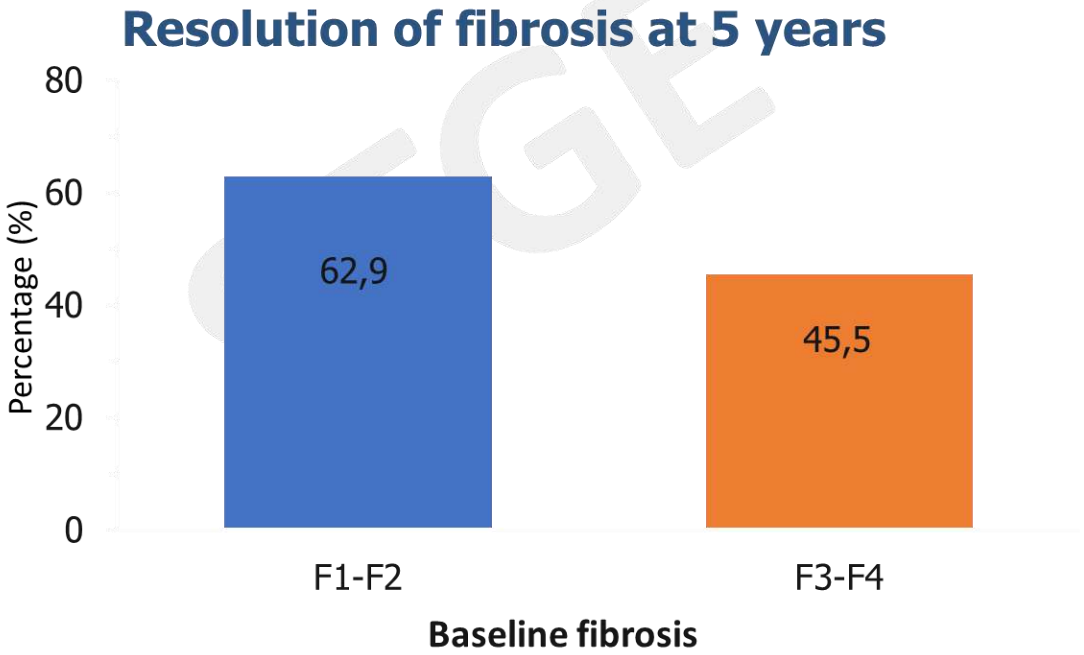
Bariatric Surgery Long-term Evolution



Lassailly G, *Gastroenterology* 2020

Bariatric Surgery Long-term Evolution

Advanced fibrosis is associated with lower response



Lassily G, Gastroenterology 2020

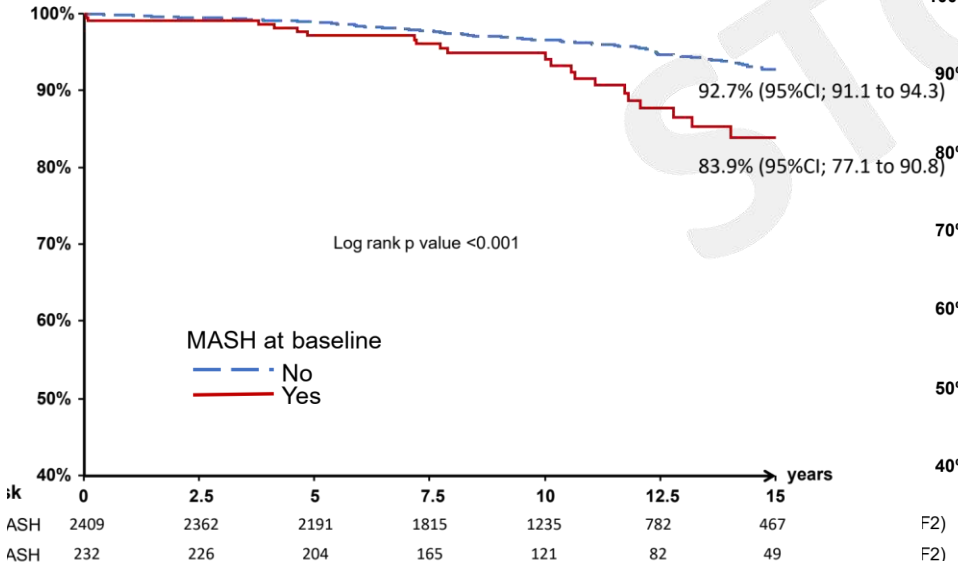
Chirurgie bariatrique et bénéfice de survie

Resolution of Metabolic Dysfunction-associated Steatohepatitis With No Worsening of Fibrosis After Bariatric Surgery Improves 15-year Survival: A Prospective Cohort Study

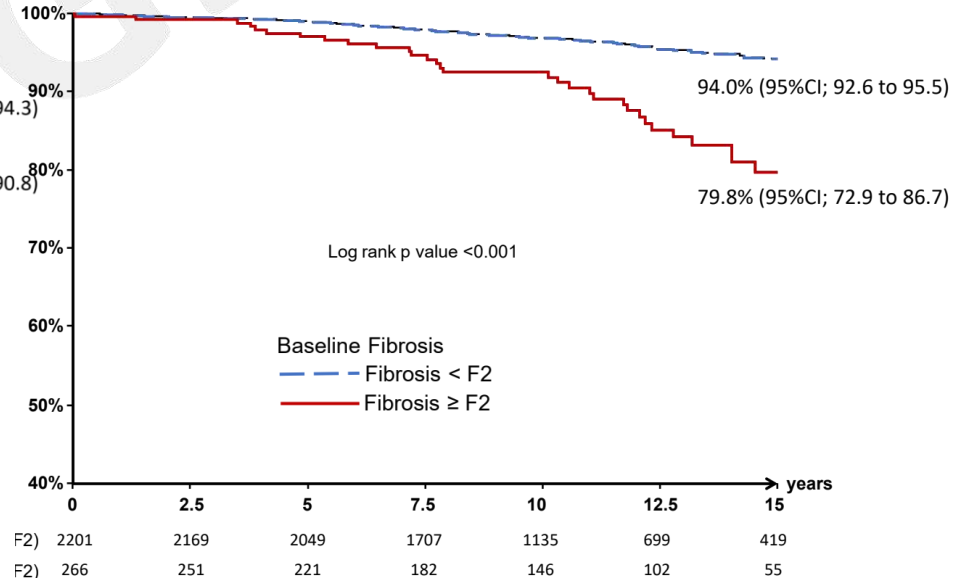
Guillaume Lassailly,[1,2,*] Robert Caiazzo,[3,4,*] Armelle Goemans,[1,2] Mikael Chetboun,[3,4] Viviane Gnemmi,[5] Julien Labreuche,[6] Gregory Baud,[3,4] Helene Verkindt,[3,4] Camille Marciniak,[3] Naima Oukhouya-Daoud,[3,4] Line-Carolle Ntandja-Wandji,[1,2] Massih Ningarhari,[1,2] Emmanuelle Leteurtre,[5] Violeta Raverdy,[3,4] Sébastien Dharancy,[1,2] Alexandre Louvet,[1,2] François Pattou,[3,4] and Philippe Mathurin[1,2]

Clinical Gastroenterology and Hepatology 2025;23:1567–1576

15-year survival according to baseline MASH



15-year survival according to baseline Fibrosis



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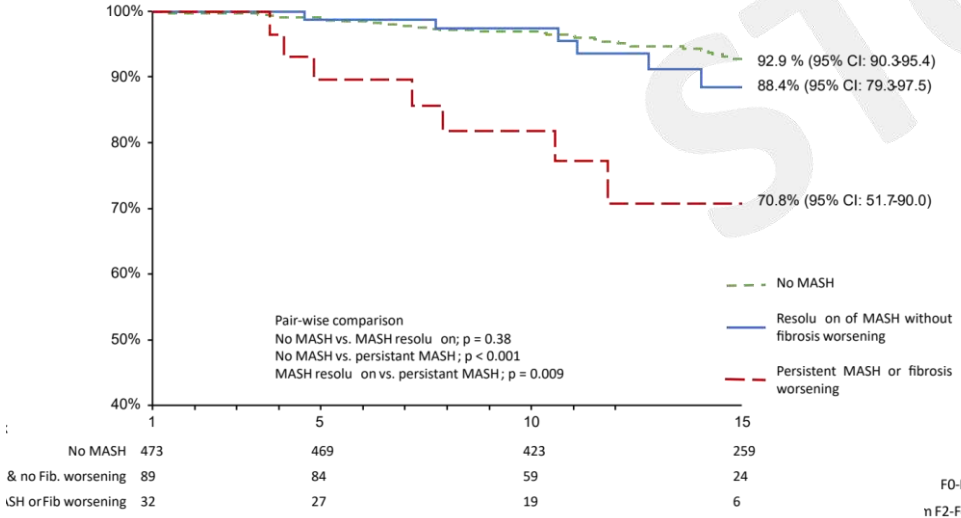
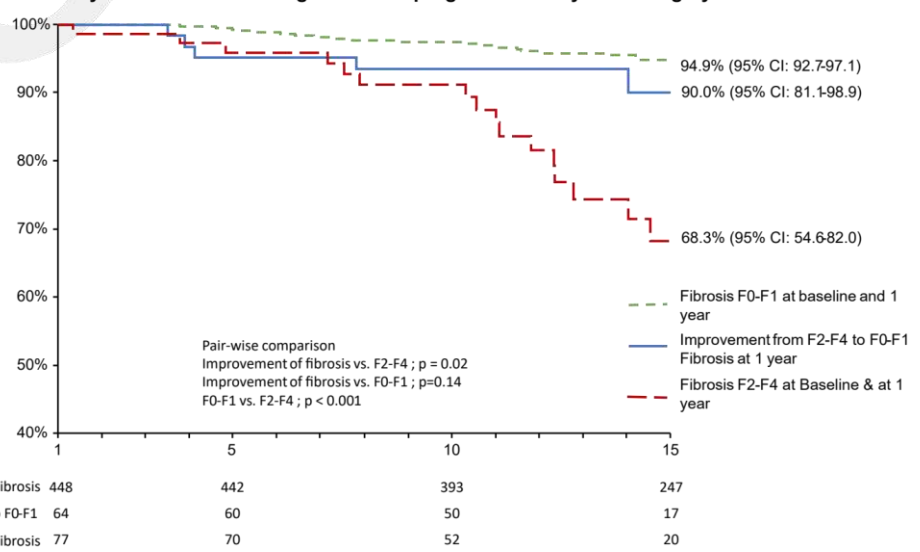
Clinical Gastroenterology and Hepatology 2025;23:1567–1576

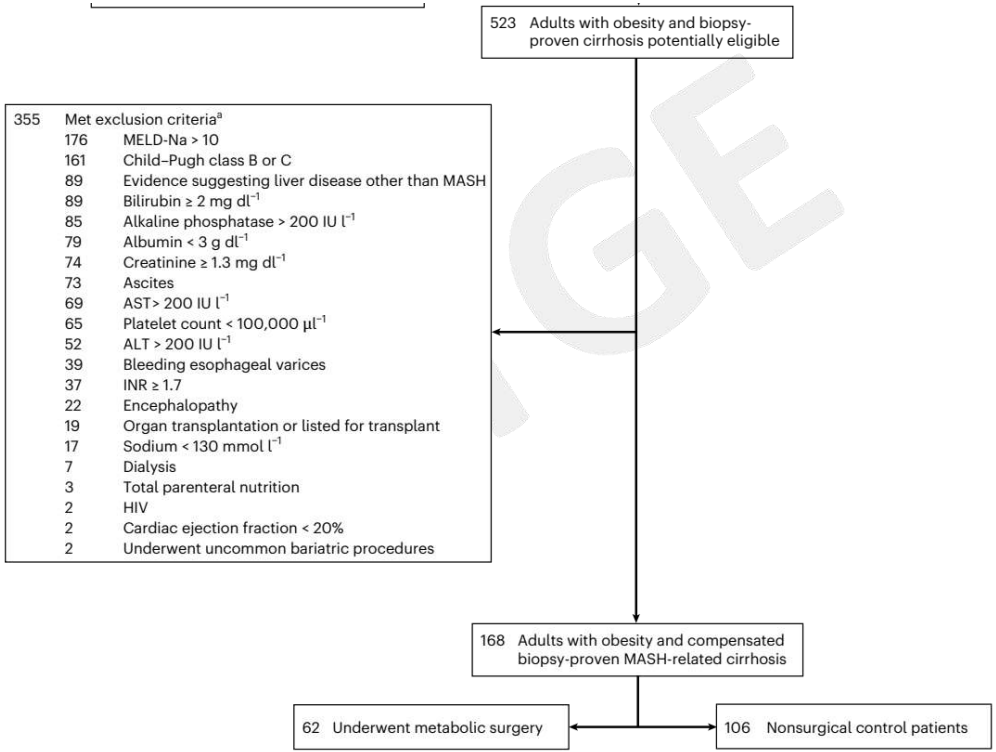
15-year survival according to resolution of MASH with no worsening of fibrosis at 1 year of surgery



15-year survival according to fibrosis progression at 1 year of surgery



Survival Benefit of Bariatric Surgery and Cirrhosis



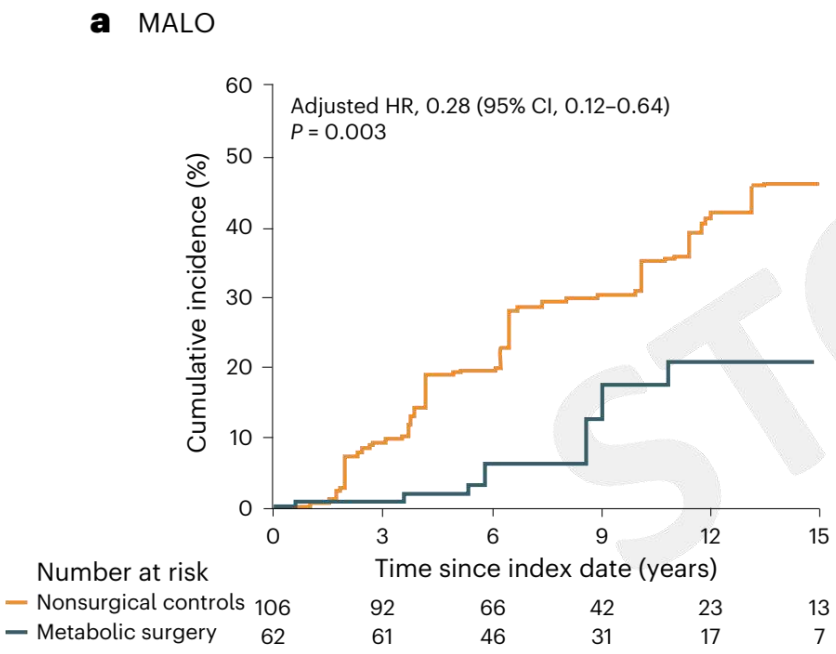
Aminian A, Nat Med 2025

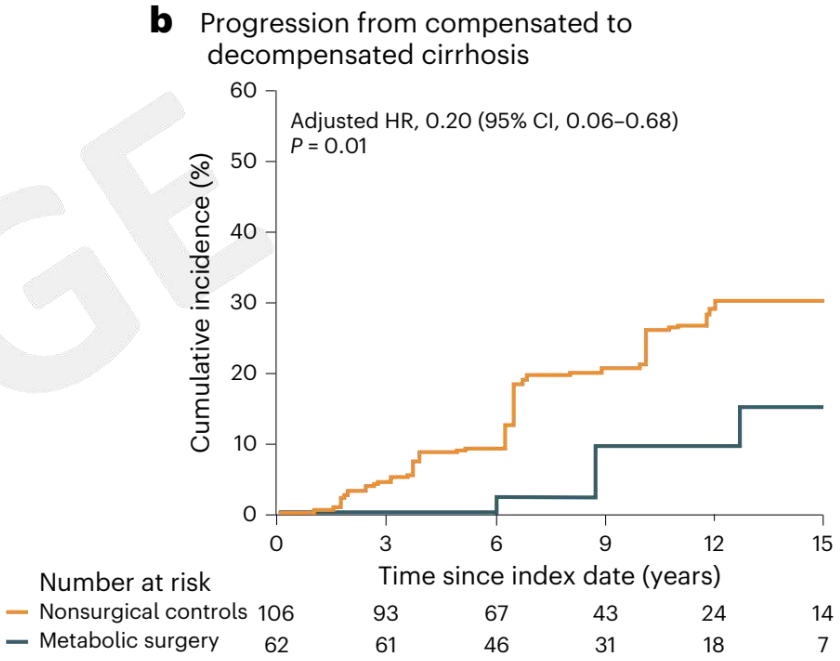
Survival Benefit of Bariatric Surgery and Cirrhosis

Outcome variable	Total cohort (*n*=168)		Metabolic surgery (*n*=62)		Nonsurgical controls (*n*=106)	
	n	Median (range) time interval (years)	*n*	Median (range) time interval (years)	*n*	Median (range) time interval (years)
Composite MALO (primary endpoint)	52	5.7 (0.7–17.2)	10	5.7 (0.7–16.6)	42	5.6 (0.8–17.2)
Encephalopathy[a]	27	6.6 (1.3–15.3)	3	8.7 (6.1–12.7)	24	6.5 (1.3–15.3)
Ascites[b]	24	5.6 (0.8–17.2)	3	5.9 (5.3–8.7)	21	5.1 (0.8–17.2)
Variceal bleeding	6	6.6 (2.8–15.8)	0	–	6	6.6 (2.8–15.8)
HCC	8	6.7 (1.8–12.6)	2	3.7, 10.9[c]	6	6.7 (1.8–12.6)
Liver transplant	9	8.4 (1.9–12.9)	1	8.2[c]	8	8.5 (1.9–12.9)
All-cause mortality	32	7.4 (0.7–16.6)	6	5.2 (0.7–16.6)	26	8.0 (1.9–16.1)
Decompensation (secondary endpoint)[d]	37	6.2 (0.8–17.2)	4	7.3 (5.3–12.7)[e]	33	6.2 (0.8–17.2)

Aminian A, Nat Med 2025

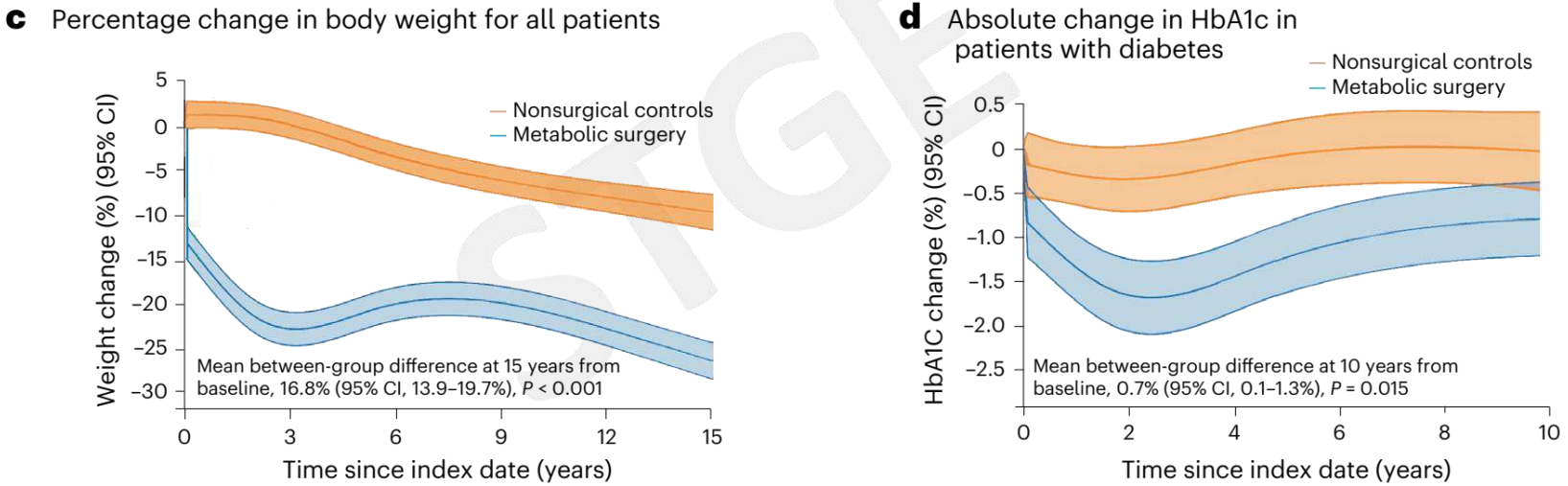
Survival Benefit of Bariatric Surgery and Cirrhosis





Aminian A, Nat Med 2025

Survival Benefit of Bariatric Surgery and Cirrhosis



Aminian A, Nat Med 2025

Conclusions

- L’approche diagnostique pour les patients MAFLD est mieux codifiée
- Parmi les critères métaboliques, le diabète a une influence pronostique majeur dans la progression de la fibrose et le développement du CHC
- Le concept de MetALD ne résistera pas à l’approche basée sur les évidences scientifiques
- L’utilisation des méthodes diagnostiques non invasives de la fibrose sera indispensable tant pour le suivi que pour la sélection des patients candidats à un traitement moléculaire ou une chriurgie bariatrique

Conclusions

- Nous sommes proches de l'utilisation thérapeutique des molécules dans la MASH
  - L'Agence européenne des médicaments (EMA) a recommandé l'autorisation de mise sur le marché (AMM) conditionnelle du Rezdiffra (resmetirom)
  - Analyse de l'EMA du Semaglutide est en cours

- La plupart des molécules en phase II sont actuellement évalués dans le cadre d'étude de phase III

Conclusions

- La mise sur le marché définitive est conditionnée par la démonstration de données sur les critères robustes tels qu!
  - Incidence cirrhose
  - MELD≥15
  - Décompensation
  - Transplantation
  - Mortalité (globale et hépatique)

- Les stratégies combinant les voies ciblant les lésions inflammatoires (Resmerirom et FGF21) et autres voies GLP-1 sont des pistes d'intérêt

- La chirurgie bariatrique aura une place importante dans l'algorithme thérapeutique des patients ayant une cirrhose ou un profil métabolique sévère avec une progression rapide de la cirrhose