
EVALUACION DE LA FIBROSIS HEPATICA 2024

Dr Francisco Fuster
Hepatólogo
Cedid Viña del Mar



- CONFLICTOS DE INTERES:
- I.P. ESTUDIO FASE 3 NATIV, LANIFIBRANOR en MASH + FIBROSIS 2/3
- REALIZO FIBROSCAN EN LA ZONA

RESUMEN

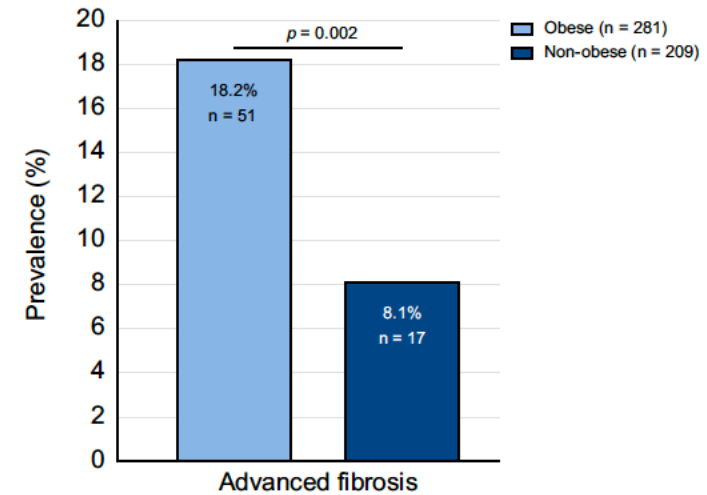
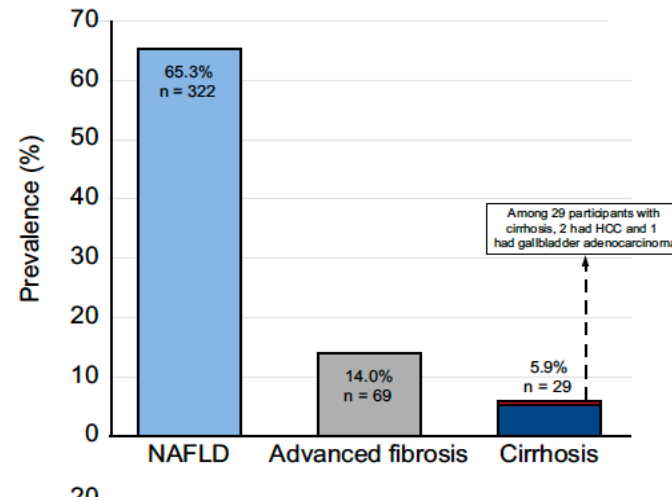
- EVALUACION DE LA FIBROSIS HEPATICA
- ¿COMO?
- ¿A QUIÉN ?
- CASO CLINICO

RESUMEN

- EVALUACION DE LA FIBROSIS HEPATICA
- **¿POR QUE?**
- ¿A QUIÉN ?
- ¿COMO?
- CASO CLINICO

A prospective study on the prevalence of NAFLD, advanced fibrosis, cirrhosis and hepatocellular carcinoma in people with type 2 diabetes

The prevalence of NAFLD, advanced fibrosis and cirrhosis were 65%, 14% and 6% respectively.



EVALUACION DE LA FIBROSIS HEPATICA

- ¿Por qué?
- Cirrosis puede no ser evidente: Ex físico, Ex. lab e imágenes son normales
- Conocer si un paciente es cirrótico o no, es muy relevante
- Permite prevenir o tratar precozmente complicaciones que cambian su pronóstico vital

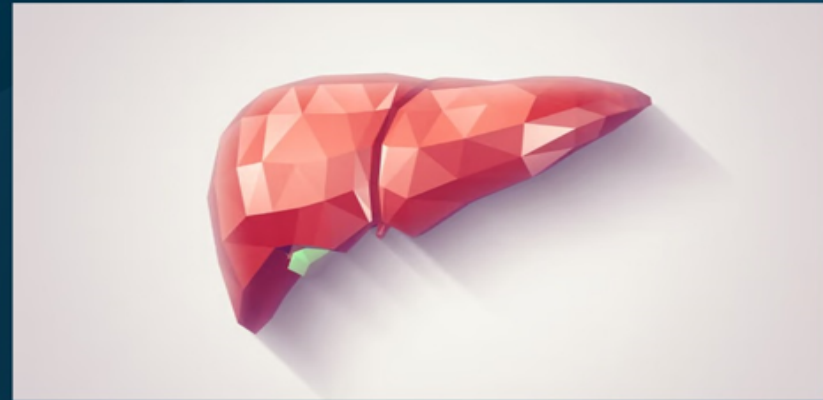
- Pesquisa de Hipertensión portal clínicamente significativa (HPCS)
Estrecha correlación con el grado de fibrosis y la rigidez hepática

- Conocer estadios pre cirróticos de mal pronostico

EVALUACION DE LA FIBROSIS HEPATICA

- ¿ por que?
- ***Estadios pre cirróticos de mal pronostico***
- Fibrosis Moderada o Severa = (puentes de fibrosis) F2 Y F3
- Pueden tener rápida progresión a la cirrosis, >> peor sobrevida
- Indicación de terapia mas agresivas (c. metabólico/sobre peso)
- Indicación de nuevos fármacos (2024****)

Marzo 2024 FDA aprueba primer fármaco en MASH con fibrosis (F2/F3): RESMETIROM



PHARMA

FDA approves first drug for MASH in Madrigal's Rezdiffra

The drug emerged from a notorious drug development graveyard about four decades after the prior term for the disease, NASH, was coined by researchers.

CONOCER EL GRADO DE FIBROSIS

- EXISTE CIRROSIS??
- HAY HPCS??
- HAY FIBROSIS SIGNIFICATIVA?
- (F2 F3)
- PREVENIR HDA
- TRATAR PRECOZMENTE HCC
- INICIAR B. BLOQUEO NCS
- TERAPIA MAS AGRESIVA DE CONDICIÓN ASOCIADA
- ACCESO A NUEVOS FARMACOS

RESUMEN

- EVALUACION DE LA FIBROSIS HEPATICA
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- CASO CLINICO

Available non-invasive tests: Context of use

« Biological » approach

- AST/ALT ratio
- APRI
- FIB-4
- NFS

Non-patented

- FibroTest®
- ELF™
- FibroMètre®
- Hepascore

Patented

« Physical » approach



VCTE

ARFI / 2D SWE

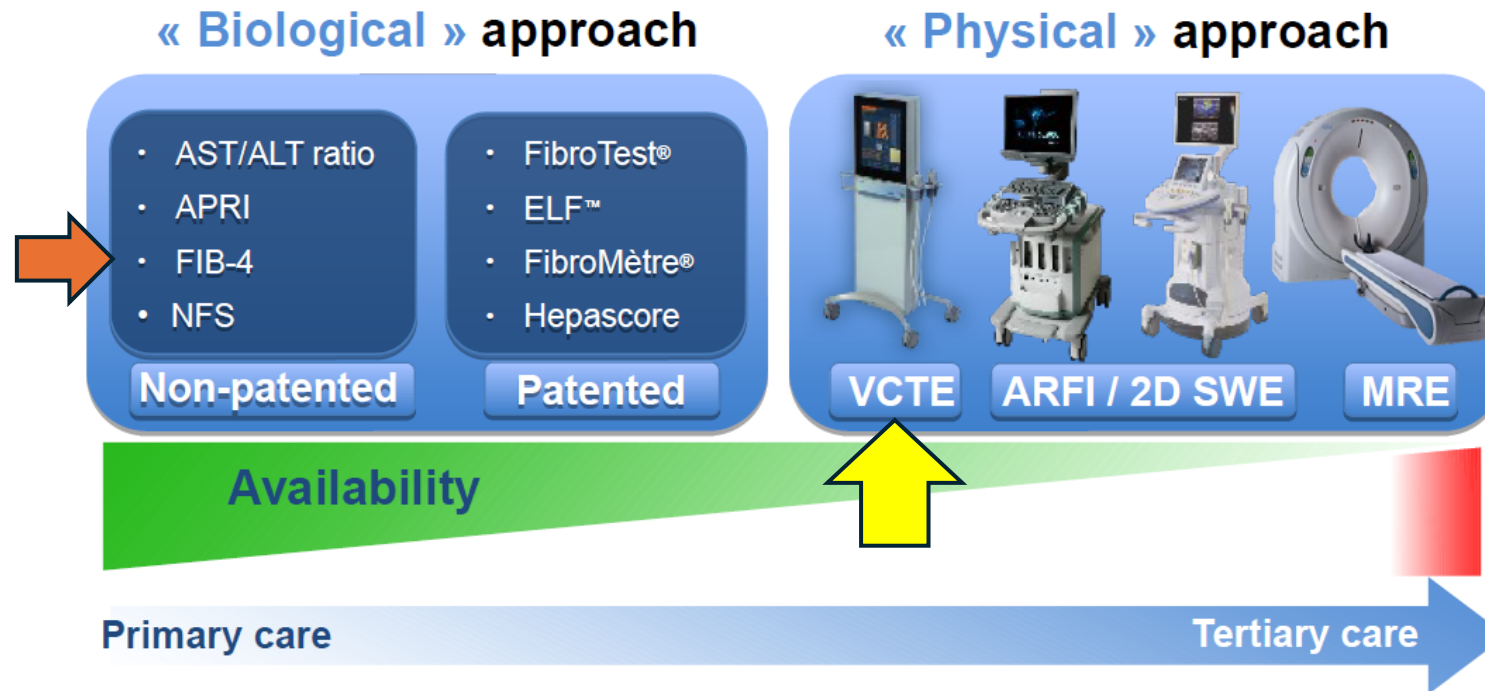
MRE

Availability

Primary care

Tertiary care

Available non-invasive tests: Context of use



FIB 4: ORIGEN

Filters applied: Abstract, Clinical Trial, Meta-Analysis, Randomized Controlled Trial, Review, 1 year. [Clear all](#)

[Comparative Study](#) > [Hepatology](#). 2006 Jun;43(6):1317-25. doi: 10.1002/hep.21178.

Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection

Richard K Sterling ¹, Eduardo Lissen, Nathan Clumeck, Ricard Sola, Mendes Cassia Correa, Julio Montaner, Mark S Sulkowski, Francesca J Torriani, Doug T Dieterich, David L Thomas, Diethelm Messinger, Mark Nelson; APRICOT Clinical Investigators

Affiliations + expand

PMID: 16729309 DOI: 10.1002/hep.21178

FIB 4: GRAN VALOR >>>ACCESO UNIVERSAL Y ALTO VALOR PREDICIVO NEGATIVO PARA FIBROSIS AVANZADA (CIRROSIS)

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}}$$

Figure 4 - Fib4

The Fib4 represents an easy-to-use test for predicting severe hepatic fibrosis or cirrhosis. Abbreviations: AST = aspartate aminotransferase; ALT = alanine aminotransferase

Source: Vallet-Pichard A, Mallet V, Nalpas B, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. Hepatology. 2007;46:32-6.

Puntuación de FIB 4 (< 65 AÑOS)

VALOR ENCONTRADO DE FIB 4

- PUNTAJE < 1,3
- PUNTAJE DE 1,3 A 2,67
- PUNTAJE > 2,67

INTERPRETACIÓN

- AUSENCIA DE CIRROSIS (F0-F1)
- VALOR INTERMEDIO, REQUIERE VALIDACIÓN DE OTRO MÉTODO
- FIBROSIS AVANZADA O CIRROSIS (F3-F4)

FIB 4 : FALSOS POSITIVOS

- **Edad** > 65AÑOS,
- VALOR DE CORTE 1,3>>>2,0
- **Ejercicio físico** suele elevar transaminasas, GOT > GTP
- Investigar otras causas de plaquetopenia

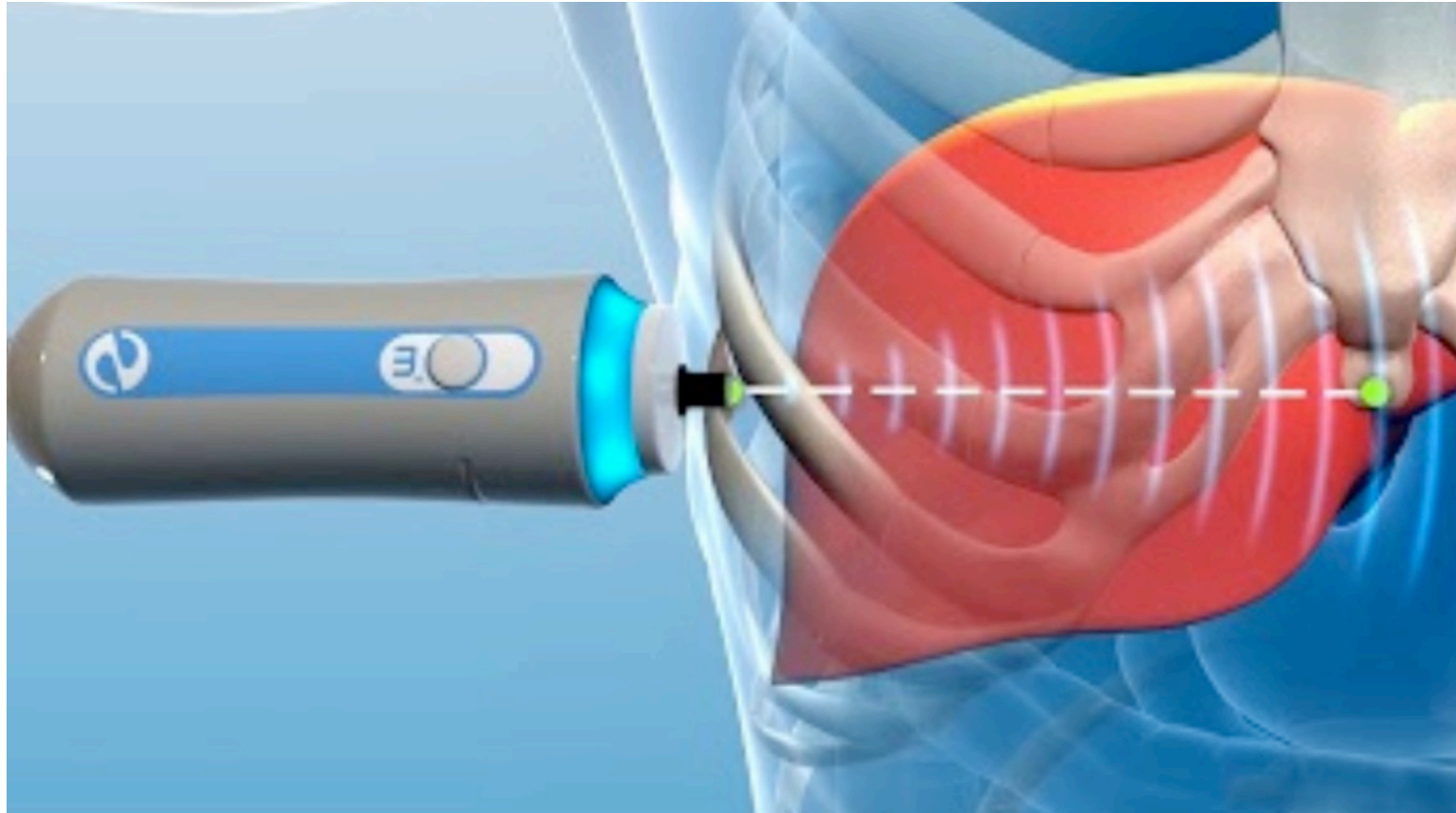
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FIBROSCAN / *Vibration controlled transient elastography (VCTE)*



FIBROSCAN: DOS PALABRAS

- EVALUA UNA PORCIÓN 100 VECES MAYOR QUE BIOPSIA HEPATICA PERCUTANEA (equivale a una pila AA)
- NO HAY LIMITACIONES POR EDAD NI POR PATOLOGÍA
- RECOMENDACIONES CLASICAS DE NO REALIZAR ELASTOGRAFIA:
- ASCITIS O ELEVACION IMPORTANTE DE GOT/GTP O DE FA /GGTP, CONGESTION HEPATICA (ICC) O DILATACION DE VIA BILIAR
- OBESIDAD, IMC > 40, RESULTADOS MAS INCIERTOS

FIBROSCAN: DOS PALABRAS

- MUY BUENA CORRELACIÓN ENTRE VALORES DE RIGIDEZ HEPÁTICA GRADO DE FIBROSIS (DESDE F0 A F4)
- MAS RECIENTEMENTE, SE HA DEMOSTRADO UNA MUY BUENA CORRELACIÓN CON LA PRESION PORTAL.
- VALORES <10Kpa, EXCLUYEN HPCS
- VALORES > 25Kpa, MUY PROBABLE HPCS

RESUMEN

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- ¿COMO?
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Cirrhosis Prevention in NAFLD

High-risk groups for NAFLD

Prediabetes
or
T2D

Obesity
and/or
≥2 cardiometabolic
risk factors

Steatosis
(on imaging)
or
↑ AST or ALT



Fibrosis Risk Stratification

Low
Risk

FIB-4: <1.3

FIB-4 Index

FIB-4: >2.67

High
Risk

FIB-4: 1.3 - 2.67

Indeterminate Risk

Order second test

Liver Stiffness Measurement (LSM)
by Elastography
or
ELF Blood Test

Cirrhosis risk
higher if:

- T2D
(or prediabetes)
- Age >50
- Higher BMI
(40 kg/m²)
- More metabolic
risk factors
- Genetic factors
(i.e., PNIPA3)

Low Risk

FIB-4 <1.3 or LSM <8 kPa or ELF <7.7
(or if a liver biopsy was performed
fibrosis stage is F0-F1)

Indeterminate Risk

FIB-4 1.3 - 2.67 or LSM 8 - 12 kPa
or ELF 7.7 - 9.8
(liver specialist to consider need for biopsy)

High Risk

FIB-4 >2.67 or LSM >12 kPa or ELF >9.8
(or if a liver biopsy was performed
fibrosis stage is F2-F4)

- Managed by primary care team, endocrinologist, other
- Focus care on obesity management & CVD prevention

- Referral to liver specialist for additional proprietary biomarkers or imaging (MRE, cT1, other)
- Multidisciplinary team to prevent cirrhosis and CVD

Caso clínico:

MARZO 2023

Hombre 61 años

DHC X TAC >>MASH+OH moderado (1 a 3 x día)

PESO AL DIAGNOSTICO: 92kg = IMC 31

GOT y GTP 2x FA1x GGTP 2x PLAQ 98000

AFP 18 Y FE 730

RM+ ENDO+ Cineética hierro

Dieta saludable+ susp. OH y ejercicio +

Control periódico con nutricionista (AJ)

FIBROSCAN MAYO 2023 Y JUNIO 2024

FibroScan basal 2023

FibroScan[®]

Barbara Zamora
Errazuriz 634
Viña del Mar
Chile
322556024

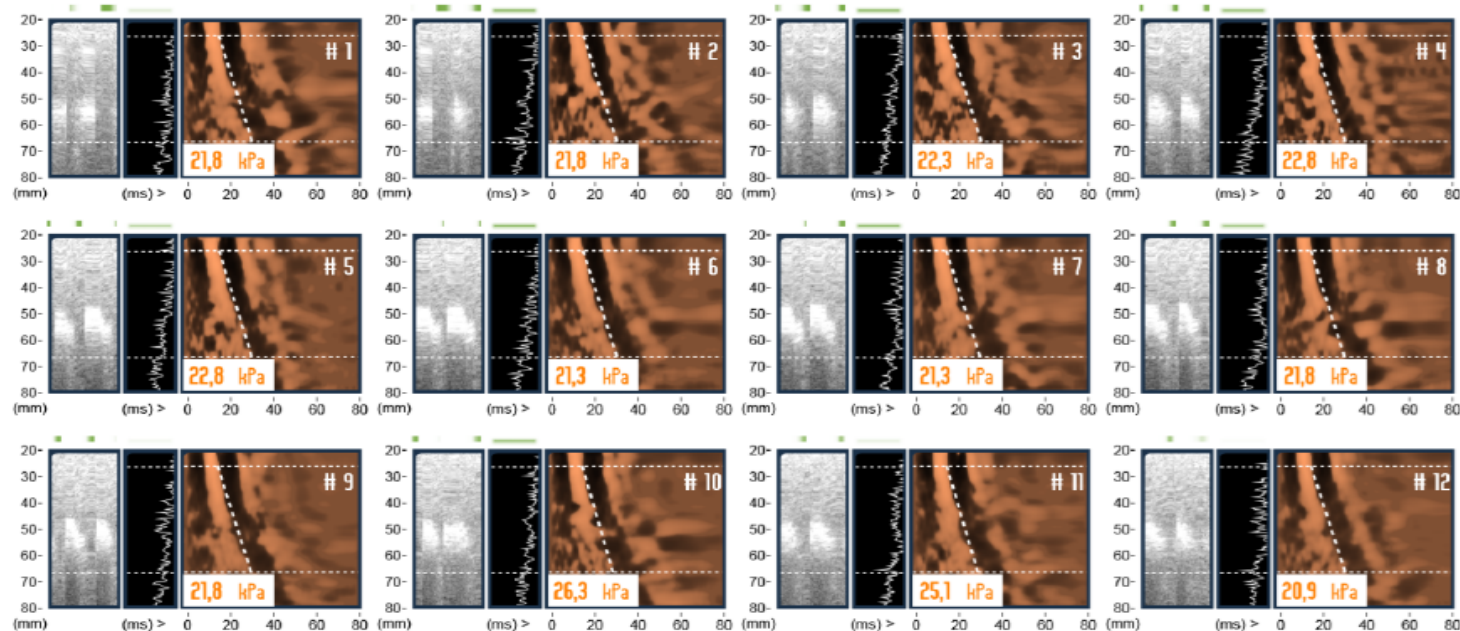
03/05/2023

14:13:54

SALINAS GUZMAN
VICTOR
17/09/1962 (V)
9243809-0
Indicación : DANO HEPATICO
Médico referente : DR FUSTER

E (kPa)
MEDIANA IQR
21,8 1,1
IQR/med.
5 %

Examen M (Hígado)
Operador : DR FUSTER
Mediciones válidas : 12
Total de mediciones : 13



Notas :

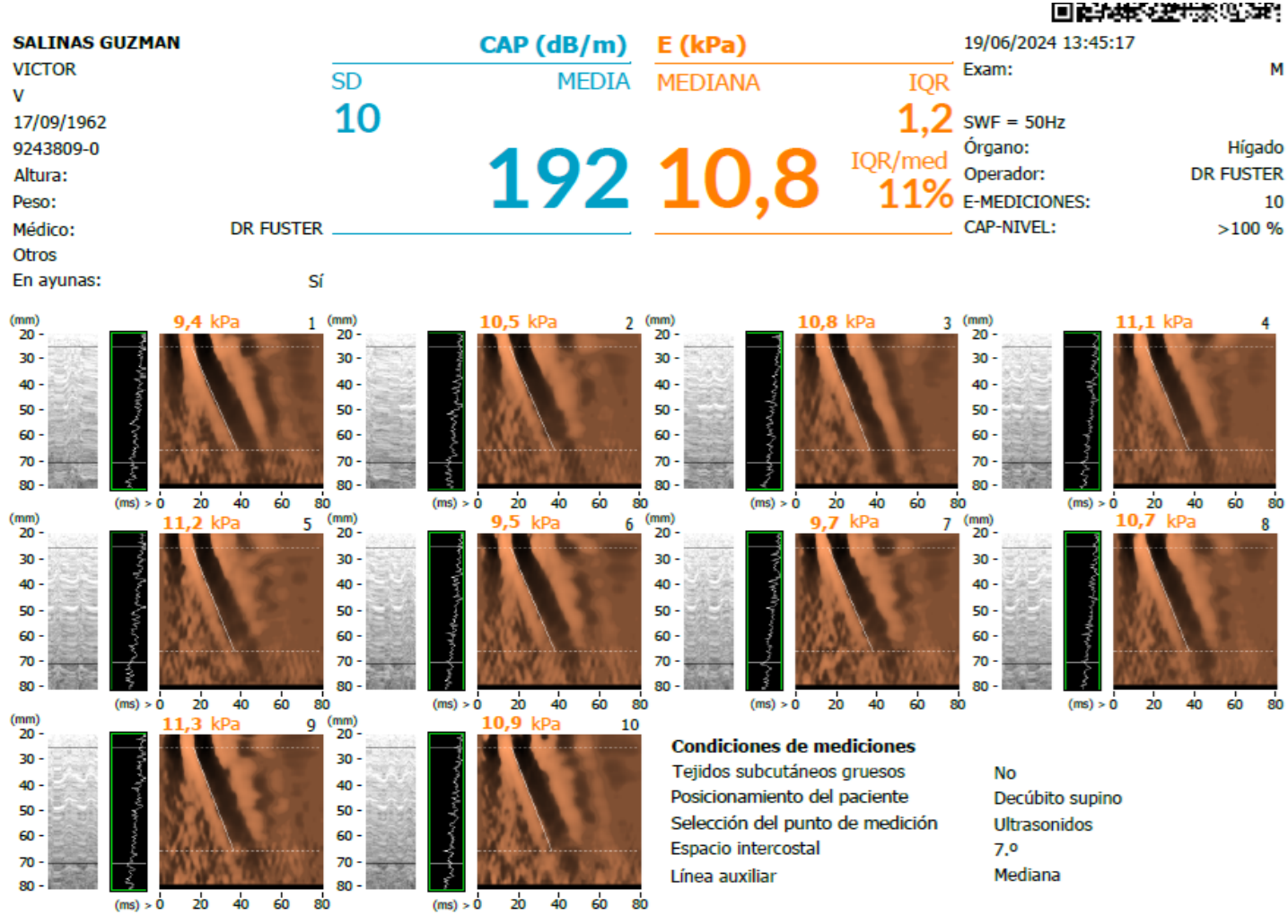
Caso clínico:

- MARZO 2023
- Hombre 61 años
- DHC X TAC >>MASH+OH moderado (<2 x día)
- PESO AL DIAGNOSTICO: 92kg = IMC 31
- GOT y GTP 2x FA1x GGTP 2x PLAQ 98000
- AFP 18 Y FE 730
- RM+ ECO+ ENDO
- Dieta saludable+ susp. OH y ejercicio +
- Control periódico con nutricionista (AJ)

- **PESO ACTUAL : 77kg (- 15KG)**
- **LAB HEPATICO ACTUAL NORMAL**
- **AFP 6, FE 330 Y PLAQ 115000**

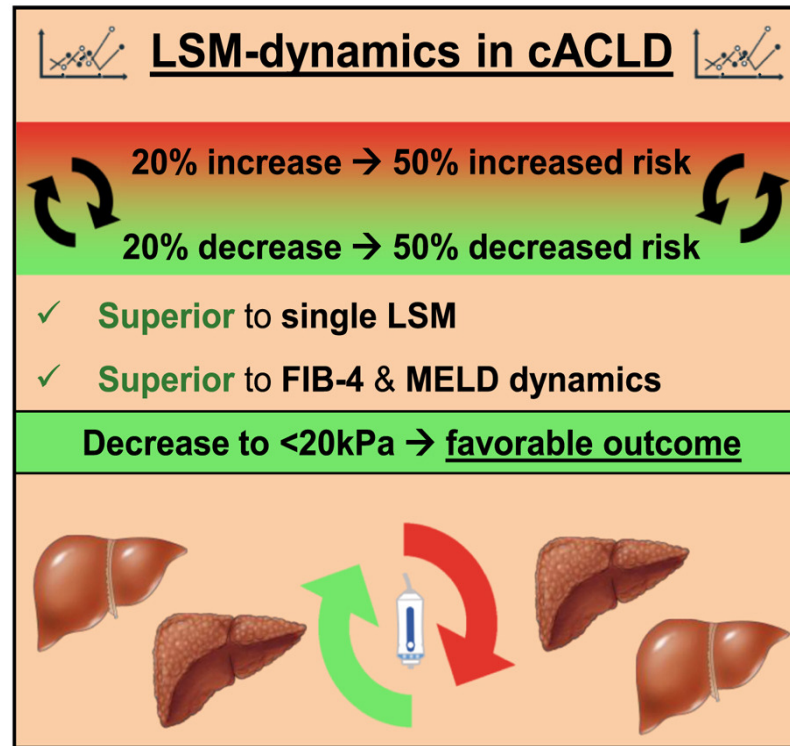
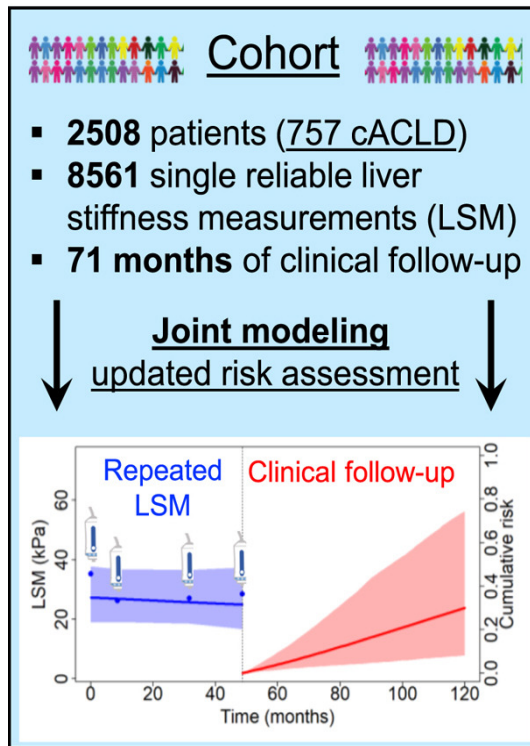
- FIBROSCAN MAYO 2023 Y JUNIO 2024

Fibroscan actual junio 2024




Consenso Baveno VII 2022: Fibroscan anual en DHC compensado

Dynamics in liver stiffness measurements predict outcomes in advanced chronic liver disease



Repeat LSM

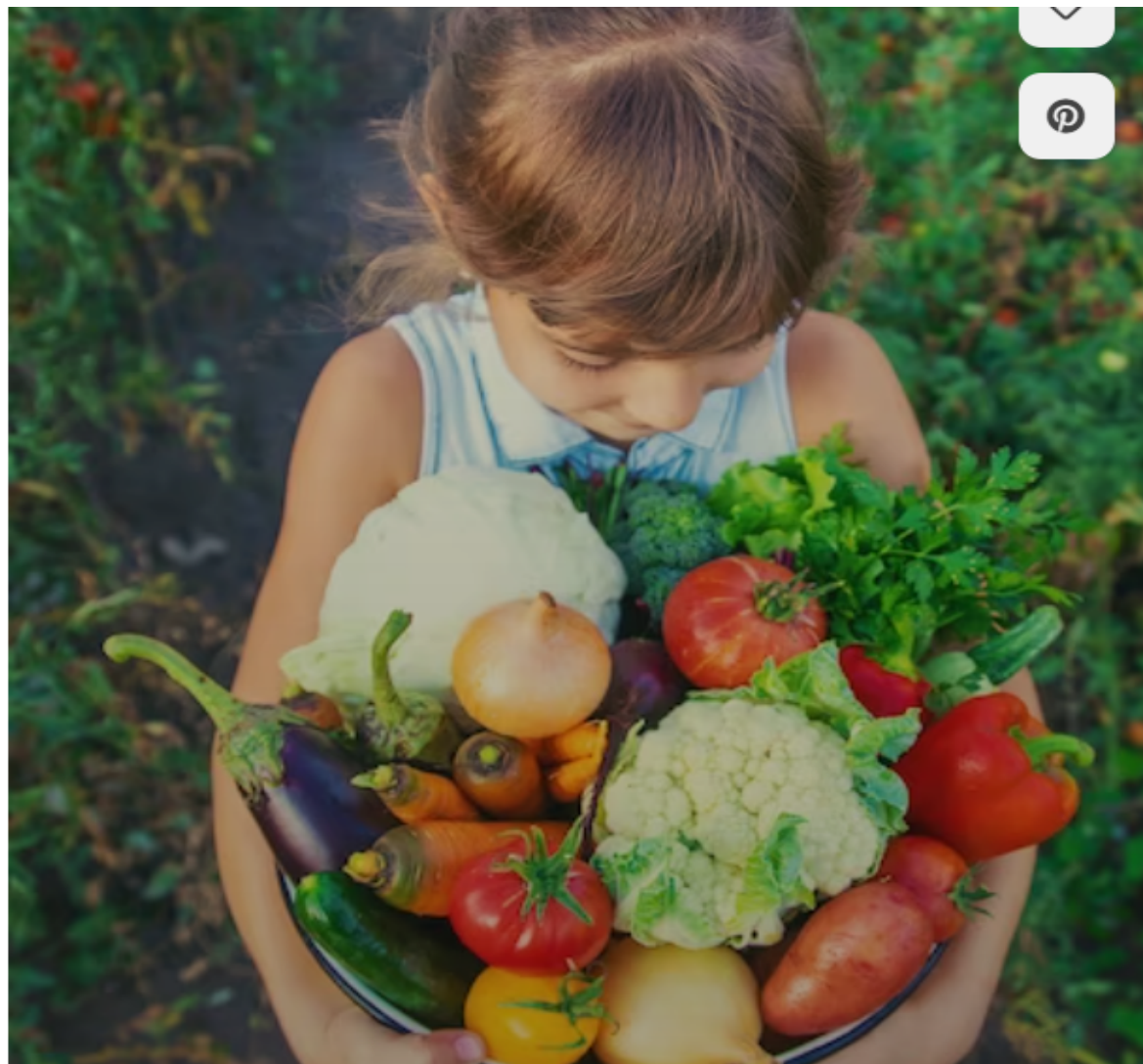
- ✓ to monitor progression (nonACLD)
- ✓ to predict outcome (cACLD + dACLD)



WE WANT YOU!

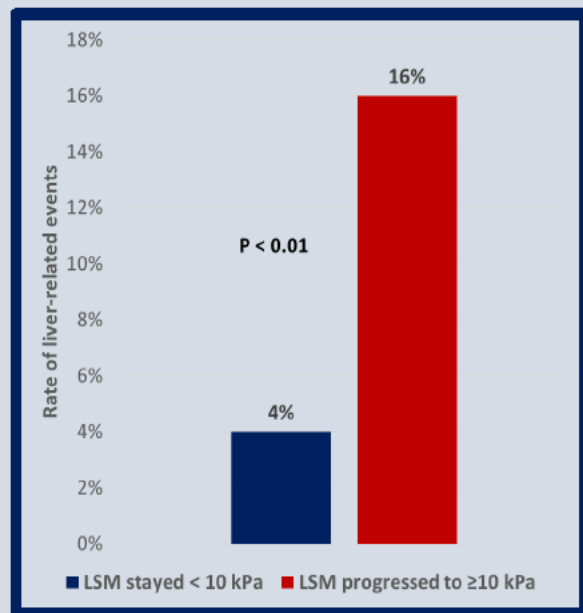
Gastroenterology

MUCHAS GRACIAS

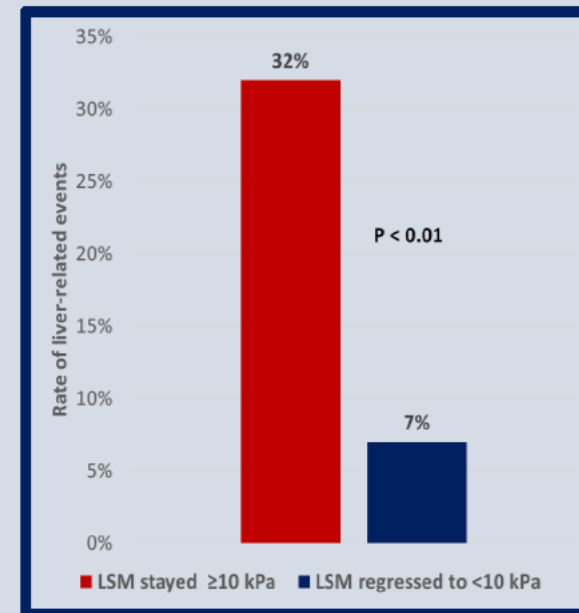
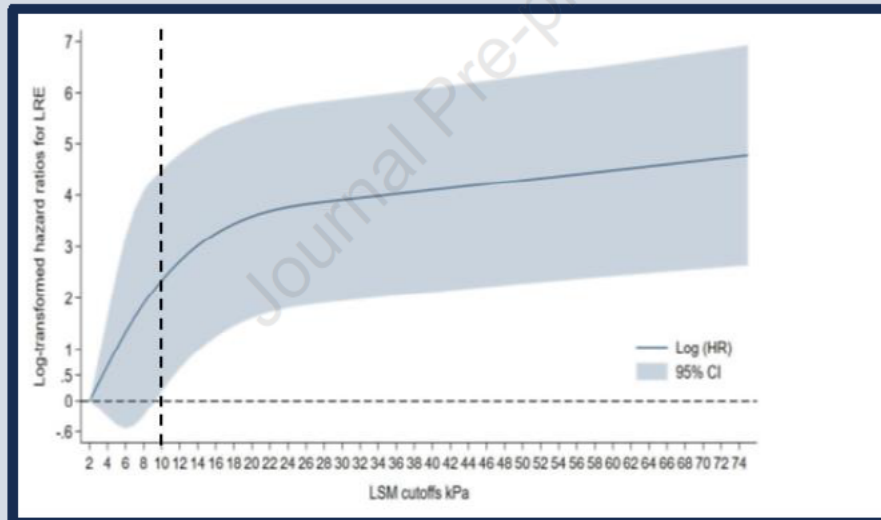


Progression & regression of LSM are associated with risk of liver-related events in NAFLD

- 1,403 adult participants in NASH CRN studies
- Annual prospective follow-up with annual VCTE exam
- 4.4 years mean follow-up with 89 liver-related events (LRE)



Risk of LRE begins to rise at LSM 10 kPa



Progressors to LSM ≥10 kPa
Adj.HR: 3.8, 95% CI [2.3-6.5]

Regressors to LSM <10 kPa
Adj.HR: 0.25, 95% CI [0.10-0.61]

380%



Risk of LRE



75%

EVALUACION DE LA FIBROSIS HEPATICA

- ¿Por qué?
- Cirrosis puede no ser evidente: Ex físico, lab e imágenes normales
- Conocer si un paciente es cirrótico (DHCC) o no es, muy relevante
- Permite prevenir complicaciones que cambian su pronóstico vital
- Pesquisa de HCC, prevención de HDA
- Pesquisa de Hipertensión portal clínicamente significativa (HPCS)
- Alto riesgo de descompensaciones relacionadas como ascitis, encefalopatía PBE y HDA>>>> BB no cardio selectivo
- Conducta ante eventos concomitantes como:
- cirugías, infecciones, IAM, cáncer etc

RESMETIRON MECANISMO DE ACCION

- Agonista del receptor beta de hormona tiroidea en el hígado (TRHbeta), el cual es responsable de varias de sus vías metabólicas.
- En Mash su disfunción es frecuente, con < niveles de actividad hormona tiroidea en el hígado>>>“Hipotiroidismo Hepático”
- Disfunción mitocondrial, y en la oxidación de ac. grasos, junto con estrés oxidativo y activación de fibrosis.
- Agonistas selectivos en el hígado de TRH beta, han mostrado en Estudios en fase 2 buenos resultados en disminuir la esteatosis y también el MASH, sin efectos colaterales significativos.

Nueva terapia en MASH

nature medicine



Article

<https://doi.org/10.1038/s41591-023-02603-1>

Resmetirom for nonalcoholic fatty liver disease: a randomized, double-blind, placebo-controlled phase 3 trial

Received: 6 March 2023

Accepted: 20 September 2023

Published online: 16 October 2023

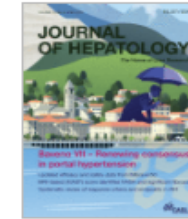
Check for updates

Stephen A. Harrison¹✉, Rebecca Taub², Guy W. Neff³, K. Jean Lucas⁴,
Dominic Labriola², Sam E. Moussa⁵, Naim Alkhouri⁶ & Mustafa R. Bashir⁷

Nonalcoholic steatohepatitis (NASH) is a progressive liver disease with no approved treatment. MAESTRO-NAFLD-1 was a 52-week randomized,





Journal of Hepatology
Volume 76, Issue 4, April 2022, Pages 959-974



Seminar

Baveno VII – Renewing consensus in portal hypertension

Roberto de Franchis¹  , Jaime Bosch^{2 3}, Guadalupe Garcia-Tsao^{4 5},

Thomas Reiberger^{6 7}, Cristina Ripoll⁸

Baveno VII Faculty[§]

Show more 



Gastroenterology



Volume 165, Issue 4, October 2023, Pages 1041-1052



Original Research

Full Report: Hepatobiliary

Dynamics in Liver Stiffness Measurements Predict Outcomes in Advanced Chronic Liver Disease

Georg Semmler^{1,2}, Zhenwei Yang³, Laurenz Fritz¹, Fiona Köck¹,
Benedikt Silvester Hofer^{1,2,4}, Lorenz Balcar^{1,2}, Lukas Hartl^{1,2}, Mathias Jachs^{1,2},
Katharina Stopfer^{1,2}, Anna Schedlbauer¹, Daniela Neumayer¹, Jurij Maurer¹,
Theresa Müllner-Bucsics^{1,2}, Benedikt Simbrunner^{1,2,4}, Bernhard Scheiner^{1,2},
Michael Trauner¹, Mattias Mandorfer^{1,2}, Thomas Reiberger^{1,2,4}  

Journal Pre-proof

Increases and decreases in liver stiffness measurements are independently associated with the risk of liver-related events in NAFLD

Samer Gawrieh, Eduardo Vilar-Gomez, Laura A. Wilson, Francis Pike, David E. Kleiner, Brent A. Neuschwander-Tetri, Anna Mae Diehl, Srinivasan Dasarathy, Kris V. Kowdley, Bilal Hameed, James Tonascia, Rohit Loomba, Arun J. Sanyal, Naga Chalasani, for the NASH Clinical Research Network

PII: S0168-8278(24)00343-X

DOI: <https://doi.org/10.1016/j.jhep.2024.05.008>

Reference: JHEPAT 9623

To appear in: *Journal of Hepatology*

Received Date: 5 July 2023

Revised Date: 29 April 2024

Accepted Date: 6 May 2024





Digestive and Liver Disease
Volume 55, Issue 11, November 2023, Pages 1472-1479



Liver, Pancreas and Biliary Tract

Dynamics of liver stiffness predicts complications in patients with HCV related cirrhosis treated with direct-acting antivirals

Alberto Nicoletti^a, Maria Elena Ainora^a, Marco Cintoni^b, Matteo Garcovich^a,
Barbara Funaro^a, Silvia Pecere^a, Martina De Siena^a, Francesco Santopaolo^a,
Francesca Romana Ponziani^a, Laura Riccardi^a, Antonio Grieco^c, Maurizio Pompili^a,

NUEVO DE ELASTOGRAFIA HEPATICA

Research Article

MASLD and Alcohol-Related Liver Diseases

JOURNAL
OF HEPATOLOGY

Using liver stiffness to predict and monitor the risk of decompensation and mortality in patients with alcohol-related liver disease

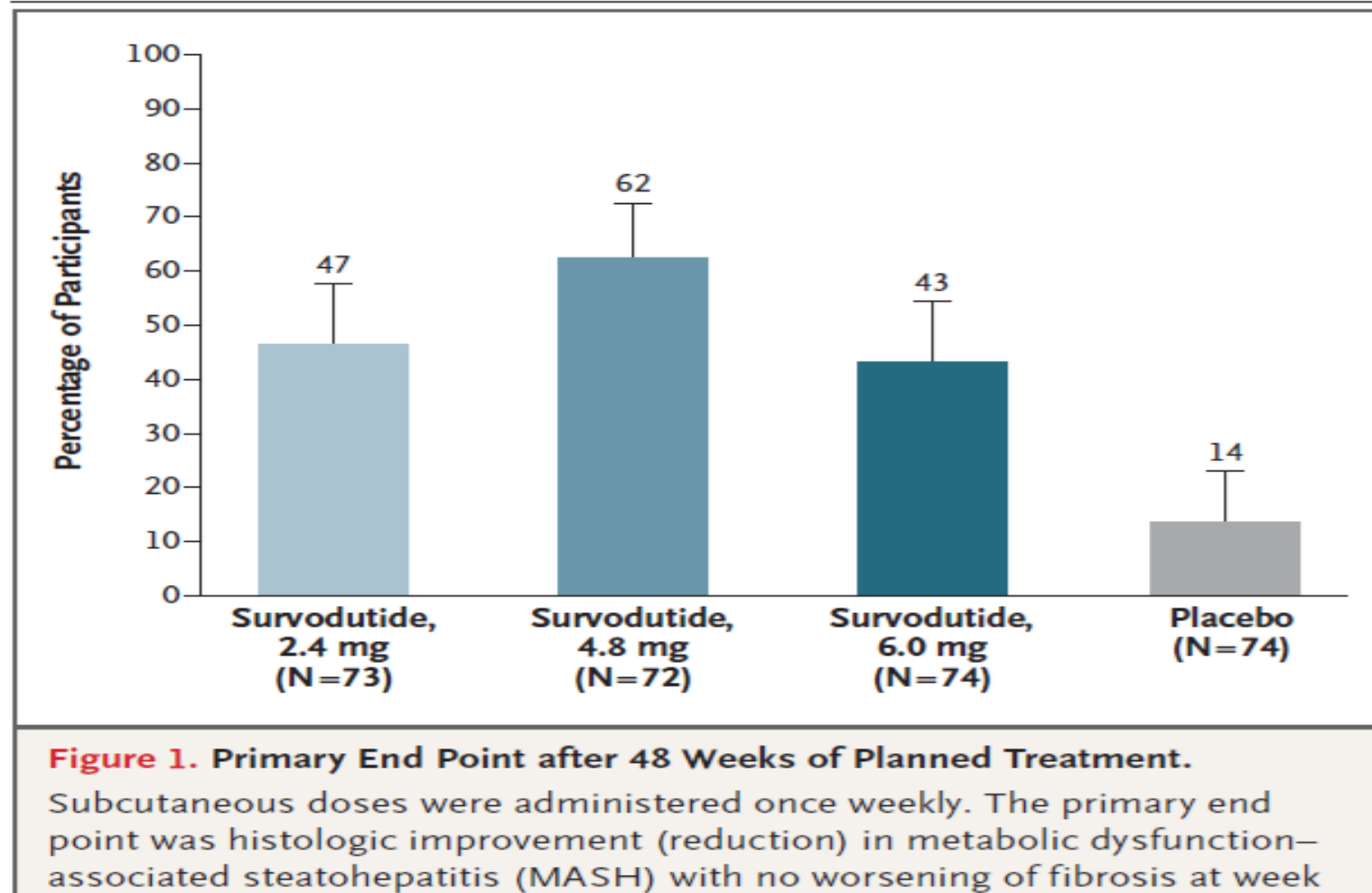
Katrine Holtz Thorhauge^{1,2}, Georg Semmler³, Stine Johansen^{1,2}, Katrine Prier Lindvig^{1,2}, Maria Kjærsgaard^{1,2}, Johanne Kragh Hansen^{1,2}, Nikolaj Torp^{1,2}, Camilla Dalby Hansen^{1,2}, Peter Andersen¹, Benedikt Silvester Hofer³, Wenyi Gu⁴, Mads Israelsen^{1,2}, Mattias Mandorfer³, Thomas Reiberger³, Jonel Trebicka⁴, Maja Thiele^{1,2,*}, Aleksander Krag^{1,2}, on behalf of the Microb-Predict, Galaxy and MicrobLiver consortia

Journal of Hepatology 2024. vol. 81 | 23–32



SURVODUTIDE ESTUDIO FASE 2

MEJORA MASH A 48 SEMANAS DE USO



Nuevos fármacos con buenos resultados (EASL 2024)

Survovutide

Clinical Trial > [Lancet Diabetes Endocrinol. 2024 Mar;12\(3\):162-173.](#)

doi: [10.1016/S2213-8587\(23\)00356-X](https://doi.org/10.1016/S2213-8587(23)00356-X). Epub 2024 Feb 5.

Glucagon and GLP-1 receptor dual agonist survodutide for obesity: a randomised, double-blind, placebo-controlled, dose-finding phase 2 trial

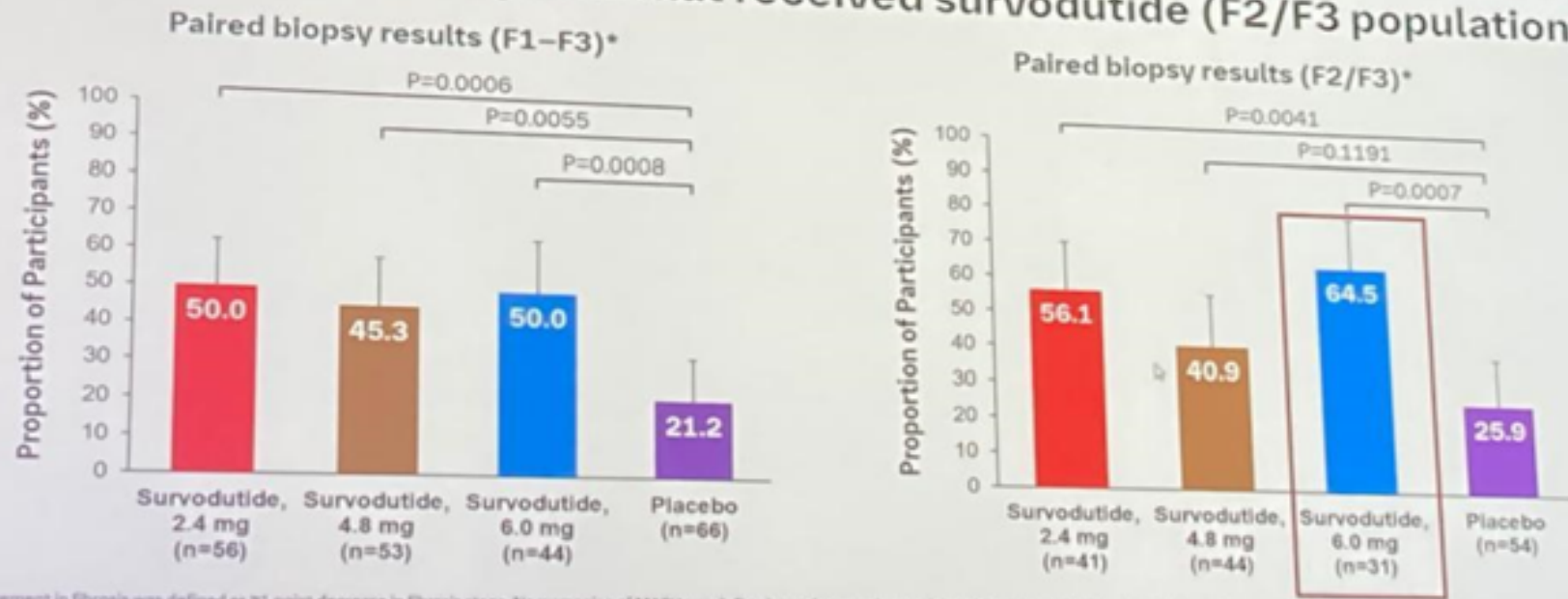
[Carel W le Roux](#)¹, [Oren Steen](#)², [Kathryn J Lucas](#)³, [Elena Startseva](#)⁴, [Anna Unseld](#)⁵,
[Anita M Hennige](#)⁶

Affiliations + expand

PMID: 38330987 DOI: [10.1016/S2213-8587\(23\)00356-X](https://doi.org/10.1016/S2213-8587(23)00356-X)

SURVODUTIDE ESTUDIO FASE 2 MEJORA FIBROSIS A 48 SEMANAS

Improvement in liver fibrosis with no worsening in MASH was observed in up to 64.5%* of participants that received survodutide (F2/F3 population)



Improvement in fibrosis was defined as ≥ 1 point decrease in fibrosis stage. No worsening of MASH was defined as no increase in any of the NAS subscores (ballooning, inflammation, or steatosis). P-values are nominal. *A sensitivity analysis based on participants with paired biopsy results at baseline and end of treatment. Error bars represent 95% confidence intervals. MASH, metabolic dysfunction-associated steatohepatitis; NAS, non-alcoholic fatty liver disease activity score. Sanyal et al. NEJM 2024.

Review

> *Diabetes Ther.* 2024 May;15(5):1069-1084. doi: 10.1007/s13300-024-01566-x.

Epub 2024 Apr 4.

Dual and Triple Incretin-Based Co-agonists: Novel Therapeutics for Obesity and Diabetes

Robert M Gutgesell ^{1 2}, Rubén Nogueiras ^{3 4}, Matthias H Tschöp ^{5 6}, Timo D Müller ^{7 8 9}

Affiliations + expand

PMID: 38573467 PMCID: [PMC11043266](#) DOI: [10.1007/s13300-024-01566-x](#)