MASLD

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Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης
Ιατρική Σχολή

ΙΠΠΟΚΡΑΤΕΙΟ
ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ
ΘΕΣΣΑΛΟΝΙΚΗΣ

Σύνοψη AASLD 2023

Αθήνα, Σάββατο 2 Δεκεμβρίου 2023

Δήλωση σύγκρουσης συμφερόντων

- Ερευνητής σε Κλινική Μελέτη: **GSK, Novo Nordisk**

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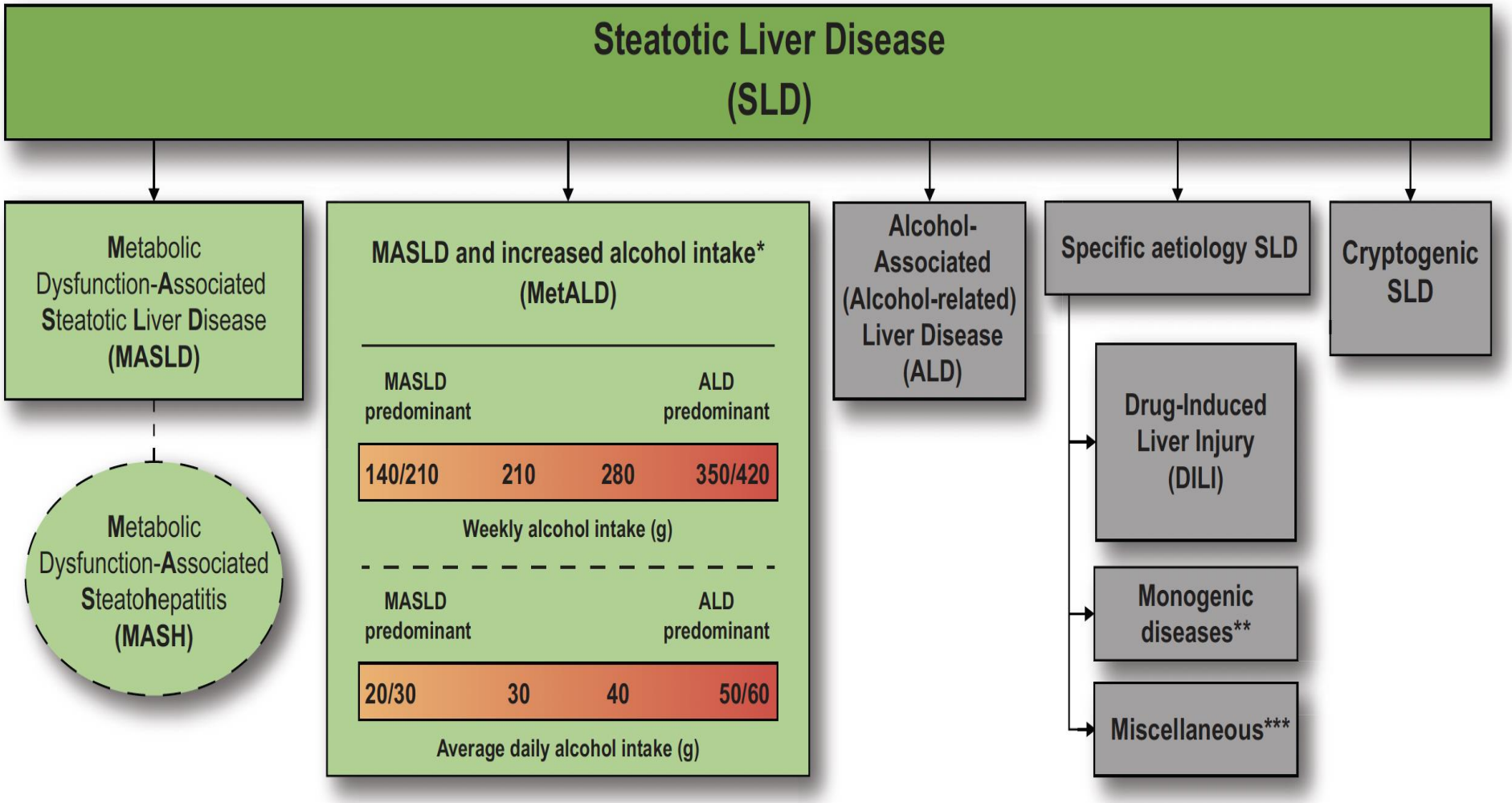
Νέα ονοματολογία



*Weekly intake 140-350g female, 210-420g male (average daily 20-50g female, 30-60g male)

**e.g. Lysosomal Acid Lipase Deficiency (LALD), Wilson disease, hypobetalipoproteinemia, inborn errors of metabolism

***e.g. Hepatitis C virus (HCV), malnutrition, celiac disease, human immunodeficiency virus (HIV)

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Ελληνική μετάφραση

- MASLD = Metabolic Dysfunction-Associated Steatotic Liver Disease
- **ΜΕΣΣΝΗ** = **ΜΕ**ταβολικά **Σ**χετιζόμενη **Σ**τεατωτική **Ν**όσος του **Ή**πατος

Γενική εντύπωση

- Οι εργασίες για τη MASLD (~550) «κυριάρχησαν», τουλάχιστον ποσοτικά, στο συνέδριο.

- Συνεχίζεται η έμφαση της έρευνας στην αναίμακτη διάγνωση της νόσου με τη χρήση καθιερωμένων, αλλά και καινοτόμων μεθόδων, συμπεριλαμβανομένης της τεχνητής νοημοσύνης.

- Παρουσιάστηκαν τα αποτελέσματα κλινικών δοκιμών ποικίλων φαρμακευτικών παραγόντων, κυρίως φάσης 2, που συμπεριέλαβαν σε σημαντικό ποσοστό και κιρρωτικούς ασθενείς.

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Ενότητες παρουσίασης

- Φυσική ιστορία
- Διάγνωση
- Θεραπεία

Φυσική ιστορία

Σχόλια

- **Μελέτες, που βασίζονται σε στατιστική ανάλυση στοιχείων μεγάλων βάσεων δεδομένων.**

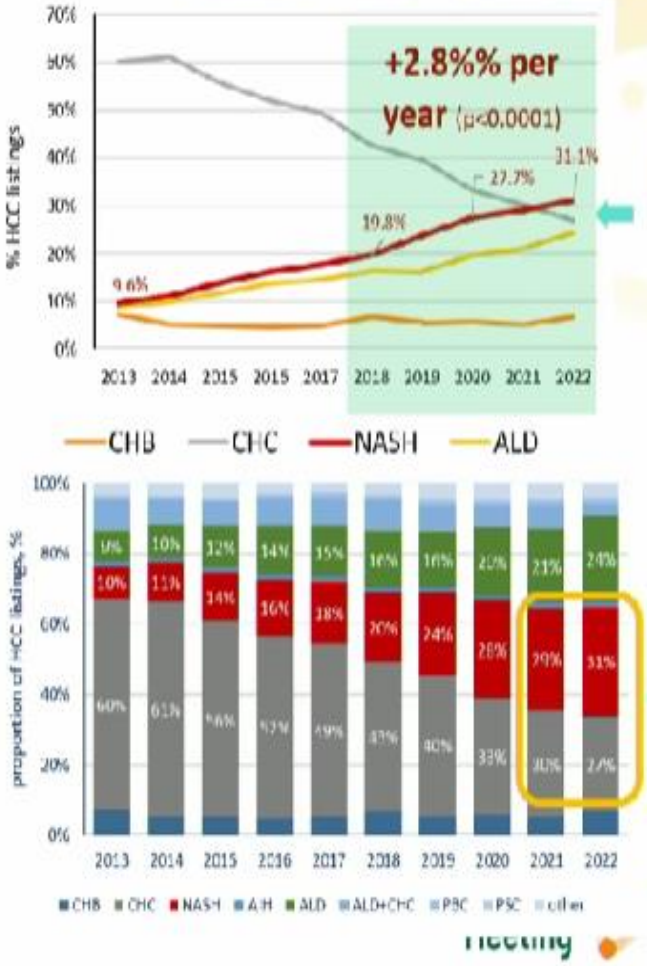
- **Επιβεβαιώνεται η σημαντική συσχέτιση της MASLD με εκβάσεις σχετιζόμενες με ηπατική νόσο.**

- **Αναδεικνύεται η δυνατότητα παρέμβασης στη φυσική ιστορία της νόσου με την τροποποίηση περιβαλλοντικών παραγόντων κινδύνου.**

#232: MASH Has Become the Most Common Indication for Liver Transplantation Among Candidates with Hepatocellular Carcinoma in the United States

Younossi et al; Inova Health System, University of the Philippines, Johns Hopkins University

- Scientific Registry of Transplant Recipients (SRTR)
- **Etiology of liver disease in patients waitlisted for LT for HCC, 2013 to 2022:**
  - **HCV-HCC: 25% → 17%**
  - **MASH-HCC: 10% → 31%**
  - **ALD-HCC: 9% → 24%**
  - **HBV-HCC: 5% → 7% (NS)**
- The increasing trend remained significant after adjustment for changes in candidates' age, sex, ethnicity, obesity, and type 2 diabetes ($p<0.0001$).



Η επίδραση των στατινών

#141: Maximizing the Benefits of Statin Therapy for Liver Disease Prevention: Targeting Patients with Unmet Statin Therapy Needs

Vell MS et al; University Hospital Rwth Aachen, West Virginia University School of Medicine, Mayo Clinic, University of Pennsylvania, University Hospital Münster, University of California San Diego, King Faisal Hospital

- UK Biobank study
  - n=205,057
- Propensity score-matched analysis
- **Statin-users showed a 15.4% reduced risk of developing new liver diseases (HR = 0.846**, 95% CI, 0.782-0.915; P < .001).[1]
- When comparing statin users to non-users **with an indication for statin therapy** but without a prescription, the risk reduction for new liver disease increased to **23.6% (HR = 0.764,** 95% CI, 0.693-0.842; P < .001).
- Likewise, **MASLD showed an additional** risk reduction of 15.9% with an overall risk reduction of **29.9% (HR=0.701**, 95% CI, 0.608-0.808; P<.001).

Table

Table: Statin use compared with non-users with indication for statin intake at baseline and the development of liver disease, hepatocellular carcinoma, and liver-related mortality in UKB

Event and Treatment Group	No. with Event/ Total No.	Hazard Ratio (95% CI)	P-value
New Liver Disease[a]			
No Statin intake	801/43,114	1.00 (reference)	-
Statin intake	902/56,109	0.764 (0.693 to 0.842)	<.001[c]
Subdiagnoses[b]			
Alcohol-associated liver disease (K70)	95/56,109	0.690 (0.509 to 0.936)	.02[c]
Fatty liver (K76.0)	392/56,109	0.701 (0.608 to 0.808)	<.001[c]
Liver cell carcinoma (C22.0)	21/56,109	0.57 (0.30 to 1.07)	.08
Liver-related Death			
No Statin intake	126/43,114	1.00 (reference)	-
Statin intake	138/56,109	0.728 (0.564 to 0.939)	.02[c]

#155: Negative impact of PNPLA3 rs738409 C>G is significantly modified by dietary factors, caffeine and non-heavy alcohol consumption in the US population

Vilar-Gomez E, & Chalasani N, et al. et al; Indiana University School of Medicine

- This study **examined the effect of *PNPLA3* rs738409-environmental interactions on risk of liver-related death (LRD) in a US-based population study.**
- Analyses were adjusted for caloric intake, age, sex, race/ethnicity, diabetes mellitus, hypertension, smoking status, and physical activity.

Association of *PNPLA3* and environmental factors with LRD

Variables	Subhazard ratios (95% CI)
PNPLA3 rs738409	2.91 (1.45-5.83)
BMI (kg/m^2)	1.1 (1.02-1.18)
Alcohol intake <2 (women) or <3 (men)/day	2.2 (1.1-4.5)
Coffee/tea ≥3 cups/day	0.35 (0.04-0.99)
MUFA (%)/day (top quartile)	0.43 (0.12-0.99)
Cholesterol (mg)/day (top quartile)	2.6 (1.0-8.8)

***PNPLA3*-by-environmental factors interactions and risk of LRD**

Comparator: *PNPLA3* CC	Subhazard ratios (95% CI)		
BMI (kg/m^2) *	<25	25-29.9	≥30
G allele effect	2.7 (1.3-5.8)	2.5 (0.9-7.1)	**3.0 (1.5-6.3)**

Cholesterol (mg) *	Q1	Q2	Q3	Q4
G allele effect	2.4 (1.2-5.2)	1.9 (0.5-7.8)	**3.3 (1.1-10.2)**	**3.7 (1.4-9.8)**

Coffee/tea (cups/day) *	<1	≥1 to <2	≥ 2 to <3	≥ 3
G allele effect	3.1 (1.4-6.9)	3.3 (1.6-7.2)	2.7 (0.8-9.1)	**0.06 (0.006-0.59)**

MUFA (%) *	Q1	Q2	Q3	Q4
G allele effect	2.3 (0.9-5.9)	3.3 (1.7-6.8)	4.3 (2.2-8.4)	**0.4 (0.1-0.9)**

* P value for interaction <0.01. Q represents quartiles

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Διάγνωση

Σχόλια

- **Επί του παρόντος, η κατηγοριοποίηση του κινδύνου των ασθενών προτείνεται να γίνεται με scores, που βασίζονται στο Fibroscan.**

- **Μελλοντικά, μπορεί να χρησιμοποιούνται μέθοδοι βασισμένες στην τεχνητή νοημοσύνη.**

MASLD

Αξιολόγηση κινδύνου

Age

0

Years

BMI

0

kg/m^2

Diabetes

Yes | No

AST

0

U/L

ALT

0

U/L

Globulin

0

g/dL

Platelets

0

Wrong Path! The Current AASLD Guidance tients with MASLD And Significant Fibrosis

ford University School of Medicine

Non-invasive Test	FIB-4			SAFE		
Thresholds	<1.3	1.3-2.67	>2.67	<0	0-99	>100
Total (row%)	55.5M (76%)	16.7M (23%)	1.2M (2%)	34.4M (47%)	26.0M (35%)	13.0M (18%)
LSM ≥8 kPa (row%)	8.7M (71%)	3.0M (24%)	522K* (4%)	2.8M* (23%)	4.6M (38%)	4.8M (39%)
LSM ≥12 kPa (row%)	2.7M (63%)	1.3M (29%)	357K (8%)	619K* (14%)	1.3M* (31%)	2.4M (55%)

represents F2+ fibrosis missed by the score

represents F3+ fibrosis missed by the score

M(million), K(thousand) *Estimates are based on effective cell sample size <30

NHANES 2017-2020 Sample with VCTE data (n=6,774)

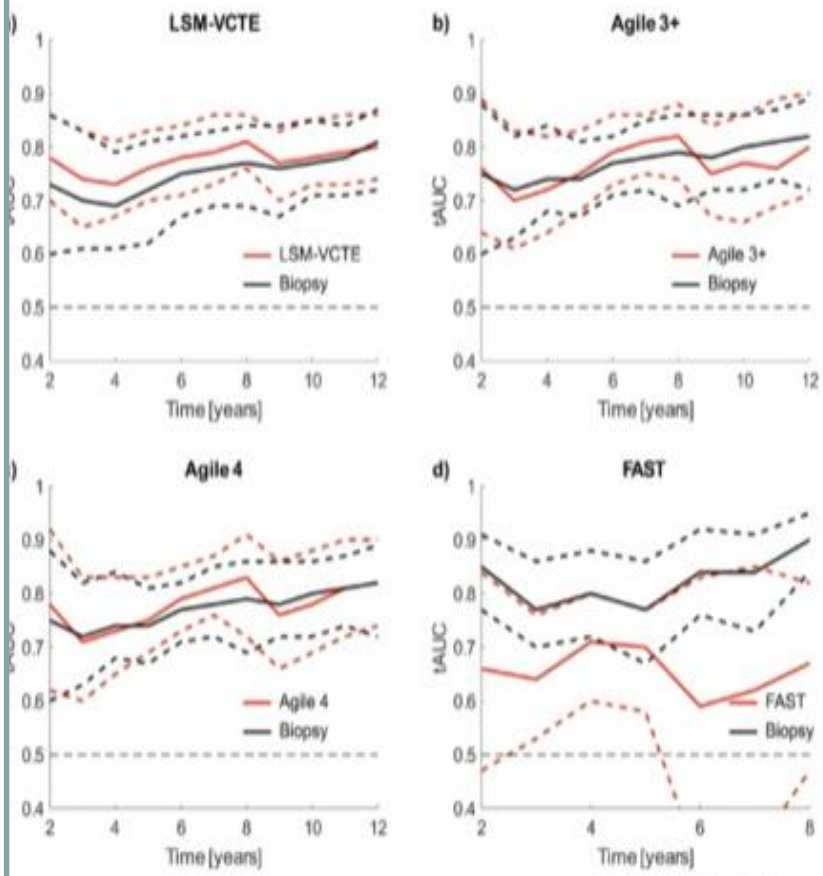
Προγνωστικά scores βασισμένα στο Fibroscan

Agile 3+ (4) scores

LSM
AST, ALT
Αιμοπετάλια
Παρουσία διαβήτη
(Ηλικία)
Φύλο

t Based Composite Scores Have
istologically Assessed Fibrosis Stage

ford/ LITMUS consortium



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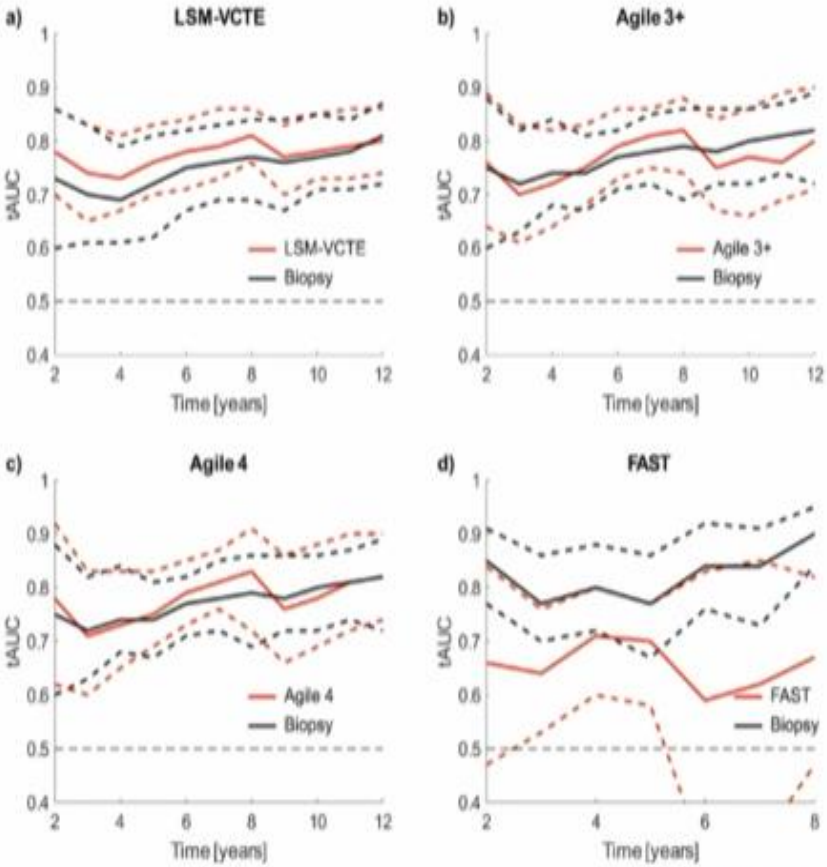
#2212-A: Liver Stiffness Measurement Based Composite Scores Have Comparable Prognostic Performance to Histologically Assessed Fibrosis Stage

Mózes FE et al; University of Oxford/ LITMUS consortium

- Aim: To compare the **prognostic performance of** histologically assessed fibrosis to that of liver stiffness measurement (LSM) by FibroScan, **FAST, Agile 3+, and Agile 4**
- **Primary endpoint: liver-related events or all-cause mortality**
- This was an individual patient data meta-analysis of patients **of ~2500 patients**
- LSM-VCTE, Agile 3+, and Agile 4 have comparable prognostic accuracy to histologically assessed fibrosis stage, making them attractive for stratifying MASLD patients
- The FAST score analysis is limited by shorter follow-up



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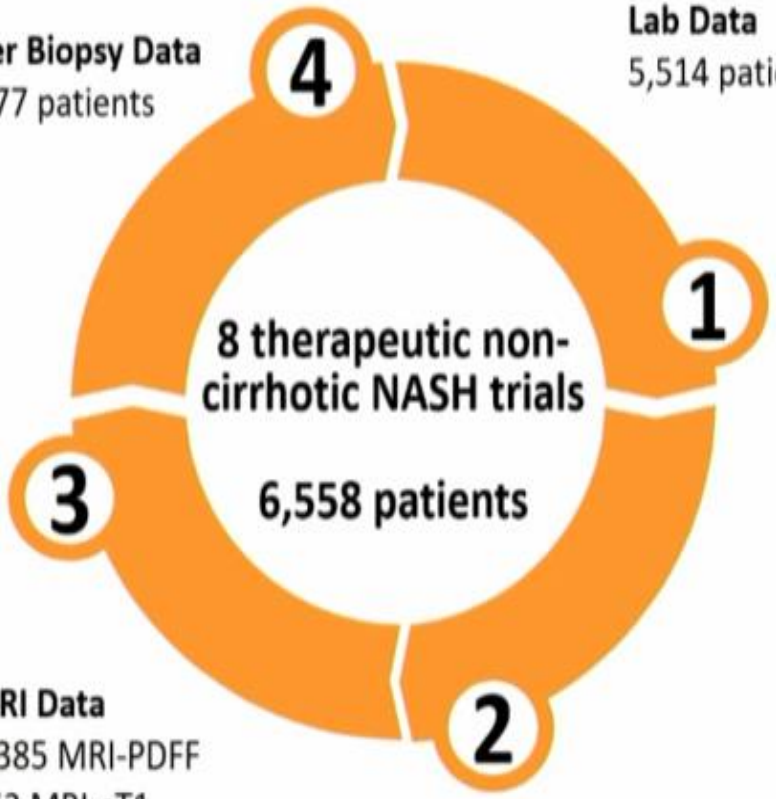
Βρίσκοντας τους ασθενείς σε κίνδυνο

#239: Predictors of At-Risk MASH Combining Data from Multiple Therapeutics Trials Including More than 6,000 Patients in Collaboration with NAIL-NIT Consortium

Harrison SA, et al; Summit Clinical Research /NAIL-NIT consortium

Liver Biopsy Data
2,277 patients

Lab Data
5,514 patients



MRI Data
2,385 MRI-PDFF
563 MRI-cT1

FibroScan Data
2,514 patients

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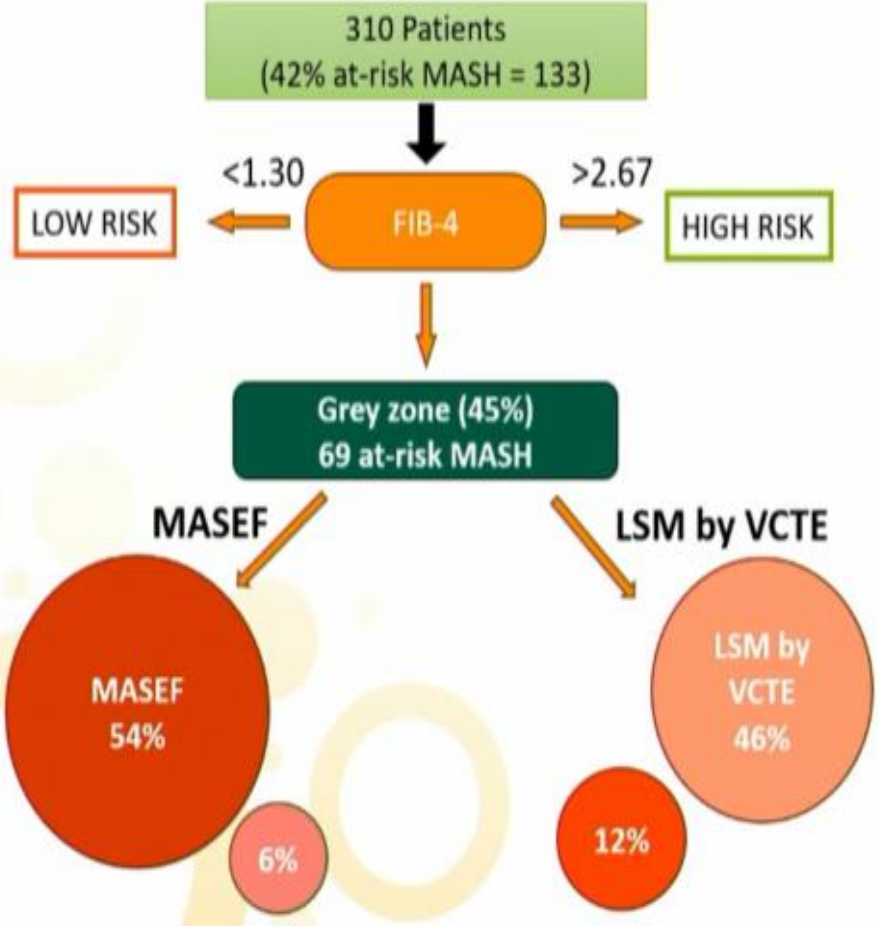
MASLD Βρίσκοντας τους ασθενείς σε κίνδυνο

- **Ideal population for trial enrichment:**
  - Middle-aged patients with multiple comorbidities (Type 2 Diabetes ++)
- **Recommended Trial Exclusion Criteria**
  - FibroScan < 8.5 kPa
  - AST < 20
- **Target NITs:**
  - if HbA1c < 6.5%
    - AST ≥ 40
    - FAST ≥ 0.67
  - if HbA1c ≥ 6.5%
    - AST ≥ 30
    - FAST ≥ 0.50

#2105: At-risk MASH identification using an algorithm that combines FIB-4 + MASEF (Metabolomics Advanced SteatohEpatitis Fibrosis score)

Noureddin-Troung-Mayo et al. (Multi Center Study)



FIB-4 + MASEF[1] and **FIB-4 + LSM by VCTE** were tested on 310 samples (42% at-risk MASH)

- FIB-4 has an accuracy of 72.4% but leaves a **45% of gray zone:** then MASEF score or LSM by VCTE were applied.
- **MASEF** correctly classified **54%** of at-risk MASH patients within FIB-4 gray zone, only misclassifying 6% of at-risk MASH patients.
- **LSM by VCTE** correctly classified **46%** of at-risk MASH patients within FIB-4 gray zone, misclassifying 12% of at-risk MASH patients.
- The overall performance/accuracy of **FIB-4 + MASEF** compared to **FIB-4 + LSM by VCTE**, though higher, was not statistically different (p = 0.69).

MASEF can be used alternatively to LSM by VCTE in the FIB-4 + LSM by VCTE algorithm that is currently recommended by the AGA and EASL.

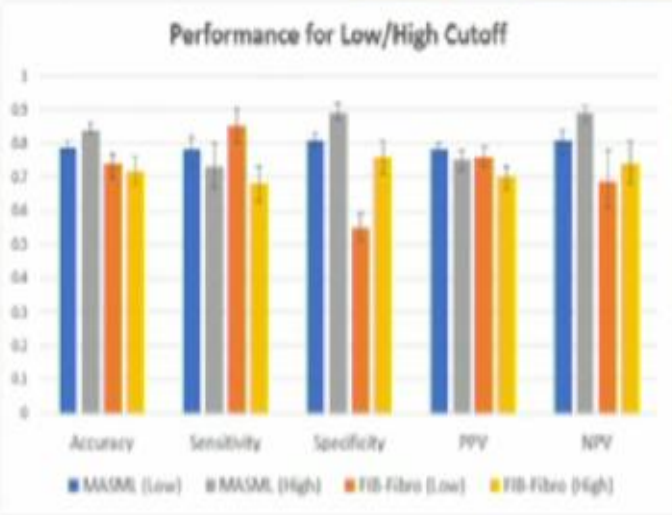
[1] Hepatology 2023. **Serum Identification of At-Risk MASH: The Metabolomics-Advanced Steatohepatitis Fibrosis Score (MASEF).** DOI:10.1097/HEP.0000000000000542

Μηχανική μάθηση

#2418-C: Single Testing with MASLD Machine Learning Models (MASMLs) Perform Equally To Current Guideline Algorithms of Sequential Testing Using FIB-4 Index & VCTE

Chang et al; Arnold O. Beckman High School, Cedars-Sinai Medical Center, Arizona Liver Health, Pinnacle Clinical Research, Houston Research Institute, Houston Methodist Hospital

- Compared machine learning models, including logistic regression, artificial neural network, and the established MASML model (Chang et al. *Hepatology* 2022), a random forests model, to FIB-Fibro in predicting significant/advanced fibrosis.
- Examined 17 routine demographic/clinical features in **1223 MASLD patients**.
- One-step MASML has similar or superior performance to multistep FIB-Fibro.



	Correctly Classified (CC) Measurement (%)	Percentage of Indeterminate-Risk Patients (%)
MASML (RF)	67.47 [64.67, 70.27]	14.16 [12.47, 15.86]
FIB-Fibro	70.53 [66.51, 74.55]	11.51 [10.13, 12.89]

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Θεραπεία

Σχόλια

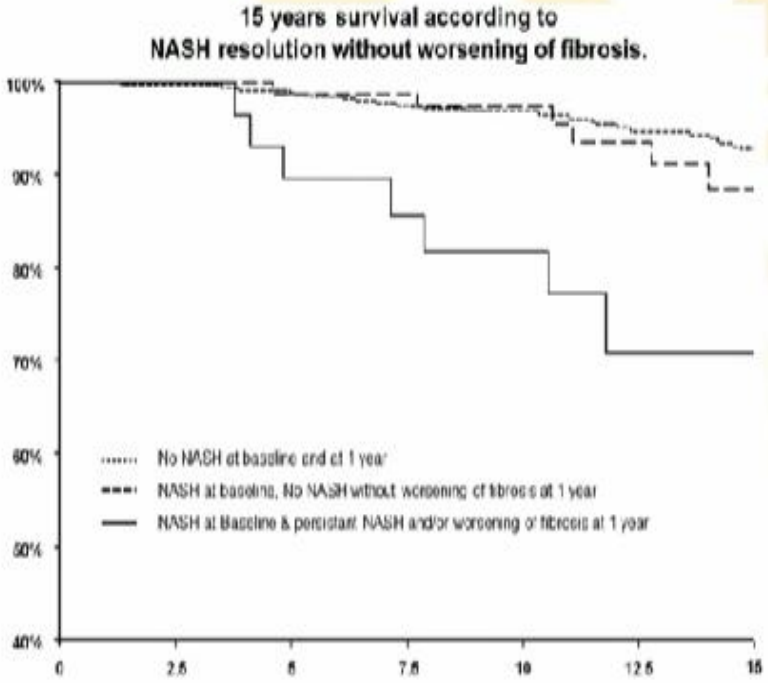
- Επιβεβαιώνονται οι κατηγορίες των φαρμακευτικών παραγόντων, που δυνητικά θα αδειοδοτηθούν.
- Αρχίζουν να διαφαίνονται δοκιμές συνδυασμού παραγόντων.
- Υπάρχουν ελπιδοφόρα μηνύματα για την αντιμετώπιση των κιρρωτικών ασθενών.

Η αποδρομή της MASH οδηγεί σε μακρότερη επιβίωση

#1: MASH Resolution without Fibrosis Worsening after Bariatric Surgery Improves Long-Term Survival

Lassailly G et al; CHU De Lille

- Aim: to determine the impact of histological evolution on long-term survival in MASH patients treated with bariatric surgery
- At baseline, **8.6% of patients** had biopsy-proven MASH
- **Patients with MASH and patients with significant fibrosis (≥ F2) had lower 15-year survival (p<0.001)**
- After surgery, MASH resolution without worsening of fibrosis was associated with better biological and histological improvement of steatosis, fibrosis, and LFTs
- MASH resolution was associated with a better 15-year survival in univariate analysis (88.4% vs. 70.8%, p = 0.009) and multivariate analysis (HR 0.37, p = 0.02)
- 15-year survival of patients with MASH resolution became similar than those without baseline MASH



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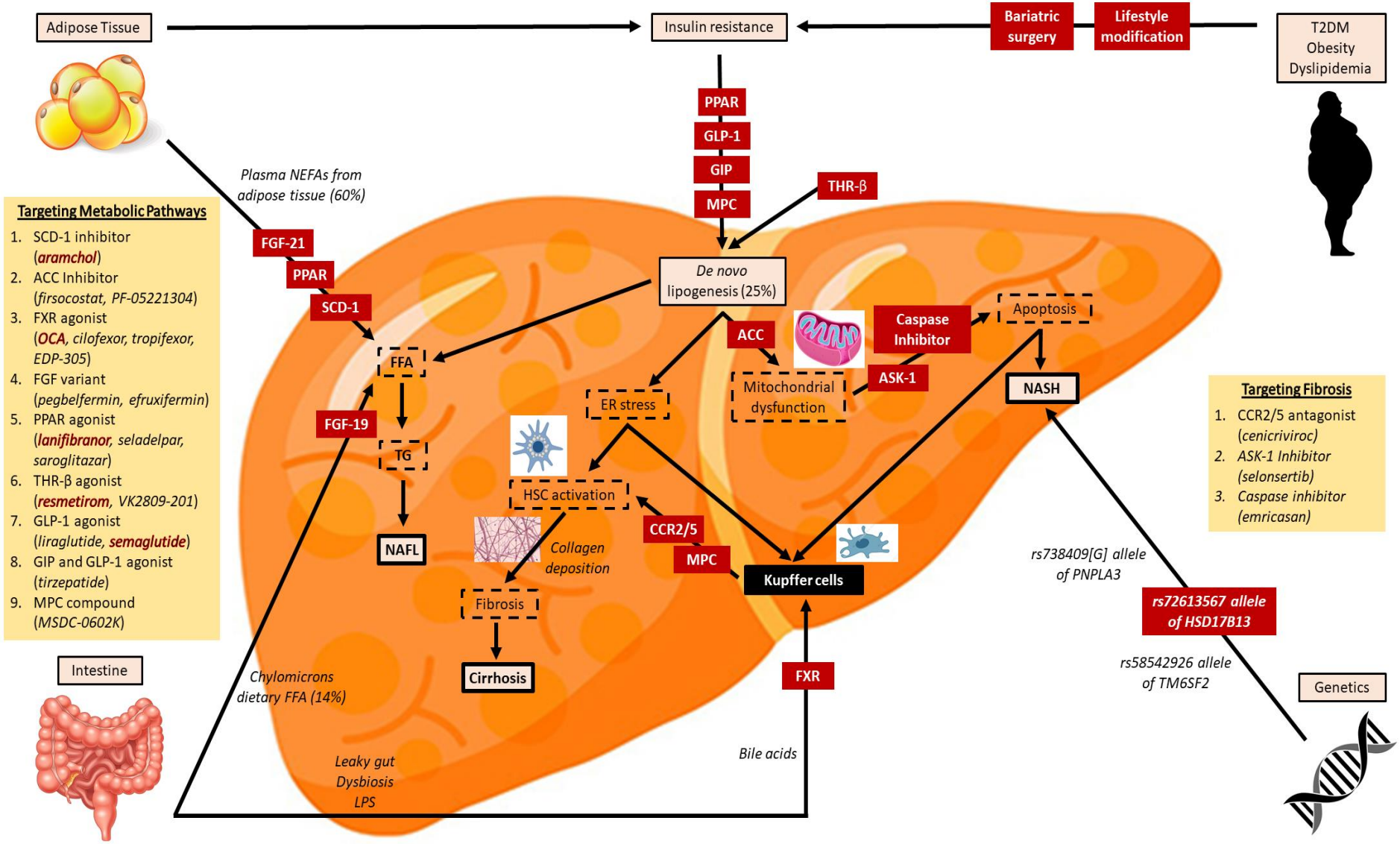
MASH Παθοφυσιολογία – στόχοι θεραπείας

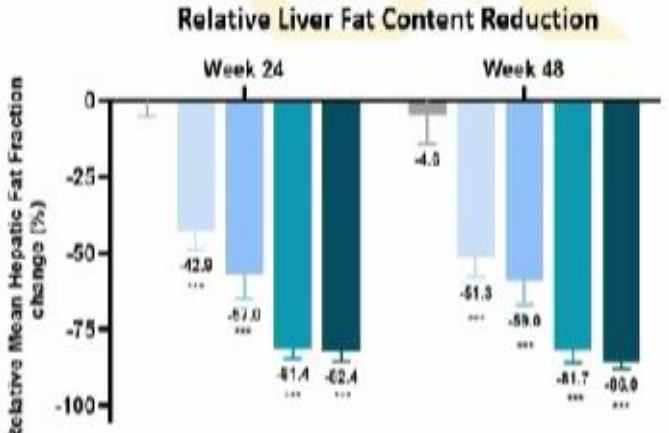


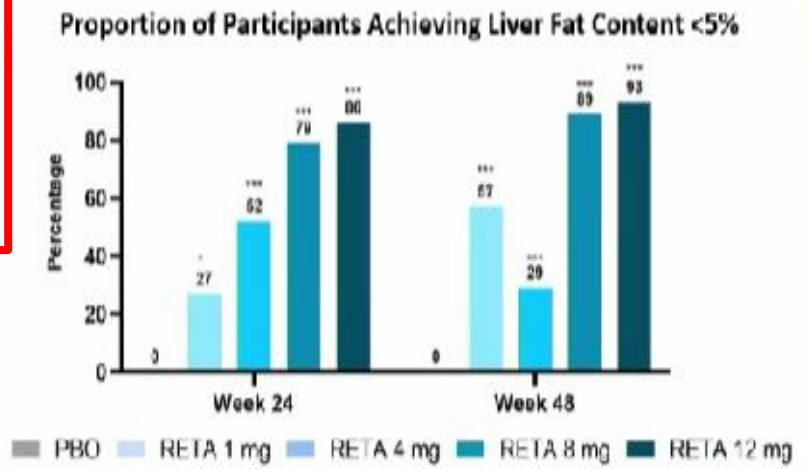
Sinakos E, Liava C & Loomba R. Ann Gastroenterol 2022

#148: Triple Hormone Receptor Agonist Retatrutide Resolves Steatosis in >85% of Subjects with MASLD & Obesity in Association with Improved Metabolic Health

Sanyal A et al; Virginia Commonwealth University, Velocity Clinical Research, Eli Lilly and Company

- Retatrutide (RETA) is a novel triple agonist of the GIP, GLP-1, and glucagon receptors
- A 48-week phase 2 obesity study demonstrated weigh loss of −22.8% and −24.2% with RETA 8 mg and 12 mg[2]
- The MASLD substudy required baseline liver fat content of ≥10% as assessed by MRI-PDFF
- Mean relative liver fat reduction was >80% with RETA 8 mg and 12 mg
- With RETA 8 mg and 12 mg, hepatic steatosis resolved in >85% of participants at Week 48
- Liver fat reductions were significantly related to reductions in body weight, waist circumference, abdominal fat, and improvements in insulin sensitivity, serum lipids, K-18 and Pro-C3





GIP=glucose-dependent insulinotropic polypeptide; GLP-1=glucagon-like peptide-1; PBO=placebo

1. Sanyal A et al, AASLD Abstract #148
2. Jastreboff A et al. *N Engl J Med* 2023; 389:514-526

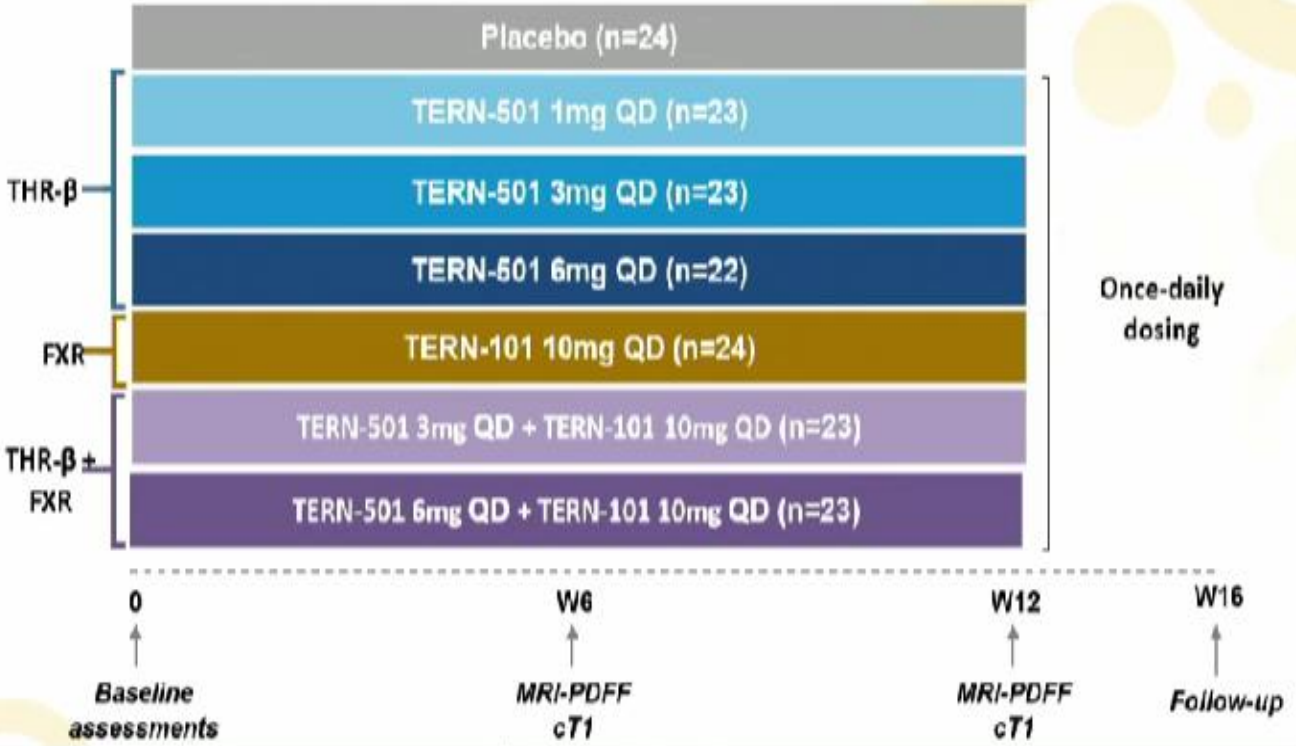
#5000: Topline Results from a 12-Week Phase 2a Tial (DUET) Evaluating TERN-501 Monotherapy or in Combination with TERN-101 (FXR) Agonist

Noureddin et al; Houston Methodist Hospital, Houston Research Institute

Randomized, double-blind, placebo-controlled trial (N=162)

Key Entry Criteria

- Non-cirrhotic; presumed MASH
- BMI ≥25 kg/m^2
- MRI-PDFF ≥10%
- MRI-cT1 ≥800 msec
- HbA1c ≤ 9.5%
- LDL <150 mg/dL; TG ≤ 500 mg/dL



Endpoints At Week 12

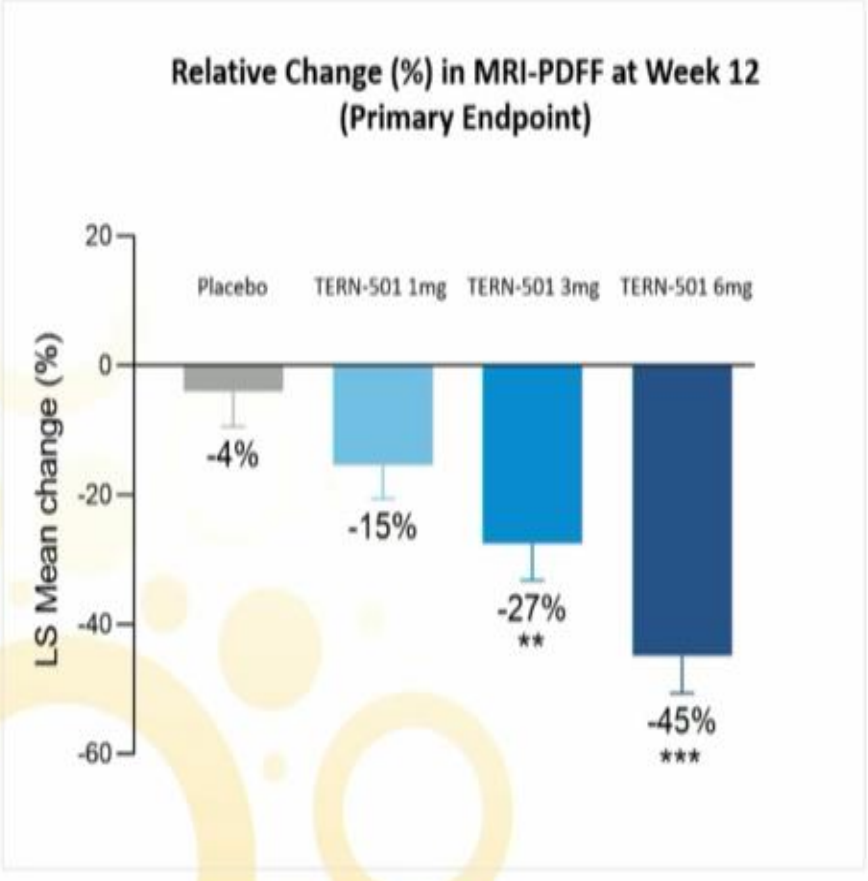
Primary Endpoint

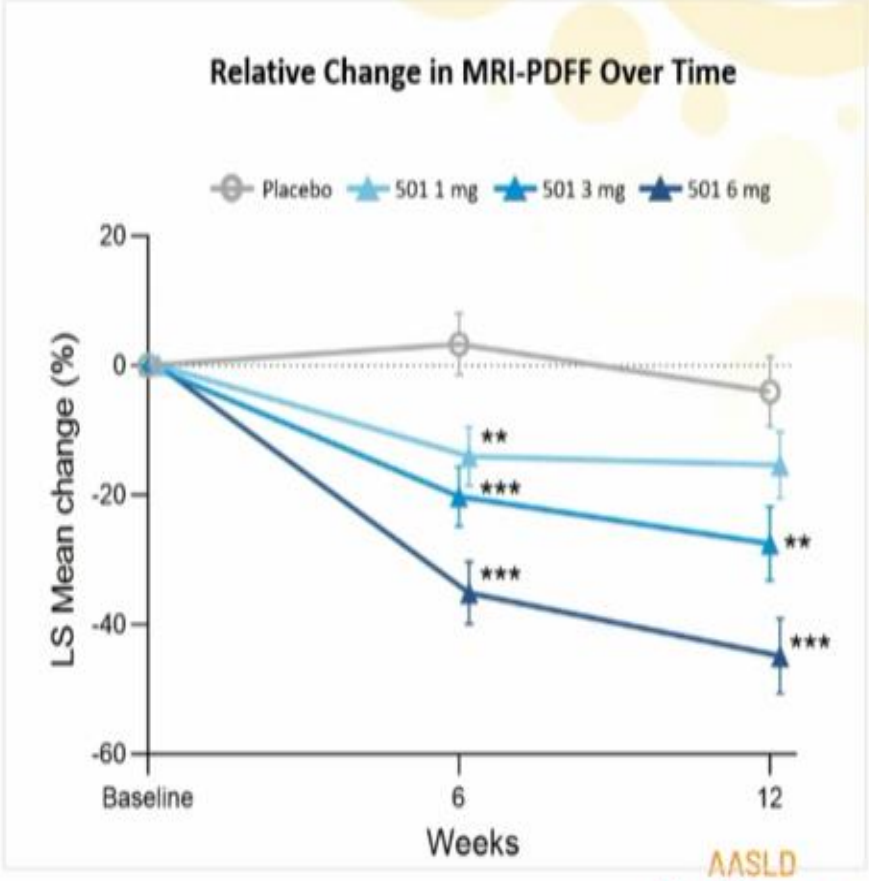
- Relative change in MRI PDFF of TERN-501 vs placebo

Secondary Endpoints

- Relative change in MRI-PDFF of '501+'101 vs placebo
- Changes in cT1 of TERN-501 vs placebo and of '501+'101 vs placebo
- Safety and tolerability

DUET Trial, Continued





**p-value <0.01; ***p-value <0.001 for TERN-501 monotherapy vs. placebo
Error bars represent standard error
ANCOVA, analysis of covariance; LS Mean, least squares mean from ANCOVA model

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MASH

Icosabutate (αγωνιστής υποδοχέων FFA)

#5011: Icosabutate in NASH/MASH with Fibrosis: Results from a Randomised, Multicentre, Double Blind, Placebo Controlled Phase 2b Trial (ICONA)

Harrison et al; Pinnacle Clinical Research, Arizona Liver Health, FDI Clinical Research, Northsea Therapeutics, Virginia Commonwealth University

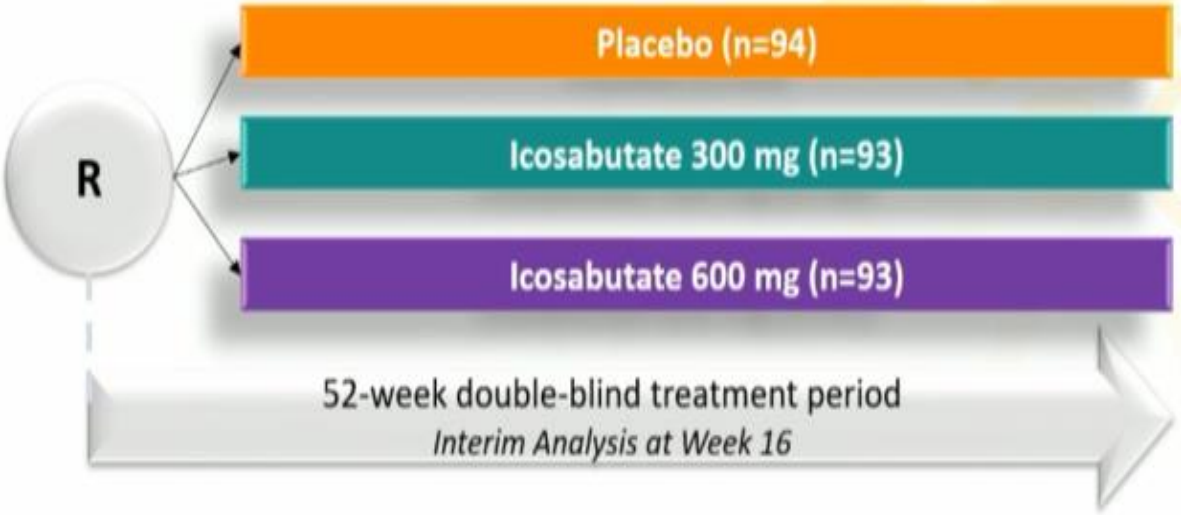
PHASE 2B DESIGN

KEY ELIGIBILITY CRITERIA

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

Fibrosis stage F1 or F2 or F3

≥8% hepatic fat by MRI-PDFF



Primary Endpoint

NASH Resolution with no worsening of Fibrosis

Secondary Endpoints

≥ 1 stage Improvement in fibrosis with no worsening in NASH

Liver chemistry, fibrosis, metabolic and inflammatory biomarkers

Meeting

Icosabutate - αποτελέσματα

#5011: Icosabutate in NASH/MASH with Fibrosis: Results from a Randomised, Multicentre, Double Blind, Placebo Controlled Phase 2b Trial (ICONA)

Harrison et al; Pinnacle Clinical Research, Arizona Liver Health, FDI Clinical Research, Northsea Therapeutics, Virginia Commonwealth University

Key Takeaways:

- While not meeting primary endpoint, ICONA study demonstrates broad, beneficial effects of icosabutate therapy in NASH patients, with greatest effects in T2D patients
- Icosabutate was well-tolerated with mild to moderate TEAEs and no reports of DILI
- The overall data, both histology and non-invasive biomarkers, and the mechanism of action targeting FFARs provide a strong rationale for further clinical development of icosabutate in diabetic NASH patients

Κίρρωση

Aldafermin

#8 A Randomized, Double-blind, Placebo-controlled, Multicenter, Phase 2b Trial Evaluating Multiple Doses of the FGF19 Analogue Aldafermin in Patients with Compensated Cirrhosis Due to NASH

Rinella et al; University of Chicago and other Centers

Key Inclusion Criteria

- Biopsy-confirmed NASH with stage 4 fibrosis (NASH CRN criteria)
- Compensated cirrhosis, Child-Pugh A
- Clinically diagnosed NASH cirrhosis [1] allowed to enroll (capped at 10%)

Must meet one of the following:

- Plt ≤140 and LSM ≥ 13.6 kPa
- FIB-4 ≥ 3.25
- Agile 4 ≥ 0.57

Study Endpoints

- **Primary endpoint:** Change from baseline in Enhanced Liver Fibrosis (ELF) score at Week 48
- **Secondary endpoints** include: fibrosis improvement ≥1-stage (NASH CRN criteria), Pro-C3, ALT, AST, C4, bile acids and LSM at Week 48

ALT, alanine aminotransferase; AST, aspartate aminotransferase; C4, 7alpha-hydroxy-4-cholesten-3-one; ELF, Enhanced Liver Fibrosis; LSM, liver stiffness measure; QD, once daily; SC, subcutaneous

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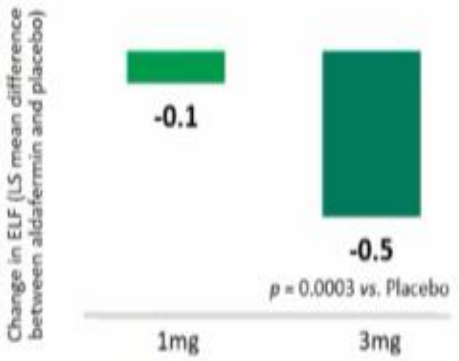
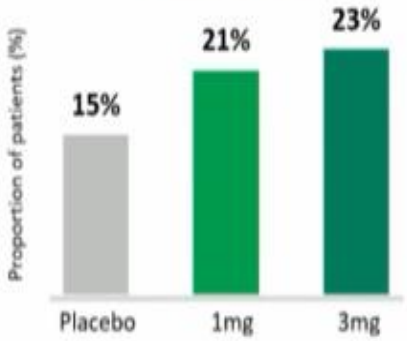
Aldafermin

#8: Positive Results from the ALPINE-4 Study, Continued

Enhanced Liver Fibrosis (ELF)



Fibrosis Improvement ≥ 1-Stage (NASH CRN)



Change from baseline to week 48	Placebo (n=56)	Aldafermin 1mg (n=42)	Aldafermin 3mg (n=55)
Δ ALT, %	-6.3%	-35.9%; *p*<0.0001	-41.5%; *p*<0.0001
Δ AST, %	-0.4%	-19.2%; *p*=0.0043	-28.3%; *p*<0.0001
Δ C4, %	-1.8%	-66.8%; *p*<0.0001	-73.5%; *p*<0.0001
Δ Total Bile Acids, %	31.7%	-35.5%; *p*=0.0008	-50.5%; *p*<0.0001
Δ Pro-C3, %	47.6%	-6.3%; *p*=0.067	-12.1%; *p=0.032*
Δ LSM, %	15.0%	-15.1%; *p*=0.036	-6.3%; *p*=0.12

ITT population; *p* values *vs.* placebo; study not powered for comparison of histological fibrosis endpoint between groups

- **Primary endpoint was met:** aldafermin 3 mg resulted in a significant reduction in ELF in patients with compensated NASH cirrhosis.
- Fibrosis improvement of ≥ 1-stage was achieved in 15%, 21%, and 23% patients in the PBO, 1mg and 3mg groups, respectively.
- Aldafermin also achieved dose-dependent benefits in multiple non-invasive markers of inflammation and fibrosis
- Six (6%) patients discontinued use due to side effects. There were 19 (12%) SAEs, but none were drug-related

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Efruxifermin

#5005: Efruxifermin in Compensated Cirrhosis Due to NASH/MASH: Results from a Randomized, Double-Blind, Placebo-Controlled, Phase 2b Trial (SYMMETRY)

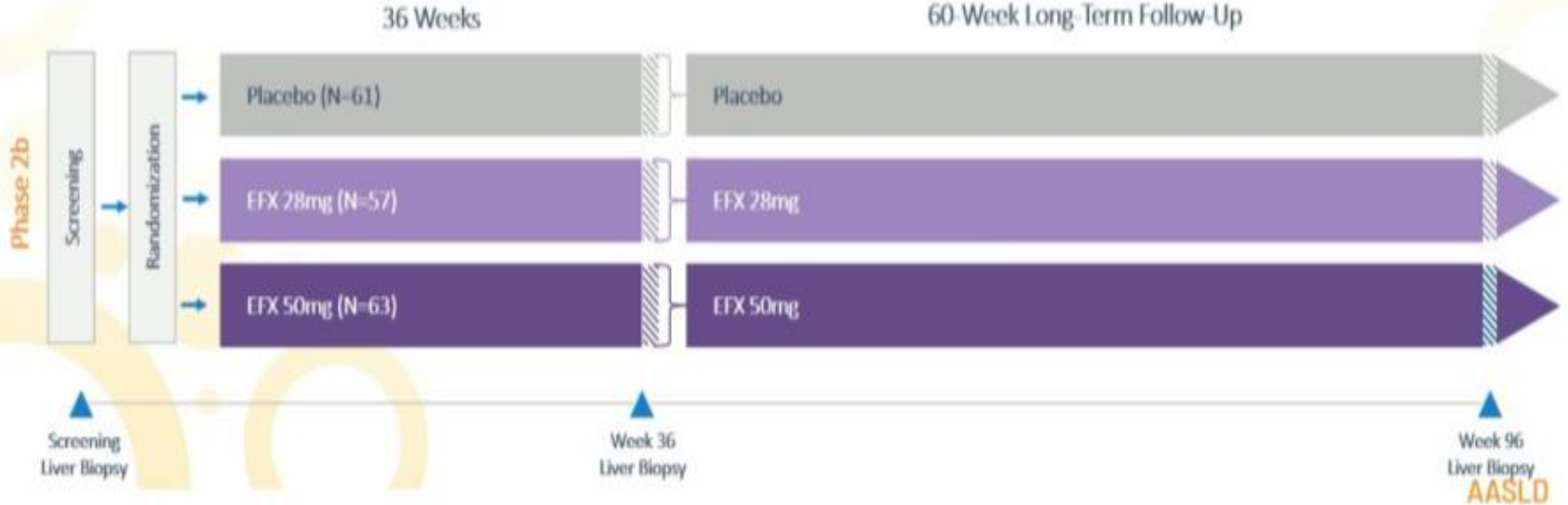
Harrison SA et al; Pinnacle Clinical Research and other Centers

- SYMMETRY is a study of efruxifermin (EFX) in Compensated Cirrhosis Due to NASH (F4)

Key Inclusion Criteria[1]
- F4 NASH (compensated)
- T2D or 2 of 4 components of metabolic syndrome

Phase 2b Primary Endpoint
- ≥1 Stage Fibrosis Improvement with no Worsening of NASH at Week 36

Key Secondary Efficacy Endpoints
- NASH Resolution
- Fibrosis Markers
- Lipoproteins
- Glycemic Control
- Weight Change
- Liver Injury Markers



[1] All patients had biopsy-proven compensated cirrhosis (fibrosis stage 4) due to definitive NASH or cryptogenic cirrhosis presumed secondary to NASH. Subjects with cryptogenic cirrhosis were limited to approximately 20% of the total study population.

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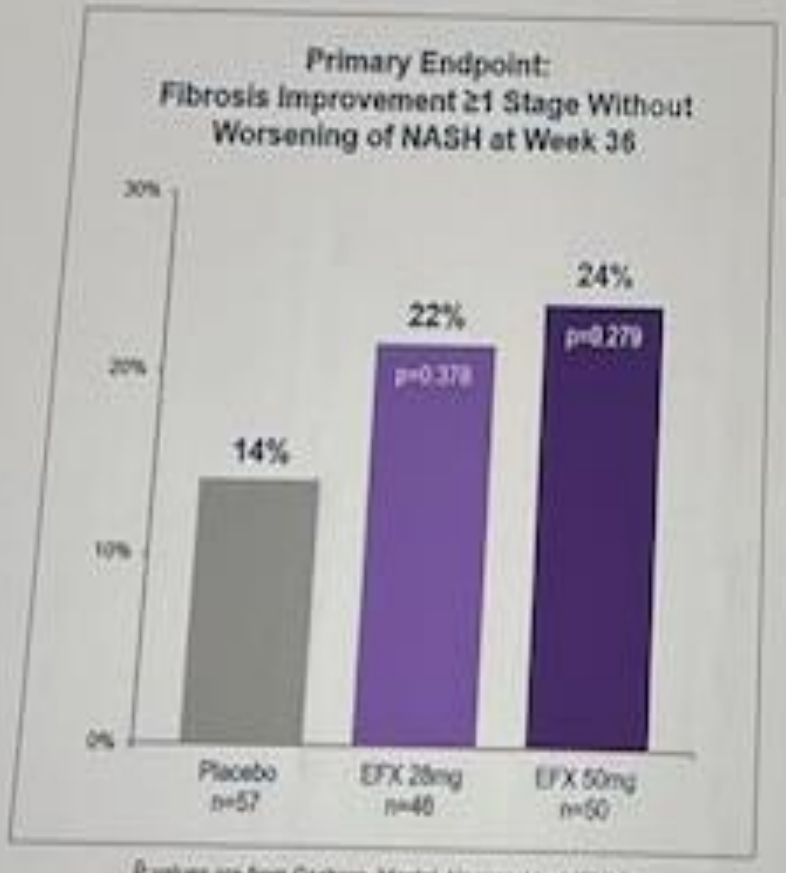
Κίρρωση

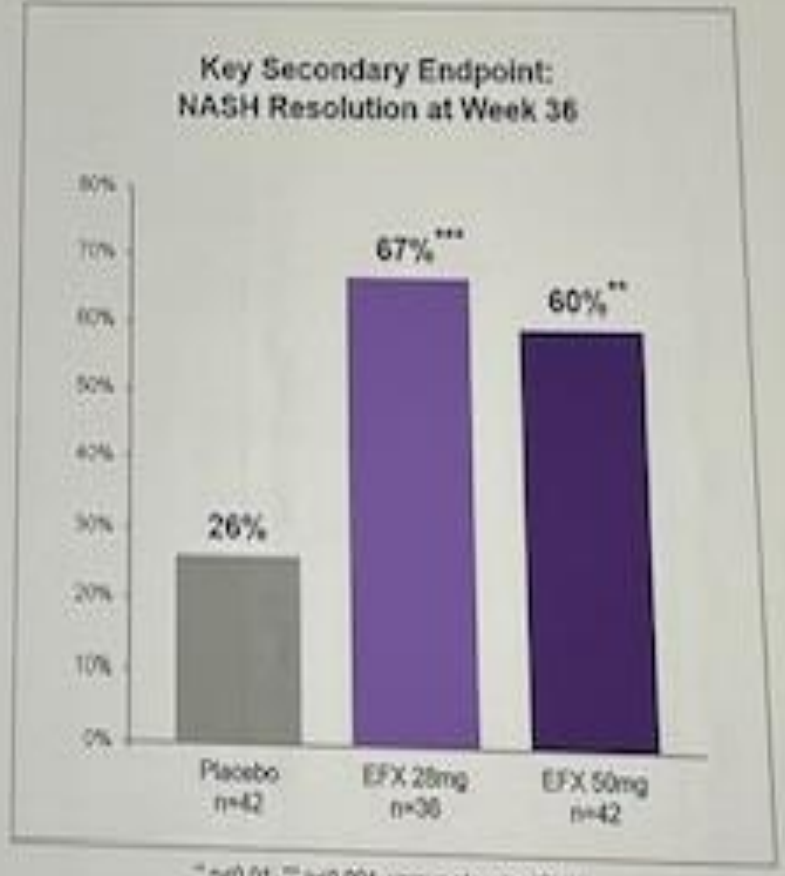
Efruxifermin - αποτελέσματα

Fibrosis Improvement and NASH Resolution

akero



P values are from Cochran-Mantel-Haenszel test (CMH)



** p<0.01, *** p<0.001, versus placebo (CMH)

Source Data: Fibrosis Improvement (Liver Biopsy Analysis Set); NASH Resolution (Liver Biopsy Analysis Set [definitive NASH only]). Topline preliminary data

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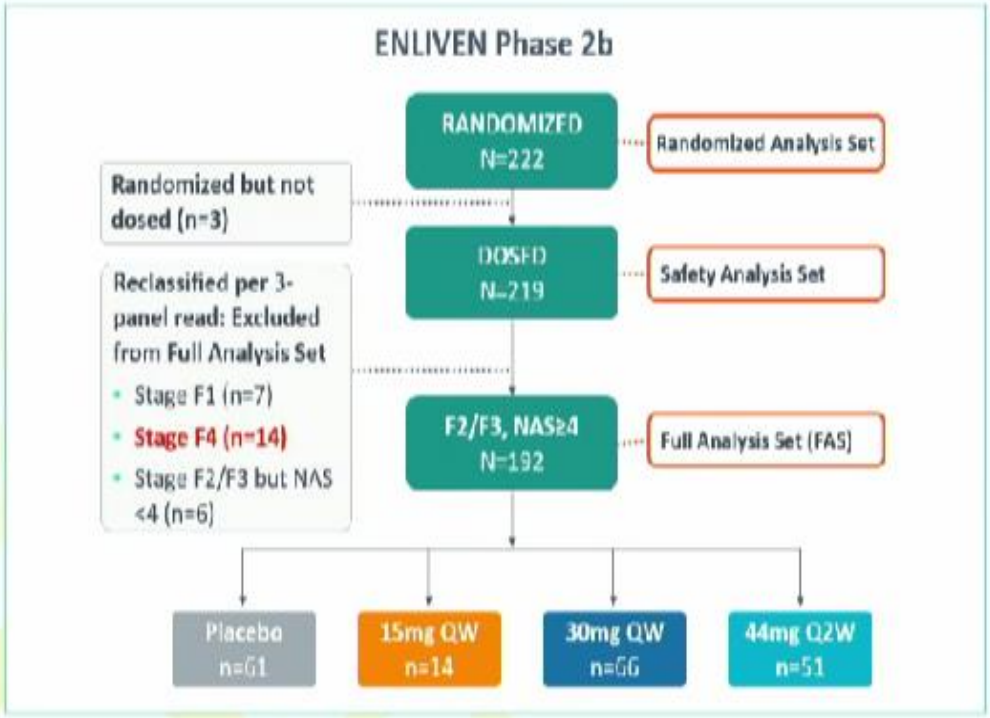
#4: Fibrosis Improvement with Pegozafermin (PGZ) Treatment in MASH Patients with F4 Fibrosis: Analysis From A 24-Week Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial (EVLIVEN)

Loomba R et al; University of California San Diego and Other Centers



PRIMARY OUTCOME: Proportion of patients achieving either:

1. Improvement of fibrosis by ≥1 stage with no worsening of NASH; or
2. Resolution of NASH without worsening of fibrosis.

SECONDARY OUTCOME: Additional liver histology measures, changes in LFC by MRI-PDFF, fibrosis and inflammatory markers, metabolic effects, safety and tolerability.

AIM: This *post hoc* analysis evaluated the efficacy and safety of PGZ versus placebo on histologic measures and biomarkers in patients with MASH with F4 fibrosis by 3-panel consensus read.

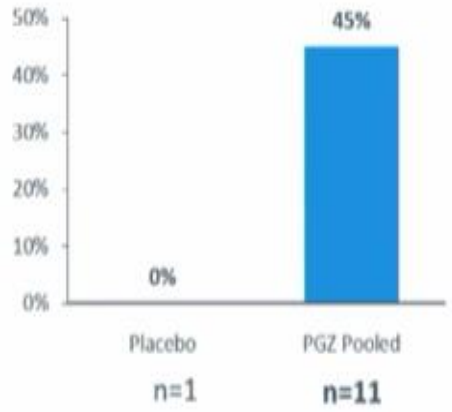
Pegozafermin

#4: EVLIVEN Trial Results, Continued

RESULTS

Baseline characteristics	N=14
Age, years, mean	56
Sex, female, %	57
BMI, kg/m², mean	37
T2D, %	86
PRO-C3 (ng/mL)	67

NIT	Responder (%) PGZ (n=12)	Fibrosis Improvement in responder (%)
ALT	64%	86%
ELF	45%	80%
PRO-C3	55%	83%
VCTE	45%	60%
FAST	45%	80%



- Five patients (45%) achieved a ≥1-stage improvement in fibrosis without worsening of NASH compared to 0 in the placebo group
- Responder rates varied between 45% and 64% for non-invasive tests in PGZ treated patients
  - Fibrosis improvement was highly correlated to responder rates (range 60%-86%)
- Tolerability profile in F4 was similar to the noncirrhotic population

CONCLUSION

- PGZ treatment improved hepatic fibrosis and non-invasive markers of liver inflammation and fibrosis in patients with NASH and F4 fibrosis

Responders defined as: ALT reduction ≥17U/L; MRI-PDFF reduction ≥30%; ELF reduction ≥ 0.5; VCTE reduction ≥20%; PRO-C3 reduction >15%; FAST score <0.35

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