

sanofi

Essential phospholipids

Understanding the
clinical evidence across
the liver health
landscape

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**3rd GLOBAL
LIVER
HEALTH
FORUM**

Disclosures



- **Lecturer for:**

- Sanofi (UAE, & Global)
- Abbott
- Janssen
- Lunatus
- Synergy
- Dr Falk
- Takeda
- Spimaco
- Julphar
- Tabouk
- Novo Nordisk

- **Member of advisory boards for**

- Sanofi (UAE, & Global)
- Abbott
- Janssen
- Lunatus
- Synergy
- Takeda
- Novo Nordisk
- Julphar

Agenda



1. Why and how are patients with MAFLD treated?
2. What is the evidence supporting the use of EPLs in patients with NAFLD?
3. Could EPLs improve symptoms in patients with NAFLD?
4. Summary

**Why and how are patients
with MAFLD treated?**

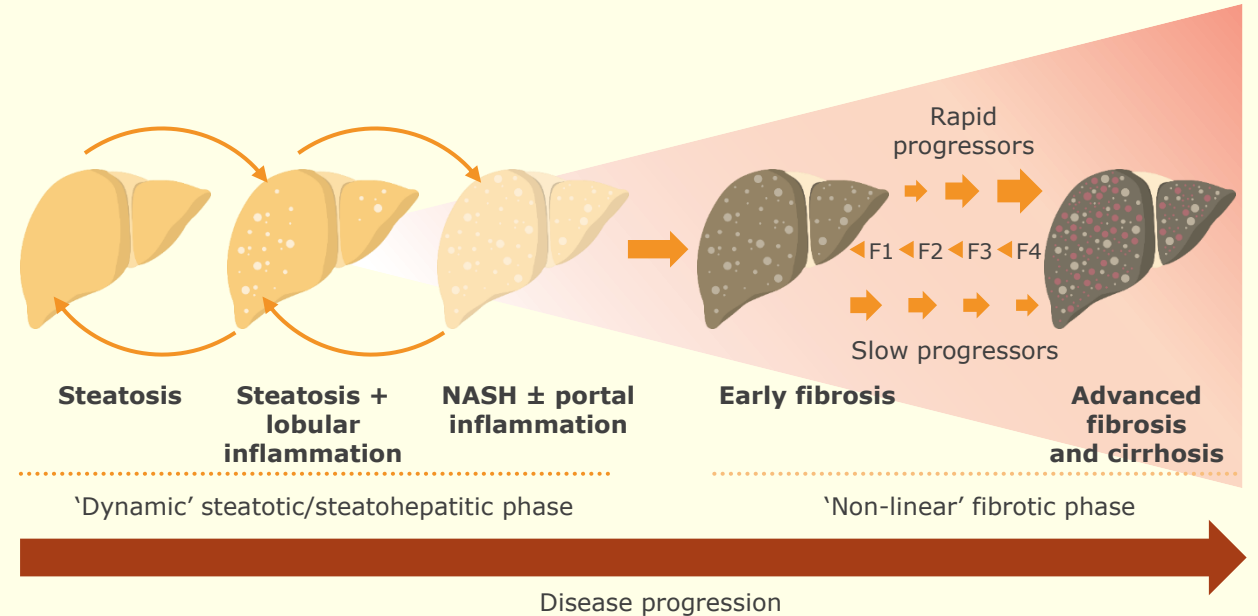
Patients with MAFLD are treated to prevent future serious comorbidities



Long-term outcomes for patients with MAFLD and NASH:

- Increased overall mortality vs people without MAFLD and NASH^{1,2}
- Increased risk of cardiovascular disease vs traditional risk factors²⁻⁴
- Together with T2DM pose a greater risk of hypertension⁵
- May be a risk factor for chronic kidney disease, colorectal cancer, endocrinopathies (including thyroid dysfunction, and osteoporosis)^{6,7}
- Have an increased rate of liver-related mortality^{1,2}
- Risk factors including obesity and an excess of insulin can result in advanced fibrosis and cirrhosis, which increases the risk for hepatocellular carcinoma⁸

MAFLD disease progression



APASL guidelines recommend lifestyle modifications to treat MAFLD



Lifestyle modifications are recommended by APASL for **patients with MAFLD without steatohepatitis and fibrosis**



Gradual weight loss (≤ 1 kg/week) of 7–10%

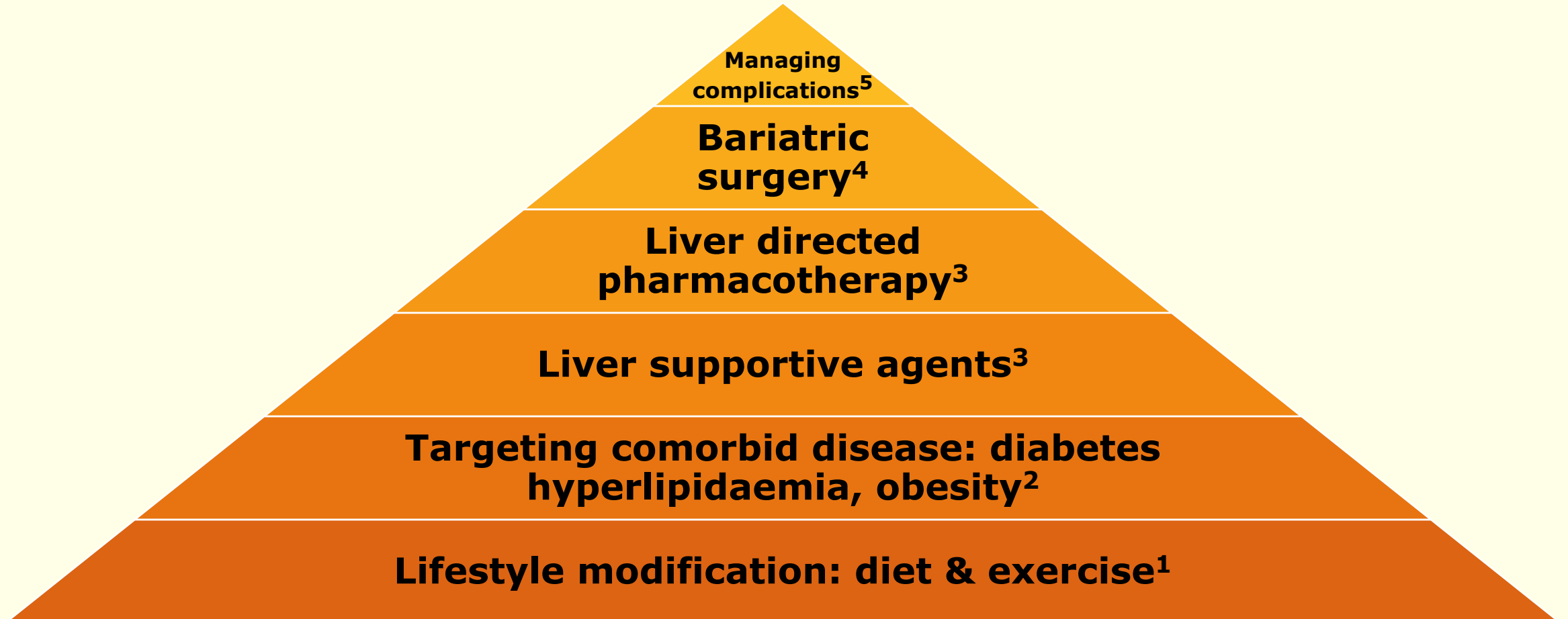


Increased **exercise** and **hypocaloric diet** (500–1,000 kcal deficit)



Pharmacological treatments are recommended by APASL for patients with **MAFLD with steatohepatitis and fibrosis** to **reduce the risk of metabolic risk factors and/or comorbidities** (e.g. pioglitazone and vitamin E)

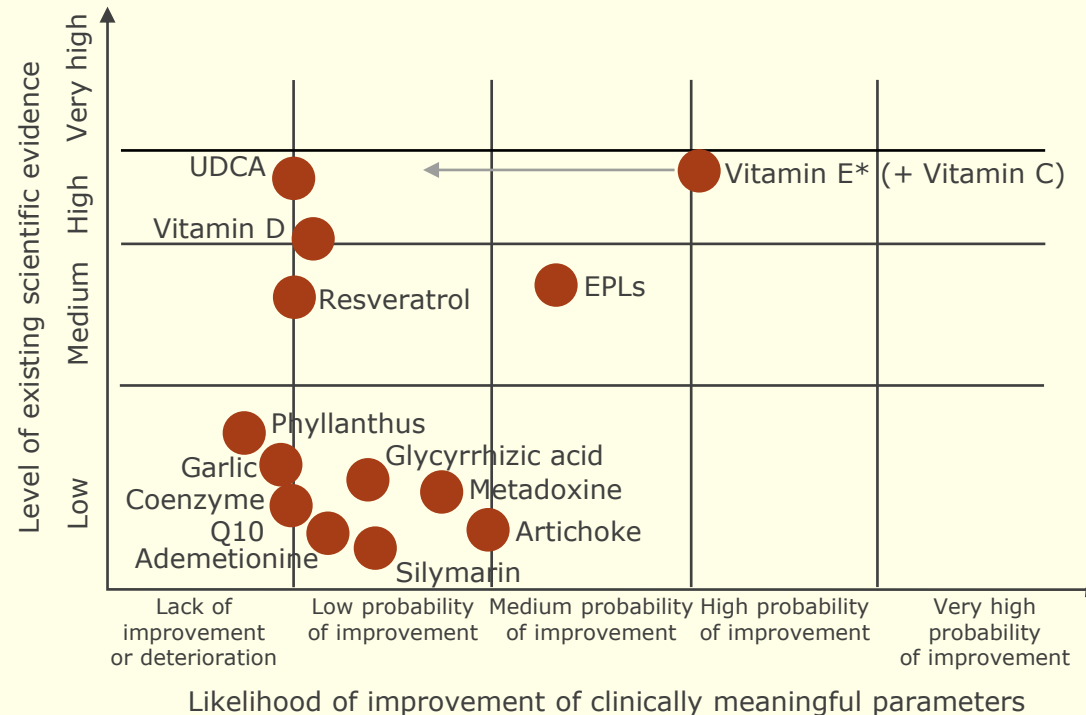
Treatment plan for NAFLD



Evidence levels supporting treatments for patients with MAFLD is inconsistent



Level of existing evidence supporting the efficacy of various treatments for MAFLD/NASH from a narrative review:



Hepatoprotective agents, including EPLs, remain an important part of the treatment of NAFLD as adjunctive therapies

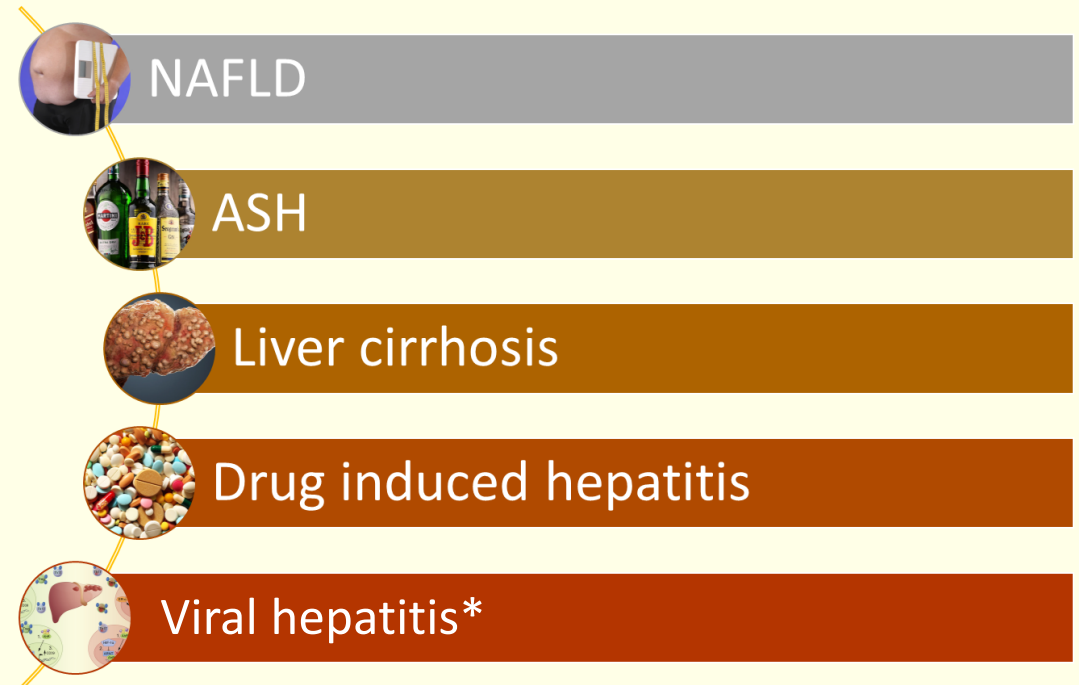
**What is the evidence
supporting the use of EPLs in
patients with NAFLD?**

Phospholipids have roles in recovery and maintenance in mammalian cells



- Activation of phospholipid-dependent enzymes
- Increase in molecular metabolism
- Improve detoxification function of the liver
- Decrease fatty infiltration of hepatocytes
- Inhibit or correct fibrogenic processes
- Influence apoptosis
- Anti-inflammatory and anti-oxidant properties

Indication

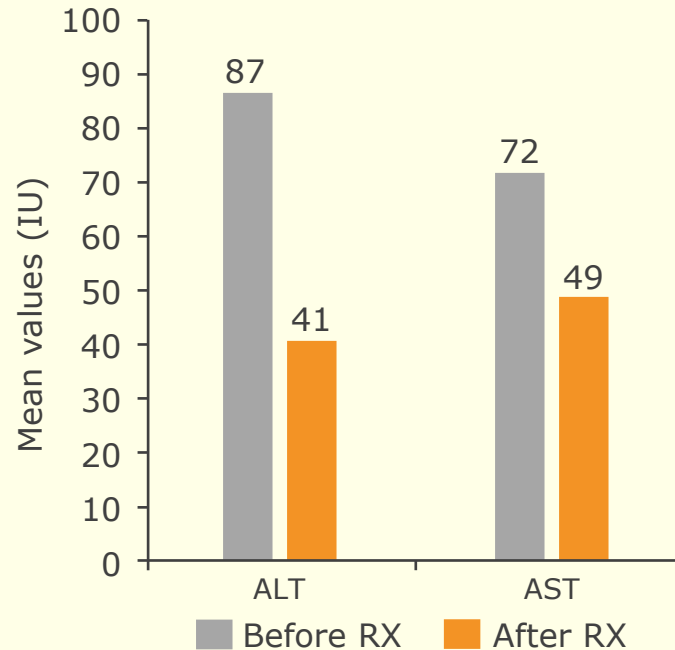


EPLs reduce transaminase levels in patients with NAFLD

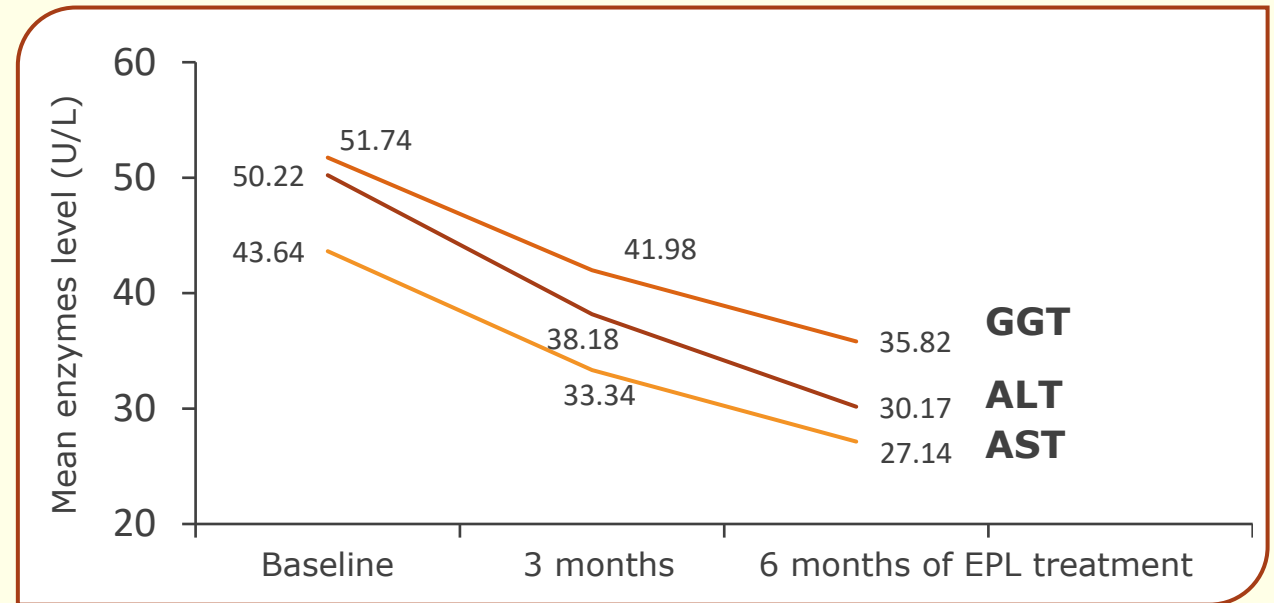


In an open-label, randomised trial (n=113):¹

Transaminase levels were reduced with treatment with EPL



In an observational, multicentre, prospective trial (MANPOWER) with patients with NAFLD and cardiometabolic comorbidities*, N=2,843

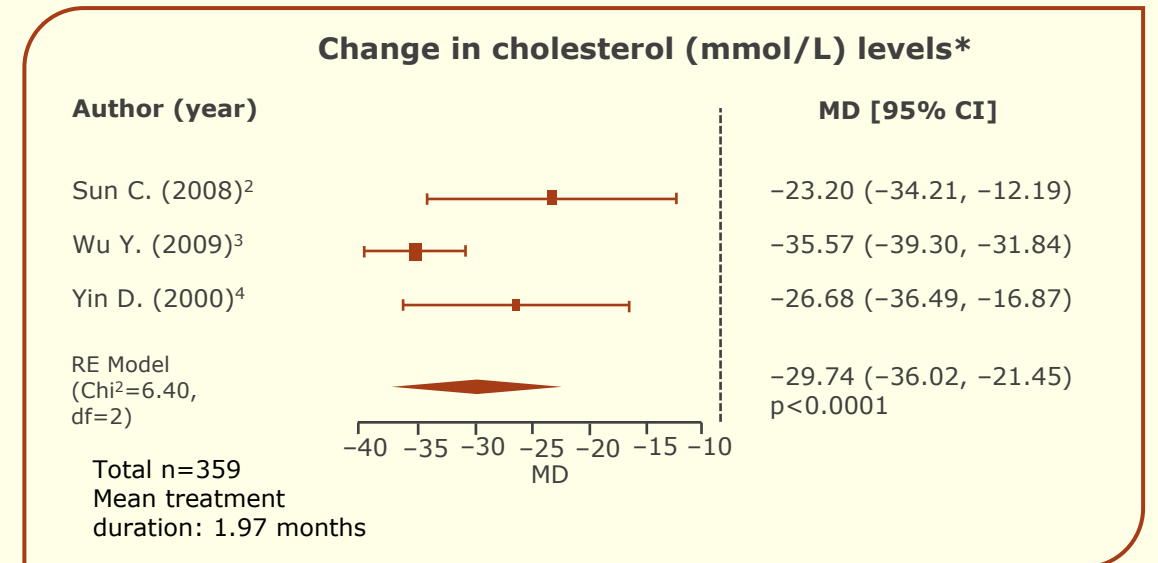
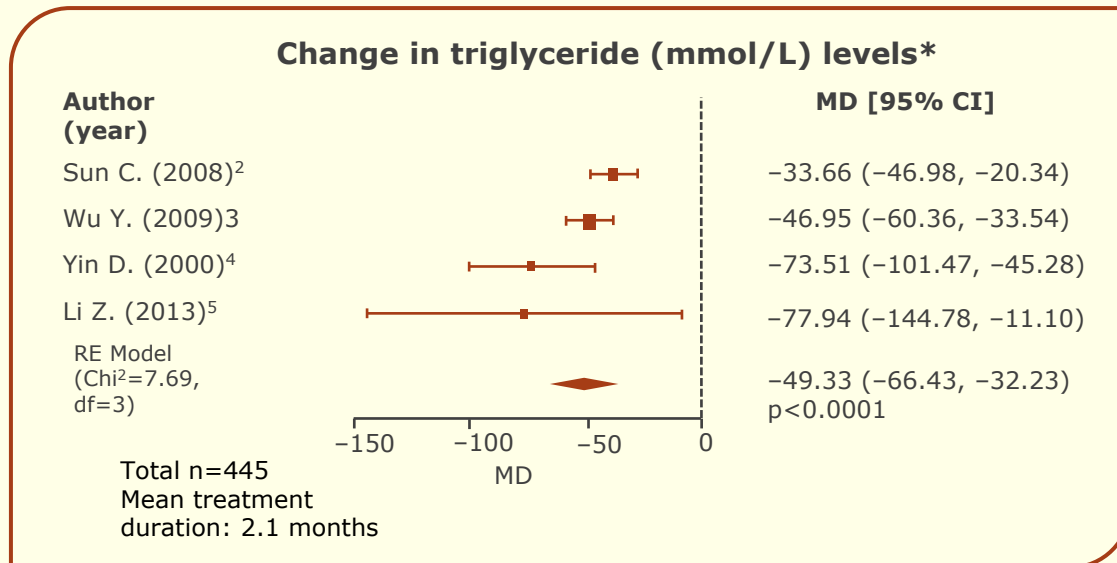


Similar trends in reduction of transaminase levels were seen in patients with NAFLD and T2DM or hyperlipidaemia¹ and in a narrative literature review of 20 studies²

EPLs plus ADs have shown consistent improvements in triglyceride and cholesterol levels



Results of a direct meta-analysis of RCTs comparing the effect of treatment with EPLs plus AD vs AD alone¹



A significantly greater reduction in **triglyceride** levels was achieved with EPL plus AD compared with AD therapy alone

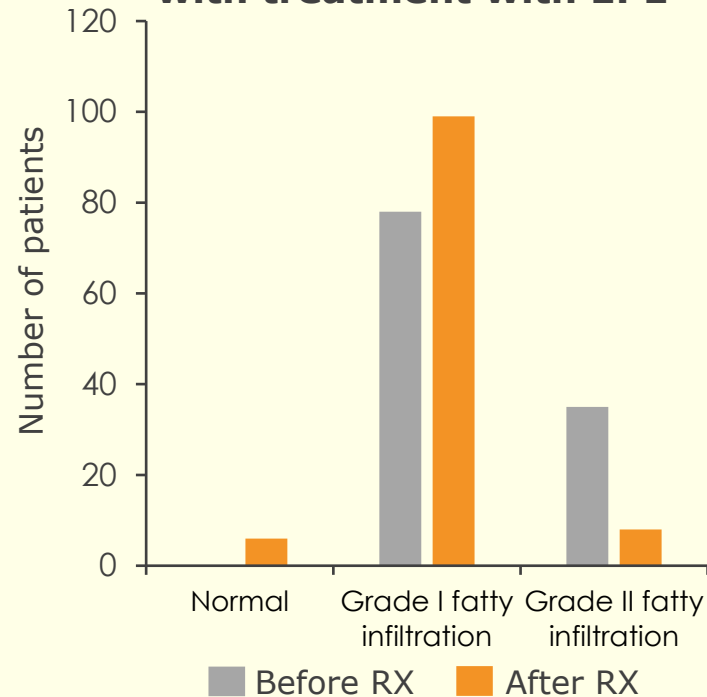
A significantly greater reduction in total **cholesterol** levels was achieved with EPL plus AD compared with AD therapy alone

EPLs improve ultrasonography and elastography results in patients with NAFLD

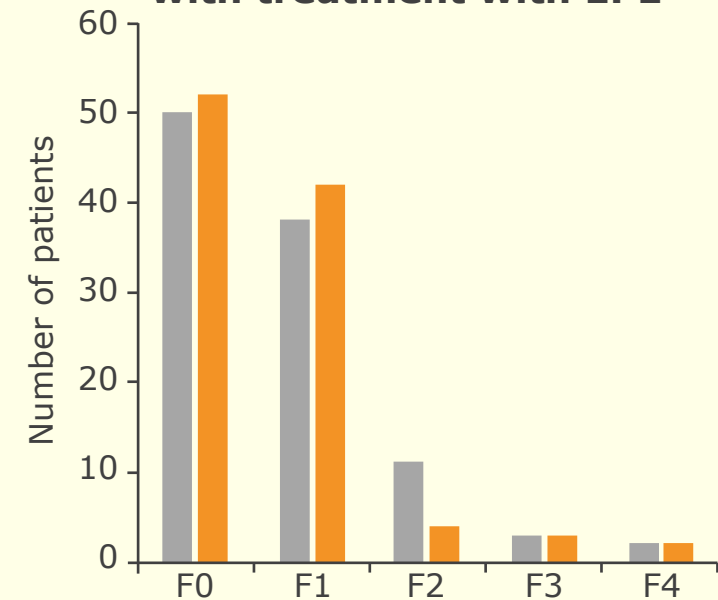


In an open-label, randomised trial (n=113):¹

Ultrasonography findings improved with treatment with EPL



Elastography findings improved with treatment with EPL

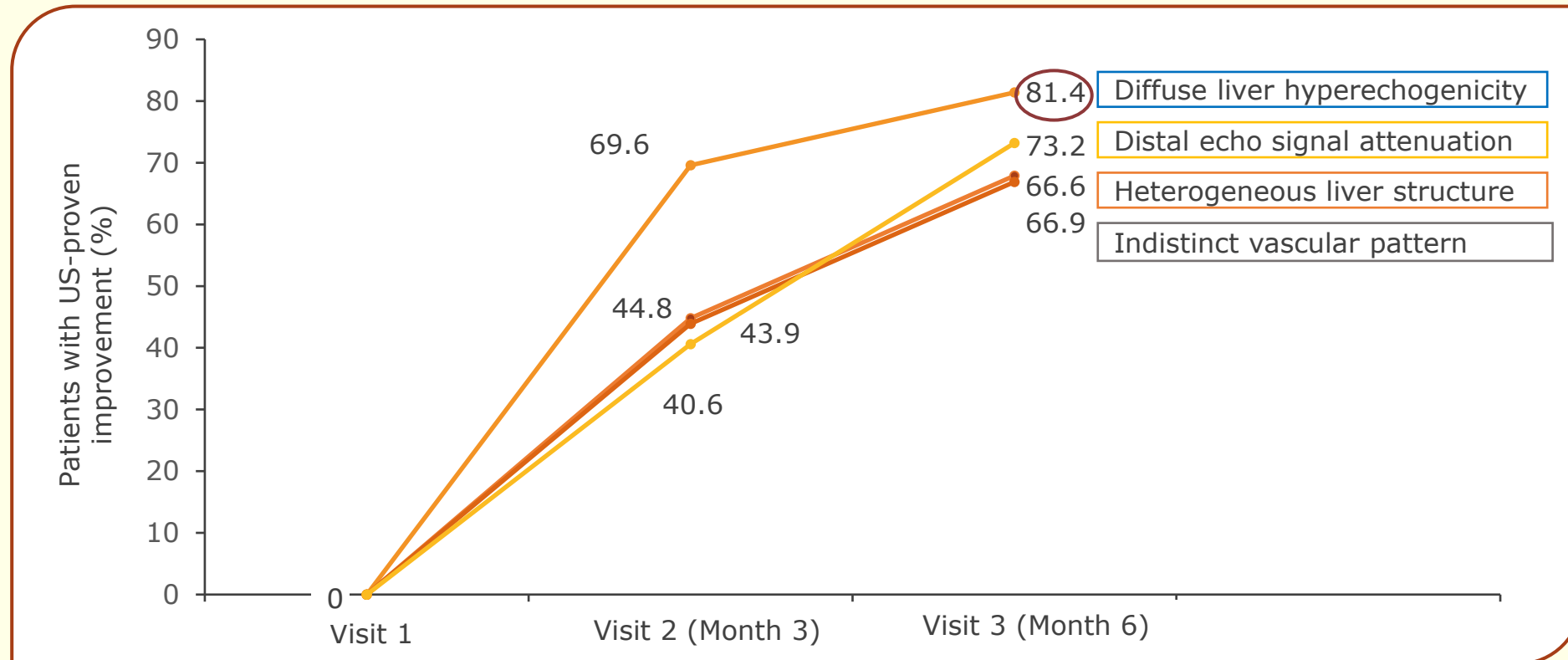


Similar trends in improvement of ultrasonography and elastography results were seen in patients with NAFLD and T2DM or hyperlipidaemia¹ and in a narrative literature review of 20 studies²

EPLs have been shown to reduce steatosis in patients with MAFLD



In an observational, multicentre, prospective trial (MANPOWER) in patients with NAFLD and cardiometabolic comorbidities*, N=2,843

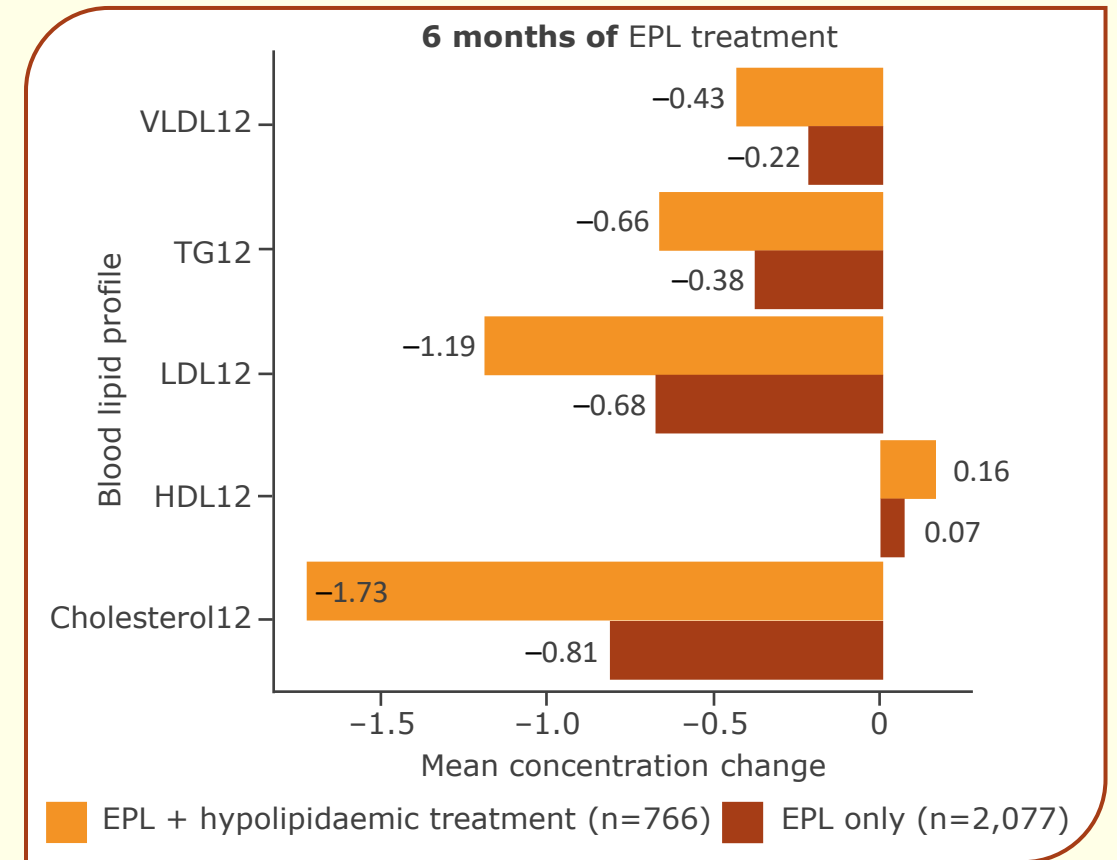
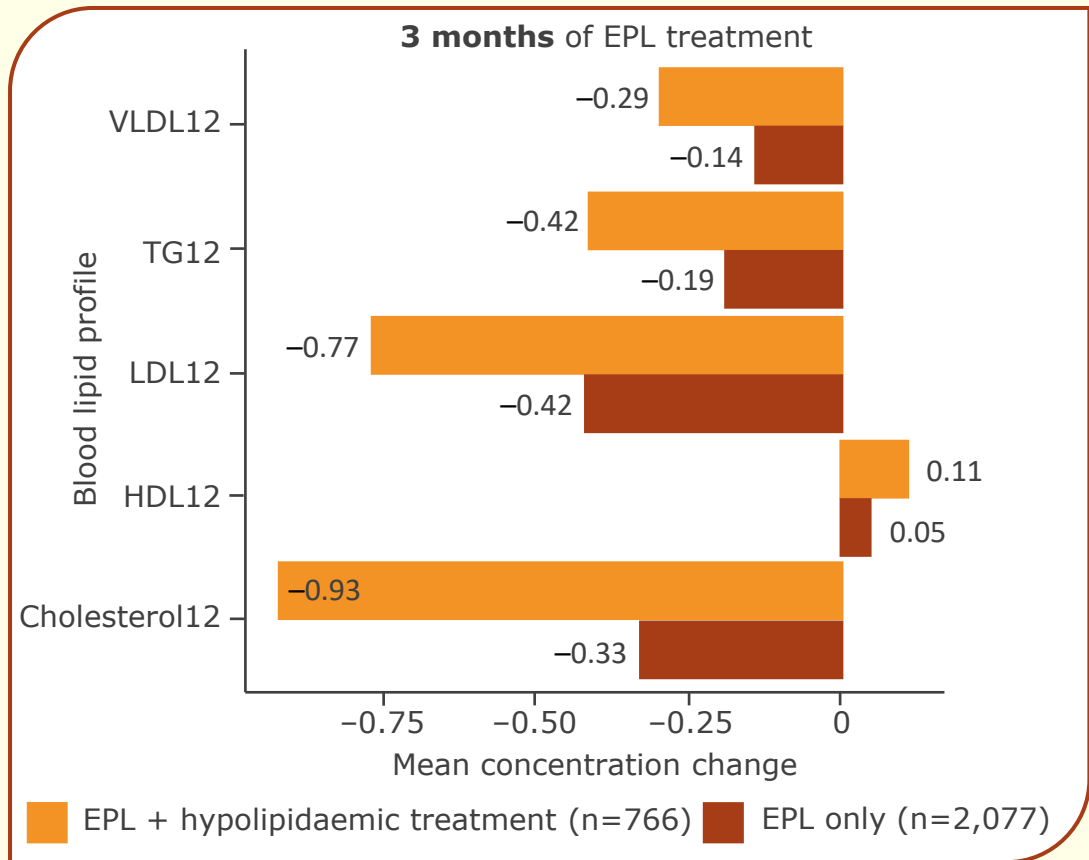


Significant improvement in ultrasound results after 3 and 6 months of treatment with EPL were seen ($p < 0.05$)

Additional benefits of EPL on lipid profiles have been observed



In an observational, multicentre, prospective trial (MANPOWER) in patients with NAFLD and cardiometabolic comorbidities*, N=2,843

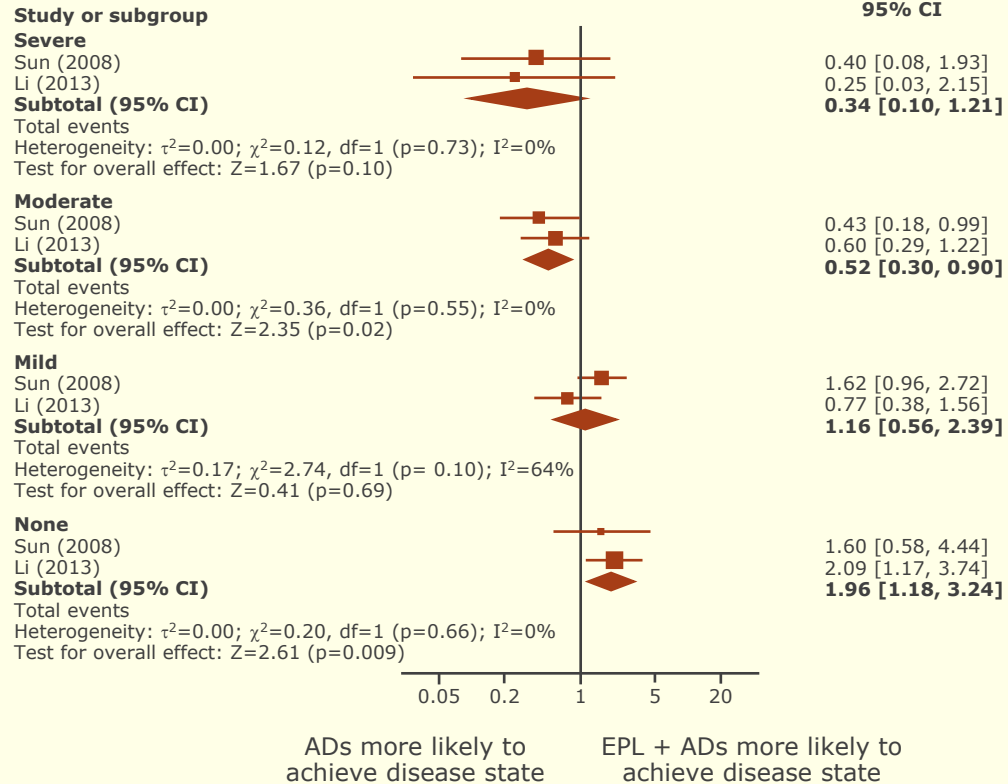


Significant improvement of lipid profile in patients receiving EPL + hypolipidaemic treatment and EPL alone ($p < 0.05$) was seen after 3 months of treatment

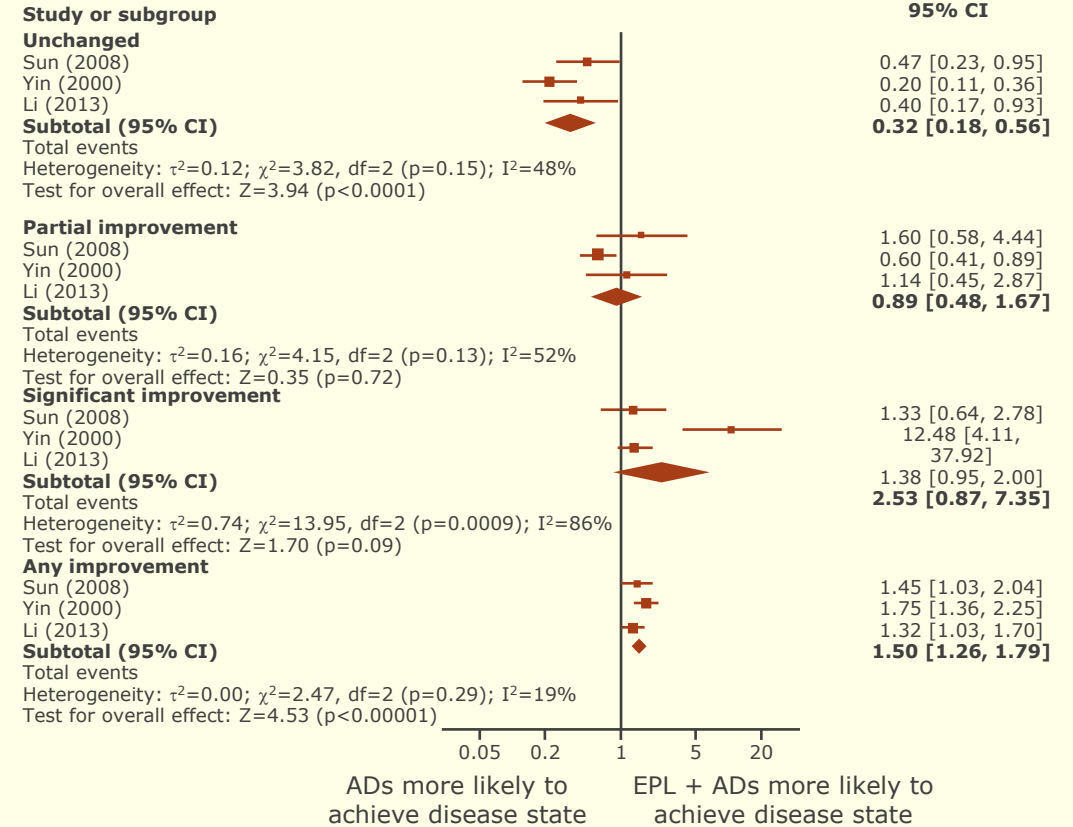
EPLs reduce disease severity and increase disease response in patients with NAFLD associated with metabolic syndrome



Disease severity



Disease response



Patients with additional risk factors showed increased biomarker improvement with EPL treatment



In a pooled analysis (EPOCH-2) of three Russian real-world studies: MANPOWER; LIDER; LIDER-2 (N=3,384)



Number of cardiovascular comorbidities

ALT, AST, postprandial glucose, TChol, HDL, LDL and TG changes were larger in patients with four comorbidities vs one comorbidity, $p < 0.001$



Eating high-fat foods

TB change was larger in patients eating fat daily vs taking fat less often, $p < 0.001$



Smoking

ALT, AST and GGT change was larger in smokers vs non-smokers, $p < 0.05$



Consuming alcohol

GGT change was larger in patients consuming alcohol 1–3 times per week vs rarely or never, $p < 0.001$

**Could EPLs improve
symptoms in patients with
NAFLD?**

How familiar are you with the clinical evidence suggesting EPL reduces patient's NAFLD symptoms?

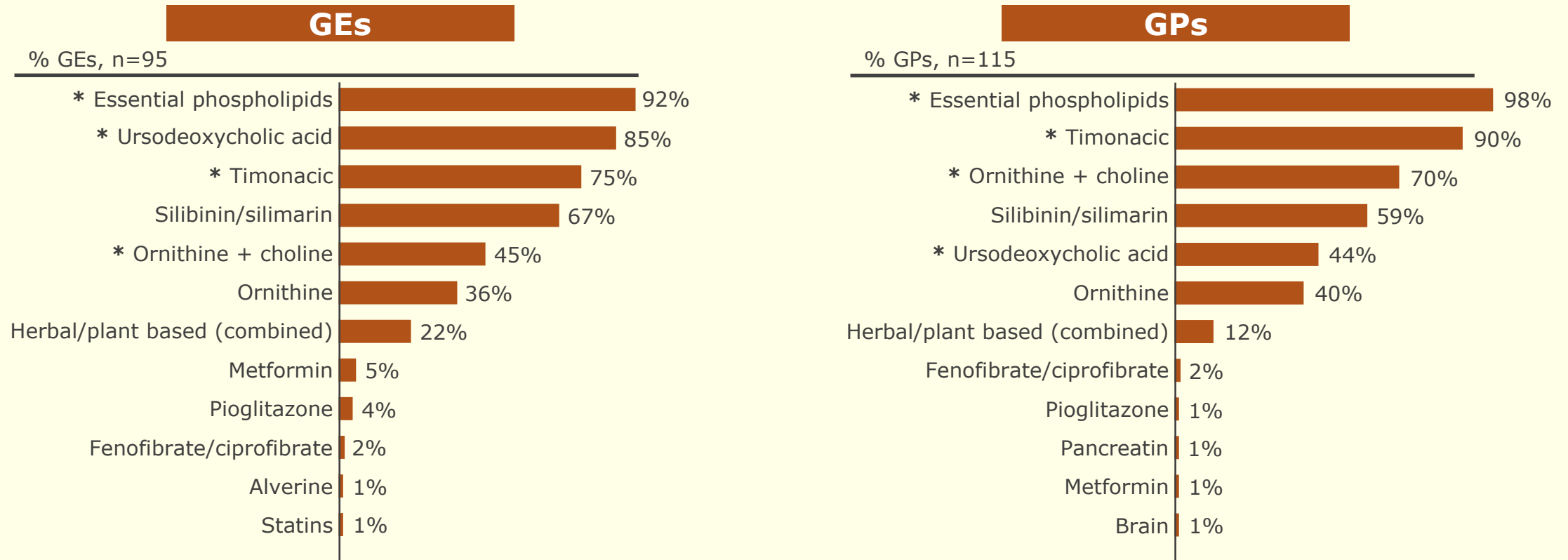


- 1 I am fully up to date with the latest data on the use of EPL and reducing NAFLD symptoms
- 2 I am aware of some data on EPL and reducing NAFLD symptoms
- 3 I am aware of data for other hepatoprotective agents, but not for EPL
- 4 I am not aware of data on EPL and reducing NAFLD symptoms

EPLs were the most frequently prescribed drug for NAFLD, in >90% of GEs and GPs



In an observational, cross-sectional, real-world survey

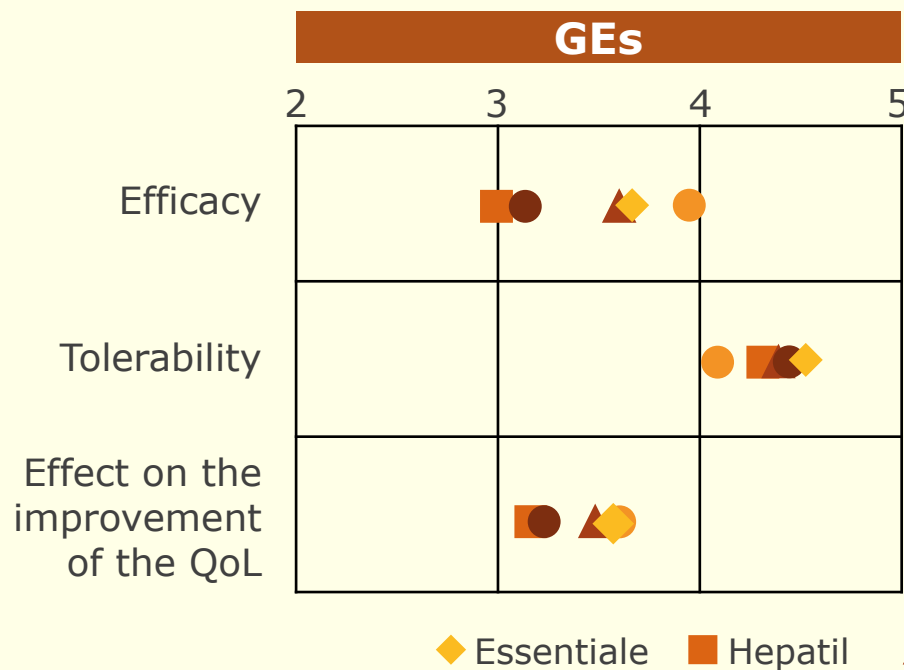


GEs and GPs ranked efficacy, tolerability and QoL improvement as the top three criteria impacting drug choice

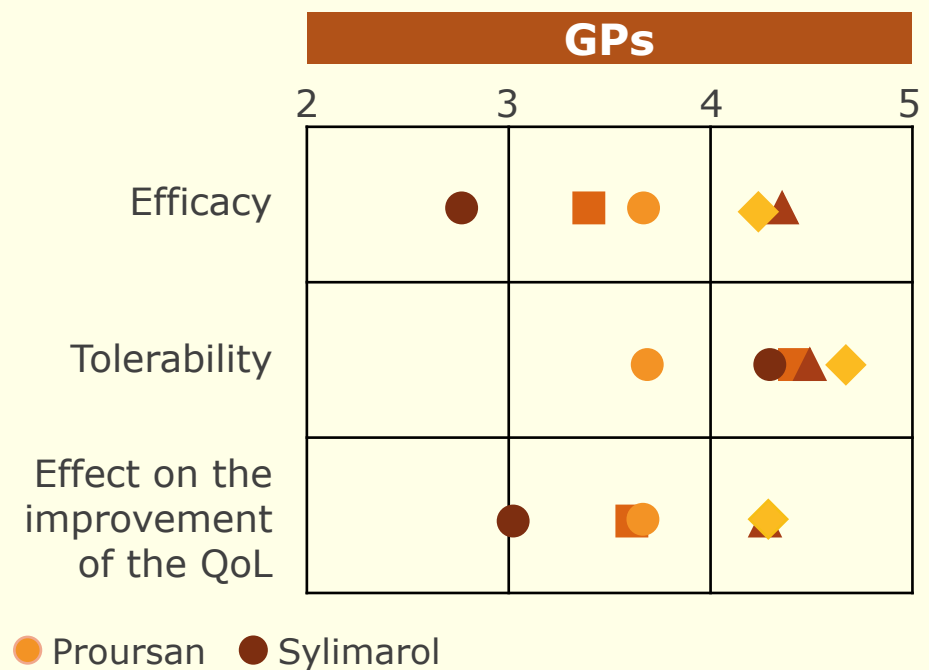


In an observational, cross-sectional, real-world survey the top 5 most frequently prescribed drugs were ranked based on the top three prescribing criteria:

Average score, n=95 GEs, scale 1–5



Average score, n=115 GPs, scale 1–5



Patients report symptoms of NAFLD



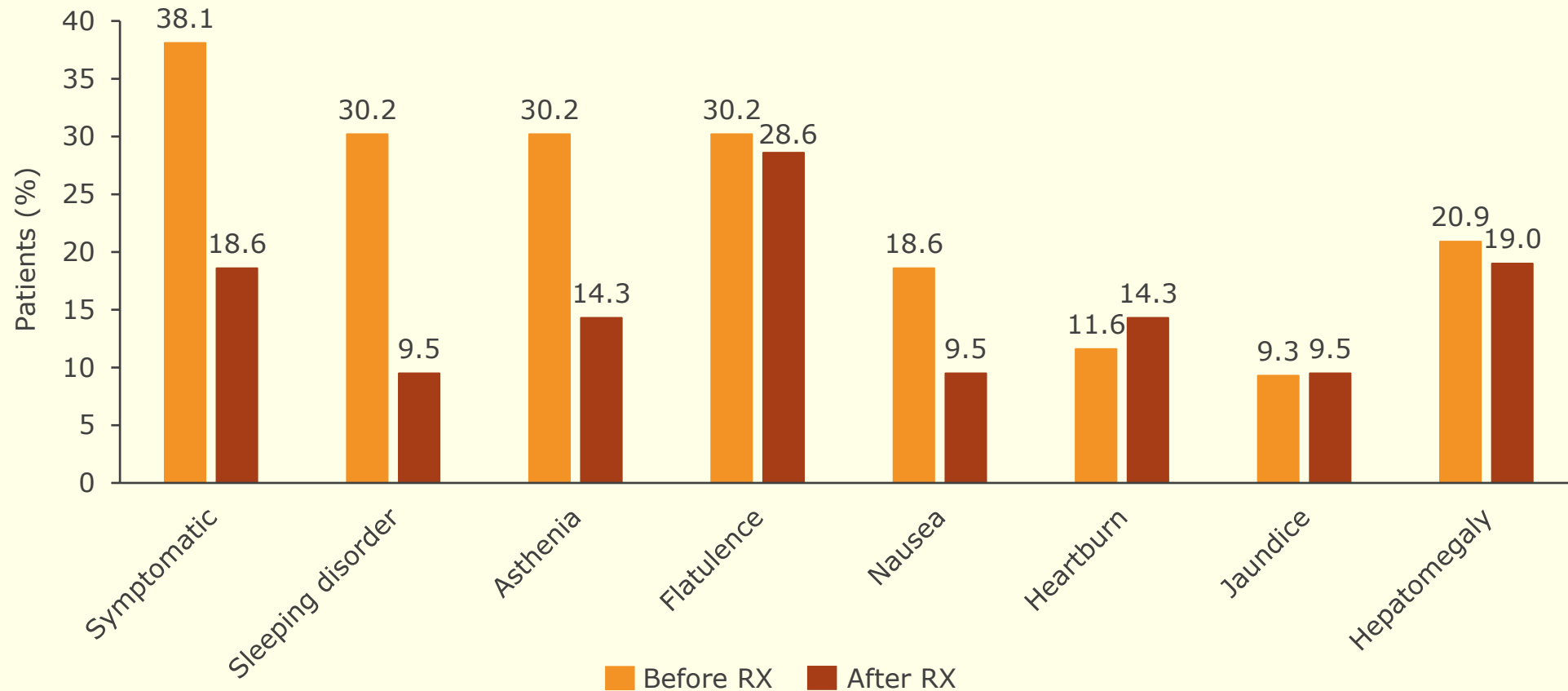
In an observational, cross-sectional, real-world survey (RESTORE) the top five most common symptoms of NAFLD reported by GEs and GPs using patients' language were:

GEs n=95		GPs n=115	
Symptom	GEs (%)	Symptom	GPs (%)
Bloating	62	Bloating	57
Weakening	33	Pain*	47
Tiredness/fatigue	31	Weakening	21
Pain*	28	Feeling of fullness	27
Feeling of fullness	24	Stomach aches	26

Treatment with EPLs reduces symptoms in patients with NAFLD



In an open-label, randomised trial (n=113):



Similar trends in reduction symptoms were seen in patients with NAFLD and T2DM or hyperlipidaemia

Patient satisfaction correlates with objective laboratory improvements for patients with NAFLD receiving EPLs



In a pooled analysis (EPOCH-2) of three Russian real-world studies: MANPOWER; LIDER; LIDER-2 (N=3,384)

Clinician satisfaction and laboratory improvements

Laboratory improvements, median change from baseline	Clinician satisfaction		
	Low + very low	High + very high	p value [†]
ALT (U/L)	-8.00	-15.00	<0.001
AST (U/L)	-7.00	-13.00	<0.001
GGT (U/L)	-6.00	-10.00	<0.001
HbA1c (%)	-0.10	-0.15	0.029
Total cholesterol (mmol/L)	-0.60	-1.10	<0.001
HDL (mmol/L)	0.10	0.10	0.028
LDL (mmol/L)	-0.40	-0.80	<0.001
VLDL (mmol/L)	0.00	-0.20	<0.001
Triglycerides (mmol/L)	-0.20	-0.40	<0.001
ALP (U/L)	-8.50	-13.60	<0.001
Total bilirubin (µmol/L)	-1.00	-2.00	<0.001

Patient satisfaction and liver structure improvements

Patient's satisfaction, %*	Improvement		
	Low + very low	High + very high	p value [‡]
Diffuse hyperechogenicity of the liver parenchyma on ultrasound	65.3	84.6	<0.001
Heterogeneity of liver structure on ultrasound	61.8	81.2	<0.001
Vascular blurring and/or underlined vascular pattern on ultrasound	67.4	87.9	<0.001
Distal attenuation of the echo-signal	51.8	77.8	<0.001

Summary



1

Patients with NAFLD are treated with lifestyle modifications, hepatoprotective agents and pharmacological treatments to prevent disease progression and serious comorbidities

2

Treatment with EPLs have reduced transaminase levels, improved ultrasonography and elastography results, reduced steatosis and reduced disease severity in patients with NAFLD

3

EPLs were viewed as being efficacious, tolerable and having a positive impact on patient QoL by GEs and GPs

4

Patient satisfaction and symptom reduction could be used as a diagnostic or monitoring tool for NAFLD