

Guiding the care of hypertriglyceridemia-induced acute pancreatitis

Multidisciplinary care and the role of new
therapies through apoC-III inhibition



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No identifiable patient-specific information is included.

Introductions



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Disclosures

	Prof. Vinciane Rebours	Prof. Gabriele Capurso	Prof. Clara Viñals
Research support/PI			
Employee			
Consultant/Honoraria	Mayoly Spindler, Sobi	Amgen, Boston Scientific, Pangenix, Sobi, Viatris	Sanofi, Sobi
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Guiding the care of hypertriglyceridemia-induced acute pancreatitis: Multidisciplinary care and the role of new therapies through apoC-III inhibition

Agenda

Welcome and introduction	Prof. Vinciane Rebours (Chair)
Warning bells: Pathophysiology and risks of hypertriglyceridemia-associated acute pancreatitis	Prof. Vinciane Rebours
Rowing in harmony: Working together to recognise the causal role of hypertriglyceridemia in acute pancreatitis	Prof. Gabriele Capurso
A shining beacon: apoC-III inhibition for acute pancreatitis prevention	Prof. Clara Viñals
Panel discussion and conclusion	All (moderated by Chair)

Warning bells: Pathophysiology and Risks of Hypertriglyceridemia- associated acute pancreatitis

Vinciane Rebours

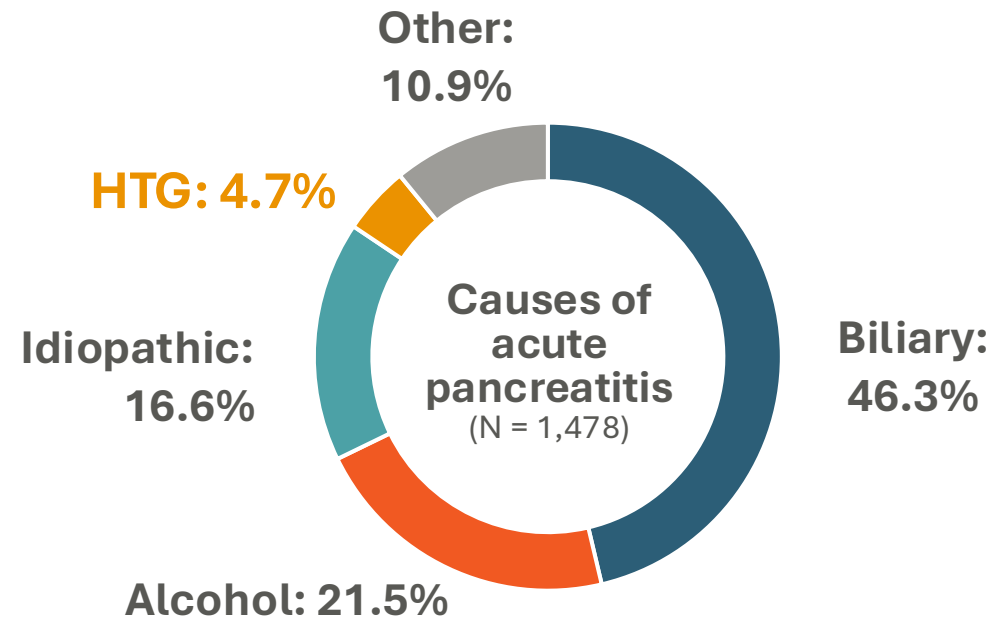
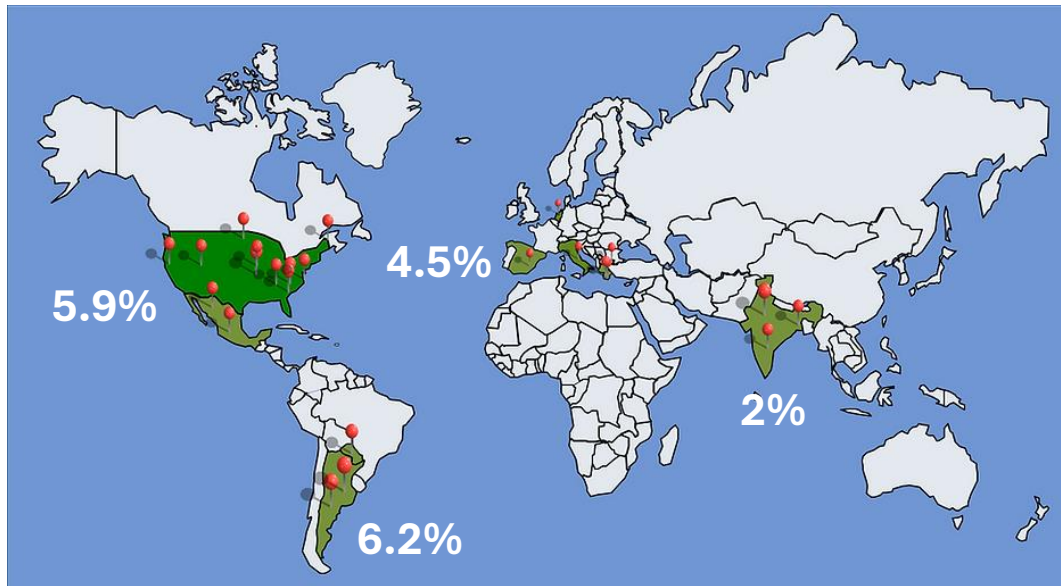
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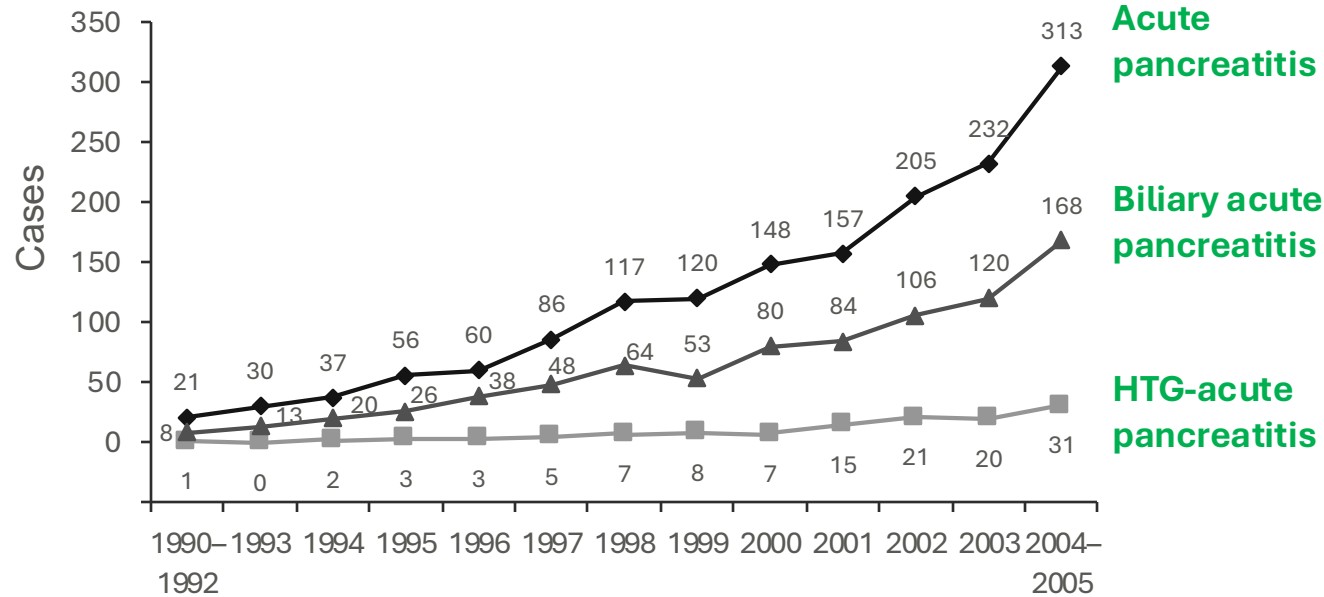


Clinical features of hypertriglyceridemia-associated acute pancreatitis (HTG-AP): International cohort

- **APPRENTICE consortium¹:**
International, multicentre, prospective cohort study
 - 22 centres
 - 2015–2018
- HTG-AP definition: Triglycerides >500 mg/dL (>5.65 mmol/L)*
- **1,478 patients**
 - 785/1,478 (53%) with triglyceride rate available
 - 69/1,478 (4.7%) with hypertriglyceridemia-associated acute pancreatitis



Hypertriglyceridemia-associated acute pancreatitis incidence: Chinese cohort



- Retrospective, multicentre study¹: 1,582 patients with serum lipids tested within 24 hours of admission
- Diagnosis: Acute pancreatitis
- 4 Guangdong hospitals, follow-up, 15 years (1990–2005)
- HTG-AP definition: Triglycerides $\geq 1,000$ mg/dL (≥ 11.3 mmol/L), or >500 mg/dL (>5.6 mmol/L) with lactescent serum on admission

	Cases of acute pancreatitis	Percentage of lipid test	Cases of HTG-acute pancreatitis, n (%)	Cases of biliary acute pancreatitis, n (%)	Cases of other acute pancreatitis, n (%)
Guangzhou	613	68.8%	35 (5.7)	387 (63.1)	191 (31.1)
Shantou	529	80.9%	31 (5.9)	273 (51.6)	225 (42.5)
Meizhou	349	72.7%	54 (15.5)	122 (34.9)	173 (49.6)
Shaoguan	91	26.6%	3 (3.3)	46 (50.6)	42 (46.2)
Total	1,582	66.8%	123 (7.8)	828 (52.3)	631 (39.9)

Adapted from Huang et al. 2014.¹ AP, acute pancreatitis; HTG-AP, hypertriglyceridemia-associated acute pancreatitis.

1. Huang et al. *Pancreas* 2014.

Aetiology of acute pancreatitis: Hungarian cohort

Aetiology of acute pancreatitis ¹	Number	%	Male	Female	Mild	Moderate	Severe
Biliary	263	43.83%	31.94%	58.87%*	64.26%	28.52%	7.22%
Alcohol	102	17.00%	27.16%†	4.15%	61.76%	30.39%	7.84%
Alcohol + high fat	57	9.50%	11.94%‡	6.42%	57.89%	29.82%	12.28%
Idiopathic	98	16.33%	16.12%	16.60%	62.24%	28.57%	9.18%
Hyperlipidemia	37	6.17%	8.06%§	3.77%	32.43%	48.65%¶	18.92%**
Post-ERCP	22	3.67%	1.79%	6.04%††	68.18%	22.73%	9.09%
Other	21	3.50%	2.99%	4.15%	66.67%	28.57%	4.76%
Total	600	100.0%					

* p<0.001; † p<0.001; ‡ p=0.022; § p=0.030; || p<0.001; ¶ p=0.011; ** p=0.025; †† p=0.006.

ERCP, endoscopic retrograde cholangiopancreatography.

1. Párnitzky et al. *PLoS One* 2016.

Distinguishing FCS from other causes of sHTG



Genetic factors

Secondary factors



Mono-causal genetic

Deficiencies due to mutations in:

- *LPL*^{1,2}
- *APOC2*^{2,3}
- *APOA5*^{2,3}
- *LMF1*^{2,3}
- *GPIHBP1*²⁻⁴
- Additional: *GPD1*, *CREB3L3*⁵

Familial

chylomicronemia syndrome (FCS)

Multifactorial

Genetic predisposition^{2,3,6} +

- **Comorbidities** (diabetes, obesity, metabolic syndrome, kidney disease, etc.) and/or²
- **Medications** and/or²
- **Lifestyle** (alcohol, high-fat/high-glycaemic index diet)²

Mono-causal secondary

Very rare⁷

- Paraproteinemia^{2,3}
- Anti-GPIHBP1 autoantibodies⁷

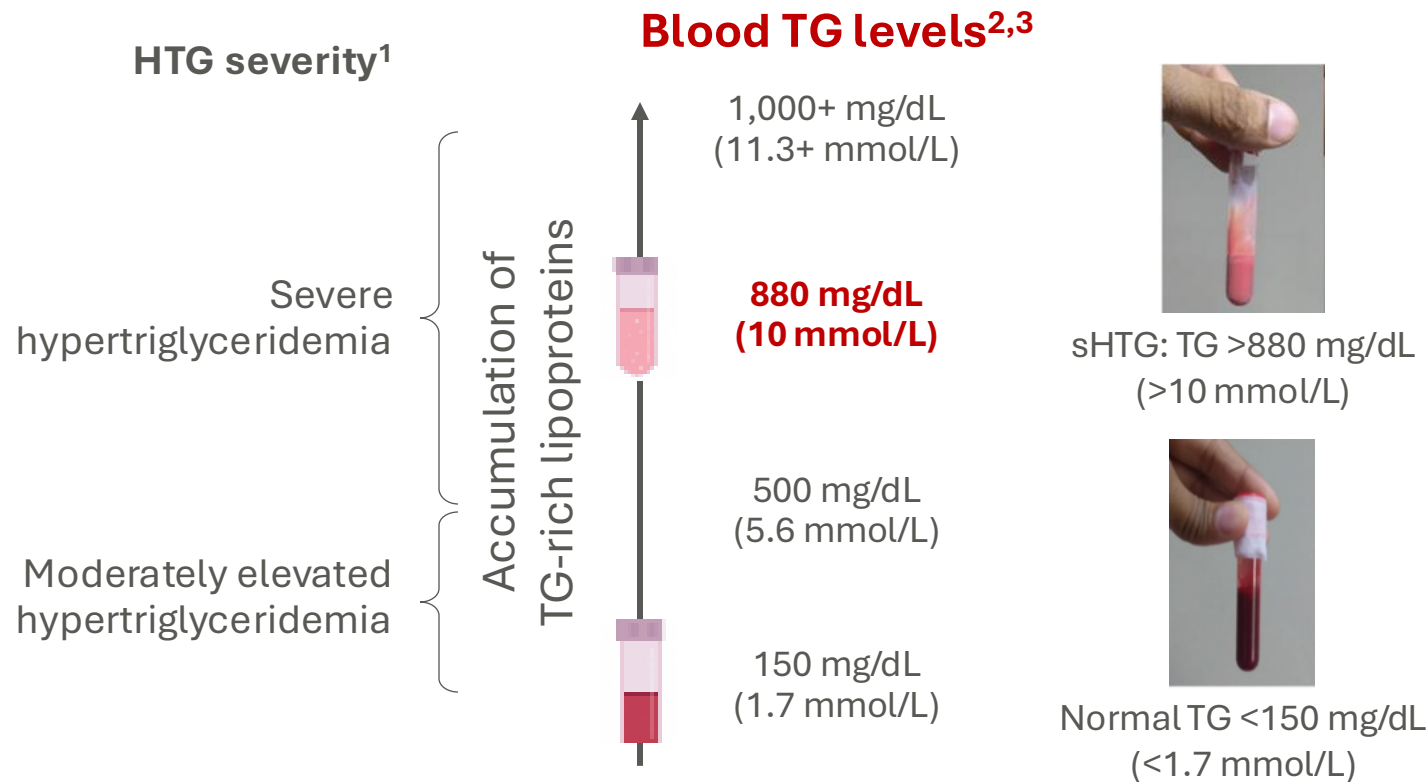
Multifactorial or secondary sHTG

FCS, familial chylomicronemia syndrome; sHTG, severe hypertriglyceridemia.

1. Karanchi et al. *StatPearls* 2023 2. Laufs et al. *Eur Heart J* 2020 3. Hegele et al. *Lancet Diabetes Endocrinol* 2014 4. Ginsberg et al. *Eur Heart J* 2021 5. Bashir et al. *Metabolites* 2023

6. D'Erasmus et al. *Arterioscler Thromb Vasc Biol* 2019 7. Baass et al. *J Intern Med* 2020.

Hypertriglyceridemia-related acute pancreatitis



Severe hypertriglyceridemia (>880 mg/dL or 10 mmol/L) is associated with accumulation of chylomicrons^{2,3}

- Lactescent serum²
- Short half-life of chylomicrons & VLDL: early triglyceride dosage⁴
- **Risk of acute pancreatitis is greatly elevated for TG levels >10 mmol/L⁵**

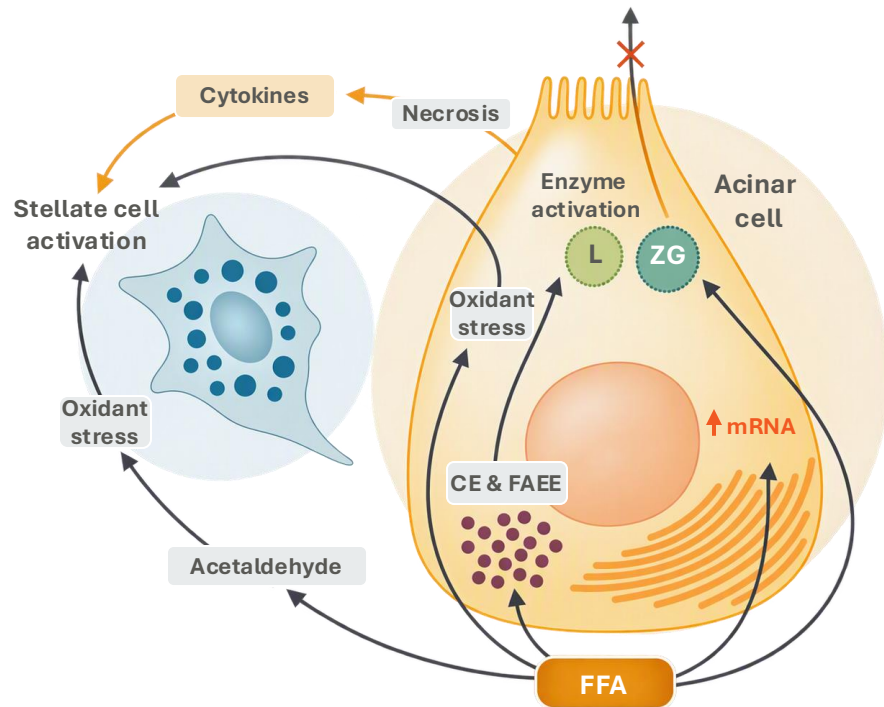
Cut-off points used to define hypertriglyceridemia categories vary across published guidelines and consensus statements

Images from Susheela et al. 2021 are for illustrative purposes only and do not reflect exact TG values.⁶

EAS, European Atherosclerosis Society; ESC, European Society of Cardiology; HTG, hypertriglyceridemia; sHTG, severe hypertriglyceridemia; TG, triglyceride.

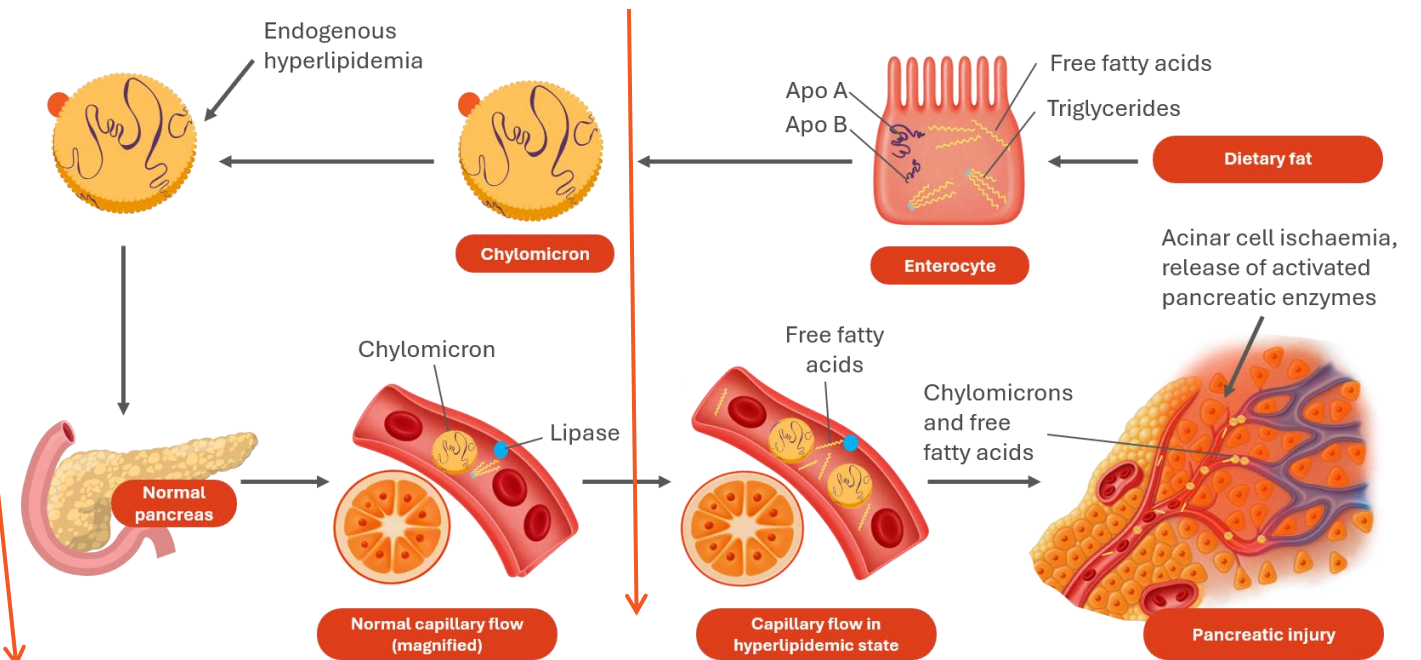
1. Ginsberg et al. *Eur Heart J* 2021 2. Mach et al. *Eur Heart J* 2020 3. Laufs et al. *Eur Heart J* 2020 4. Huang et al. *Pancreas* 2014 5. Patel et al. *Cardiovasc Diabetol* 2022 6. Susheela et al. *J Med Case Rep* 2021.

Triglyceride hydrolysis^{1,2}
Free fatty acid toxicity^{1,2}



**TOXICITY
ACINUS**

Hypertriglyceridemia^{3,4}
High level of chylomicrons^{1,3}
Microthrombi²



ISCHAEMIA

Figures made with MindTheGraph using data from published papers.¹⁻⁴

Apo, apolipoprotein; CE, cholesteryl esters; FAEE, fatty acid ethyl esters; FFA, free fatty acid; L, lysosome; mRNA, messenger RNA; TG, triglyceride; ZG, zymogen granule.

1. Kiss et al. *Acta Physiol* 2023 2. Qiu et al. *Ann Med* 2023 3. de Pretis et al. *United European Gastroenterol J* 2018 4. Kimura & Mössner. *Int J Pancreatol* 1996.

The role of FFA, pancreatic lipase and Ca^{2+} signalling sobi in acinar cell injury: pancreatitis model

Lipoprotein lipase-
deficient mice



Caerulein-induced
acute pancreatitis

Observed injury^{1,*}



↑ Necrosis

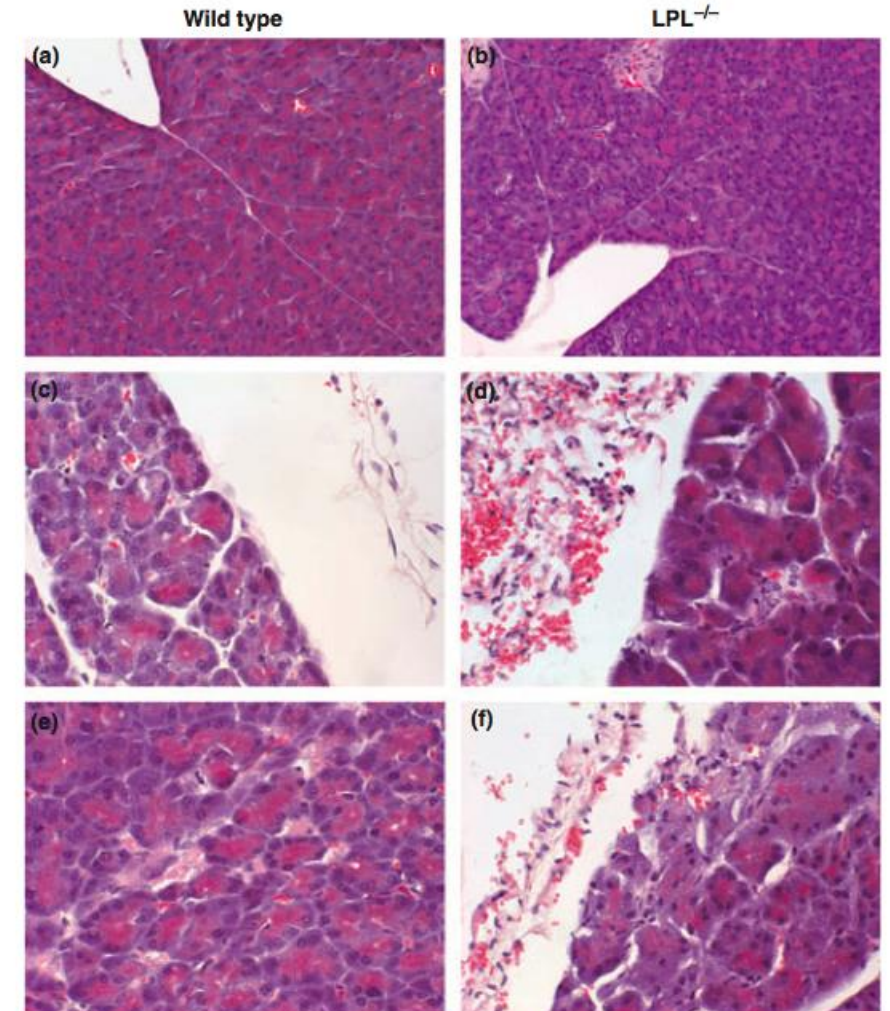


↑ Oedema

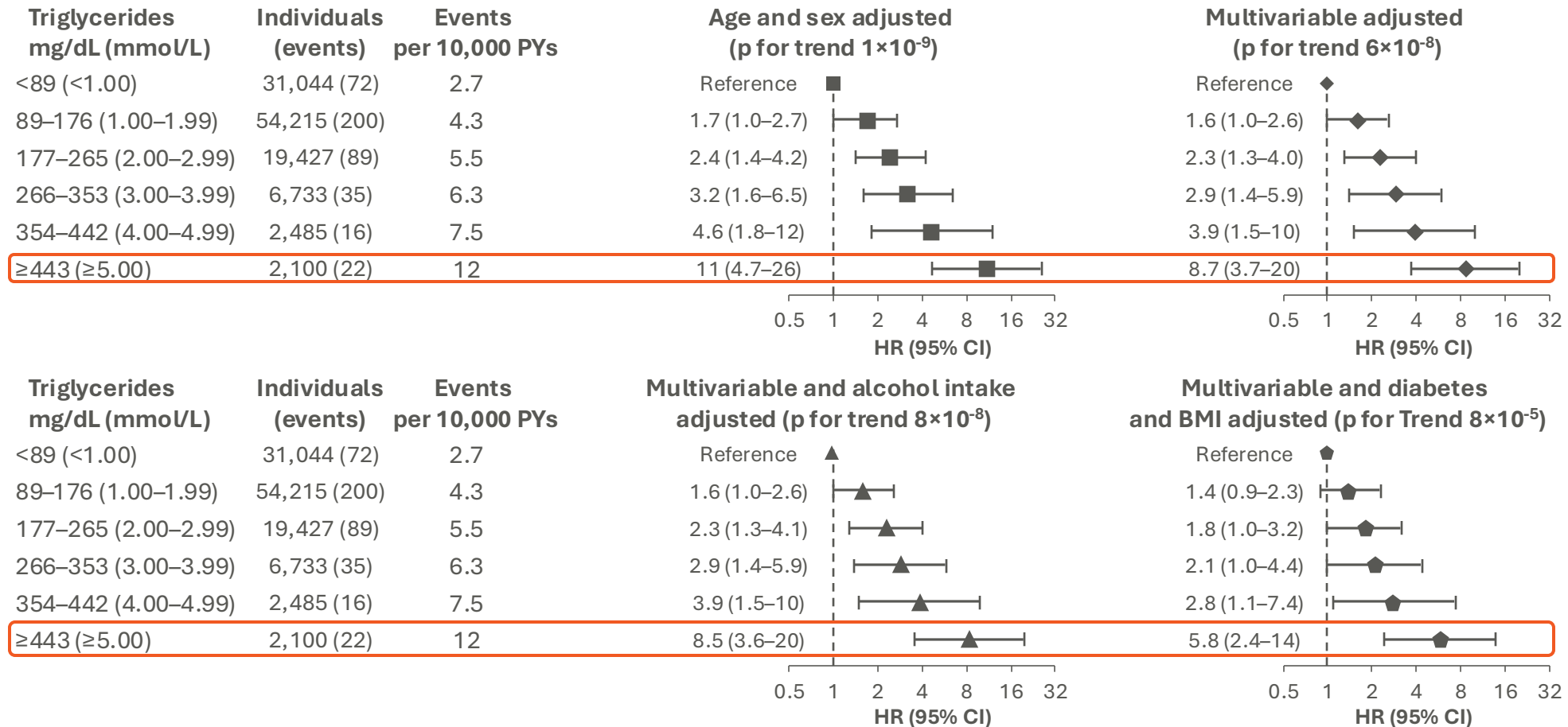


↑ Haemorrhage

↑ Ischaemia



Risk of acute pancreatitis is associated with plasma triglyceride level¹



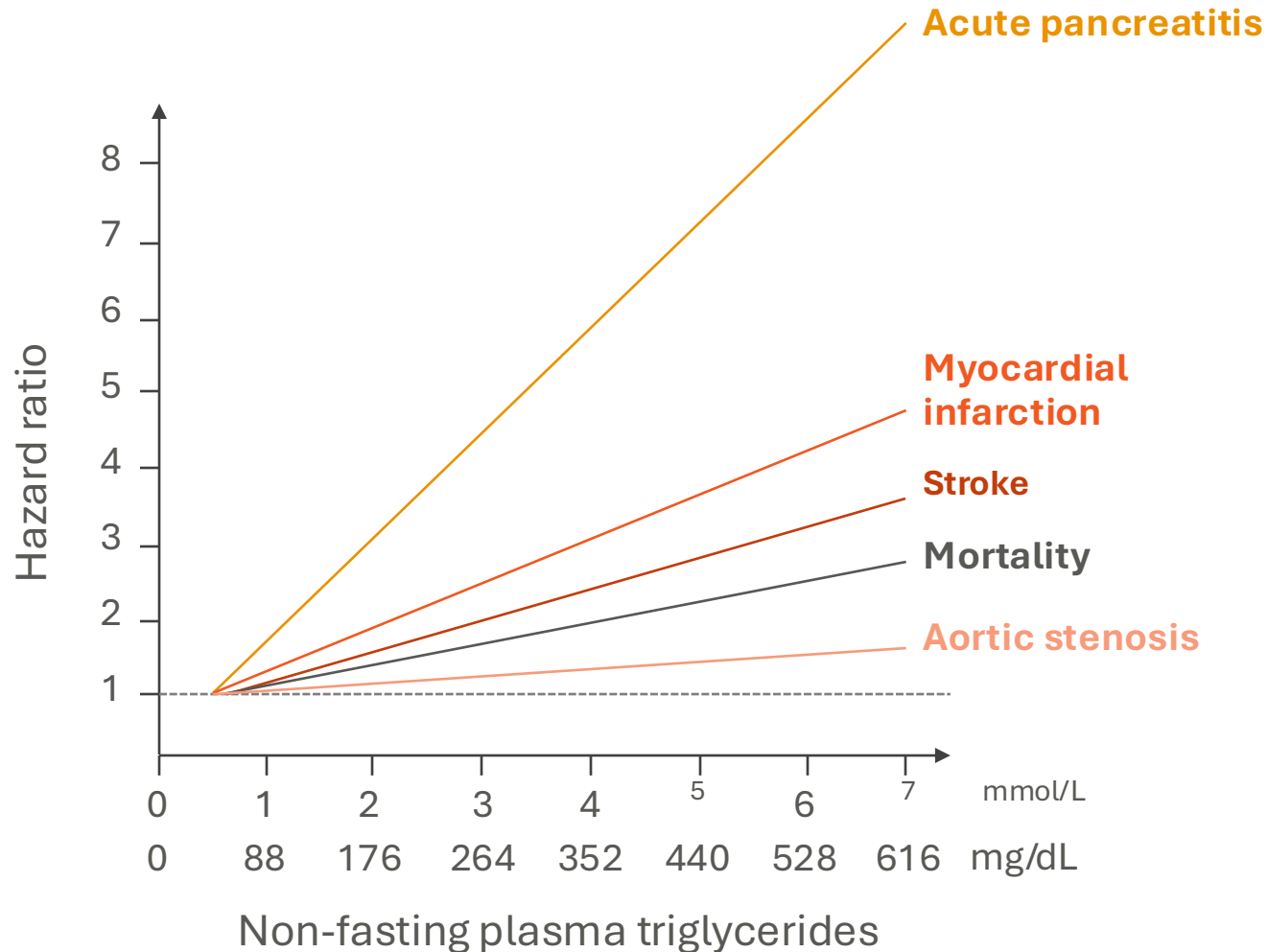
Acute pancreatitis risk: Multivariable adjusted for age, sex, education, smoking, hypertension, statin use, birth year*

* Multivariable adjusted also for study cohort. Corrected for regression dilution bias. BMI, body-mass index; HR, hazard ratio; PY, person year.

1. Pedersen et al. *JAMA Intern Med* 2016.

Hypertriglyceridemia and associated risks¹

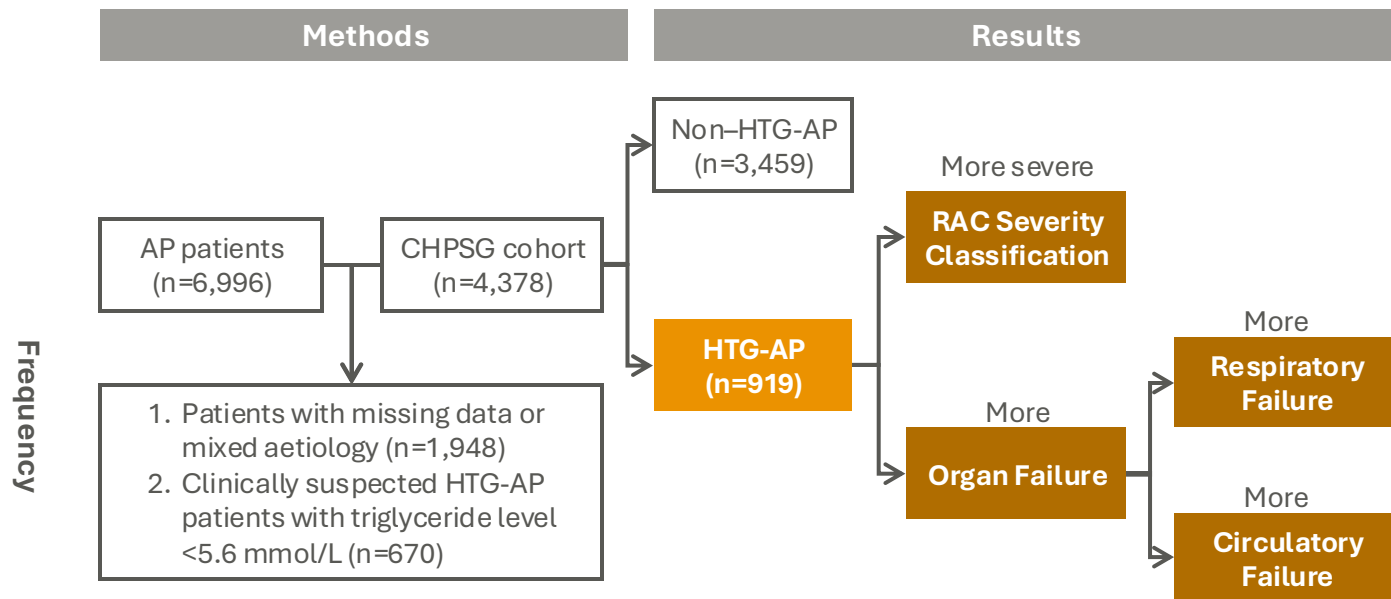
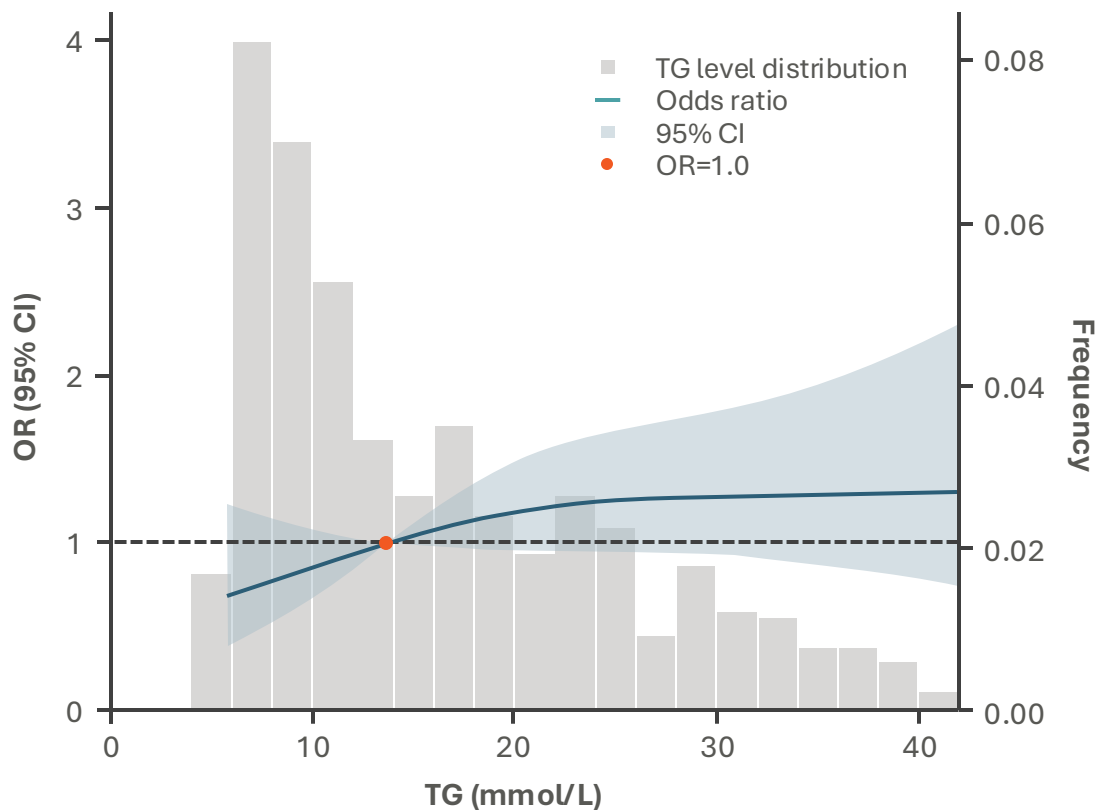
Relationship of progressive increase in non-fasting plasma TG
with progressive increase in risk of morbidity and mortality



Based on data from roughly 100,000 individuals participating in the **Copenhagen General Population Study** and the **Copenhagen City Heart Study**

Observational relationships are shown.

Clinical outcomes in patients with hypertriglyceridemia-associated acute pancreatitis

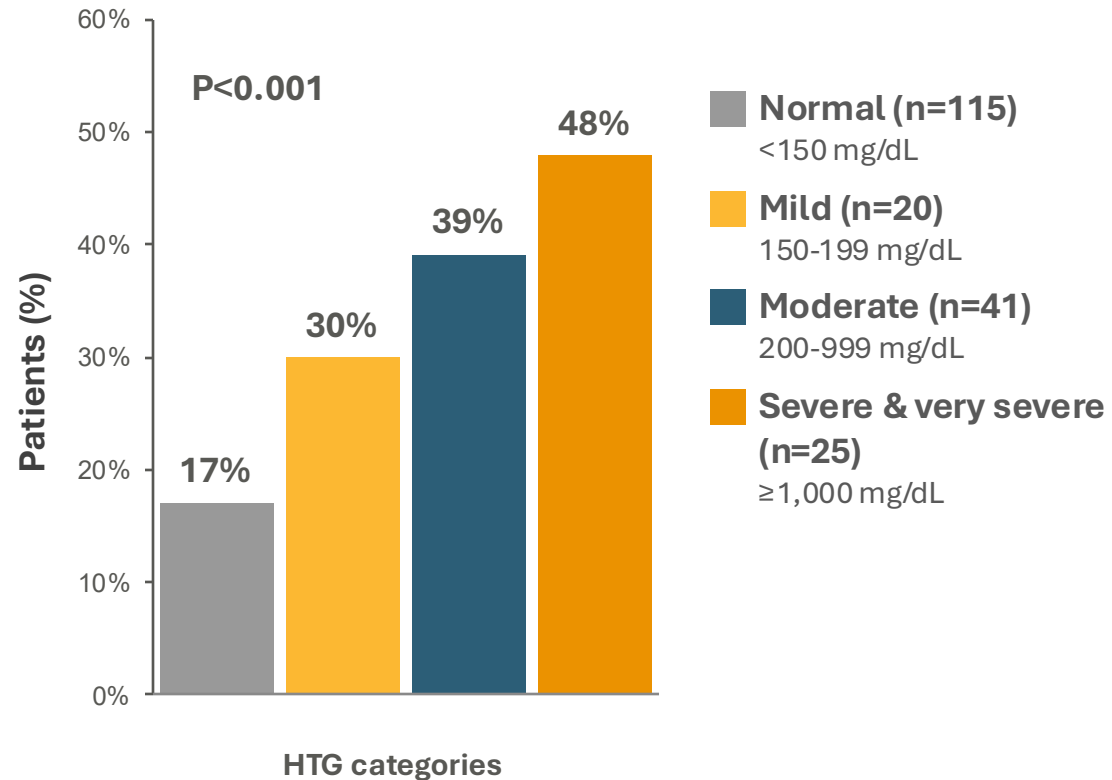


Severe pancreatitis
Triglyceride threshold: 13.64 mmol/L

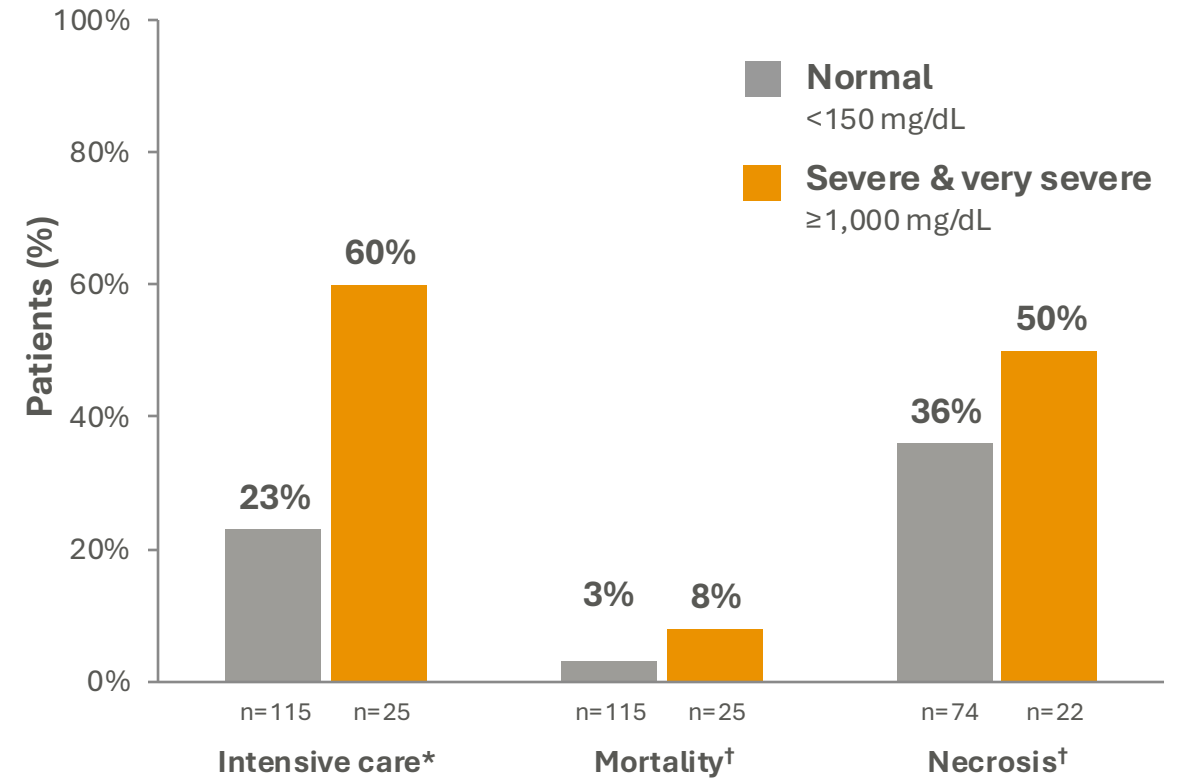
Restricted cubic spline analysis in patients with HTG-AP only (n=919), adjusted for the four risk factors identified in multivariable analysis (age, fasting glucose, white blood cell count and pleural effusion); the red point indicates OR = 1.0 (TG 13.64 mmol/L).
AP, acute pancreatitis; CHPSG, Chinese HTG-associated Pancreatitis Study Group; CI, confidence interval; HTG, hypertriglyceridemia; HTG-AP, hypertriglyceridemia-associated acute pancreatitis;
OR, odds ratio; RAC, Revised Atlanta Classification; TG, triglyceride.
1. Deng et al. *Am J Gastroenterol* 2025.

Outcomes in patients with HTG-AP¹

Persistent organ failure



Hospital utilisation, mortality, & necrosis



**Serum TG level:
an independent risk factor of severity**

Duration of hospitalisation:
<150 mg/dL: **7** days
≥1,000 mg/dL: **17** days

* p<0.001. † Not significant. HTG-AP, hypertriglyceridemia-associated acute pancreatitis; TG, triglyceride.
1. Nawaz et al. *Am J Gastroenterol* 2015.

Clinical significance of elevated serum TG in early AP

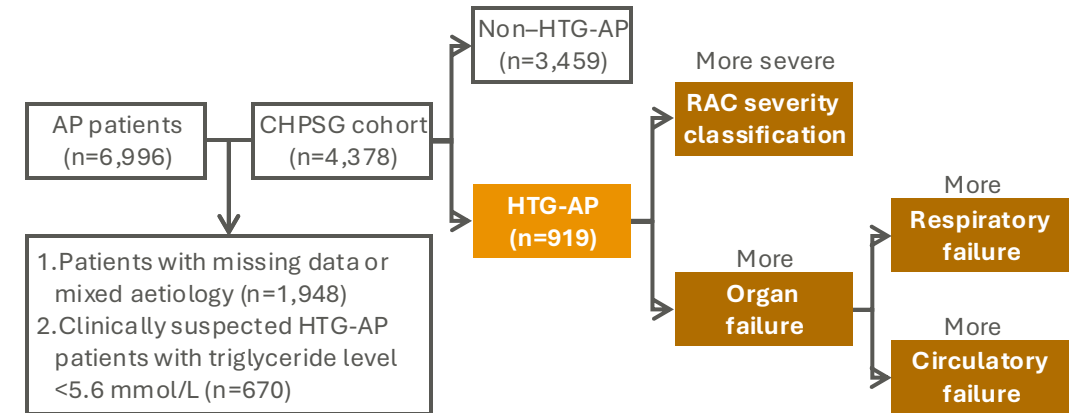
TG level category:
Mild: 1.7–2.3 mmol/L
Moderate: 2.3–11.2 mmol/L
Severe: 11.2–22.4 mmol/L
Very severe: ≥22.4 mmol/L

Variable	Serum TG Level (mg/dL) within 72 h of hospital admission				P_{trend}
	Normal $N = 1078$	Mild $N = 107$	Moderate $N = 242$	Severe and very severe $N = 112$	
Severity classification, N (%)					<0.001
MAP	424 (39)	43 (40)	85 (35)	21 (19)	
MSAP	440 (41)	34 (32)	98 (41)	49 (44)	
SAP	214 (20)	30 (28)	59 (24)	42 (38)	
APFC, N (%)	221 (21)	18 (17)	59 (24)	29 (26)	0.125
ANC, N (%)	150 (14)	17 (16)	43 (18)	32 (29)	0.001
Pancreatic necrosis, N (%)	210 (20)	25 (23)	62 (26)	39 (35)	0.001
OF, N (%)	368 (34)	48 (45)	91 (38)	59 (53)	<0.001
POF, N (%)	214 (20)	30 (28)	59 (24)	42 (38)	<0.001
MOF, N (%)	31 (3)	9 (8)	23 (10)	12 (11)	<0.001
Persistent SIRS, N (%)	221 (21)	28 (26)	70 (29)	54 (48)	<0.001
Median hospital days (IQR)	9 (6–14)	9 (5–13)	10 (6–14)	12 (7–17)	0.079
Median ICU days, (IQR)	0	0 (0–1)	0 (0–2)	1 (0–7)	0.045
Admission to ICU, N (%)	267 (25)	31 (29)	83 (34)	57 (51)	<0.001
Mortality, N (%)	53 (5)	11 (10)	15 (6)	8 (7)	0.112

ANC, acute necrotic collection; AP, acute pancreatitis; APFC, acute peripancreatic fluid collection; ICU, intensive care unit; IQR, interquartile range; MAP, mild acute pancreatitis; MOF, multiple organ failure; MSAP, moderately severe acute pancreatitis; OF, organ failure; POF, persistent organ failure; SAP, severe acute pancreatitis; SIRS, systemic inflammatory response syndrome; TG, triglyceride.

1. Wan et al. *Lipids Health Dis* 2017.

Risk factors associated with severe AP in HTG-AP



HTG-AP patients (n=919) ¹	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Sex	0.671 (0.418–1.075)	0.097	1.165 (0.571–2.38)	0.675
Age	1.022 (0.999–1.046)	0.061	1.044 (1.012–1.077)	0.007
Body mass index	1.030 (0.982–1.081)	0.218	1.047 (0.989–1.109)	0.112
Fasting glucose	1.117 (1.078–1.158)	<0.001	1.114 (1.06–1.17)	<0.001
Triglyceride	1.005 (0.998–1.013)	0.164	1.005 (0.996–1.013)	0.263
Cholesterol	1.069 (1.019–1.122)	0.006	1.017 (0.954–1.083)	0.608
Uric acid	1.000 (0.998–1.001)	0.740	0.999 (0.997–1.001)	0.460
Alcohol	1.046 (0.664–1.646)	0.848	1.211 (0.609–2.408)	0.584
Smoke	0.789 (0.500–1.245)	0.309	0.707 (0.354–1.41)	0.325
Diabetes history	0.882 (0.550–1.413)	0.601	0.649 (0.348–1.209)	0.173
Charlson Comorbidity Index	1.133 (0.941–1.365)	0.187	1.049 (0.821–1.34)	0.703
White blood cell count	1.096 (1.051–1.142)	<0.001	1.113 (1.054–1.175)	<0.001
Pleural effusion	11.297 (6.737–18.944)	<0.001	10.849 (6.026–19.533)	<0.001

AP, acute pancreatitis; CI, confidence interval; HTG, hypertriglyceridemia; HTG-AP, hypertriglyceridemia-associated acute pancreatitis; OR, odds ratio; SAP, severe acute pancreatitis.

1. Deng et al. *Am J Gastroenterol* 2025.

What are the risks of AP associated with an elevated serum TG level?

Cohort of sHTG patients with a fasting triglyceride level $\geq 1,000$ mg/dL¹

- **5,550 patients with severe hypertriglyceridemia**
- **5.4% developed acute pancreatitis**

Study covariates	Patients develop AP vs not developing incident AP OR (95% CI)
Risk factors	
Alcohol abuse	1.76 (1.28–2.40)
History of any pancreatitis*	9.27 (6.42–13.35)
Hypertension	1.39 (1.05–1.85)
Body mass index	
Not normal vs normal	2.12 (1.41–3.14)
Renal function	
CKD stage 4 vs other CKD stages	5.07 (1.86–11.89)
Prescriber specialty	
Other specialty†	1.55 (1.02–2.31)
HTG level	
HTG level ≥1,000 mg/dL	2.91 (1.72–3.31)

Bold values indicate statistical significance with $p < 0.05$. * History of any pancreatitis was defined as an international classification of diseases (ninth revision) clinical modification code of 577.xx.

† Other specialty is emergency medicine, oncology, pulmonary, gastroenterology, pharmacists, or unknown.

AP, acute pancreatitis; CI, confidence interval; CKD, chronic kidney disease; OR, odds ratio; sHTG, severe hypertriglyceridemia; TG, triglyceride.

1. Rashid et al. *J Clin Lipidol* 2016.

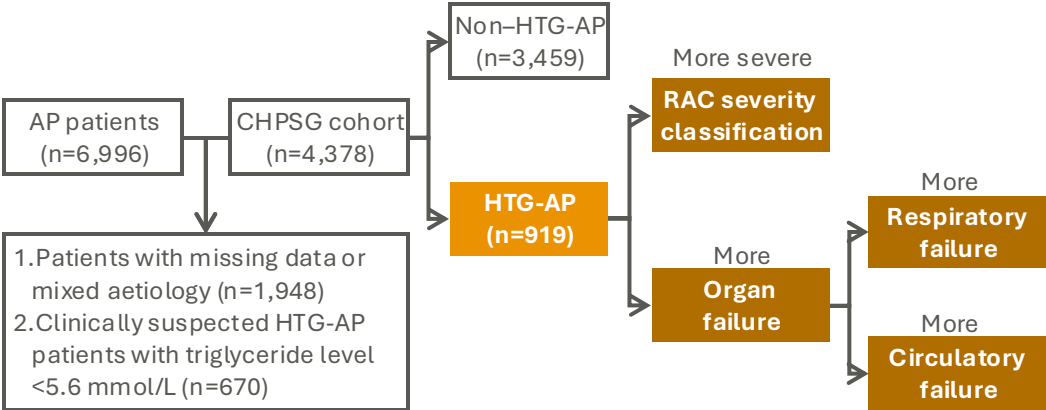
Is hypertriglyceridemia-associated acute pancreatitis more severe compared to other causes of acute pancreatitis?

Meta-analysis of 15 studies¹

- 1,564 patients with hypertriglyceridemia-related acute pancreatitis versus
- 5,721 patients with non-hypertriglyceridemia-related acute pancreatitis

	OR (95% CI)	<i>p</i> value
Persistent renal failure	3.18 (1.92–5.27)	<0.00001
Persistent respiratory failure	2.88 (1.61–5.13)	<0.0001
Persistent shock	3.78 (1.69–8.44)	<0.0001
SIRS	2.03 (1.49–2.75)	<0.00001
Mortality	1.90 (1.05–3.45)	<0.01

Clinical outcomes in patients with hypertriglyceridemia-associated acute pancreatitis



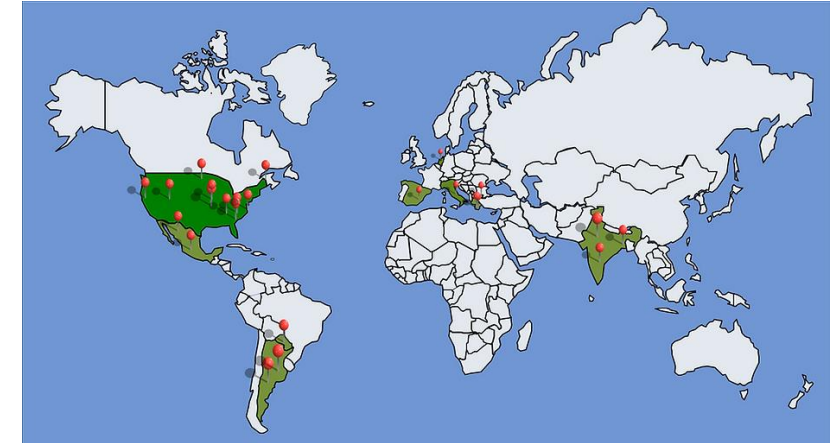
Outcomes ¹	Non-HTG-AP patients n=3,459	HTG-AP patients n=919	p value
ICU stay, median number of days (IQR)	0 (1)	0 (4)	<0.001
Total stay, median number of days (IQR)	11 (7)	11 (7)	0.994
Death, n (%)	58 (1.68)	8 (0.87)	0.075
Necrosis, n (%)	443 (12.81)	97 (10.55)	0.065
Pancreatic infection, n (%)	260 (7.52)	54 (5.88)	0.087
Pleural effusion, n (%)	916 (26.48)	250 (27.20)	0.66
Severe acute pancreatitis, n (%)	212 (6.13)	88 (9.58)	<0.001
Organ failure, n (%)	613 (17.72)	174 (18.93)	0.395
Respiratory failure, n (%)	212 (6.13)	88 (9.58)	<0.001
Acute kidney injury, n (%)	103 (2.98)	28 (3.05)	0.913
Heart failure, n (%)	50 (1.45)	20 (2.18)	0.116

Characteristics of patients with hypertriglyceridemia-associated acute pancreatitis vs other aetiologies

Compared to patients with non-HTG-AP (n=1,409), patients with HTG-AP (n=69) are more likely to have:

- **Younger age**
(40 vs 50 years; $p < 0.001$)
- **Male sex**
(67% vs 52%; $p = 0.018$)
- **Higher BMI**
(BMI 30.4 vs 27.5 kg/m²; $p = 0.0002$)
- **Active alcohol consumption**
(71% vs 49%; $p < 0.001$)
- **Diabetes**
(59% vs 15%; $p < 0.001$)
- **Past history of pancreatitis**
(41% vs 24%; $p = 0.002$)

APPRENTICE consortium¹



Clinical outcomes significantly differ in hypertriglyceridemia-associated acute pancreatitis vs other aetiologies

Prospective multicentre Italian cohort of 86 patients

Characteristics	HTG-AP (n=38)	Other aetiologies (n=48)	p value
Severity (n, %)			0.286
Mild	20 (52.6)	33 (68.8)	
Moderate	12 (31.6)	11 (22.9)	
Severe	6 (15.8)	4 (8.3)	
Necrosis (n, %)	14 (36.8)	7 (14.6)	0.017
Length of stay (median number of days, IQR)	13 (16)	11 (11)	0.356*
ICU admission (n, %)	5 (13.2)	2 (4.2)	0.130
Local complications (n, %)			
Pseudocysts/WON	6 (15.8)	1 (2.1)	0.021
Fluid collection drainage	3 (7.9)	2 (4.2)	0.463
Systemic complications (n, %)			
Acute renal failure	4 (10.5)	8 (16.7)	0.414
Respiratory failure	8 (21.1)	7 (14.6)	0.432
Cardiovascular failure	2 (5.3)	1 (2.1)	0.425
Septic shock	2 (5.3)	3 (6.3)	0.846
Death (n, %)	0	0	–

p values in bold are statistically significant. * Mann-Whitney U test.

HTG-AP, hypertriglyceridemia-associated acute pancreatitis; ICU, intensive care unit; IQR, interquartile range; WON, walled-off necrosis.

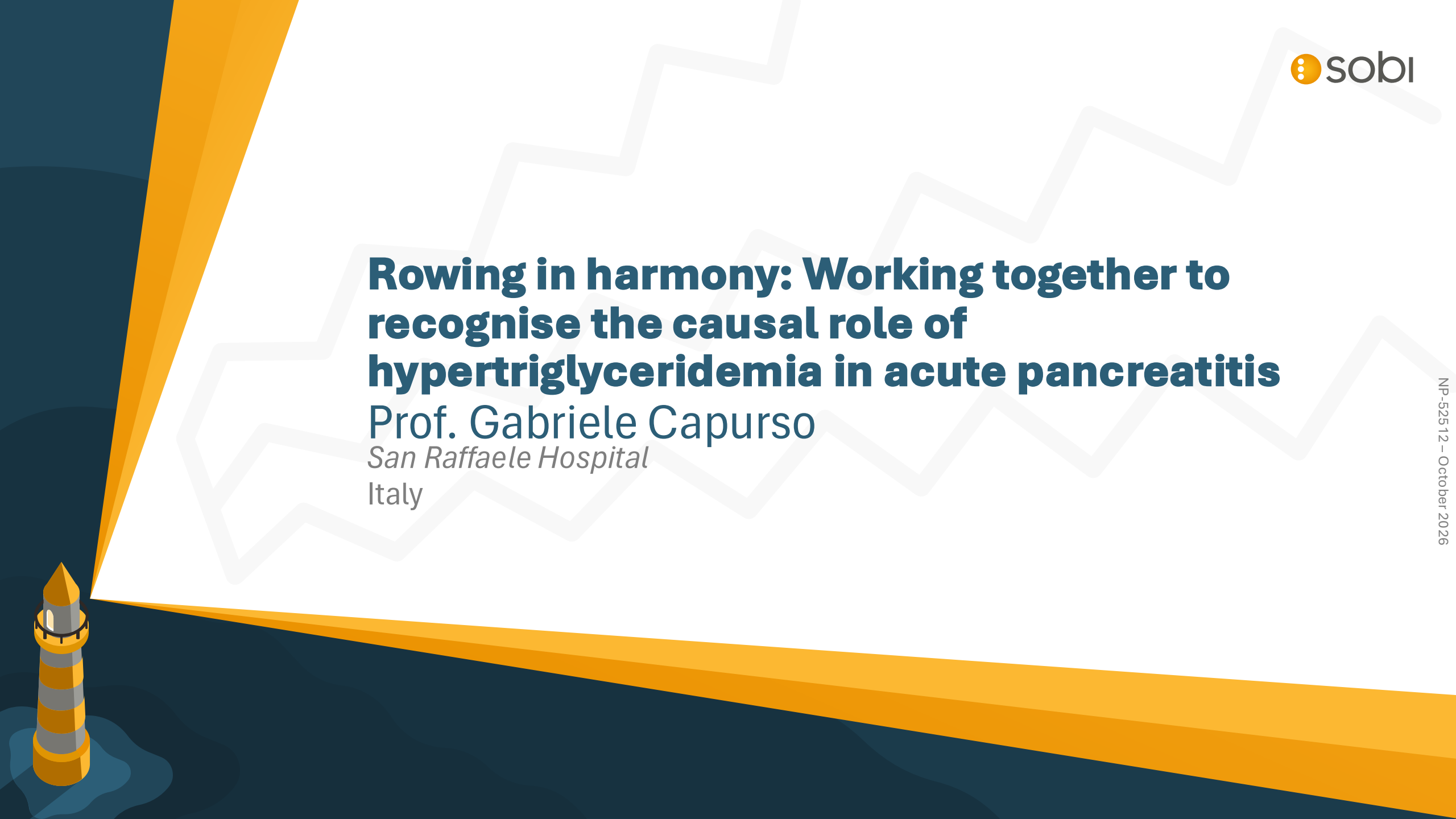
1. De Marchi et al. *Pancreatology* 2026.

HTG-related acute pancreatitis

- Severity is correlated with TG level¹
- High risk of relapse in patients with past medical history of acute pancreatitis^{2,3}
- Necrosis and organ failure are frequent^{1,4–6}
- Mortality and severity are higher compared to other causes of pancreatitis⁶

HTG-AP, hypertriglyceridemia-associated acute pancreatitis; TG, triglyceride.

1. Nawaz et al. *Am J Gastroenterol* 2015 2. Rashid et al. *J Clin Lipidol* 2016 3. Pothoulakis et al. *Pancreatol* 2020 4. Wan et al. *Lipids Health Dis* 2017
5. Deng et al. *Am J Gastroenterol* 2025 6. Wang et al. *J Clin Gastroenterol* 2017.



Rowing in harmony: Working together to recognise the causal role of hypertriglyceridemia in acute pancreatitis

Prof. Gabriele Capurso

San Raffaele Hospital
Italy

Acute pancreatitis is one of the most common gastrointestinal emergencies

Most common GI emergencies^{1,*}



Infectious gastroenteritis and colitis



Gallstone disease / Acute biliary disease



Acute pancreatitis ranked 3rd

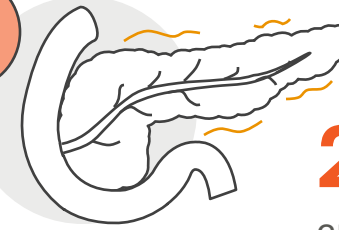


Acute gastrointestinal bleeding



Inflammatory bowel disease flares

Identifying acute pancreatitis²



2 of 3

criteria confirm the diagnosis

01



Typical upper abdominal pain

02



Lipase or amylase $>3 \times \text{ULN}$

03



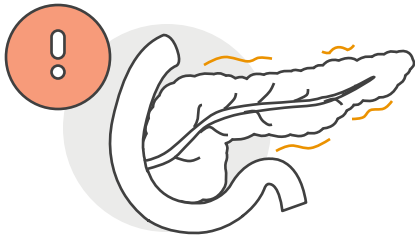
Imaging if diagnosis unclear (CT, MRI)

* In Europe.

CT, computed tomography; GI, gastrointestinal; MRI, magnetic resonance imaging; ULN, upper limit of normal.

1. Farthing et al. *United European Gastroenterol J* 2014 2. Hamesch et al. *Eur J Intern Med* 2025.

Acute pancreatitis is a medical emergency that requires hospitalisation

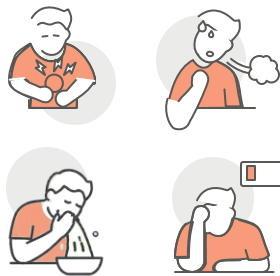


ICU admission in

~45% of people with
acute pancreatitis¹

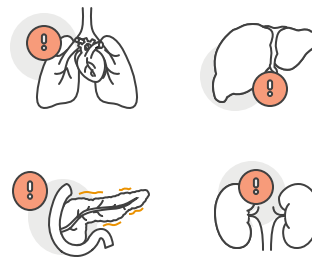
Mortality in

5–8% of people with
acute pancreatitis²



Significant symptoms

Abdominal pain, nausea,
vomiting, back pain, fatigue²



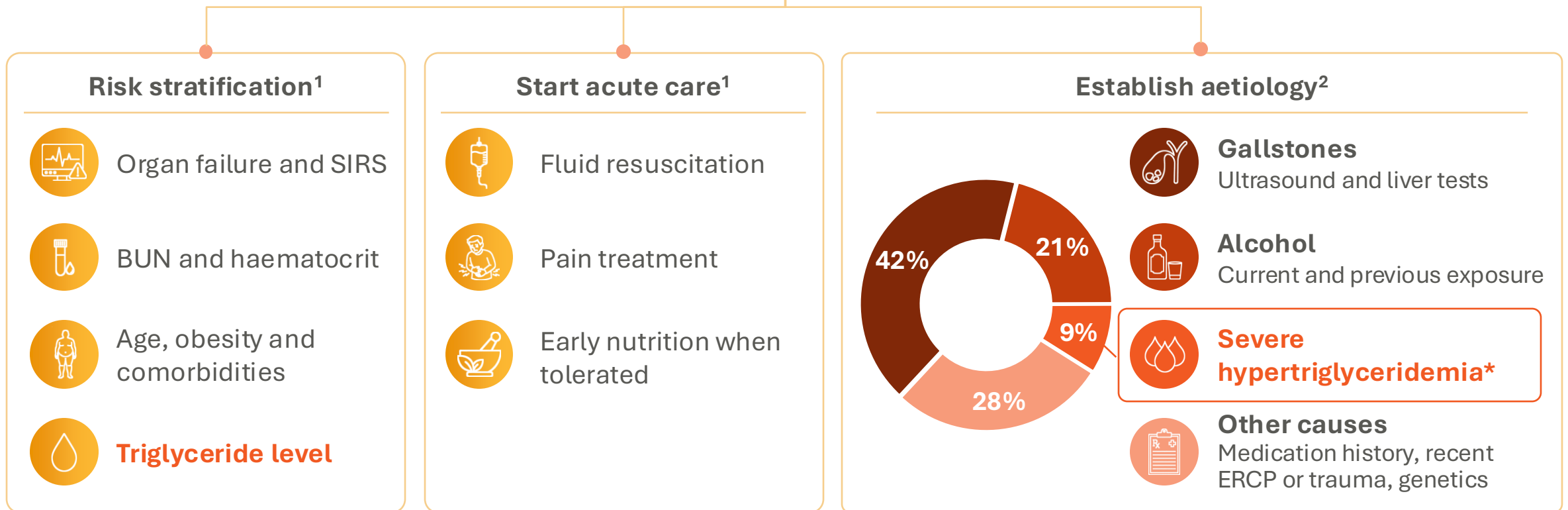
Persistent organ failure

~33% of patients²

**Mortality in
severe cases
can reach³**

30%

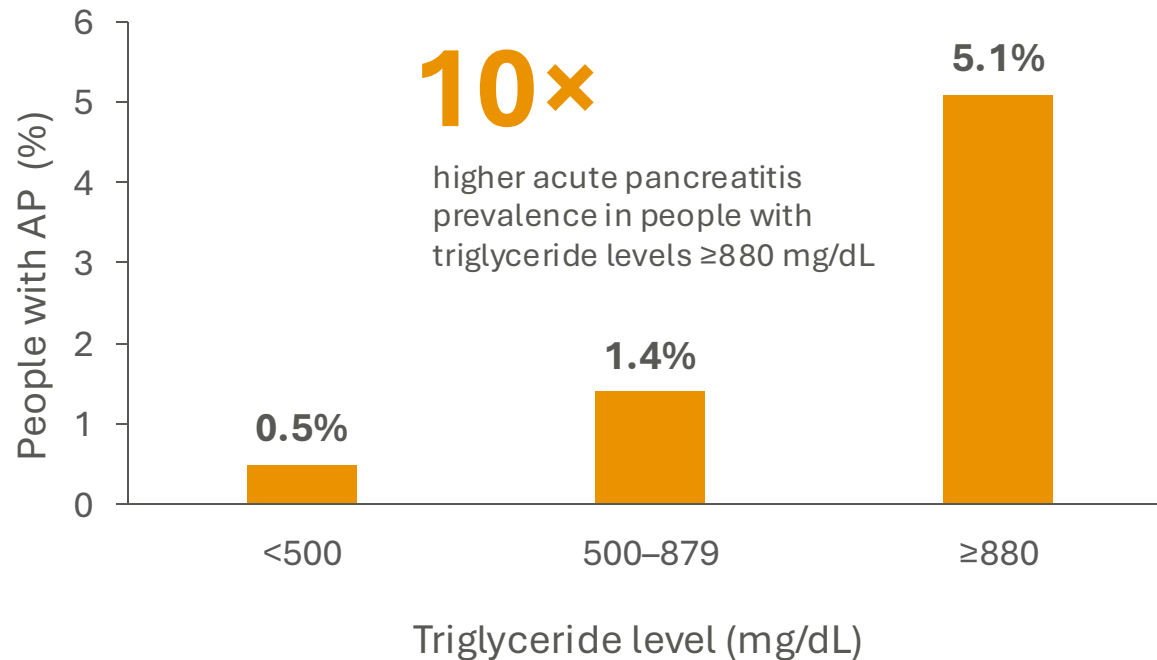
Risk stratification, acute care and aetiology run in parallel 🧠sobi after acute pancreatitis diagnosis



* Defined as serum triglyceride concentrations above 1,000 mg/dL.
BUN, blood urea nitrogen; ERCP, endoscopic retrograde cholangiopancreatography; SIRS, systemic inflammatory response syndrome.
1. Hamesch K, et al. *Eur J Intern Med* 2025 2. Bálint et al. *Sci Rep* 2020.

Testing triglycerides at diagnosis is essential to identify severe hypertriglyceridemia as a potential contributor to acute pancreatitis

Data from an electronic health record database covering 32 million people in Germany, Italy, Spain and the UK^{1,2}



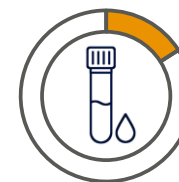
<24h

Triglyceride concentrations fall rapidly after AP onset; sampling **within 24 hours of admission** is critical to detect severe hypertriglyceridemia³



8%

of people with acute pancreatitis had a triglyceride test **within ±1 day** of the index acute pancreatitis event¹



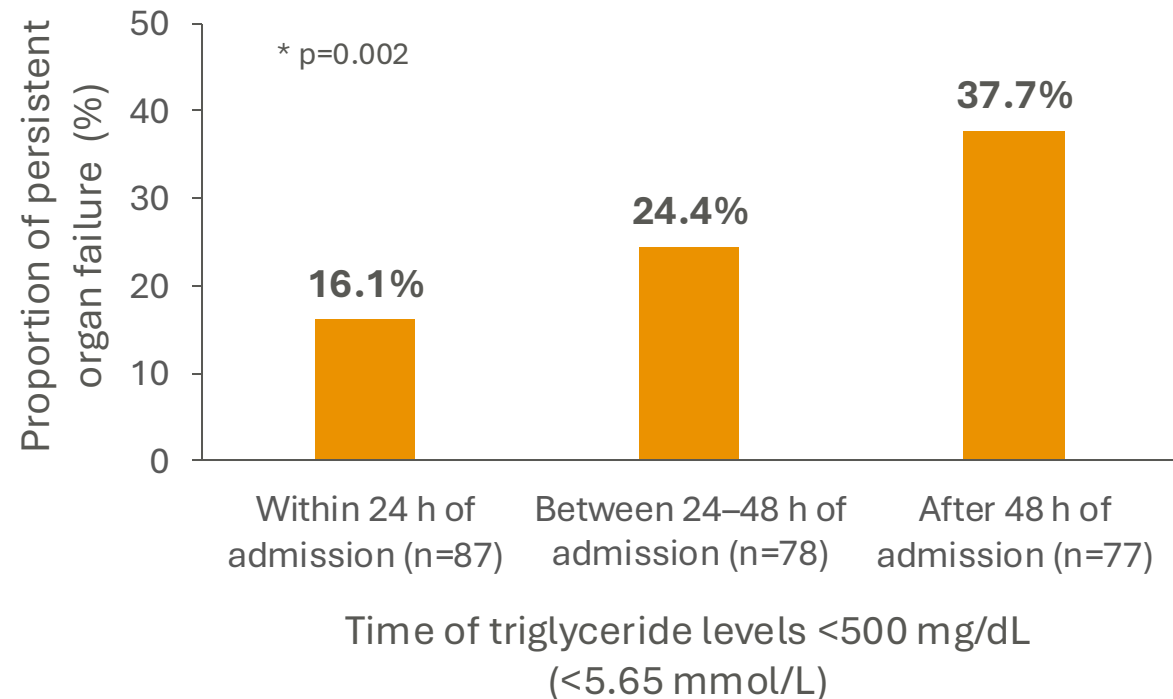
16%

of people with acute pancreatitis had a triglyceride test **within ±7 days** of the index acute pancreatitis event¹

Testing for severe hypertriglyceridemia at diagnosis is essential to start treatment soon and reduce the risk of organ failure

Time matters: Timely reduction of serum triglycerides during the early phase of hypertriglyceride-associated acute pancreatitis is proportionally associated with decreased development of persistent organ failure

Proportion developing persistent organ failure after hypertriglyceride-associated acute pancreatitis¹



Preventing the first hypertriglyceridemia-associated acute pancreatitis is crucial to prevent recurrence, which may have long-term complications

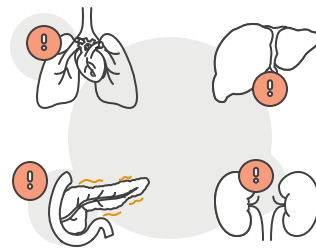
19.5x

Higher rate of recurrent acute pancreatitis in people with history of acute pancreatitis vs. overall severe hypertriglyceridemia population¹

~10x

Higher risk of severe and very severe hypertriglyceridemia-associated acute pancreatitis vs. normal triglycerides^{3,*}

People with hypertriglyceridemia-associated acute pancreatitis* vs people with no or mild hypertriglyceridemia have:²



~3x

Increase in **persistent organ failure**²



~5x

Increase in **newly diagnosed diabetes**²



~4x

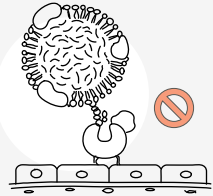
Increase in **mortality**²

A single hypertriglyceridemia-associated acute pancreatitis event can trigger a cascade leading to chronic pancreatitis, permanent organ failure with high morbidity and mortality^{2,4-7}

* With TG $\geq$ 1,000 mg/dL.

1. Kessler et al. *Lipids Health Dis* 2025 2. Zhang et al. *HPB* 2019 3. Pothoulakis et al. *Digestion* 2021 4. Gagy et al. *Therap Adv Gastroenterol* 2024 5. Hajibandeh et al. *J Gastroenterol Hepatol* 2023 6. Li et al. *Eur J Intern Med* 2023 7. de Rijk et al. *J Gastroenterol Hepatol* 2024.

Untreated severe hypertriglyceridemia can lead to more severe acute pancreatitis and higher reoccurrence rates



apoC-III in severe hypertriglyceridemia-associated acute pancreatitis

By inhibiting lipoprotein lipase activity, **apoC-III prevents triglyceride clearance** leading to **triglyceride and triglyceride-rich lipoprotein accumulation**^{1,2}

Triglyceride-rich lipoproteins **accumulate** in the circulation^{1,2}



Pancreatic **capillary ischaemia** and **acinar lipotoxicity**^{3,4}

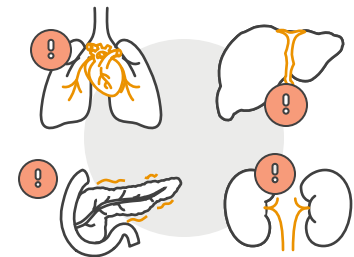


Acute pancreatitis⁴

Without triglyceride lowering:



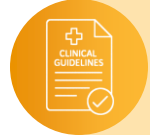
Higher recurrence rates
underlying severe hypertriglyceridemia persists
after each attack^{3,5,6}



More severe disease
necrosis, systemic inflammatory response
syndrome, multi-organ failure^{4,5}

Without sustained triglyceride lowering, the underlying severe hypertriglyceridemia persists after each attack, leading to higher severity risk and acute pancreatitis recurrence

Guidelines mandate action in severe hypertriglyceridemia to prevent acute pancreatitis



Guidelines from the **IAP/EPC**¹ and **ESC/EAS**^{2,3} recommend **TG-lowering to prevent AP**



The risk of pancreatitis is clinically significant if **TGs are >880 mg/dL (10 mmol/L)**¹

Therapeutic options to lower triglycerides and reduce risk of acute pancreatitis



Diet and lifestyle^{1,2}

- Low fat diet
- Limit carbohydrates and simple sugars
- Avoid alcohol
- Increase physical activity

Limitations

- Burdensome; triglycerides often remain elevated despite adherence⁴



Conventional therapies^{1,2}

- Statins (modest TG lowering of 10–20%)¹
- Fibrates[†]
- Omega-3 fatty acids

Limitations

- No trial evidence that fibrates prevent AP recurrence²



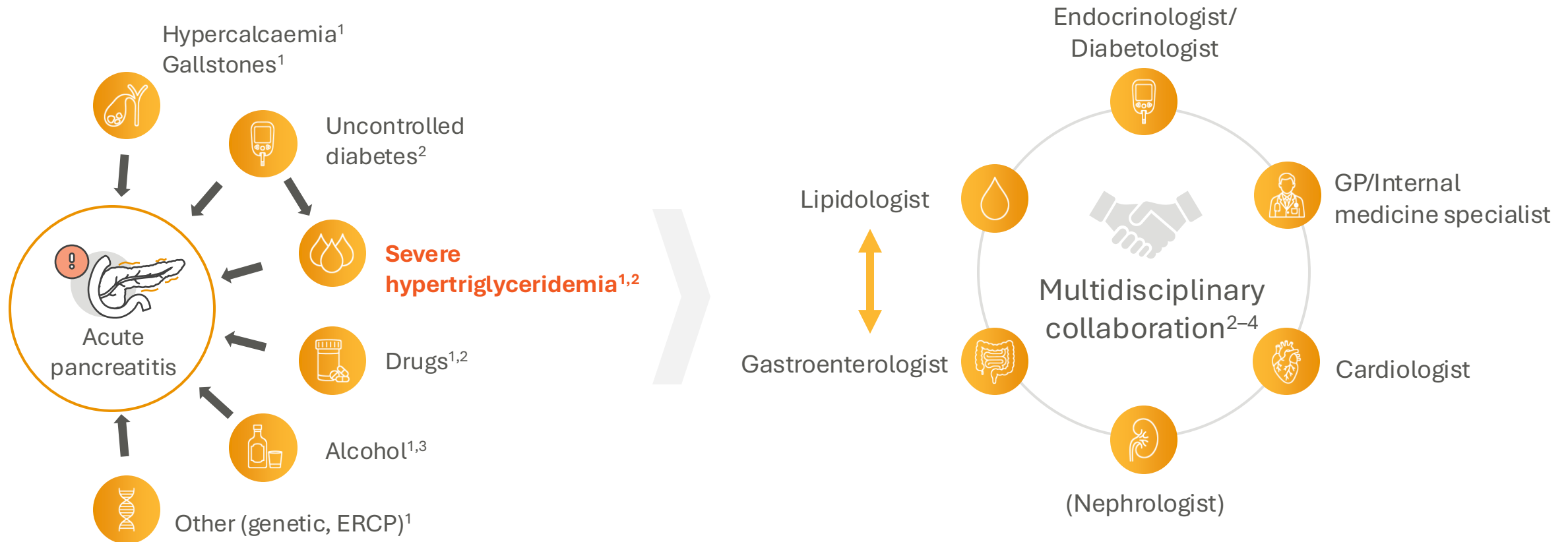
Additional therapies

- Manage secondary causes, diabetes and obesity^{1,5}
- During AP: insulin (first-line in diabetes); plasmapheresis only selectively²
- Consider lomitapide in severe hypertriglyceridemia^{1,‡,§}
- ApoC-III inhibitors olezarsen^{§,¶} and volanesorsen^{§,#} reduce AP recurrence²; volanesorsen is recommended in FCS³

† Fenofibrate, bezafibrate³. ‡ Approved only for HoFH, limited availability in many countries. § Sobi recomienda seguir la ficha técnica de cada medicamento. Sobi recommends following the prescribing information for each medication. ¶ Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsén is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis. Olezarsén no está indicado para el tratamiento de la hipertrigliceridemia en España. Hypertriglyceridemia is not an approved indication for olezarsen in Spain. # Volanesorsén no está indicado para el tratamiento de la pancreatitis aguda ni de la hipertrigliceridemia en España. Acute pancreatitis and severe hypertriglyceridemia are not approved indications for volanesorsen in Spain. AP, acute pancreatitis; EAS, European Atherosclerosis Society; EPC, European Pancreatic Club; ESC, European Society of Cardiology; FCS, familial chylomicronemia syndrome; HoFH, homozygous familial hypercholesterolemia; IAP, International Association of Pancreatology; SoC, standard of care; TG, triglyceride.

1. Pánciczky et al. *Pancreatol* 2025 2. Mach et al. *Eur Heart J* 2020 3. Mach et al. *Eur Heart J* 2025 4. Gouni-Berthold et al. *Curr Atheroscler Rep* 2023 5. Bashir et al. *Metabolites* 2023.

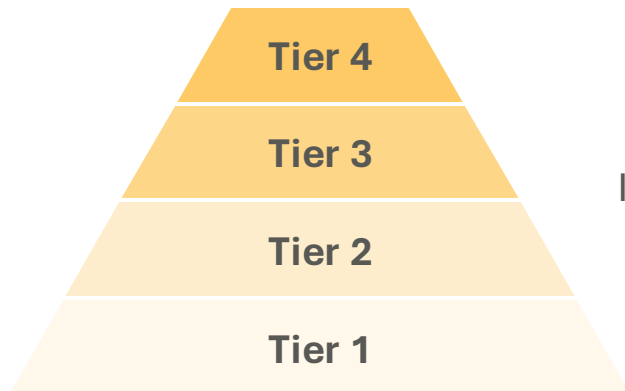
Acting early and together to prevent recurrence in case of severe hypertriglyceridemia-associated acute pancreatitis



For complex cases, multidisciplinary assessment in specialty centres may be considered



Specialty centres: e.g., pancreas centres or lipid clinics, available in some settings^{1,2}



Tiered care model
Increasing specialisation
and resources*

Cases that may benefit from specialty input:



Severe hypertriglyceridemia (**>880 mg/dL/10 mmol/L**) or suspected hypertriglyceridemia-induced pancreatitis²⁻⁴



Persistent triglyceride levels **≥500 mg/dL** despite lifestyle and secondary-cause management²



Suspected genetic/inherited lipid disorder or complex dyslipidaemia^{2,4}

*Common secondary causes (e.g., dysregulated diabetes) are usually **addressed first***²

Specialty centres input can help manage complications, prevent recurrence and guide genetic testing^{2,4}

* Dependent on country-level income. AP, acute pancreatitis; EAS, European Atherosclerosis Society; HTG, hypertriglyceridemia; TG, triglyceride.

1. Párnitzky et al. *Pancreatology* 2025 2. Bork et al. *Atherosclerosis* 2026 3. Tenner et al. *Am J Gastroenterol* 2024 4. Subramanian et al. *Eur J Intern Med* 2026.

The gastroenterologist's role goes beyond referral in severe hypertriglyceridemia-associated acute pancreatitis



- 1 Diagnose acute pancreatitis and assess aetiology** including potential **severe hypertriglyceridemia at diagnosis**¹⁻³
- 2 Manage acute pancreatitis** and in case of severe hypertriglyceridemia, **initiate triglyceride-lowering treatment**^{1,3-5}
- 3 Work together in a multidisciplinary setting to follow and manage** severe hypertriglyceridemia and **prevent recurrence**^{3,5-7}
- 4 Manage the sequelae** of acute pancreatitis⁸

Key takeaways

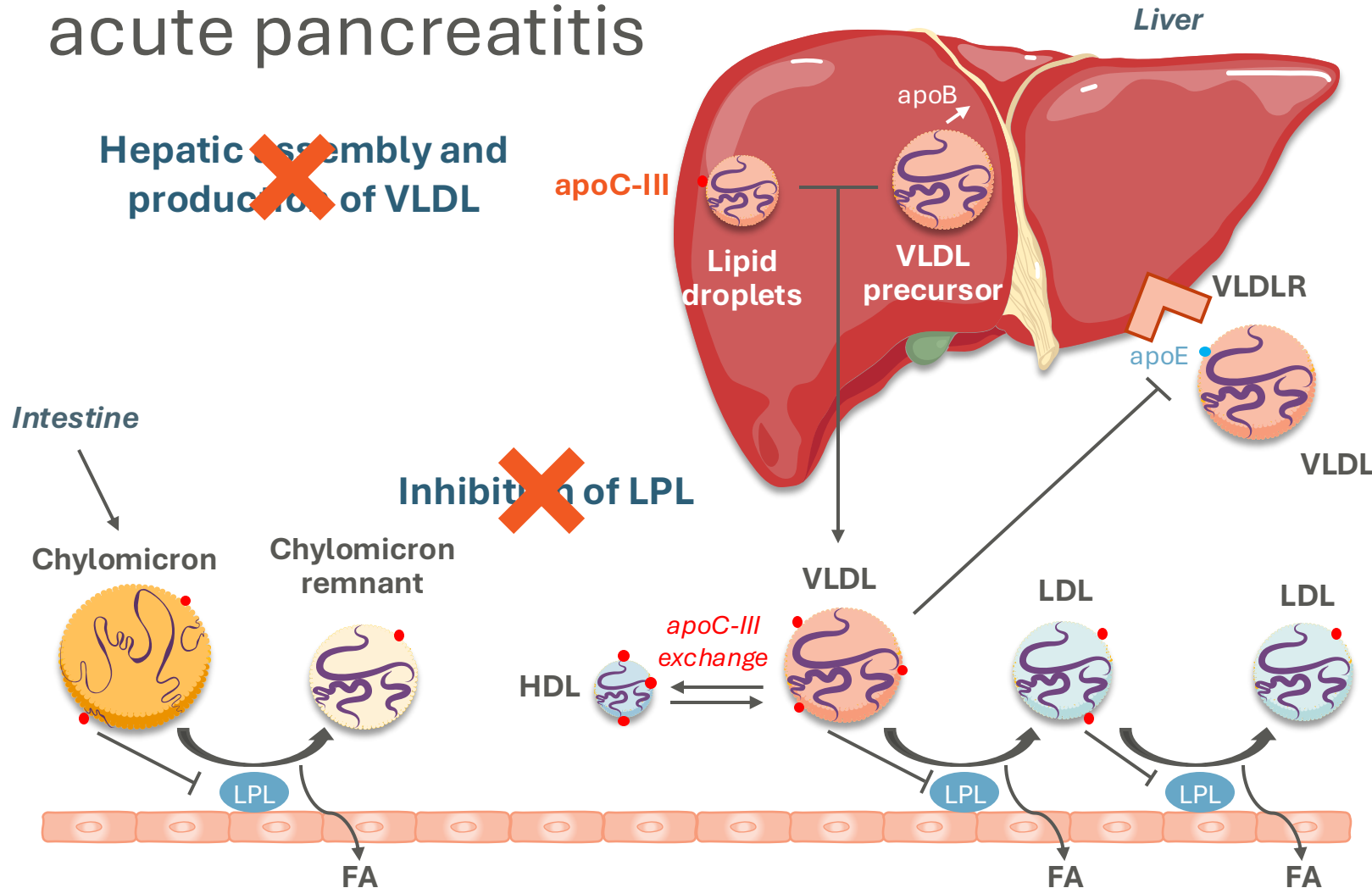
- Acute pancreatitis is a medical emergency that requires hospitalisation^{1–4}
- Testing for severe hypertriglyceridemia at diagnosis is essential to start treatment soon and reduce the risk of organ failure^{4,5}
- Acting early and in a multidisciplinary team may help to prevent recurrence in case of severe hypertriglyceridemia-associated acute pancreatitis^{4,6–8}

A shining beacon: apoC-III inhibition for acute pancreatitis prevention

Dr. Clara Viñals

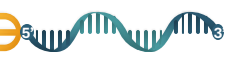
*Hospital Clínic, Barcelona
Spain*

Targeting apoC-III reduces TG levels and the risk of acute pancreatitis



Inhibiting apoC-III enhances TG catabolism¹ and is an approach to reduce the risk of acute pancreatitis* in patients with sHTG^{2,3,†}

Olezarsen (GalNAc₃-conjugated liver-directed ASO)²

GalNAc₃ conjugate  ASO targeting APOC3 mRNA

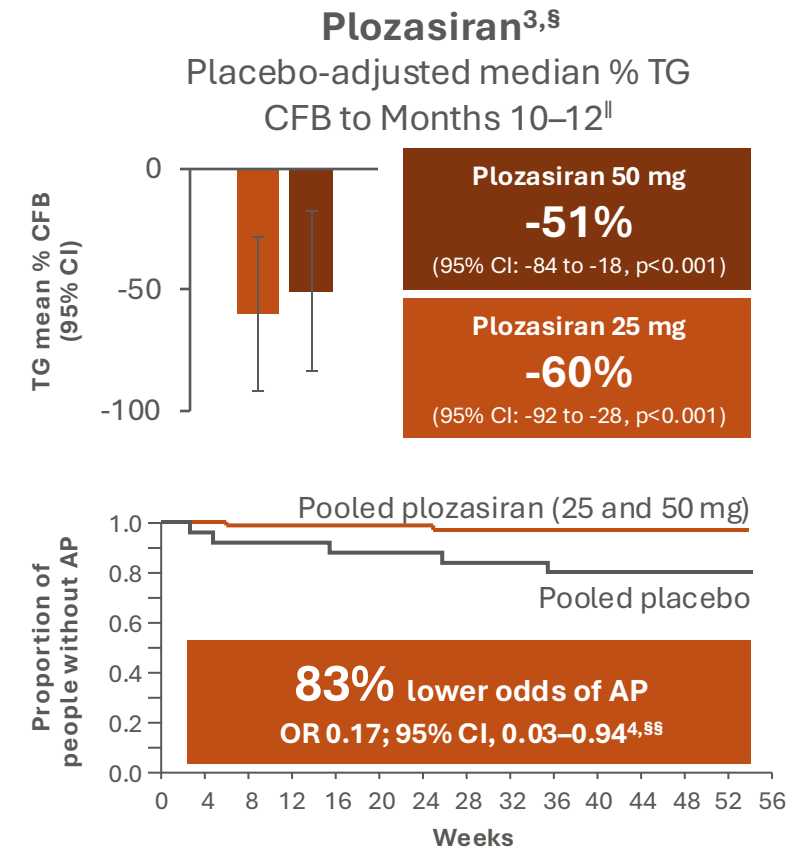
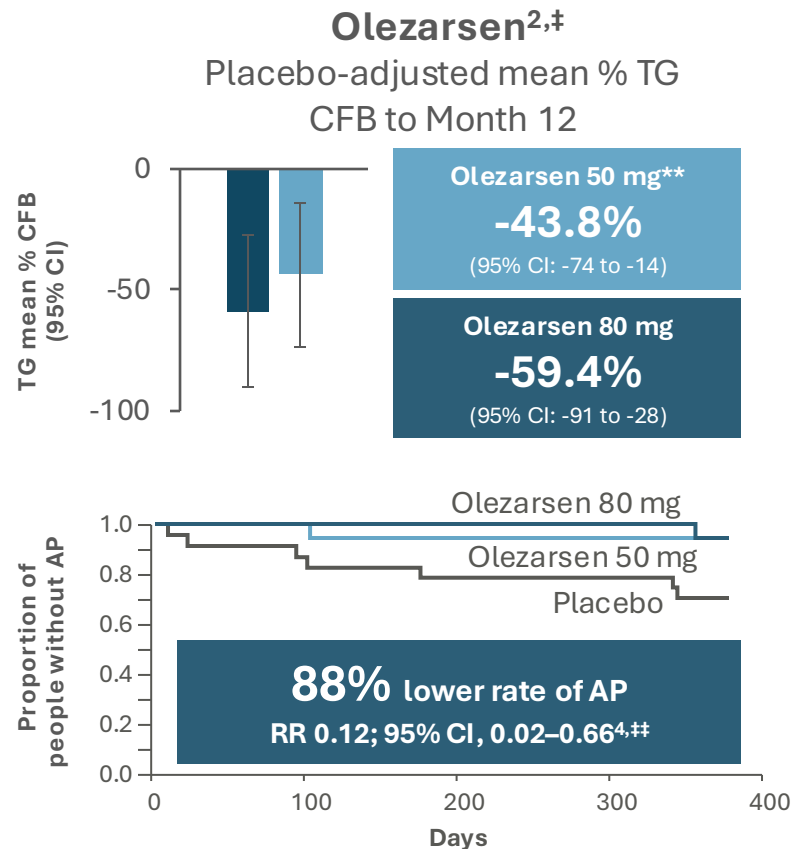
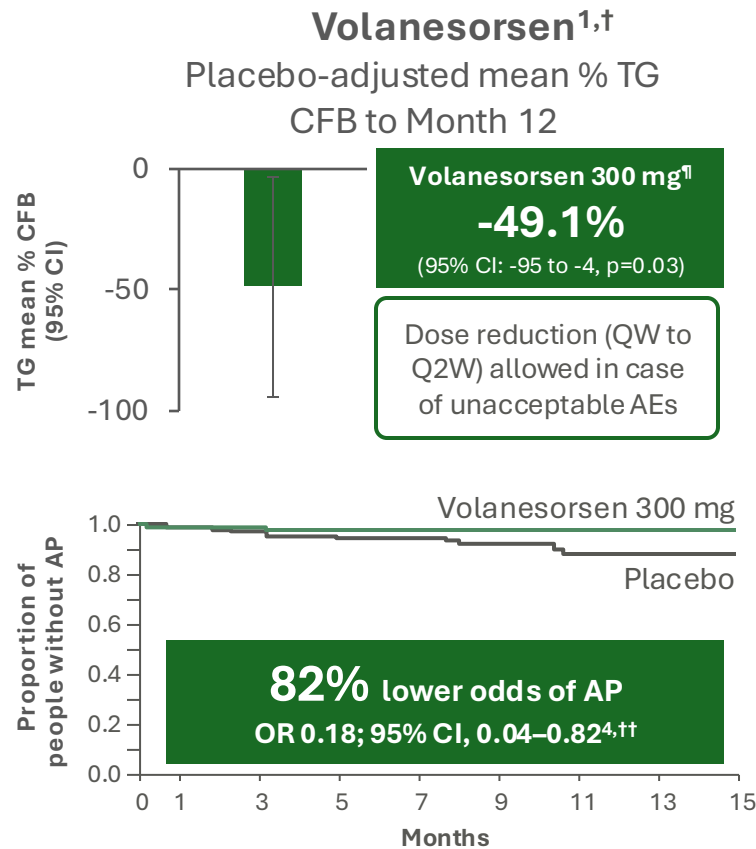
Inhibition of hepatic uptake of TG-rich lipoproteins (Inhibited)

Efficacy even if LPL is dysfunctional or complete LPL deficiency¹

Illustration made with MindTheGraph using published data.¹⁻⁴ * Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsén is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis.[†] Olezarsén no está indicado para el tratamiento de la hipertrigliceridemia en España. Hypertriglyceridemia is not an approved indication for olezarsen in Spain. ApoB, apolipoprotein B; apoC-III, apolipoprotein C-III; apoE, apolipoprotein E; ASO, antisense oligonucleotide; FA, fatty acid; FCS, familial chylomicronemia syndrome; GalNAc₃, triantennary N-acetylgalactosamine; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LPL, lipoprotein lipase; mRNA, messenger RNA; sHTG, severe hypertriglyceridaemia; TG, triglyceride; VLDL, very low-density lipoprotein; VLDLR, very low-density lipoprotein receptor.

1. Gaudet et al. *New Engl J Med* 2014 2. Mach et al. *Eur Heart J* 2025 3. Stroes et al. *N Engl J Med* 2024 4. Norata et al. *Trends Pharmacol Sci* 2013.

ApoC-III targeting effectively reduced triglyceride levels and pancreatitis events in FCS*



Disclaimer: Direct comparisons between studies may be misleading due to differences in study design, population, and methodology. The results presented should be interpreted cautiously and in the context of the individual studies.

* Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsen is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis. † Volanesorsén no está indicado para el tratamiento de la pancreatitis en España. Pancreatitis is not an approved indication for volanesorsen in Spain. ‡ Primary and secondary efficacy endpoints were tested hierarchically. As the second primary endpoint with the 50 mg olezarsen dose was not statistically significant, the secondary end points are presented as LSM changes with the 95% CI. The 95% CI for the secondary end points were not adjusted for multiplicity, and the results should not be interpreted as hypothesis tests. § Plozasiran no está comercializado en España. Plozasiran is not marketed in Spain. || Mean of the levels at 10 and 12 months. ¶ La dosis inicial recomendada es de 285 mg, 1,5 ml inyectados por vía subcutánea, una vez por semana durante 3 meses. Después de 3 meses, se reducirá la frecuencia de administración a 285 mg cada 2 semanas. The recommended starting dose of volanesorsen is 285 mg, administered as a 1.5 mL subcutaneous injection once a week for 3 months. After 3 months, the frequency of administration will be reduced to 285 mg every 2 weeks. ** La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. †† Fixed-effects meta-analysis of individual patient data from 3 randomized controlled trials (APPROACH, COMPASS, BROADEN) in patients with severe hypertriglyceridemia (TG >500 mg/dL), including but not limited to FCS; volanesorsen n=121, placebo n=86. ‡‡ Pooled olezarsen vs placebo. §§ Pooled plozasiran vs placebo. AE, adverse event; AP, acute pancreatitis; apoC-III, apolipoprotein C-III; CFB, change from baseline; CI, confidence interval; FCS, familial chylomicronemia syndrome; LSM, least-squares mean; OR, odds ratio; RR, rate ratio; TG, triglyceride; QW, weekly; Q2W, every other week. 1. Witztum et al. *N Engl J Med* 2019 2. Stroes et al. *N Engl J Med* 2024 3. Watts et al. *N Engl J Med* 2025. 4. Tsimikas et al. *Curr Atheroscler Rep* 2025.

Balance study with olezarsen in FCS: Study design

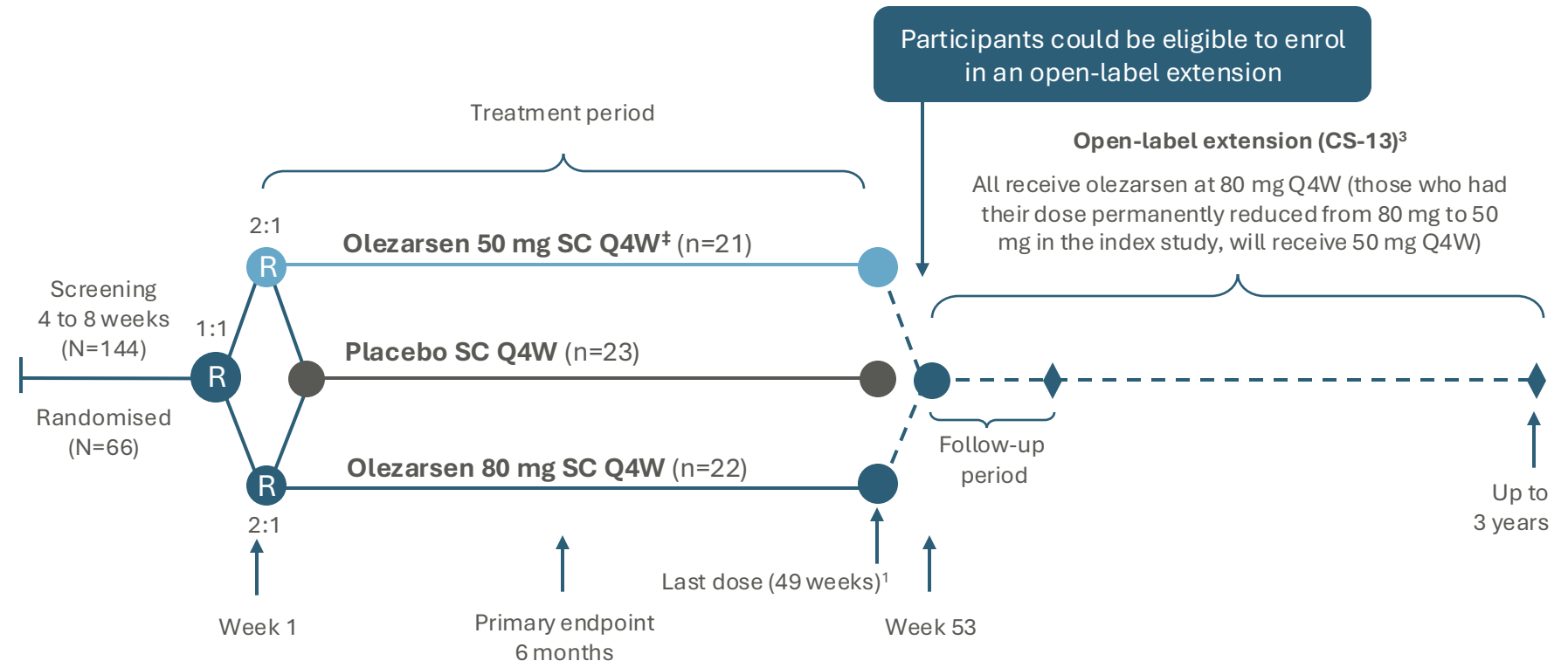
Randomised, double-blind, placebo-controlled Phase 3 trial in adults with genetically confirmed FCS and fasting TG ≥ 880 mg/dL^{1,2}

STUDY POPULATION

- Age ≥ 18 years
- Genetically confirmed FCS*
- Fasting TG ≥ 880 mg/dL at screening
- History of pancreatitis ≤ 10 years prior to screening in $\geq 65\%$ of people enrolled†
- Diet ≤ 20 g fat/day during the study

PRIMARY ENDPOINT

- **Percent change in fasting TG from baseline at 6 months vs. placebo** (mean of weeks 23, 25 and 27)
1. Primary endpoint 1: for 80 mg olezarsen
 2. Primary endpoint 2: for 50 mg olezarsen



Randomisation stratified by

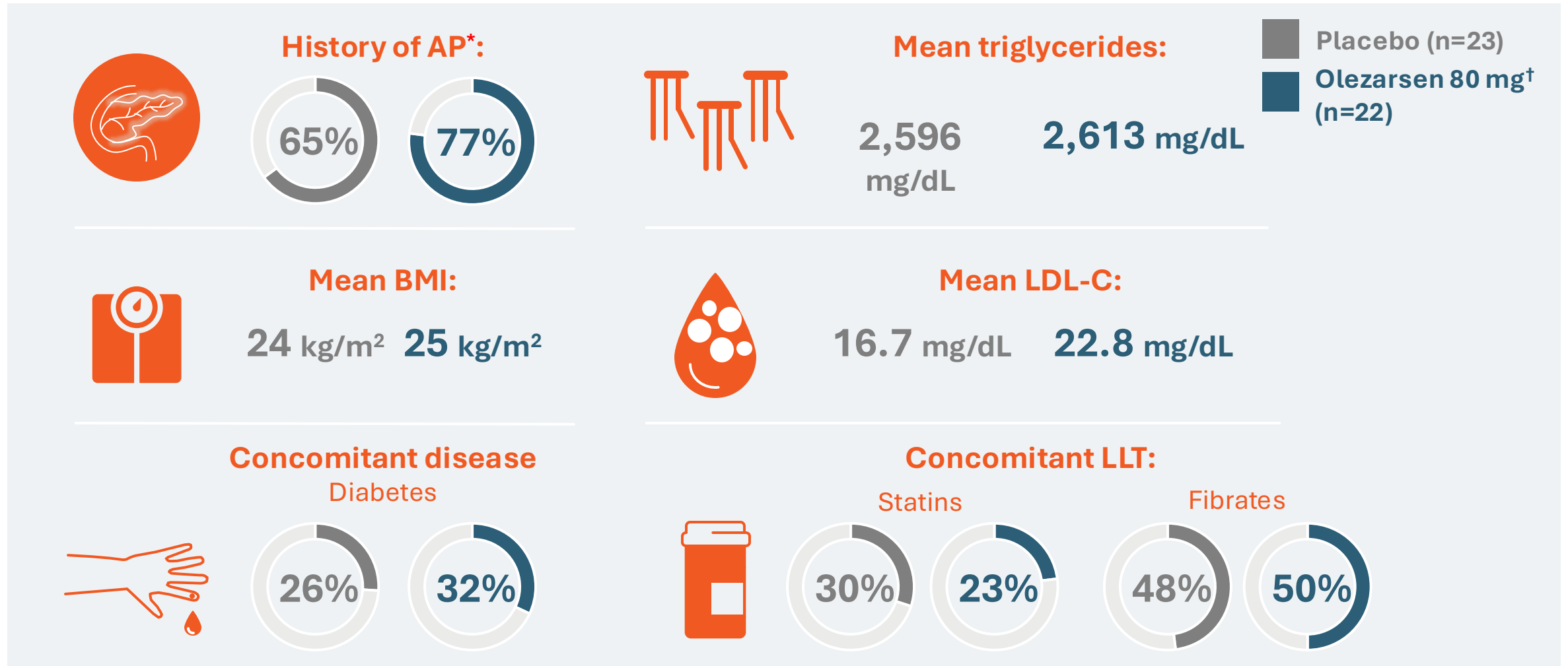
- History of pancreatitis within 10 years prior to screening, or no history of pancreatitis
- Previous treatment with volanesorsen (yes or no)

* Ho, compound / double He loss of function mutation in genes such as *LPL*, *GPIHBP1*, *APOA5*, *APOC2* or *LMF1*. † People with no history of pancreatitis capped at 35% of enrolment.

‡ La posología de 50 mg de olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. FCS, familial chylomicronemia syndrome; He, heterozygous; Ho, homozygous; Q4W, every 4 weeks; R, randomisation; SC, subcutaneous; TG, triglyceride. 1. Stroes et al. *N Engl J Med* 2024 (supplement) 2. Stroes et al. *N Engl J Med* 2024 3. ClinicalTrials.gov. NCT05130450.

Balance study in FCS: Key baseline characteristics

Placebo and olezarsen 80 mg groups¹



* History of acute pancreatitis in the previous 10 years. [†] Approved dose by EMA.²

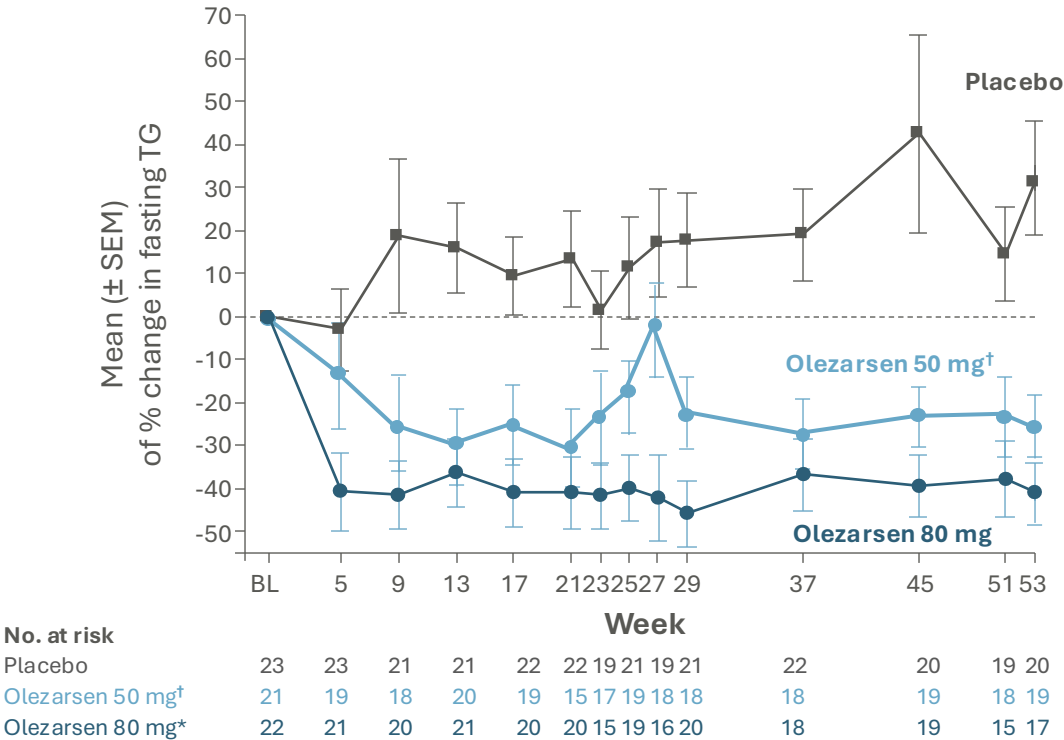
AP, acute pancreatitis; BMI, body mass index; EMA, European Medicines Agency; FCS, familial chylomicronemia syndrome; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy.

1. Stroes et al. *N Engl J Med* 2024 2. Tryngolza SmPC 2025.

Balance study in FCS: 59.4% reduction in TG vs. placebo at 12 months with olezarsen 80 mg^{1,*}



Rapid and persistent change in fasting plasma TG levels¹



LSMD vs. Placebo
6 months (primary endpoint)
Olezarsen 80 mg*
-43.5%
(95% CI: -69.1, -17.9), $p < 0.001$

12 months:
Olezarsen 80 mg*
-59.4%
(95% CI: -90.7, -28.1)

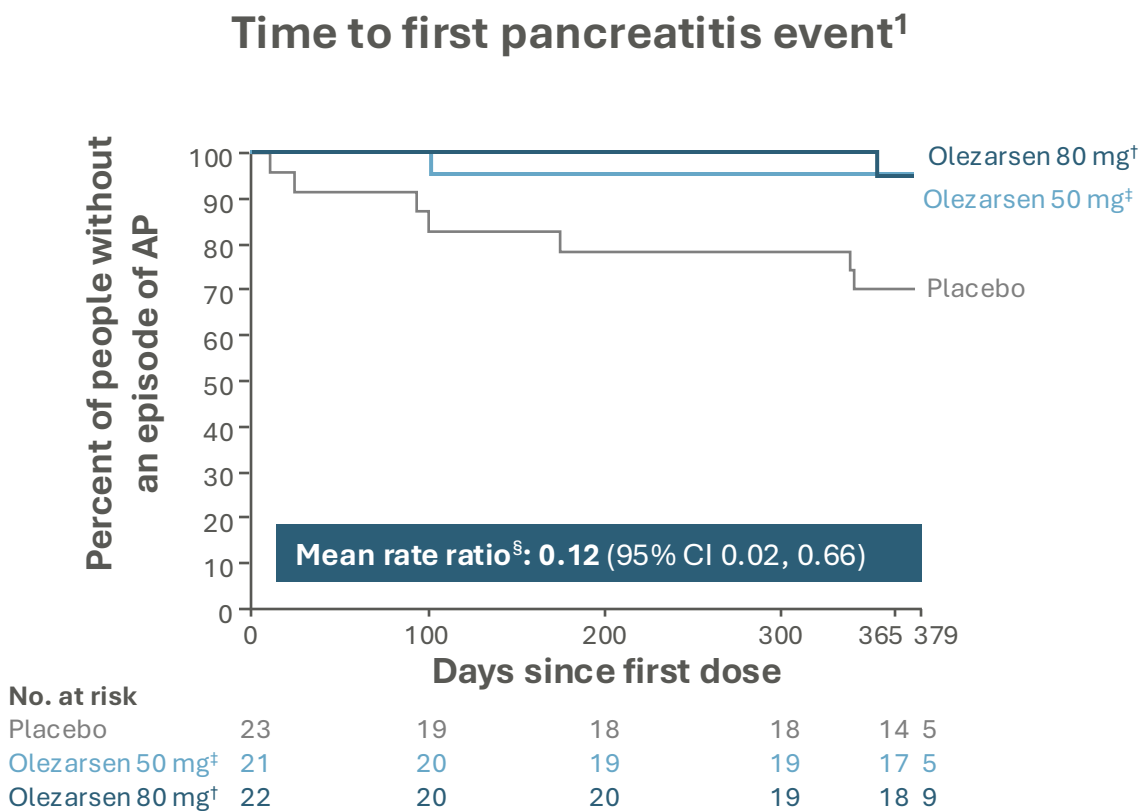
* Approved dose by the European Medicines Agency.

† La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month.

BL, baseline; CI, confidence interval; FCS, familial chylomicronemia syndrome; LSMD, least squares mean difference; SEM, standard error of the mean; TG, triglycerides.

1. Stroes et al. *N Engl J Med* 2024.

Balance study in FCS: 88% reduction in pancreatitis events* by 12 months with olezarsen¹



Pancreatitis events

	Placebo (N=23)	Olezarsen 50 mg [‡] (N=21)	Olezarsen 80 mg [†] (N=22)
People with events, n (%)	7 (30)	1 (5)	1 (5)
Pancreatitis events, n	11	1	1
First pancreatitis event, study day	9	102	357

Fewer and ‘delayed’ pancreatitis events in people treated with olezarsen compared with placebo

* Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsen is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis. † Approved dose by the European Medicines Agency. ‡ La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. § Pooled olezarsen vs placebo; exposure-adjusted event rate in the treatment group divided by the exposure-adjusted event rate in the placebo group; a ratio of 1 would indicate no difference. AP, acute pancreatitis; CI, confidence interval; FCS, familial chylomicronemia syndrome. 1. Stroes et al. *N Engl J Med* 2024.

Balance study in FCS: Safety and tolerability profile¹

	Placebo (n=23)	Olezarsen 50 mg* (n=21)	Olezarsen 80 mg† (n=22)
AEs, n (%)			
Any	22 (96)	18 (86)	19 (86)
Related to study drug	5 (22)	6 (29)	7 (32)
Mild	3 (13)	6 (29)	3 (14)
Moderate	0	0	4 (18)
Severe	2 (9)	0	0
Leading to treatment discontinuation	0	1 (5)	2 (9)‡
Leading to death	0	1 (5)§	0
Any serious	9 (39)	4 (19)	3 (14)
Serious related to study drug	0	0	0
Adverse event of interest			
Reduction in platelet count¶	0	0	0
≥1 Injection-site reaction in a person	2 (9)	3 (14)	3 (14)
≥1 Influenza-like illness in a person¶¶	0	1 (5)	1 (5)
≥1 Hypersensitivity AE in a person	3 (13)	1 (5)	0
Narrow FMQ for anaphylactic reaction	0	0	0
Narrow FMQ for hepatic failure	0	0	0

- A greater proportion of placebo-treated people experienced SAEs
- No drug-related SAEs
- No clinically meaningful changes in platelet count or in measures of hepatic and renal function

* La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. † Approved dose by the European Medicines Agency. ‡ AEs in the 80 mg group leading to treatment discontinuation were diarrhoea, vomiting, flushing, and chest discomfort in 1 person and chills, myalgia, and trismus in the other person. § AE leading to death in the 50 mg group was considered unrelated to study treatment by the investigator. ¶ A reduction in platelet count was defined as a reduction to levels <50,000/mm³ accompanied by a major bleeding event or clinically relevant nonmajor bleeding event or a reduction in platelet count to levels <25,000/mm³, irrespective of bleeding status. ¶¶ AEs with preferred terms in MedDRA, version 26.0, include influenza-like illness, pyrexia, feeling hot, body temperature increased, chills, myalgia, or arthralgia, starting on the day of injection or the next day. AE, adverse event; FCS, familial chylomicronemia syndrome; FMQ, Food and Drug Administration medical query; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event. 1. Stroes et al. *N Engl J Med* 2024.

CORE/CORE2: Two Phase 3 studies in people with sHTG with a subgroup analysis of TG levels ≥ 880 mg/dL



Two randomised, double-blind, placebo-controlled Phase 3 trials in **1,061 adults** with **fasting TG ≥ 500 mg/dL** and identical design

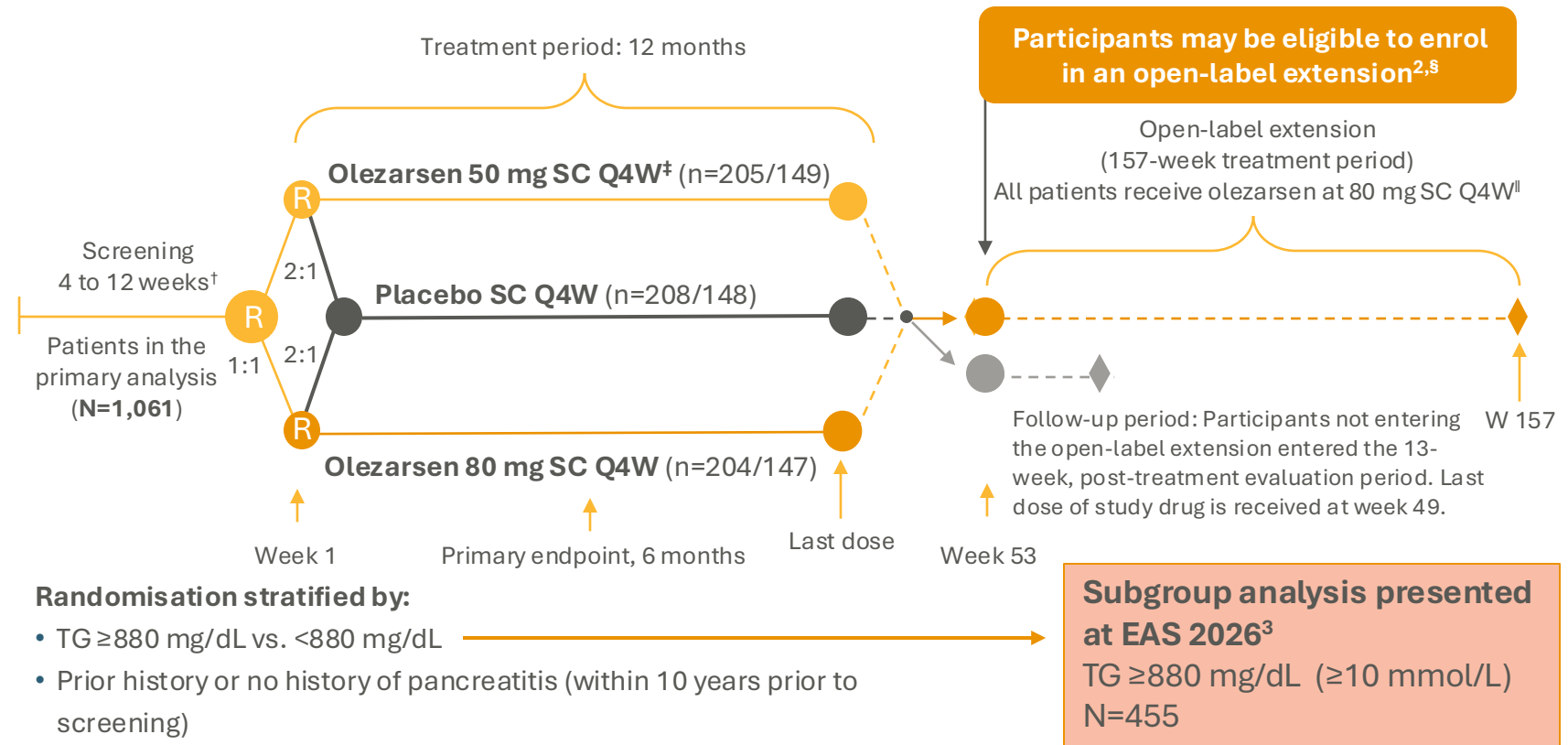
STUDY POPULATION

CORE (N=617)/CORE2 (N=444)

- Aged ≥ 18 years
- **Fasting TG ≥ 500 mg/dL** at screening & qualification
- Must be on lipid-lowering therapy that should adhere to SoC per local guidelines*

PRIMARY ENDPOINT:

- Percent change from baseline in fasting TG at 6 months

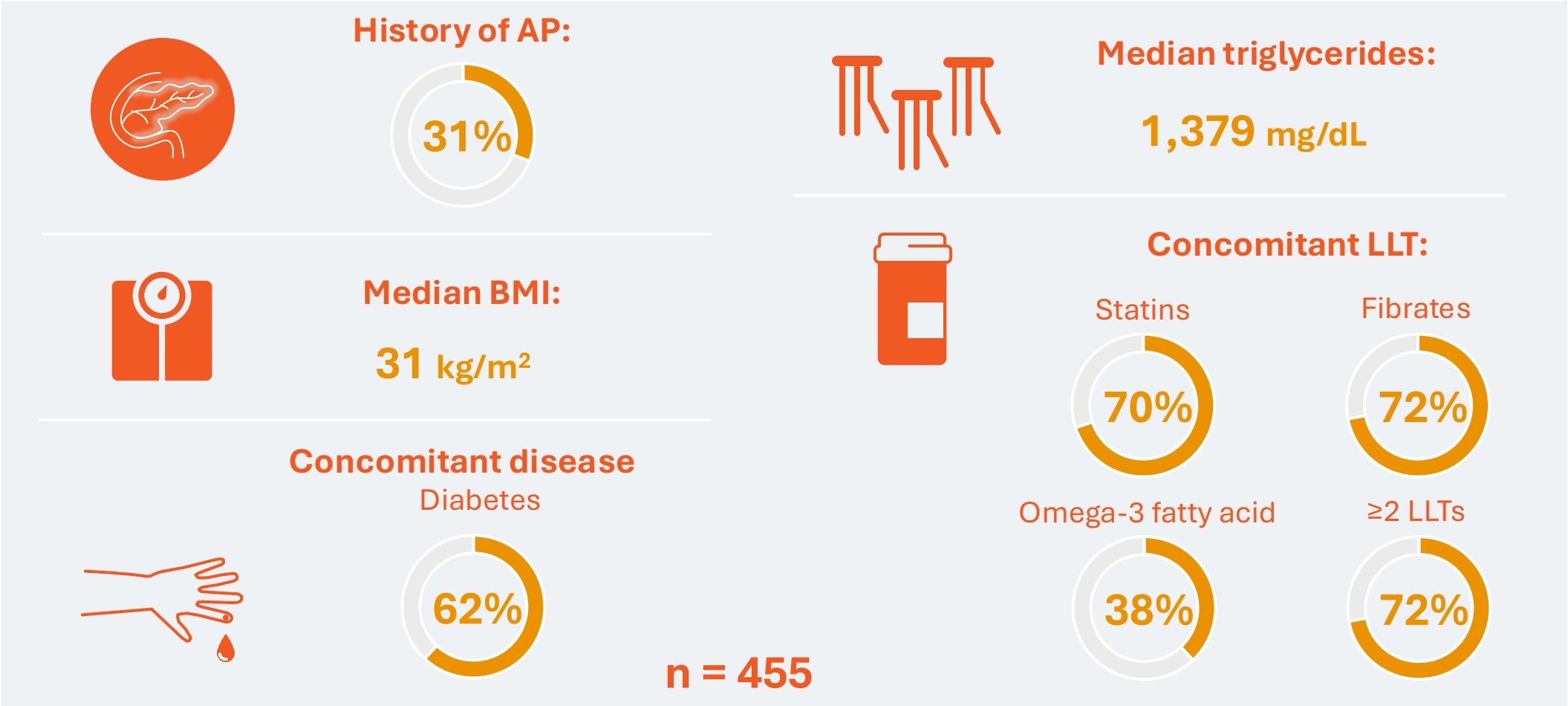


Disclaimer: Olezarsen is not an approved treatment of sHTG. Submission to EMA for label extension to sHTG ≥ 880 mg/dL (≥ 10 mmol/L) in March 2026. Olezarsen no está aprobado en el tratamiento de la HTGs.

* Lipid lowering therapy should be optimised and stabilised at least 4 weeks prior to screening. [†] Screening period of approximately 4 to 12 weeks including a 2-week diet and lifestyle stabilisation, followed by a 2 to 4-week qualification period. [‡] La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. [§] Participants not entering the open-label extension will enter the 13-week post-treatment safety evaluation period. ^{||} The open-label extension study is ongoing with an estimated completion in 2027.³ Patients who had their dose permanently reduced from 80 mg to 50 mg in the index study, will receive 50 mg Q4W. MRI, magnetic resonance imaging; Q4W, every 4 weeks; SC, subcutaneous; sHTG, severe hypertriglyceridemia; SoC, standard of care; TG, triglyceride.

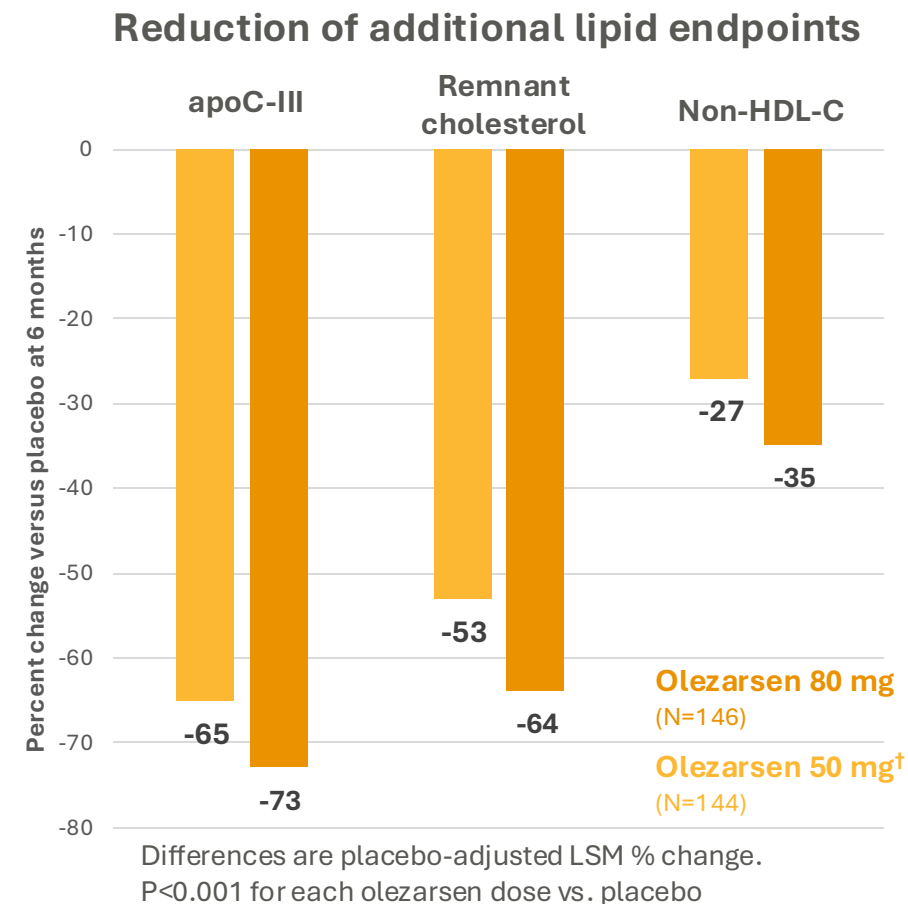
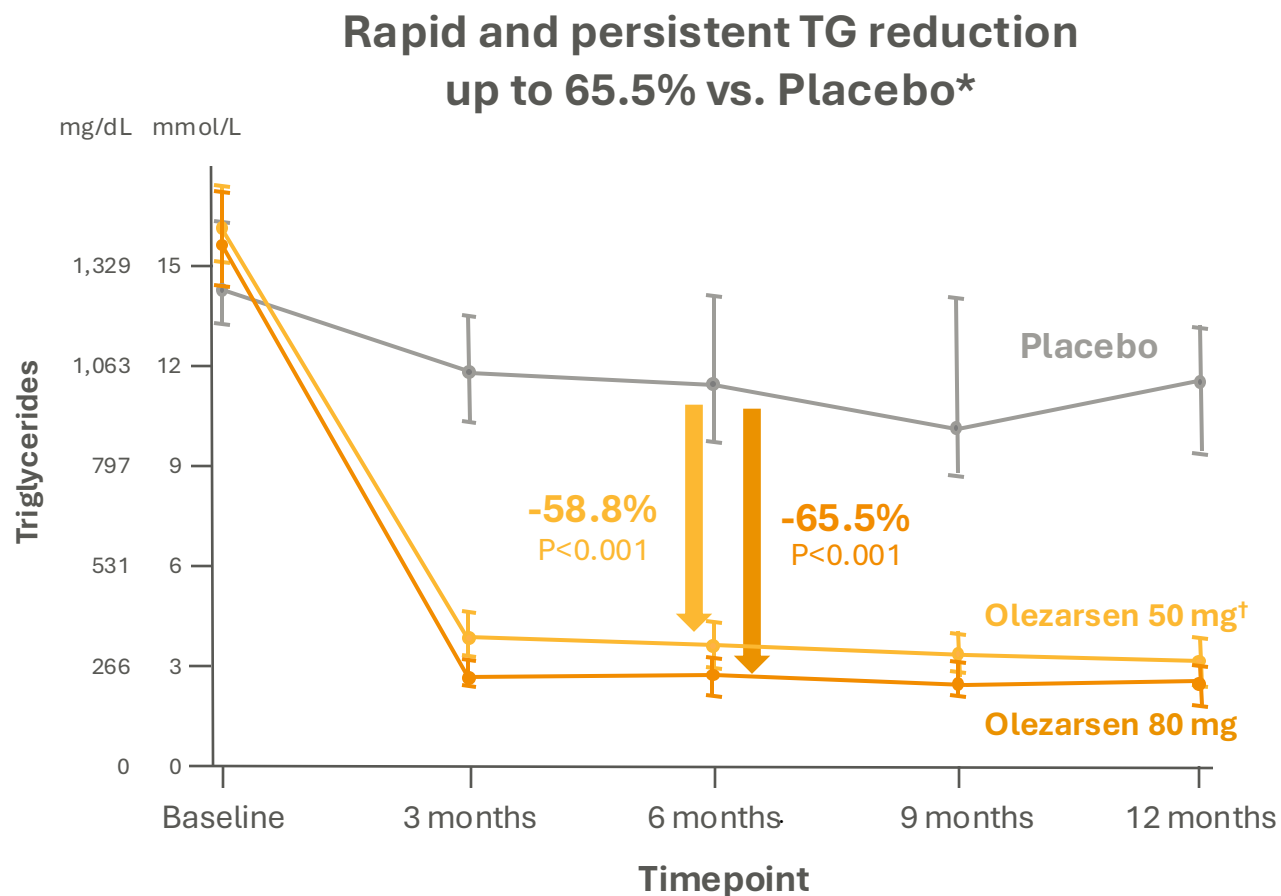
1. Marston et al. *N Engl J Med* 2026 2. Clinicaltrials.gov NCT05681351 3. Zimerman et al. Presentation at EAS 2026.

CORE/CORE2 in sHTG ≥ 880 mg/dL: Baseline characteristics reveal high comorbidity burden and concomitant LLT¹



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AP, acute pancreatitis; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy; sHTG, severe hypertriglyceridemia.
1. Zimerman et al. Presentation at EAS 2026;ID1635.

CORE/CORE2 in sHTG ≥ 880 mg/dL (≥ 10 mmol/L): Significant reduction of TG, apoC-III, remnant cholesterol and non-HDL-C¹

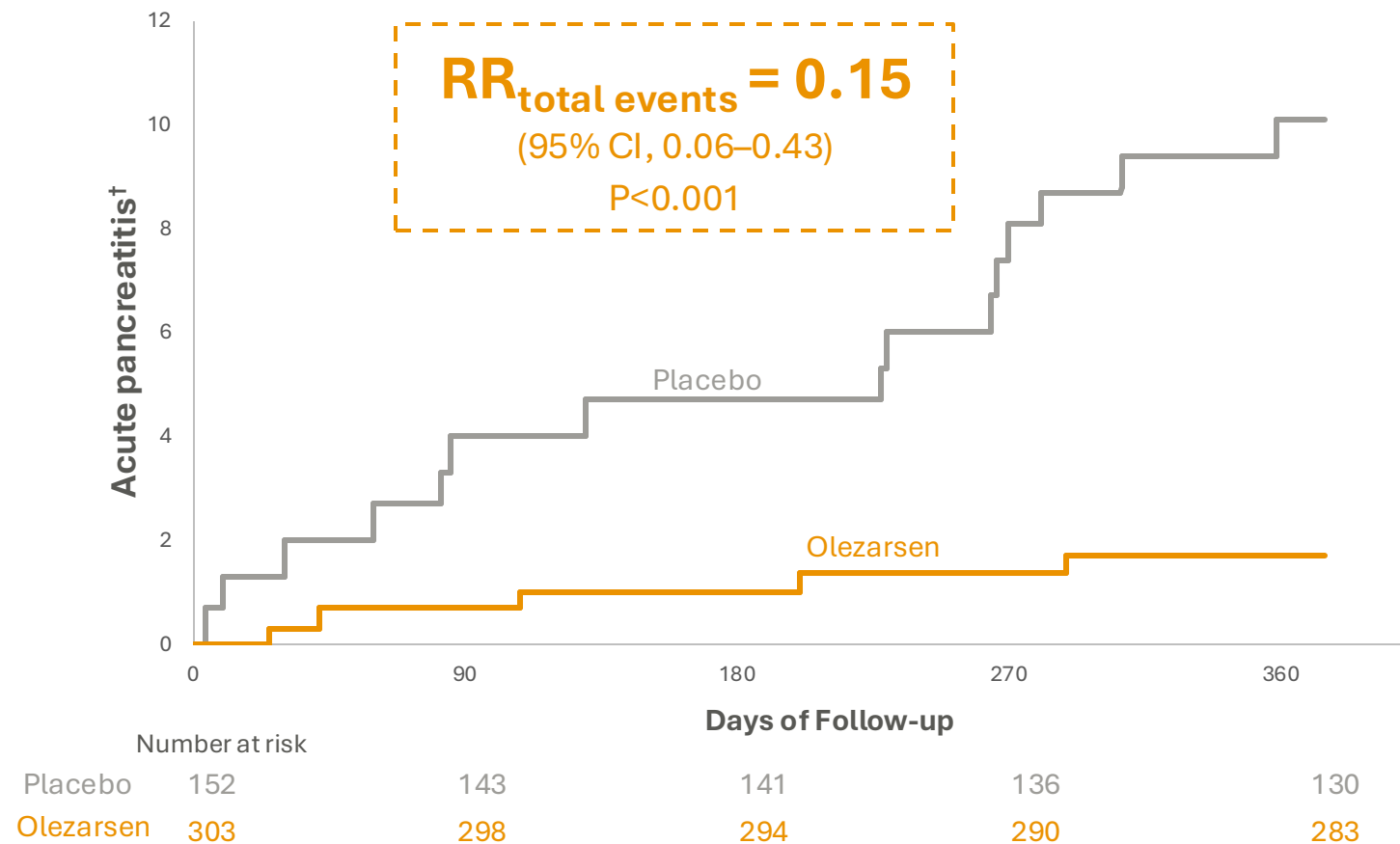


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* Points indicate median values, bands indicate 95% CI of the mean. Differences are placebo-adjusted least-squares mean change in TG levels at month 6. Data are pooled from CORE-TIMI 72a and CORE2-TIMI 72b and include patients with baseline TGs ≥ 880 mg/dL (~ 10 mmol/L). [†] La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month.

CI, confidence interval; sHTG, severe hypertriglyceridemia; TG, triglycerides. 1. Zimerman et al. Presentation at EAS 2026;ID1635.

CORE/CORE2 in sHTG ≥880 mg/dL (≥10 mmol/L):
85% reduction of pancreatitis events within 12 months^{1,*}



- Olezarsen reduced the rate of acute pancreatitis by 85%

	NNT over 1 year
Pooled olezarsen patients (n=705) ²	20
Patients with TG ≥880 mg/dL (placebo n=152, pooled olezarsen n= 303) ¹	9
Patients with TG ≥880 mg/dL + prior pancreatitis ² (placebo n=49, pooled olezarsen n=92)	4

Disclaimer: Olezarsen is not an approved treatment of sHTG. Submission to EMA for label extension to sHTG ≥880 mg/dL (≥10 mmol/L) in March 2026. Olezarsen no está aprobado en el tratamiento de la HTGs.

* Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsen is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis.

† Time to first acute pancreatitis in the pooled olezarsen groups vs. placebo in patients with baseline TGs ≥880 mg/dL (~10 mmol/L). The rate ratio and NNT were based on total pancreatitis events. CI, confidence interval; EMA, European Medicines Agency; FCS, familial chylomicronemia syndrome; NNT, number needed to treat; RR, rate ratio; sHTG, severe hypertriglyceridemia; TG, triglycerides.

1. Zimerman et al. Presentation at EAS 2026;ID1635 2. Marston et al. *N Engl J Med* 2026.

CORE/CORE2 in sHTG ≥880 mg/dL (≥10 mmol/L): Safety

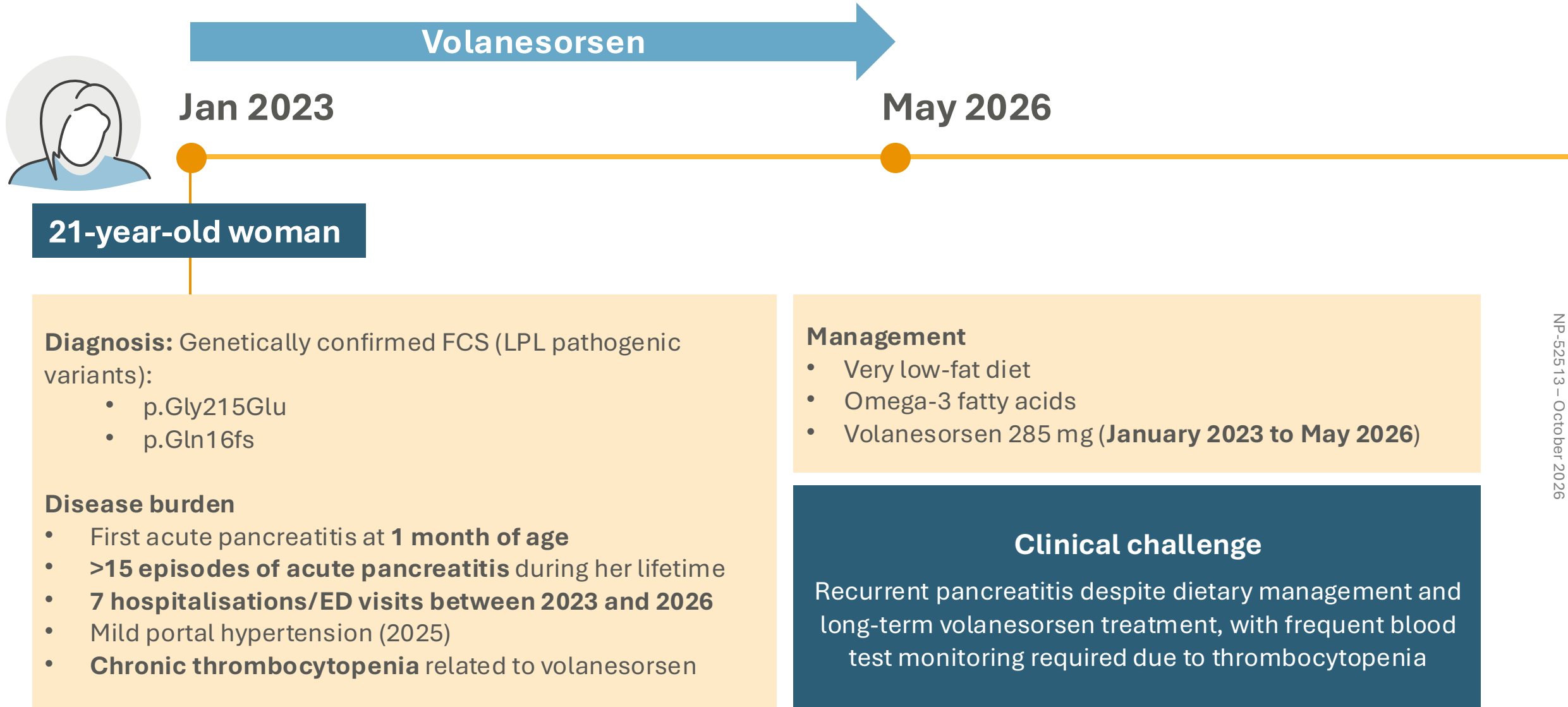
	Placebo	Olezarsen 50 mg*	P value vs placebo	Olezarsen 80 mg	P value vs placebo
Hepatic parameters					
ALT or AST ≥3× ULN	1%	3%	0.28	12%	0.003
ALT or AST ≥5× ULN	<1%	1%	0.56	3%	0.22
Absolute change in HFF (%) [†]	1.3	1.8	0.76	3.1	0.25
Platelet count					
<100K/μL	5%	3%	0.37	5%	0.80
<75K/μL	2%	<1%	0.34	1%	0.65
Glycaemic measures					
HbA1c (%), placebo-adjusted change [†]	–	0.20	0.13	0.15	0.24

The reduction in acute pancreatitis risk with olezarsen was not offset by safety concerns, supporting its safety in patients with severe hypertriglyceridemia^{1,2}

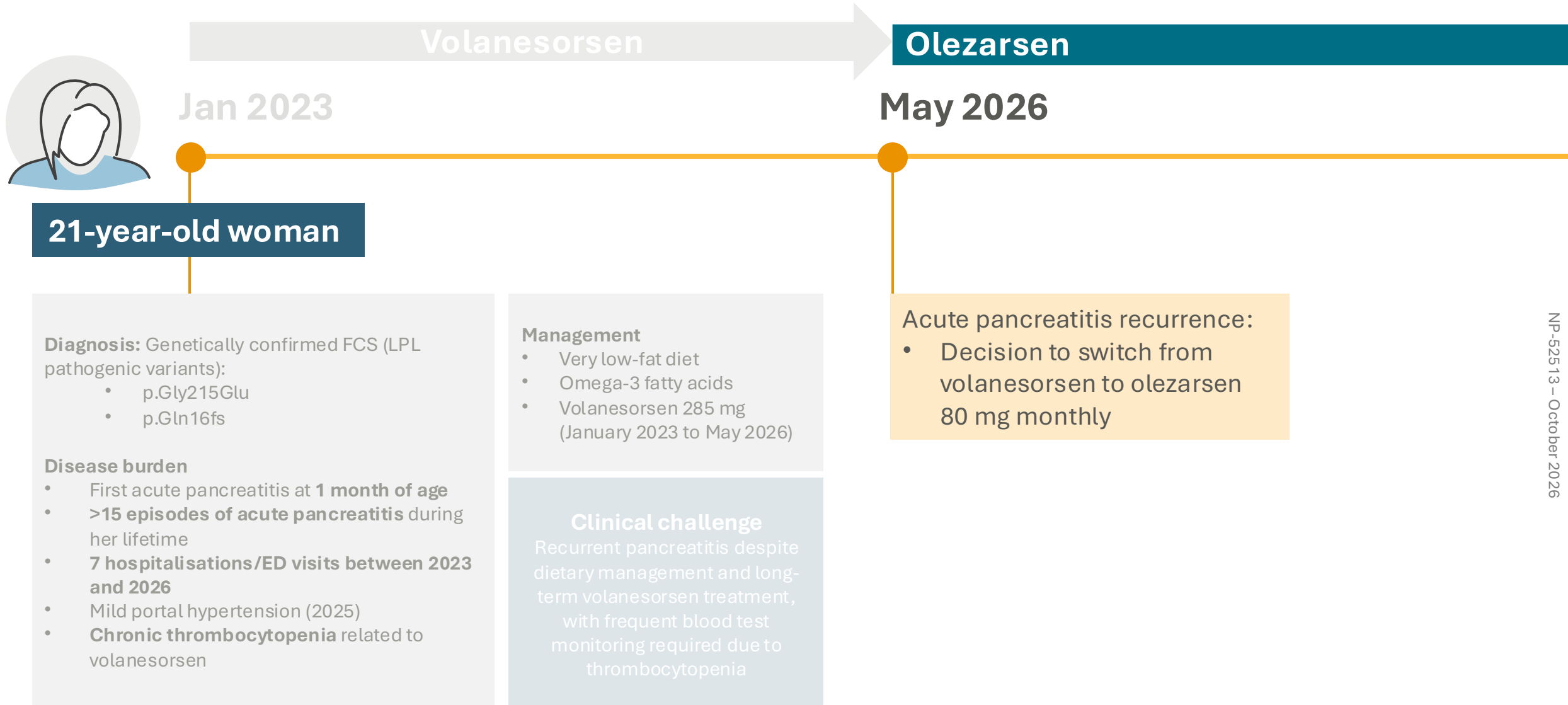
Disclaimer: Olezarsen is not an approved treatment of sHTG. Submission to EMA for label extension to sHTG ≥880 mg/dL (≥10 mmol/L) in March 2026. Olezarsen no está aprobado en el tratamiento de la HTGs. Patients with ALT/AST <3x ULN at screening/qualification were allowed to be enrolled. Elevations in total bilirubin ≥2x ULN occurred in 1 patient on olezarsen 80 mg. There were no cases meeting Hy's Law criteria. * La posología de 50 mg de Olezarsén no está autorizada. La dosis recomendada de olezarsén es de 80 mg administrados mediante inyección subcutánea una vez al mes. The 50 mg dosage of olezarsen is not approved in Spain. The recommended dose of olezarsen is 80 mg administered by subcutaneous injection once a month. † Least-squares mean change at 12 months. ALT, alanine aminotransferase; AST, aspartate aminotransferase; HbA1c, glycated haemoglobin; HFF, hepatic fat fraction; sHTG, severe hypertriglyceridemia; TG, triglycerides; ULN, upper limit of normal.

1. Zimerman et al. Presentation at EAS 2026;ID1635 2. Marston et al. *N Engl J Med* 2026.

Patient case: Patient history



Patient case: Treatment switch



Patient case: Clinical course after switching

Olezarsen

June 2026

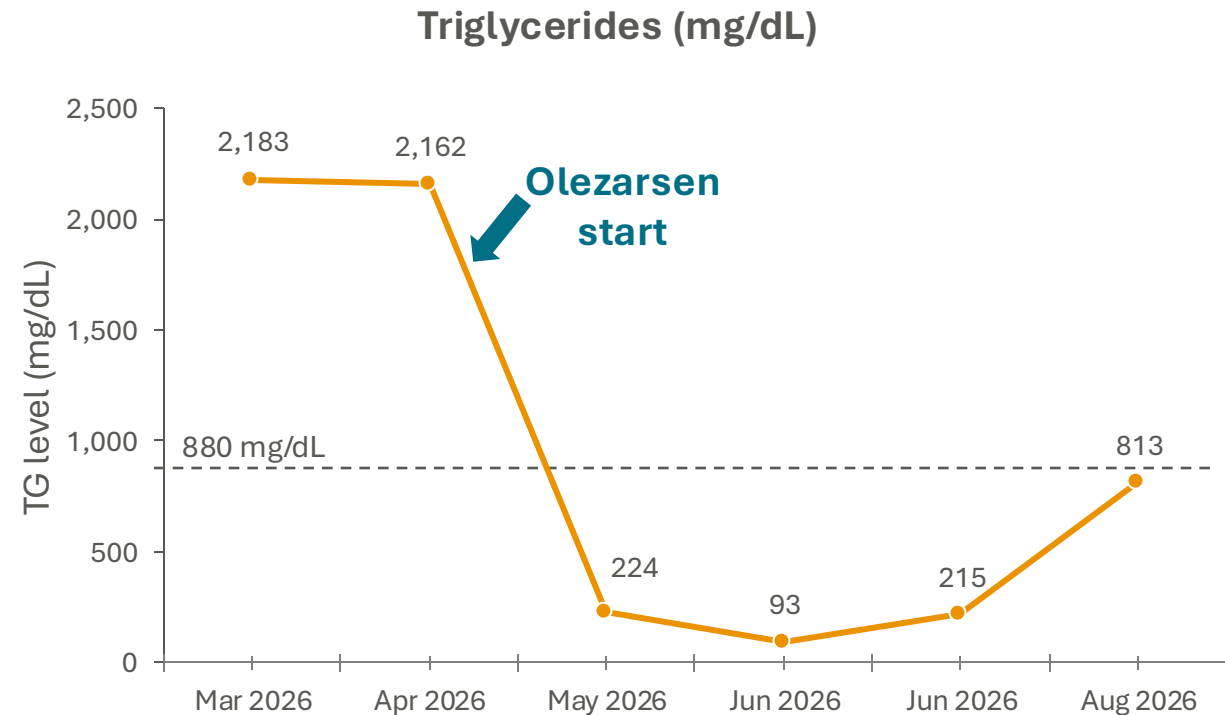
August 2026

Hospitalisation after a trip with friends

- Mild hypertriglyceridemia-induced acute pancreatitis
- TG at admission: 919 mg/dL
- Peak lipase: 438 U/L
- Haemodynamically stable, uncomplicated course

Platelets

- Improved after discontinuation of volanesorsen
- Nadir before switch: $92 \times 10^9/L$
- Generally above $100 \times 10^9/L$ after switch



Key takeaways

- Pivotal studies have shown that targeting apoC-III can significantly reduce triglycerides and acute pancreatitis* risk in patients with FCS and sHTG^{1-3,†}
- Hypertriglyceridemia is a common cause of acute pancreatitis, so routine testing of triglycerides is key⁴
- The only way to successfully manage these patients is working together as a multidisciplinary team⁴

* Olezarsén está indicado como complemento a la dieta en pacientes adultos para el tratamiento del síndrome de quilomicronemia familiar (SQF) confirmado genéticamente. Los resultados relativos a pancreatitis aguda reflejan el impacto del tratamiento en la enfermedad subyacente y no constituyen una indicación independiente para el tratamiento o la prevención de la pancreatitis aguda. Olezarsén is indicated as an adjunct to diet in adult patients for the treatment of genetically confirmed familial chylomicronemia syndrome (FCS). Results regarding acute pancreatitis reflect the impact of treatment on the underlying disease and do not constitute an independent indication for the treatment or prevention of acute pancreatitis. † Olezarsén no está indicado para el tratamiento de la hipertrigliceridemia en España. Hypertriglyceridemia is not an approved indication for olezarsén in Spain. ApoC-III, apolipoprotein C-III; ASO, antisense oligonucleotide; FCS, familial chylomicronemia syndrome; GalNAc₃, triantennary N-acetyl galactosamine; sHTG, severe hypertriglyceridemia; TG, triglyceride. 1. Stroes et al. *N Engl J Med* 2024 2. Watts et al. *N Engl J Med* 2025 3. Witztum et al. *N Engl J Med* 2019 4. Párnitzky et al. *Pancreatology* 2025.

A stylized lighthouse with orange and grey horizontal stripes, situated on a small patch of land in the bottom left corner. A large, bright orange beam of light emanates from the lighthouse, extending diagonally across the slide.

Q&A and panel discussion

All faculty

Q&A and panel discussion

All faculty

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Thank you for joining us

Guiding the care of hypertriglyceridemia-induced acute pancreatitis

Multidisciplinary care and the role of new
therapies through apoC-III inhibition

