LONG-TERM EFFICACY AND SAFETY OF OLEZARSEN IN PATIENTS WITH SEVERE HYPERTRIGLYCERIDEMIA

Interim One-Year Results of the CORE Open Label Extension (OLE) - TIMI 72c

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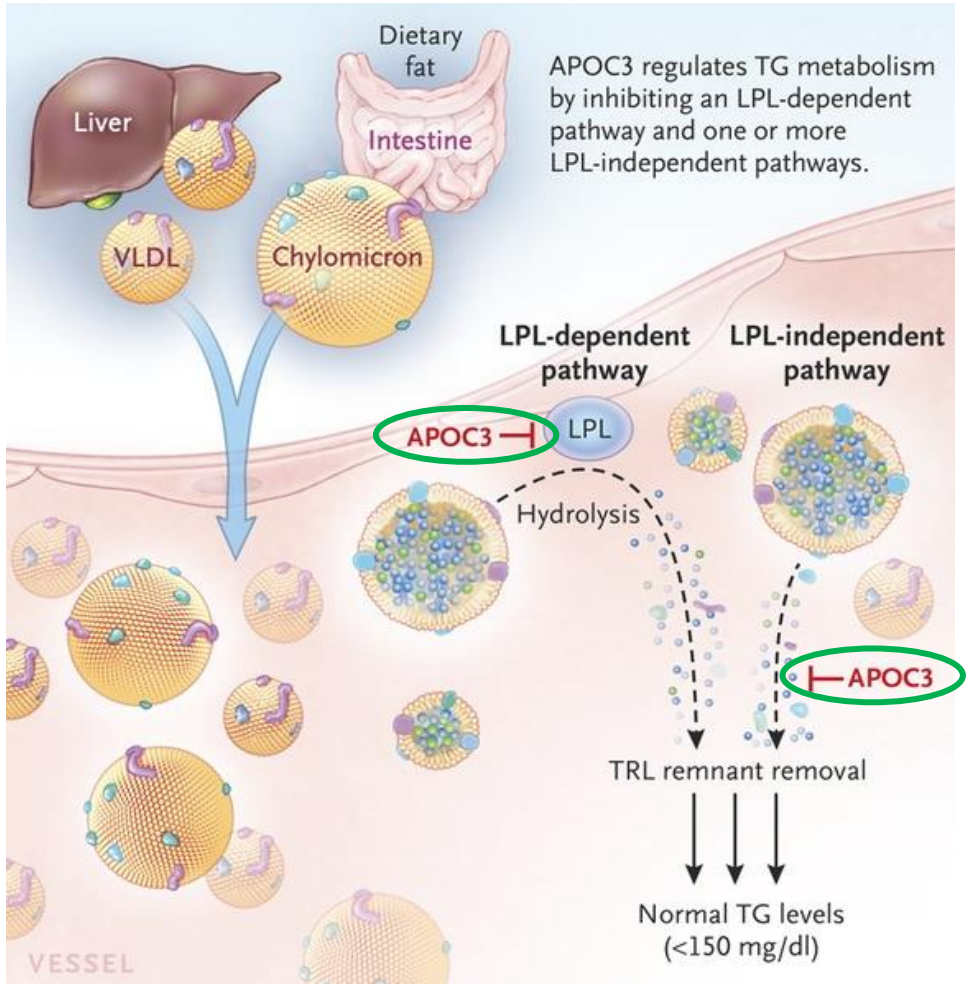
BACKGROUND

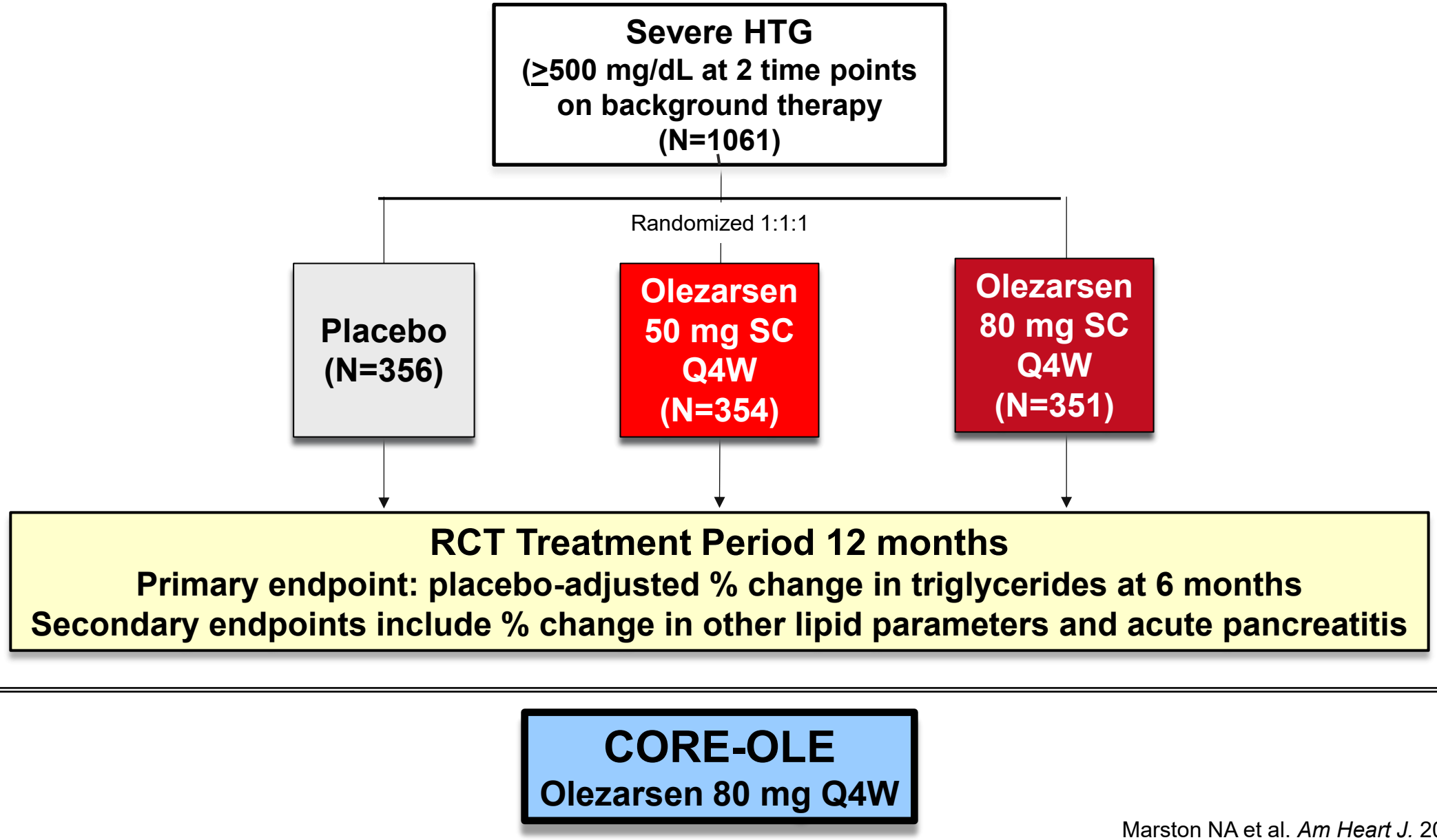


- Severe hypertriglyceridemia (sHTG), defined as triglycerides (TGs) of 500 mg/dL (5.65 mmol/L) or greater, carries an increased risk of acute pancreatitis
- Apolipoprotein C-III (APOC3) inhibits:
  - lipoprotein lipase, a key enzyme in TG metabolism
  - hepatic uptake of TG-rich lipoproteins (TRLs)
- Olezarsen is an antisense oligonucleotide targeting APOC3 that promotes the breakdown and clearance of TRLs, has demonstrated significant reduction in TGs and the risk of acute pancreatitis.
- Olezarsen is approved in the EU and US for treatment of Familial Chylomicronemia Syndrome (FCS) and in the US in patients with severe hypertriglyceridemia to reduce triglyceride levels and the risk of acute pancreatitis

Gaudet D. N Engl J Med. 2014;371:2200-6
Marston NA, et al. N Engl J Med. 2026;394:429-441

CORE-TIMI 72A & CORE2-TIMI 72B

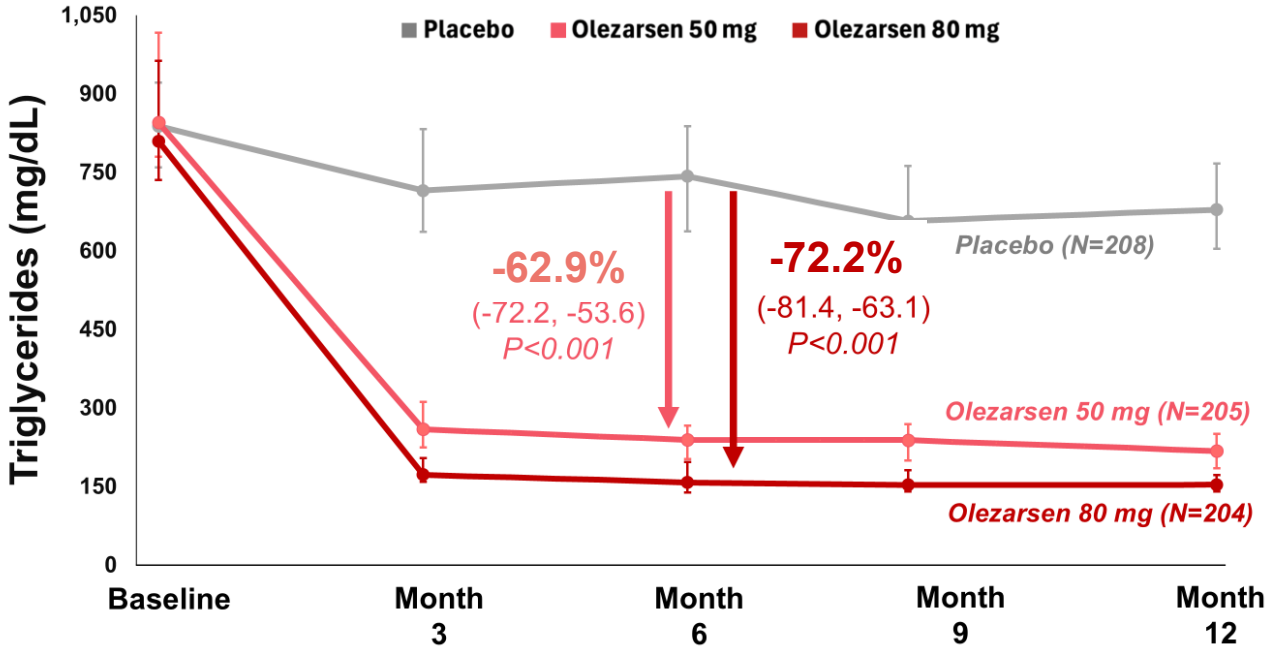
Identically designed



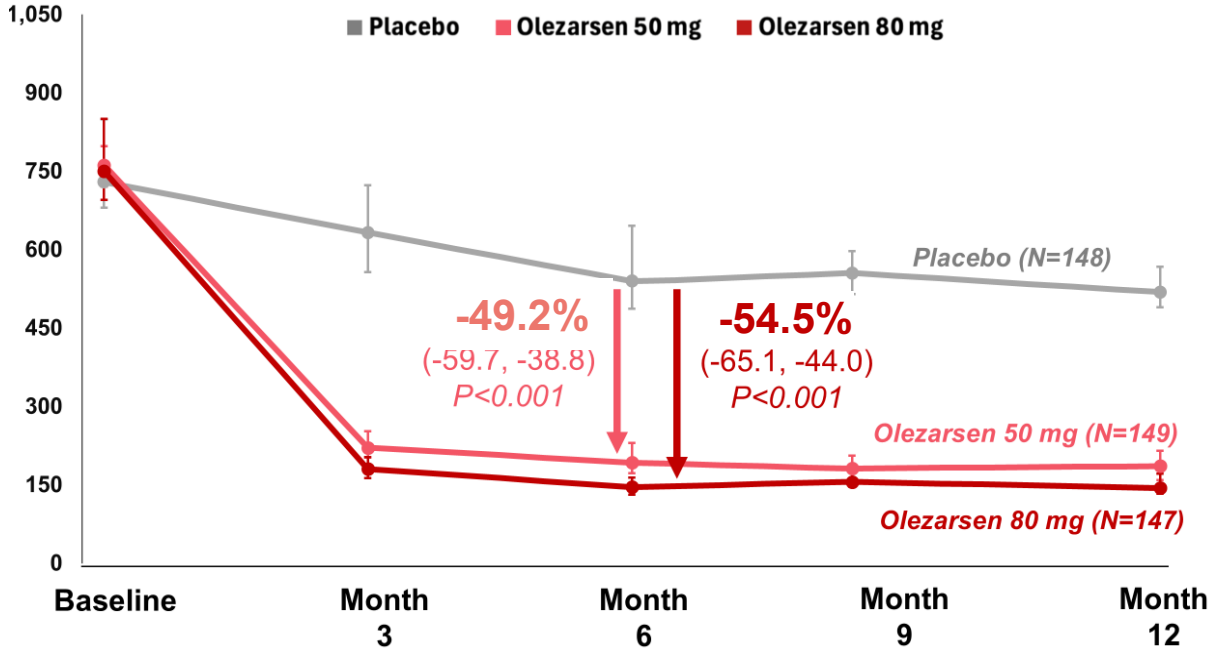
Marston NA et al. *Am Heart J.* 2025;286:125-35

PRIMARY ENDPOINT: CORE-TIMI 72A AND 72B

CORE-TIMI 72A



CORE2-TIMI 72B



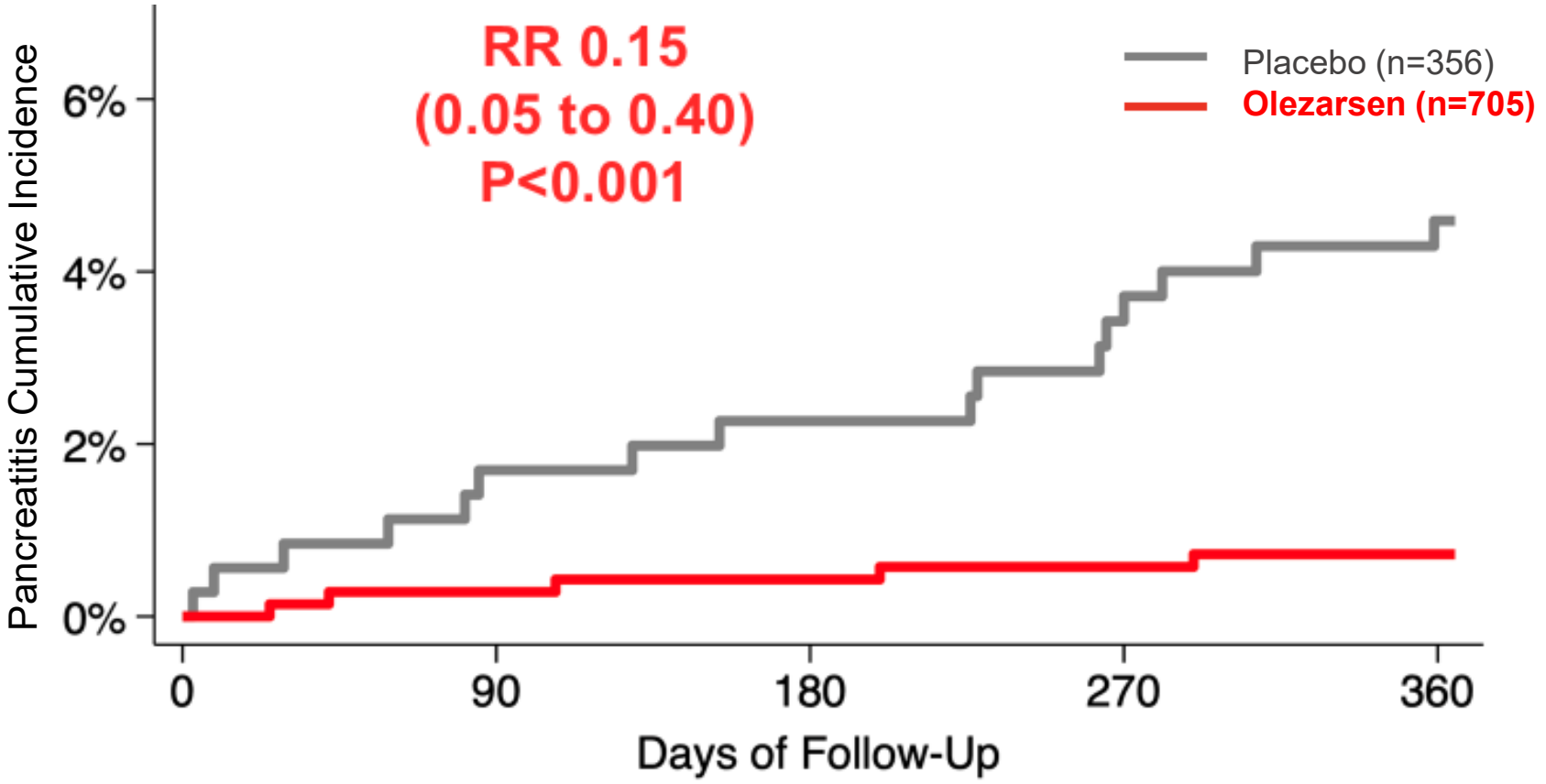
Among patients with severe hypertriglyceridemia, olezarsen:

- Lowered triglycerides by up to 72% c/w placebo on top of conventional therapies
- Resulted in >85% of patients achieving TG levels below 500 mg/dL

Marston NA, et al. N Engl J Med. 2026;394(5):429-41

ACUTE PANCREATITIS

Pooled analysis across both trials and doses



ARR in incidence of total events = 5.2%

NNT over 1 year = 20

ARR, Absolute Risk Reduction

Marston NA, et al. N Engl J Med. 2026;394(5):429-41

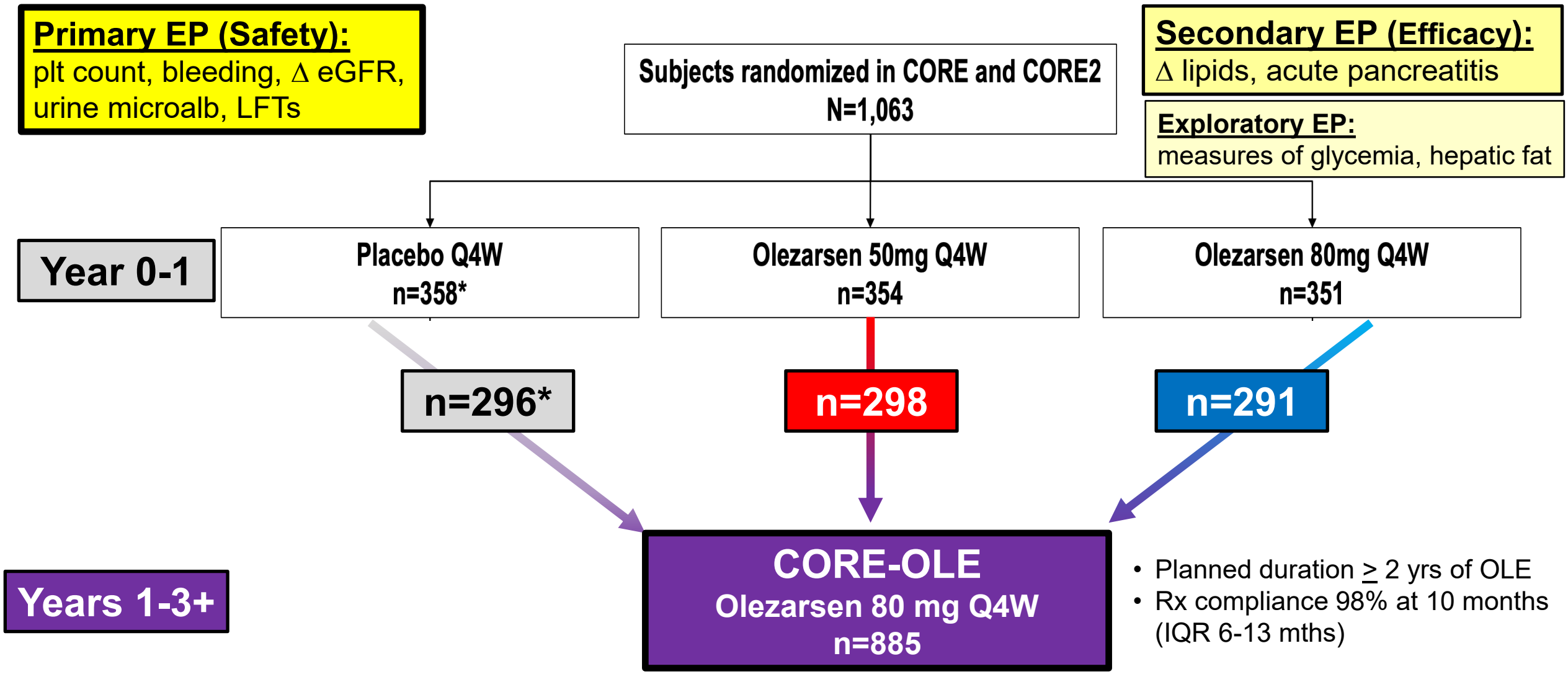
PATIENT DISPOSITION

CORE-TIMI 72a & CORE2-TIMI 72b -> CORE OLE

Primary EP (Safety):
plt count, bleeding, Δ eGFR, urine microalb, LFTs

Secondary EP (Efficacy):
Δ lipids, acute pancreatitis

Exploratory EP:
measures of glycemia, hepatic fat



- Planned duration ≥ 2 yrs of OLE
- Rx compliance 98% at 10 months (IQR 6-13 mths)

*1 patient in placebo arm did not receive olezarsen in OLE

BASELINE CHARACTERISTICS OF OLE POPULATION AT RANDOMIZATION INTO PARENT RCTs

Age (yrs)	54 [46, 61]
Female sex	23%
Race/Ethnicity	
White	89%
Hispanic/Latino	12%
Body Mass Index (kg/m²)	31 [28,35]
Diabetes mellitus	64%
Triglycerides (mg/dL)	798 [593,1277]
History of Pancreatitis	16%
Any Lipid Lowering Therapy	99%
Statin	75%
Fibrate	63%
Omega-3 fatty acid	32%

At time of entry into OLE

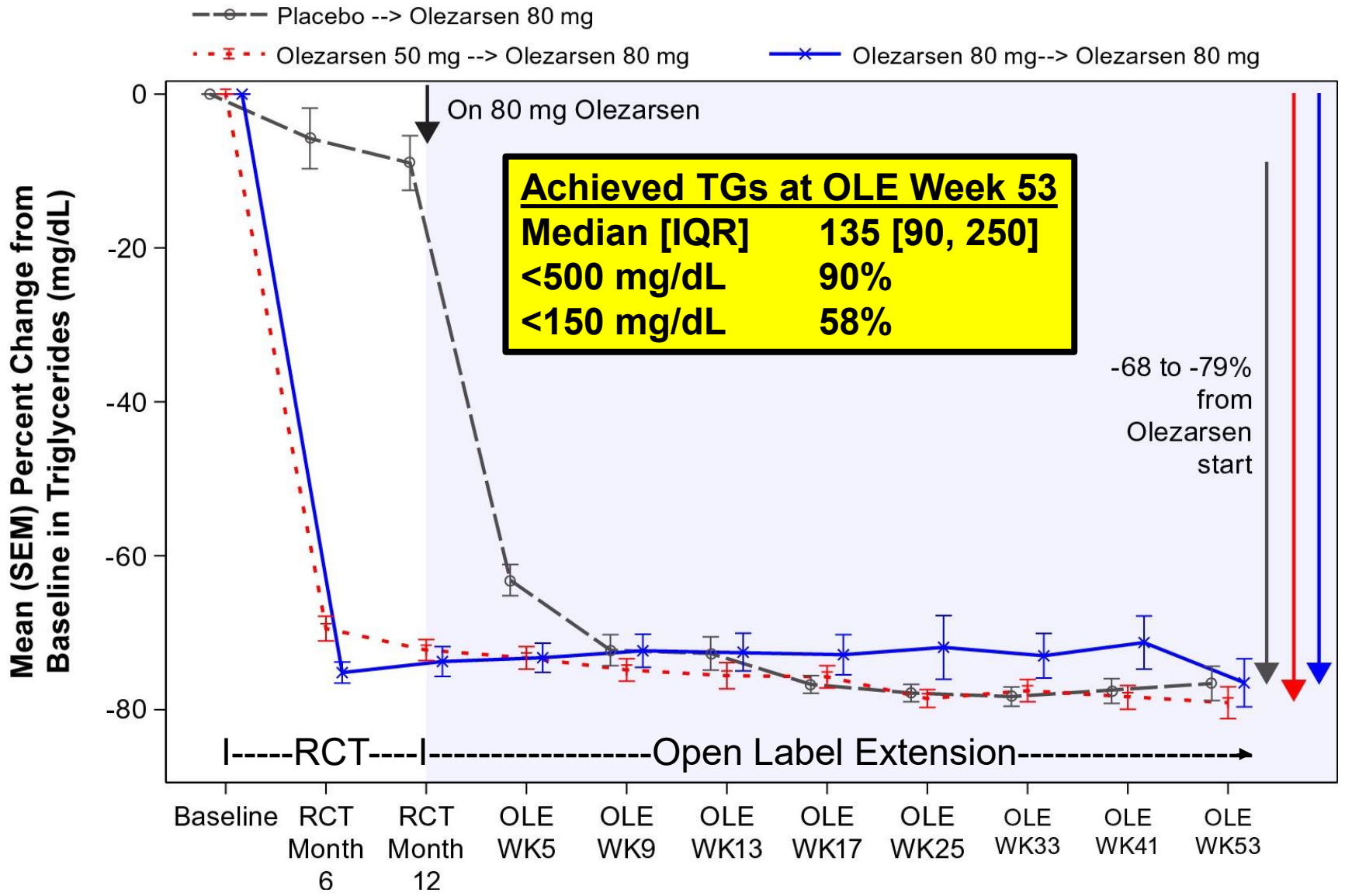
Placebo	611 [418, 1163]
Ole 50 mg	199 [127,336]
Ole 80 mg	149 [103, 311]

Continuous variables shown as median [IQR]

Baseline variables balanced by treatment arm

Preliminary data

MEAN % CHANGE IN BASELINE* TRIGLYCERIDES THROUGH OLE WEEK 53



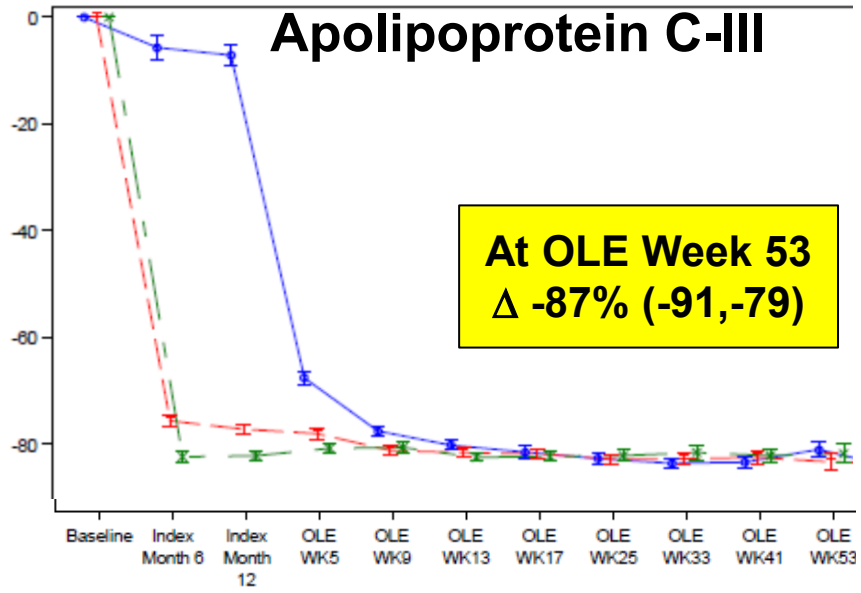
*Baseline prior to start of CORE-TIMI 72a and CORE-TIMI 72b

Error bars show the standard error of the mean

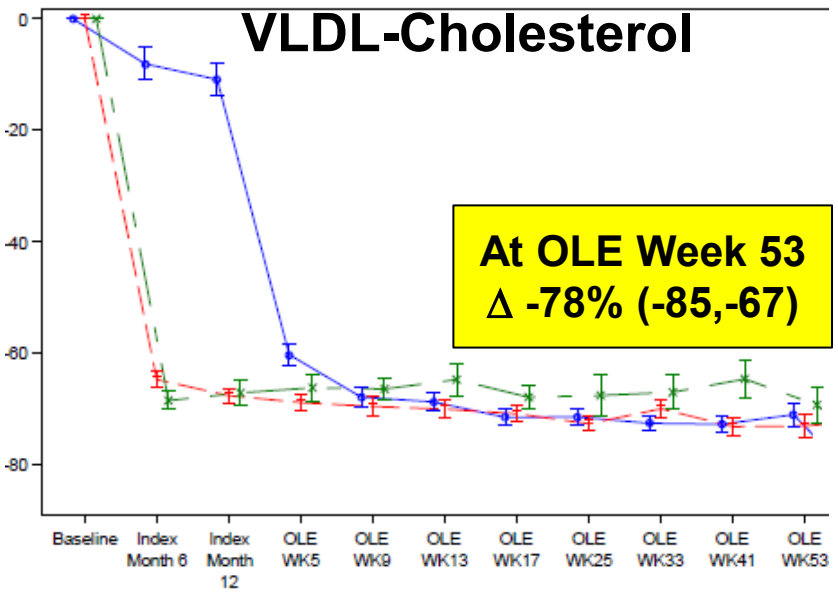
Preliminary data

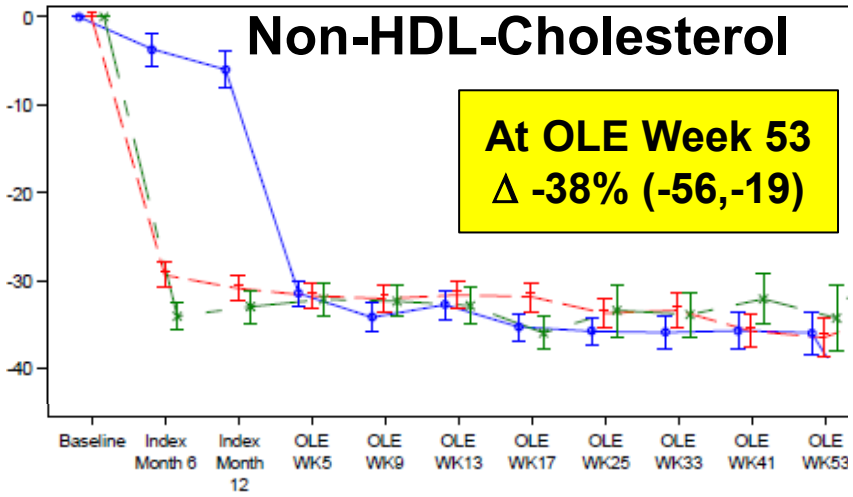
SECONDARY LIPID ENDPOINTS

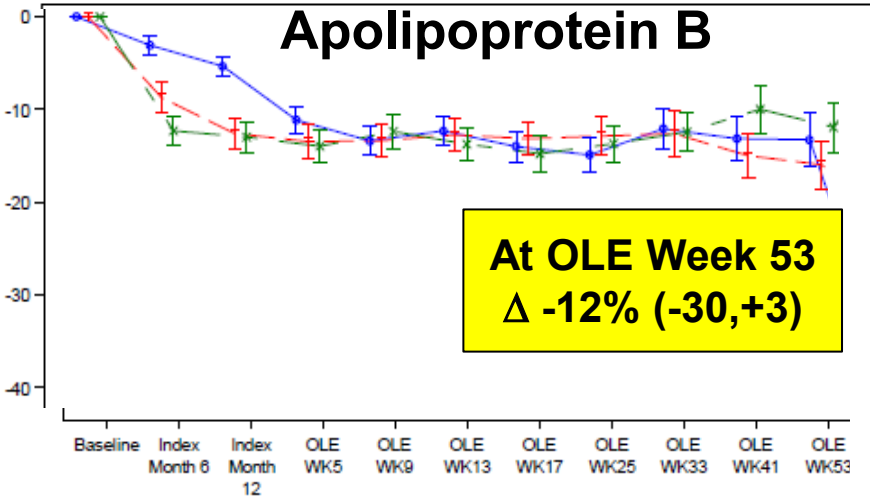
Mean % Changes from RCT Baseline



Placebo--> Ole 80
Ole 50 --> Ole 80
Ole 80 --> Ole 80







Preliminary data

PRIMARY ENDPOINTS (SAFETY)

	CORE-TIMI 72a & CORE2-TIMI 72b (pooled, N=1,061)			CORE-OLE
	Placebo (N=356)	Olezarsen 50 mg (N=354)	Olezarsen 80 mg (N=351)	Olezarsen 80 mg (n=884*)
Platelet count <75K/uL	1.7	0.6	2.0	**0.9**
Clinical bleeding events	4.8	5.9	5.4	**3.5**
Decrease in eGFR ≥ 30%	13.4	8.9	10.1	**6.2**
Decrease in eGFR ≥ 50%	2.0	0.9	2.9	**0.8**
UPCR ≥ 500 mg/g	14.2	12.1	13.6	**8.6**
UPCR ≥ 1000 mg/g	4.5	5.2	4.0	**2.8**
ALT or AST ≥ 5x ULN	0.9	0.9	1.4	**0.5**
Total bilirubin ≥ 2.0 mg/dL	0.3	0.3	0.6	**0.3**

*Excludes 1 patient enrolled in the OLE did not take any doses of olezarsen
Data shown are n/N rates
No cases of Hy's Law (AST or ALT ≥3x ULN and total bilirubin ≥ 2x ULN) were observed
NOTE: Rates shown for CORE-TIMI 72a and CORE2-TIMI 72b data are at 1 year, for CORE-OLE through median 10 months follow-up.

Preliminary data

ADVERSE EVENTS

	CORE-TIMI 72a & CORE2-TIMI 72b (pooled N=1,061)			CORE-OLE
	Placebo (N=356)	Olezarsen 50 mg (N=354)	Olezarsen 80 mg (N=351)	Olezarsen 80 mg (N=884*)
Any treatment emergent adverse event	75.0	74.6	76.1	**60.7**
Leading to drug discontinuation	2.0	3.4	4.3	**3.3**
Serious	13.8	8.8	10.8	**8.5**
Leading to drug discontinuation	0.3	1.1	0.6	**1.5**
Injection site reactions				
Any	0.8	10.2	16.5	**11.4**
Mild	0.8	9.6	14.8	**10.3**
Moderate	0	1.1	2.8	**1.1**
Severe	0	0	0	**0**

*Excludes 1 patient enrolled in the OLE did not take any doses of olezarsen
Data shown are n/N rates
NOTE: Rates shown for CORE-TIMI 72a and CORE2-TIMI 72b data are at 1 year, for CORE-OLE through median 10 months follow-up.

Preliminary data

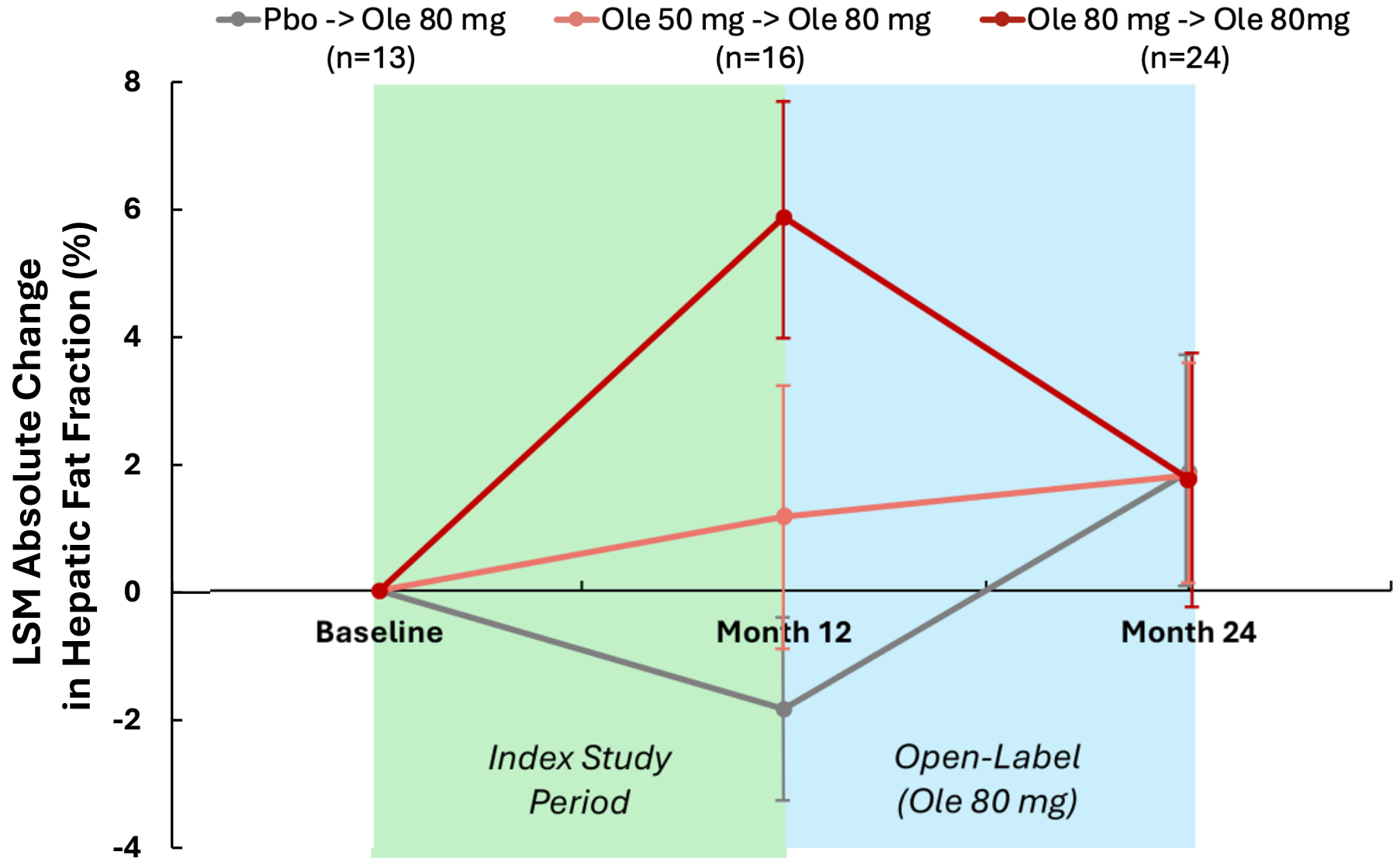
ADJUDICATED CASES OF ACUTE PANCREATITIS

	CORE-TIMI 72a & CORE2 TIMI-72b (pooled RCTs)		CORE-OLE
	All Olezarsen (N=705)	Placebo (N=356)	Olezarsen 80 mg (N=884)
Patients with an event, n(%)	5 (0.7)	17 (4.8)	10 (1.1)
Total number of events	7	22	19*
Total patient-years	696.1	352.9	711.4
Event rate per 100 pt/yr	1.01	6.23	2.67

*1 non-compliant patient had 8 events

Preliminary data

MRI Hepatic Fat Substudy
Preliminary 24-month data (n=53)



HFF = hepatic fat fraction

Baseline HFF = 13.9% in placebo, 17.6% in 50 mg, 16.0% in 80 mg

Preliminary data

SUMMARY & CONCLUSION

- **In patients with severe hypertriglyceridemia (TG >500 mg/dL), longer term use of olezarsen for up to 2 years:**
  - Was generally well tolerated, with no new safety findings
  - Sustained TG lowering of 68-79%
  - Resulted in 90% of patients achieving TG levels <500 mg/dL
  - Achieved persistent reductions in the risk of acute pancreatitis
  - Preliminary data suggest only modest (<2%) ↑ in hepatic fat fraction through 2 years
- **These findings provide additional support for the continued use of olezarsen in patients with severe hypertriglyceridemia to reduce triglyceride levels and risk of acute pancreatitis over the longer term**