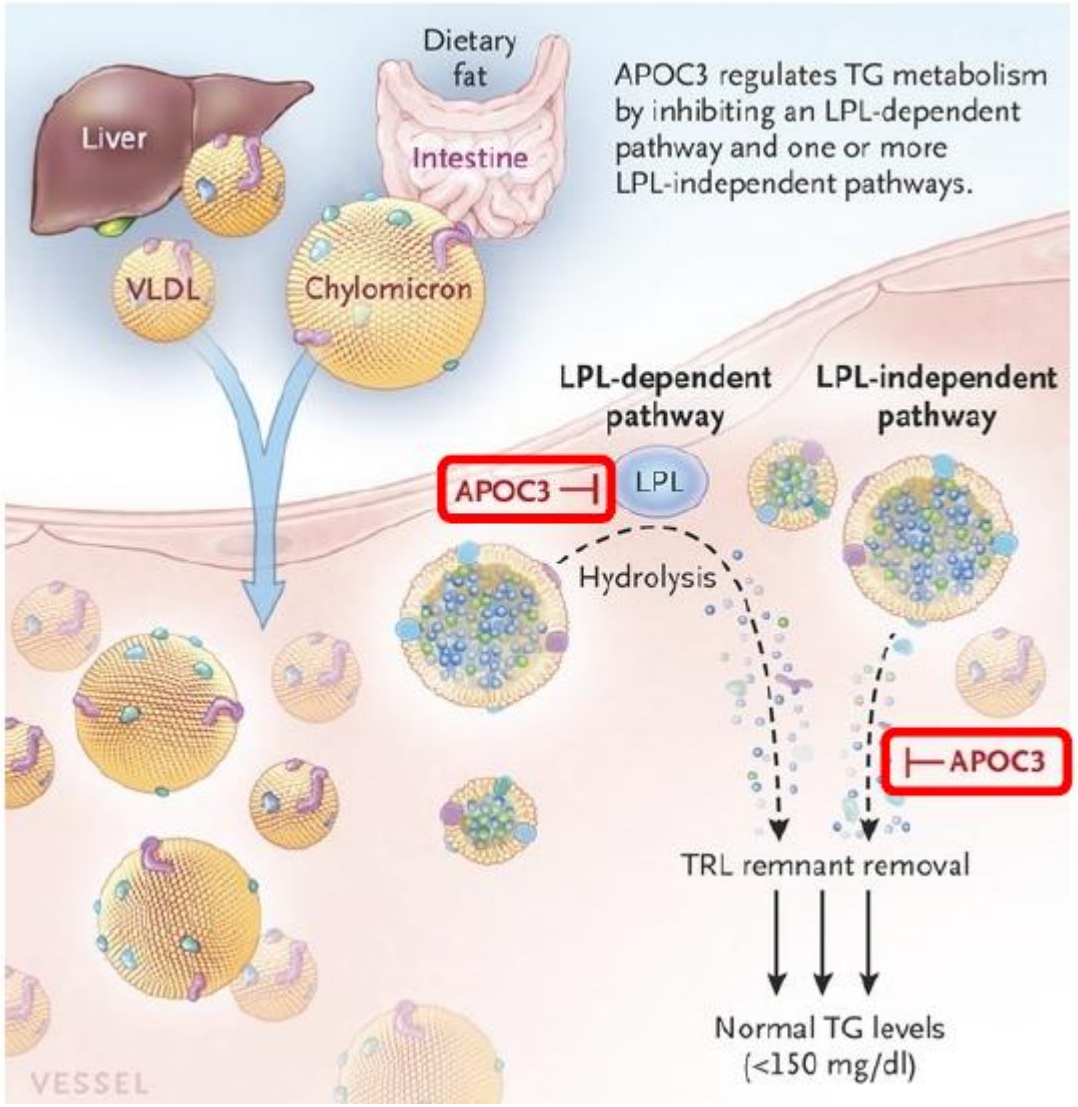
VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Studie ESSENCE s olezarsenem

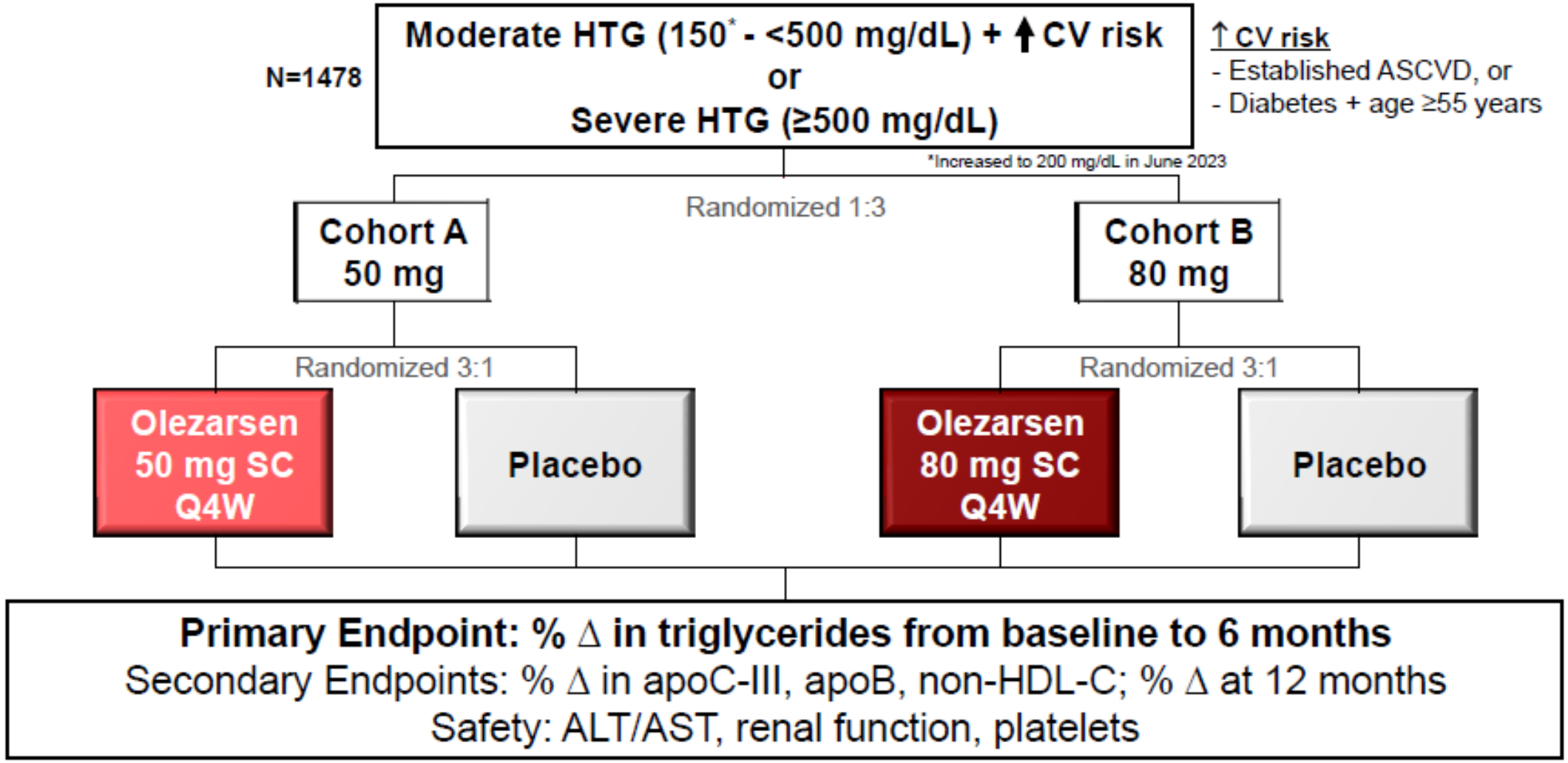
Michal Vrablík

Inhibice apolipoproteinu CIII: účinná modifikace lipoproteinového metabolismu



- Apolipoprotein C-III
  - Syntetizován v játrech
  - Inhibuje metabolismus na TG bohatých lipoproteinů
- Olezarsen
  - ASO cílící na mRNA pro *APOC3*
  - Konjugace s GalNAC (analogie s inklisiranem)
    - Předchůdce schválený pro klinické použití volanesorsen

Design studie

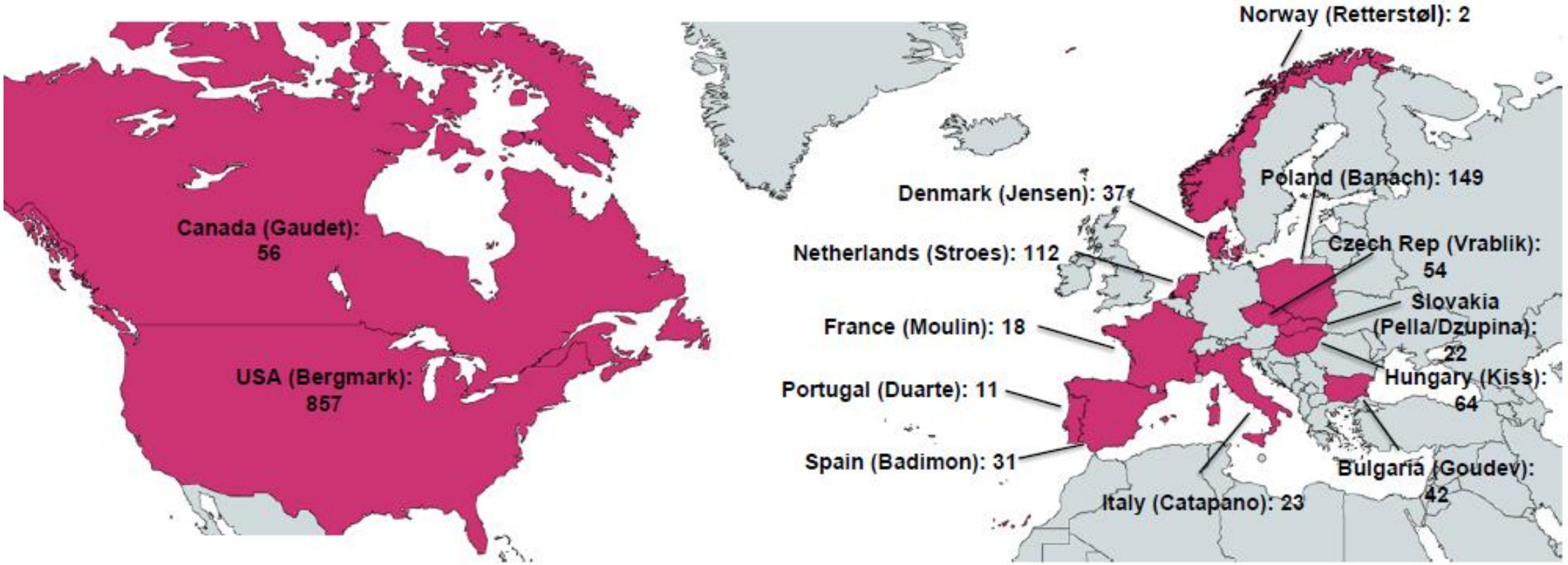


Primary efficacy analysis population: **Patients with baseline triglycerides <500 mg/dL**
Primary safety analysis population: All patients receiving at least one dose of study drug

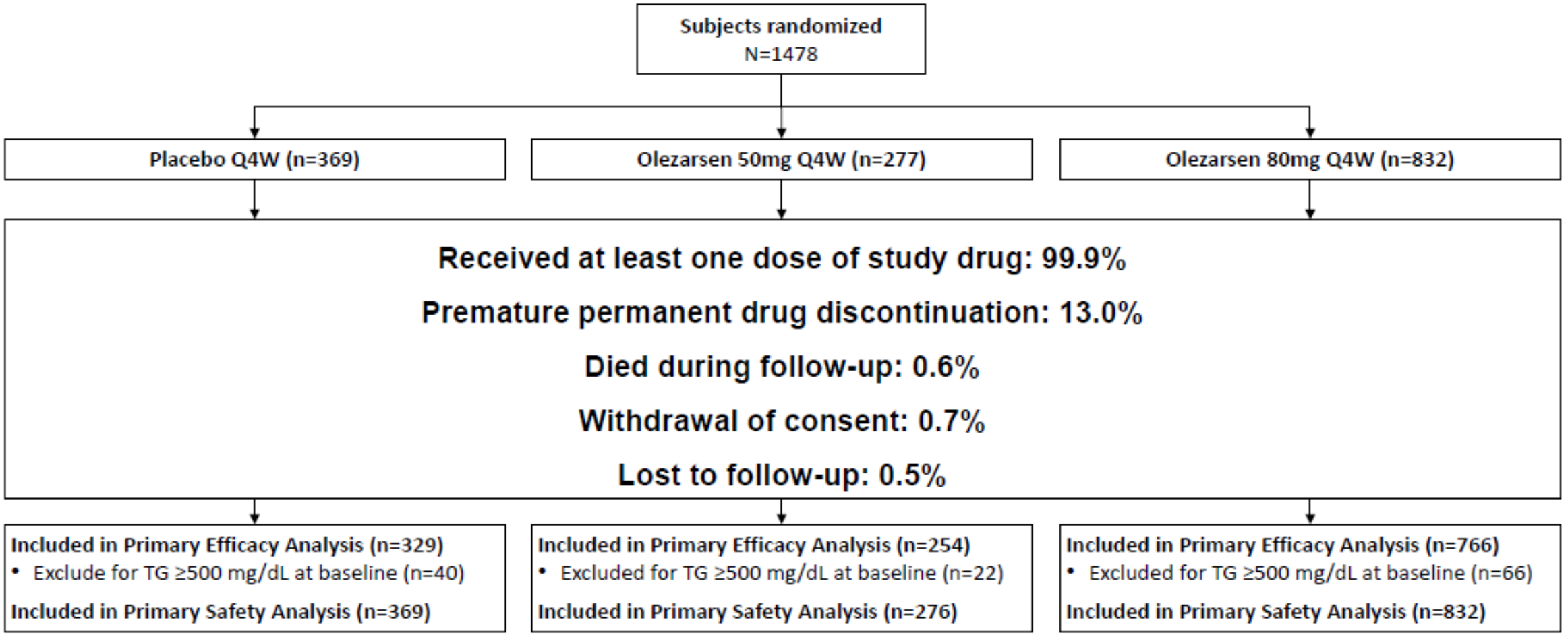
Divide TG value in mg/dL by 88.5 to calculate mmol/L
Bergmark BA, Marston NA, et al. *Am Heart J*:2025:116-24

Velké poděkování všem českým centrům

November 2022 – February 2024 | **14** Countries | **160** Sites | **1,478** Patients



Průběh studie



Primary efficacy analysis population: Patients with baseline triglycerides <500 mg/dL
Primary safety analysis population: All patients receiving at least one dose of study drug
*No deaths attributed to study medication by site investigator

An Academic Research Organization of
Brigham and Women's Hospital and Harvard Medical School

Divide TG value in mg/dL by 88.5 to calculate mmol/L

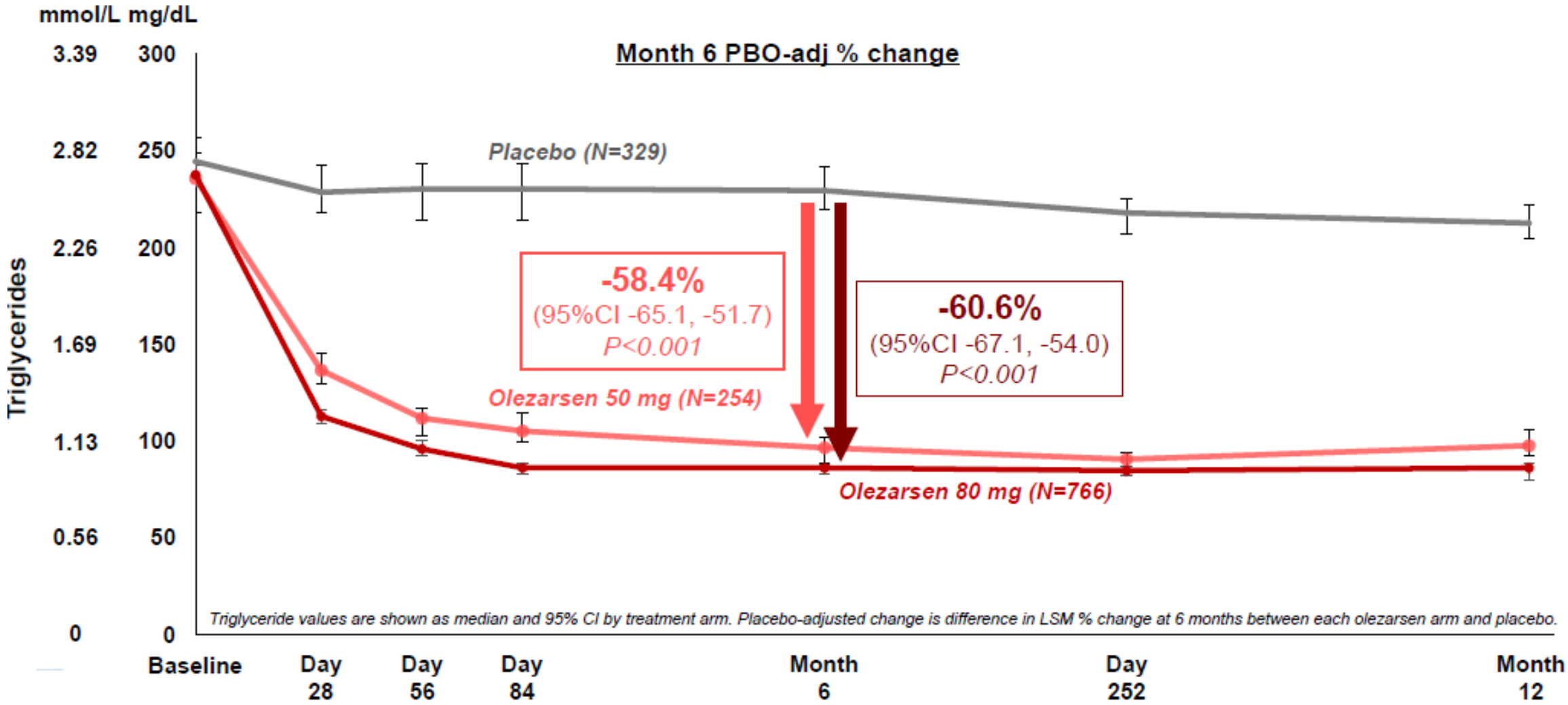
Vstupní charakteristika

	Overall N=1349
Age (yrs)	64 (56, 70)
Female sex	40
Race/Ethnicity	
White	93
Black	4
Asian	1
Hispanic/Latino	23
Diabetes mellitus	60
Chronic kidney disease	9
Triglycerides (mg/dL)	238.5 (190.5, 307.5)
Triglycerides (mmol/L)	2.7 (2.2, 3.5)
HbA1c (%)	6.2 (5.7, 7.1)

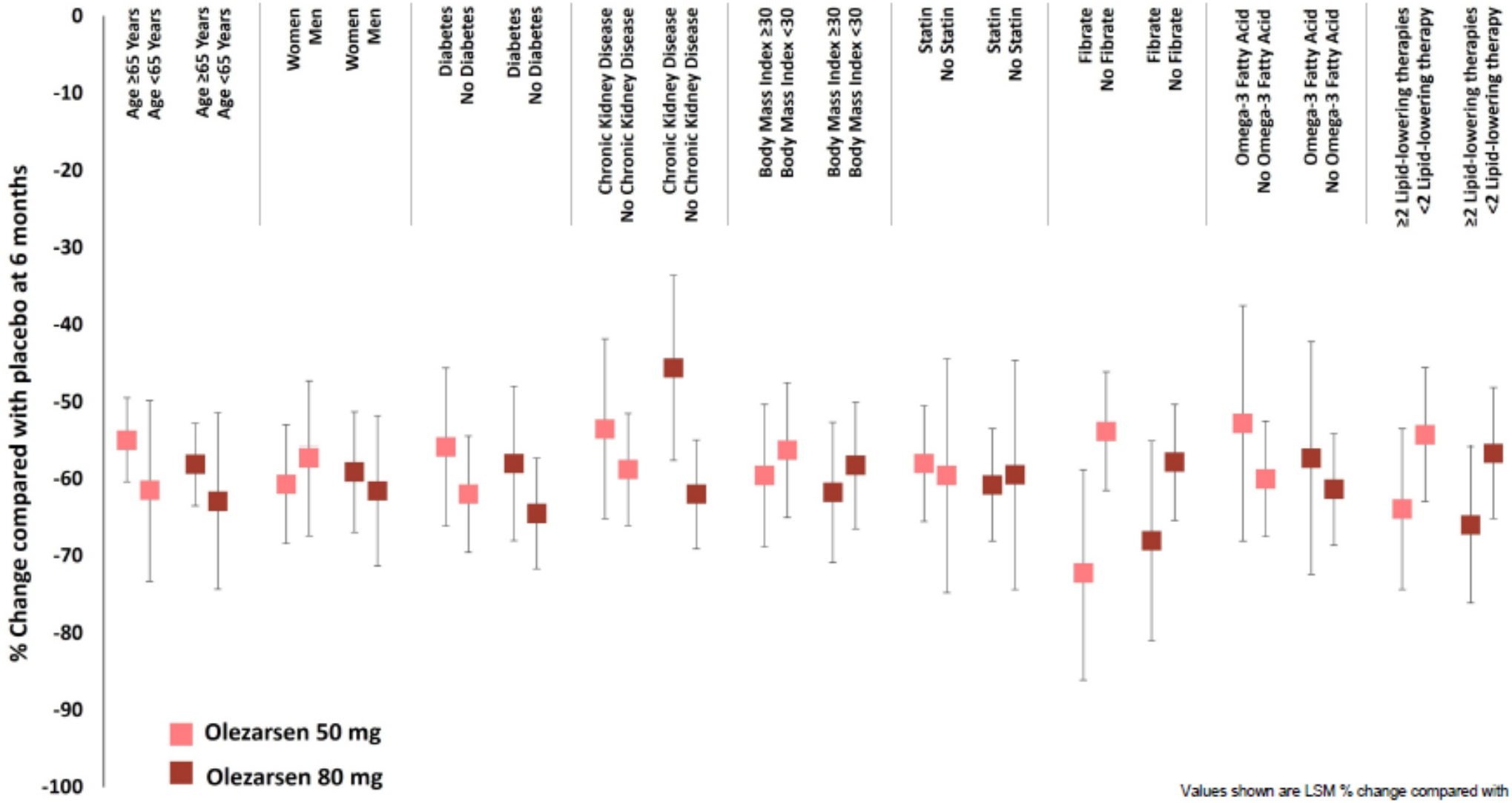
Values shown are % or median (IQR) for pooled treatment arms in the primary efficacy cohort
There were no significant differences across treatment arms

	Overall N=1349
Lipid-lowering therapy	96
Statin	81
Ezetimibe	17
Fibrate	23
Omega-3 fatty acid	17
Niacin	1
PCSK9 inhibitor	5
≥2 therapies	42

Olezarsen - účinnost

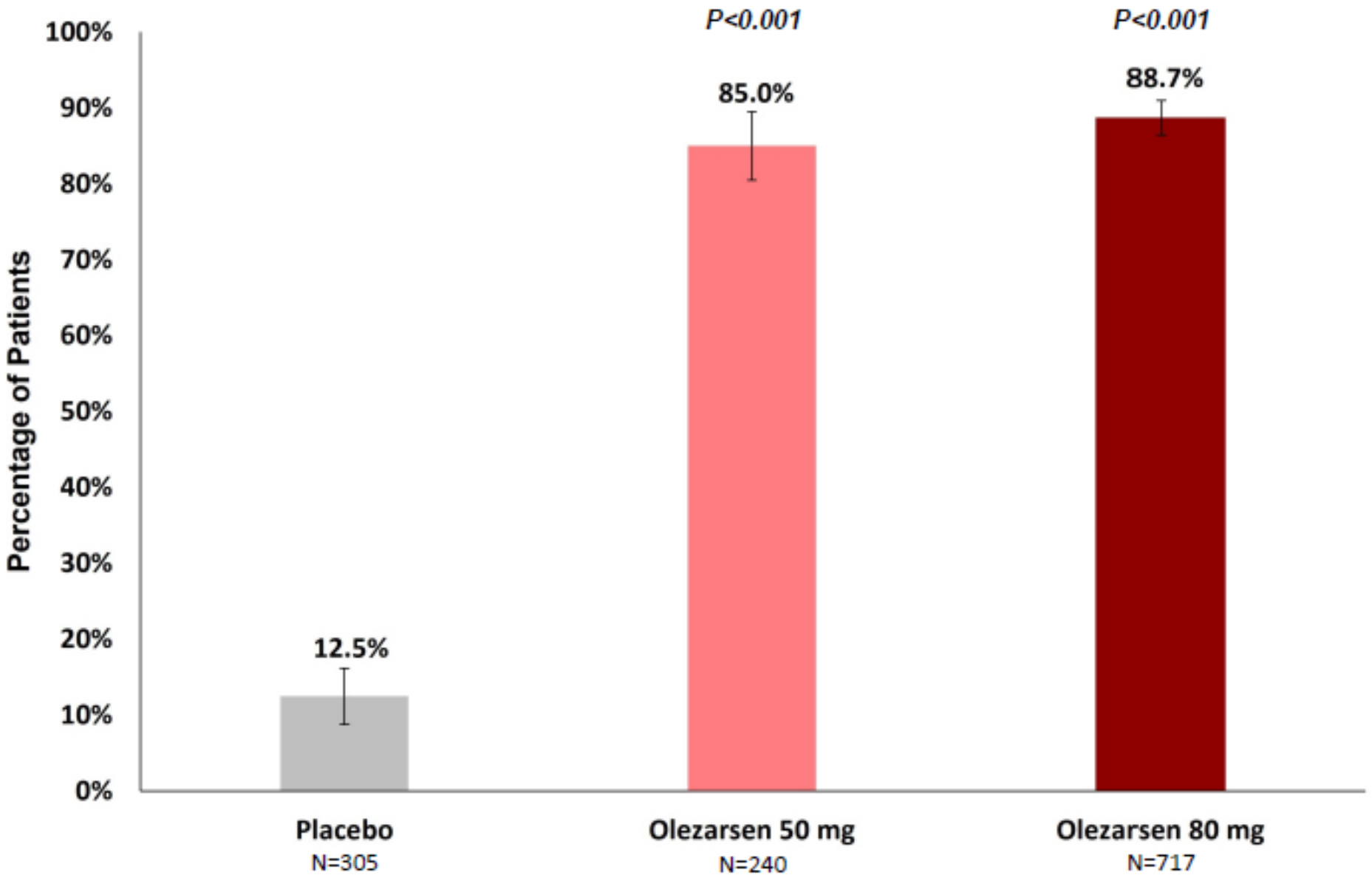


Účinnost v podskupinách



Values shown are LSM % change compared with placebo and 95% CI

Dosažení TG < 1,7 mmol/l



Klinické události ve 12. měsíci

	Placebo N=329	Olezarsen (pooled) N=1020
Major adverse cardiovascular events		
CV death, MI, ischemic stroke, or arterial revascularization	4.3	5.0
Pancreatitis		
Acute pancreatitis	0	0.3

CV – cardiovascular; MI – myocardial infarction

Event data shown as % in the primary efficacy cohort

Klíčové bezpečnostní parametry

	Placebo N=369	Olezarsen 50 mg N=276	P-value vs Placebo	Olezarsen 80 mg N=832	P-value vs Placebo
Treatment-emergent adverse events					
Any	72	73	0.84	77	0.09
Leading to drug discontinuation	5	4	0.75	7	0.22
Serious	11	9	0.42	14	0.29
Leading to drug discontinuation	1	1	0.70	2	0.49
Injection Site Reaction	2	15	<0.001	16	<0.001
Mild	2	13	<0.001	15	<0.001
Moderate	<1	3	0.006	3	0.002
Severe	0	0	-	0	-

Treatment phase data in the safety cohort shown as %

Klíčové bezpečnostní parametry

	Placebo N=369	Olezarsen 50 mg N=276	P-value vs Placebo	Olezarsen 80 mg N=832	P-value vs Placebo
Hepatic abnormalities*					
ALT or AST ≥3x ULN	1	3	0.12	2	0.15
ALT or AST ≥5x ULN	<1	1	0.58	<1	0.99
Total bilirubin ≥2x ULN	<1	<1	0.99	<1	0.52
Renal abnormalities					
eGFR decline ≥50%	1	<1	0.99	1	0.73
UPCR ≥1000 mg/g	2	1	0.77	2	0.98
UPCR ≥3000 mg/g	0	<1	0.43	<1	0.99
Platelet count reductions					
<100K/uL	1	2	0.18	2	0.10
<75K/uL	<1	1	0.32	1	0.68
<50K/uL	<1	0	0.99	<1	0.52

*There were no cases meeting Hy's Law criteria

Treatment phase data in the safety cohort shown as %

Klíčové bezpečnostní parametry

	Placebo N=369	Olezarsen 50 mg N=276	P-value vs Placebo	Olezarsen 80 mg N=832	P-value vs Placebo
Treatment-emergent adverse events					
Any	72	73	0.84	77	0.09
Leading to drug discontinuation	5	4	0.75	7	0.22
Serious	11	9	0.42	14	0.29
Leading to drug discontinuation	1	1	0.70	2	0.49
Injection Site Reaction	2	15	<0.001	16	<0.001
Mild	2	13	<0.001	15	<0.001
Moderate	<1	3	0.006	3	0.002
Severe	0	0	-	0	-

Treatment phase data in the safety cohort shown as %

- Limitace
  - Zařazeni pacienti s mírnou hypertriglyceridemií
  - Délka studie byla jenom jeden rok

ORIGINAL ARTICLE

Targeting *APOC3* with Olezarsen in Moderate Hypertriglyceridemia

Brian A. Bergmark, M.D.,[1,2] Nicholas A. Marston, M.D., M.P.H.,[1,2]
Thomas A. Prohaska, M.D., Ph.D.,[3] Veronica J. Alexander, Ph.D.,[3]
Andre Zimerman, M.D., Ph.D.,[1,4] Filipe A. Moura, M.D., Ph.D.,[1,5,6]
Yu Mi Kang, M.D., Ph.D.,[1,7] Julia Weinland, B.S.N.,[3] Sabina A. Murphy, M.P.H.,[1,2]
Erica L. Goodrich, M.S.,[1,2] Shuanglu Zhang, M.P.H.,[1,2] Dan Li, Ph.D.,[3]
Maciej Banach, M.D., Ph.D.,[8] Erik Stroes, M.D., Ph.D.,[9]
Michael T. Lu, M.D., M.P.H.,[2,10] Sotirios Tsimikas, M.D.,[3,11]
Robert P. Giugliano, M.D.,[1,2] and Marc S. Sabatine, M.D., M.P.H.,[1,2]
for the Essence–TIMI 73b Investigators*

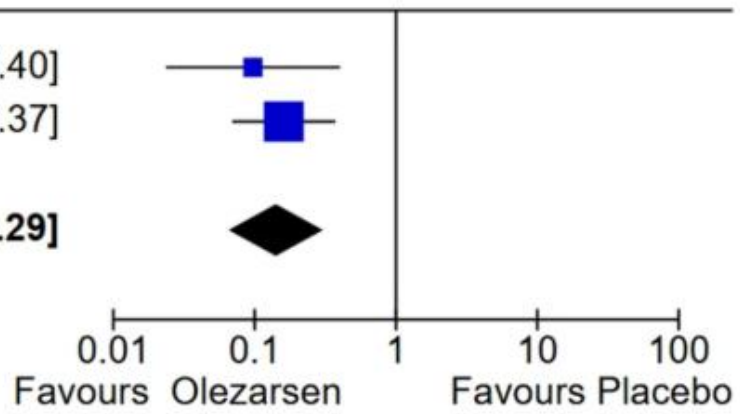
Olezarsen snižuje riziko akutní pankreatitidy

- Rehman, A., Rajdeep, D., Mohnkern, J.D. *et al.* Efficacy of Olezarsen in Severe Hypertriglyceridemia and Acute Pancreatitis Risk: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Dig Dis Sci* (2026). https://doi.org/10.1007/s10620-026-09846-1

Study or Subgroup	Olezarsen Events	Olezarsen Total	Placebo Events	Placebo Total	Weight	Risk ratio IV, Random, 95% CI
BALANCE 2024	2	43	11	23	26.0%	0.10 [0.02 , 0.40]
CORE-TIMI 2025(pooled)	7	705	22	356	74.0%	0.16 [0.07 , 0.37]
Total (Wald[a])		**748**		**379**	**100.0%**	**0.14 [0.07 , 0.29]**
Total events:	9		33			

Test for overall effect: Z = 5.31 (P < 0.00001)

Heterogeneity: Tau² (REML[b]) = 0.00; Chi² = 0.36, df = 1 (P = 0.55); I² = 0%



Reduced risk of pancreatitis in the Olezarsen group