

**Ezetimibe in Prevention of Cerebro- and
Cardiovascular Events in Middle- to High-Risk,
Elderly (75 Years Old or Over) Patients With
Elevated LDL-Cholesterol:
A Multicenter, Randomized, Controlled, Open-Label
Trial (EWTOPIA 75)**

Discussant

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SCIENTIFIC 20
SESSIONS 18

**Late-breaking clinical trials session
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Proportional reduction in major vascular/cardiovascular events in randomized trials of statins, ezetimibe, and PCSK9 monoclonal antibodies for the magnitude LDL-C reduction

EWTOPIA 75 mean age 81 y, 75% women

Ezetimibe vs usual care

LDL-C 1y 126 vs 144 mg/dl
(3.2 vs 3.72 mmol/L)

↓18 mg/dl (0.47 mmol/L) = ↓13%

MACE HR 0.66 (95% CI .50-.86)

MACE≈2%/y

CTT MVE RRR ↓22%/1 mmol/L

Expected RR 10%

MEGA mean age 58 y, 69% women

Pravastatin 10-20 (mean 8.3) mg vs usual care

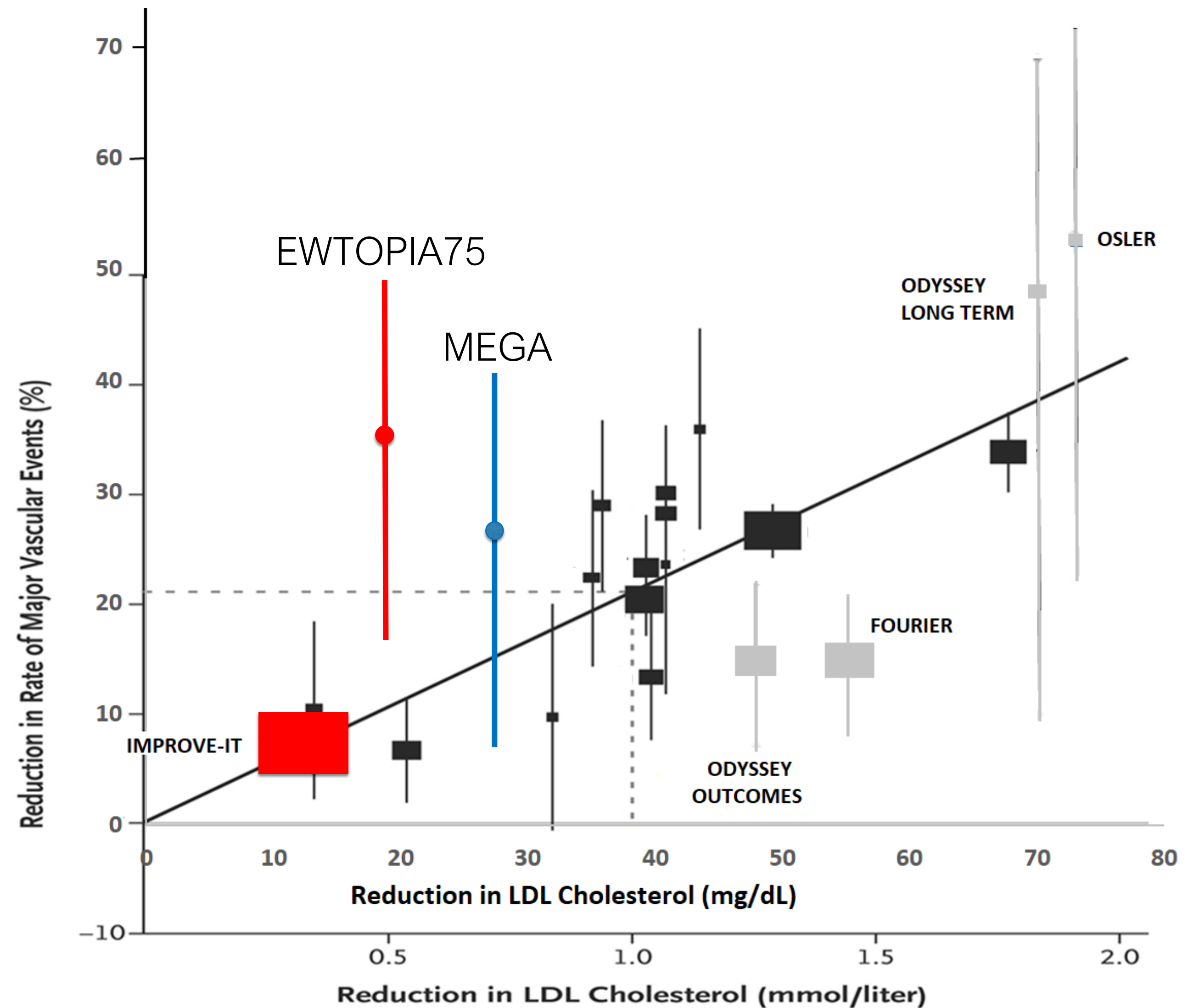
LDL-C 1 y 128 vs 154 mg/dl
(3.30 vs 3.97 mmol/L)

↓26 mg/dl (0.67 mmol/L)

CVE HR 0.74 (0.59-0.94)

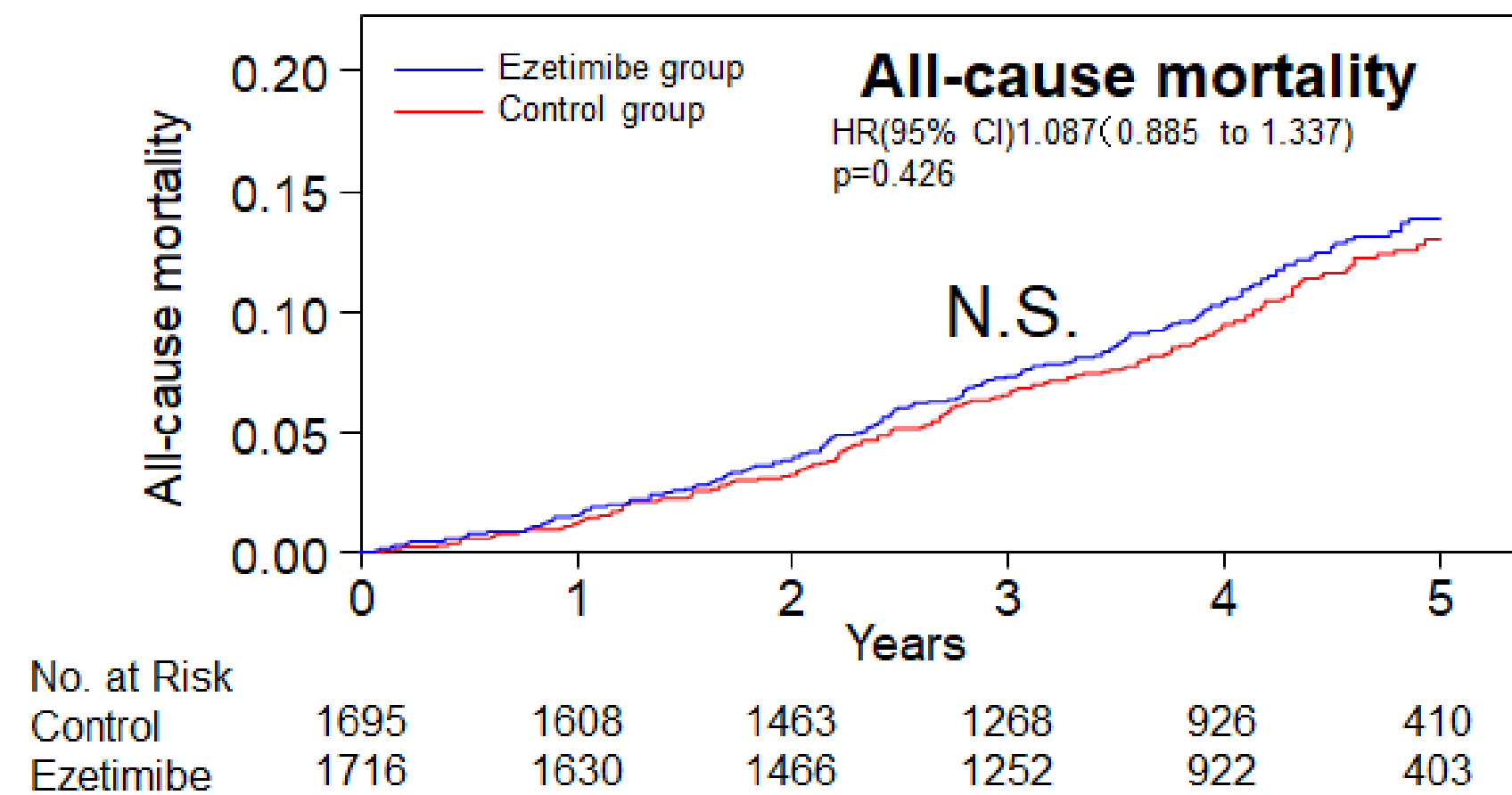
10-y ASCVD risk ≈ 5%

CTT Expected RR 15%

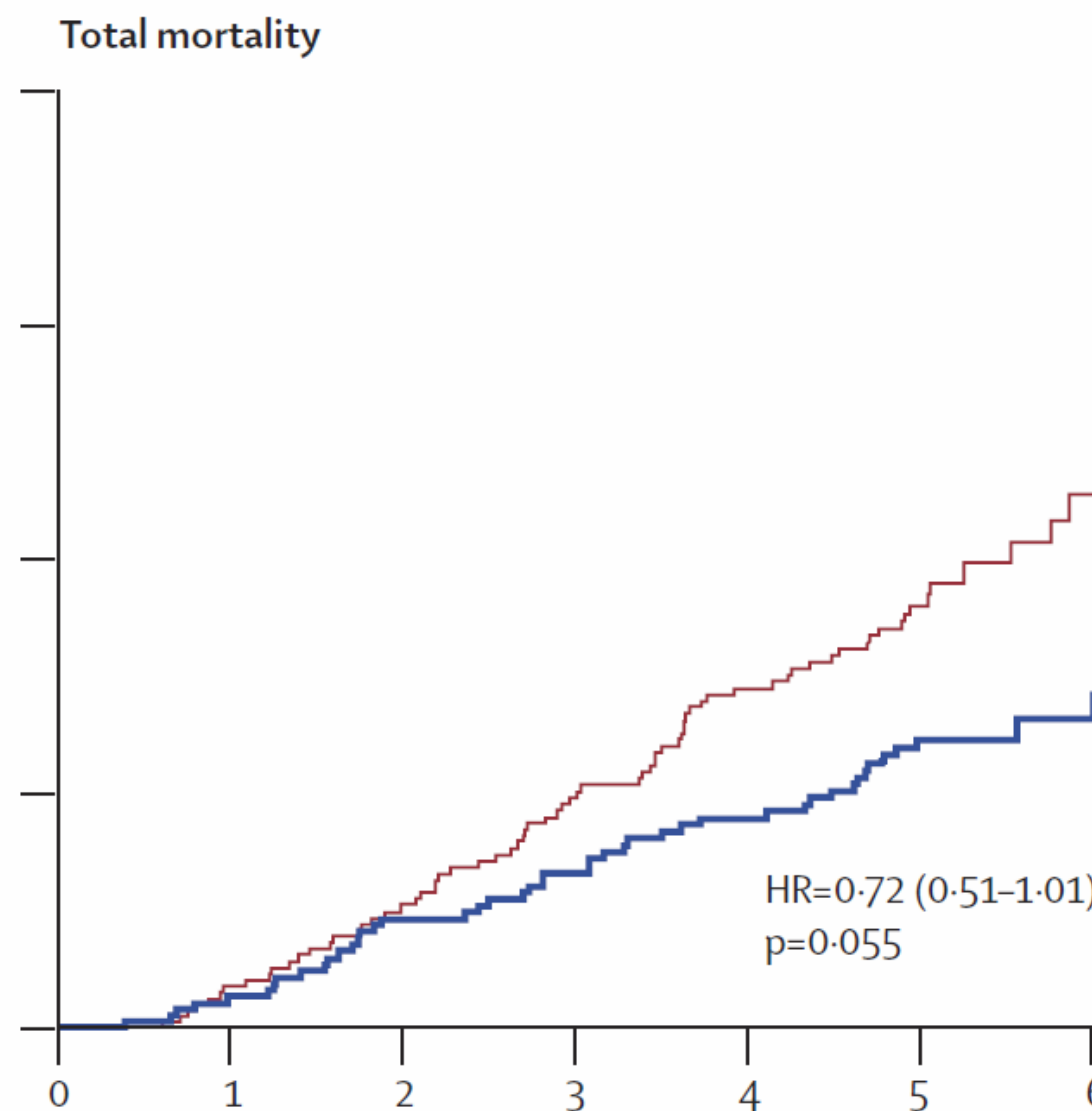


Total mortality in primary prevention RCTs

EWTOTPIA – Ezetimibe vs UC



MEGA – Pravastatin vs UC



JUPITER – Rosuvastatin 10 mg vs placebo

	Hazard ratio (HR) (95% CI)
70-97 y	0.80 (0.62-1.04) p=0.090
50-59 y	0.80 (0.60-1.04) P=0.10

Baseline CRP ≥ 2.0 mg/L
 LDL-C 1y 55 vs 110 mg/dl
 (1.42-2.85 mmol/L)
 \downarrow 55 mg/dl (1.43 mmol/L)
 ~7% 10-y ASCVD risk

Conclusions

- LDL-C lowering from ezetimibe in Japanese older adults without CVD
 - LDL-C ↓ efficacy about expected %, but greater than expected CVD reduction
 - Chance?
 - Open-label design?
 - Genetic? Japanese have different genetic polymorphisms NPC1L1
 - ? Different effect on plaque regression/stabilization
 - Japanese PRECISE-IVUS: LDL-C ↓ 10 mg/dl 9-12 months
 - PAV regression atorvastatin/ezetimibe 78% vs atorvastatin alone 58%
 - Older adults different?
- Statins may be more effective ↓ total mortality
- Need primary prevention LDL-C lowering trials in other populations aged ≥ 75 years
 - Ongoing STAREE NCT02099123 end 2022
 - Australia Age ≥ 70 y: N=18,000 Atorvastatin 40 mg vs placebo
 - USA NIH RFA-AG-19-020