ARTICLE PRESENTATION

PHASE 2B RANDOMIZED TRIAL OF THE ORAL PCSK9 INHIBITOR MK-0616

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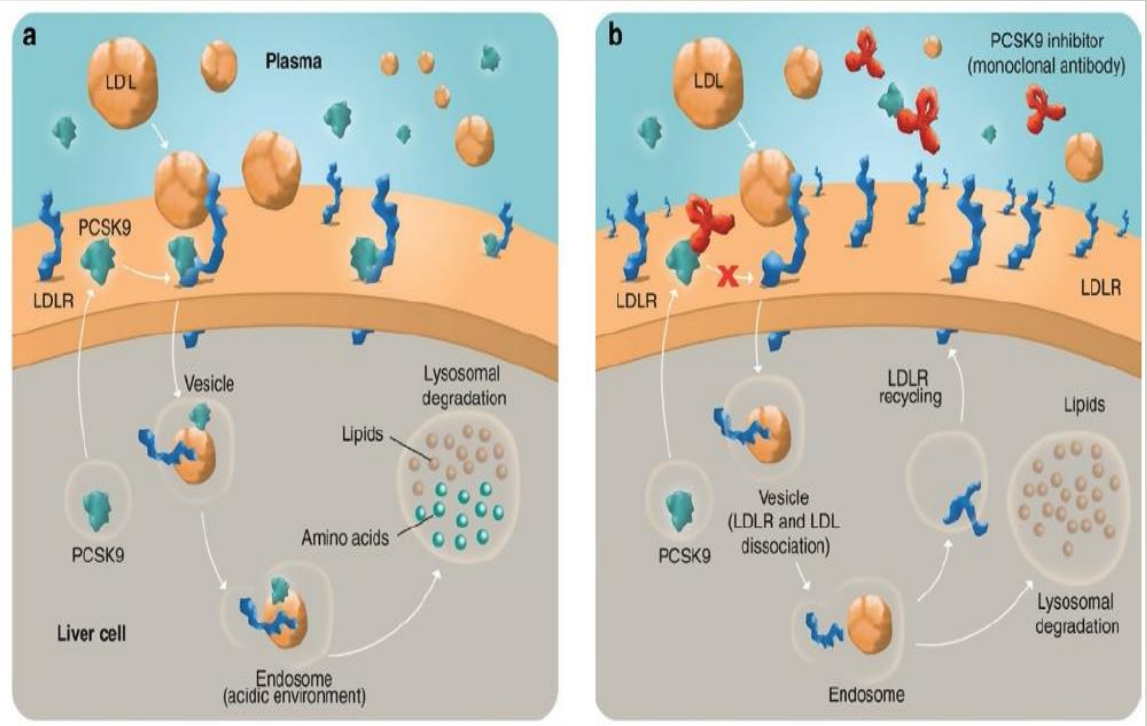
PURPOSE

- Phase 2b, randomized, double-blind, placebo-controlled, multicenter trial
- Goal: Evaluate LDL-C lowering and safety of MK-0616 in a diverse population of participants with hypercholesterolemia and a broad range of cardiovascular risk.

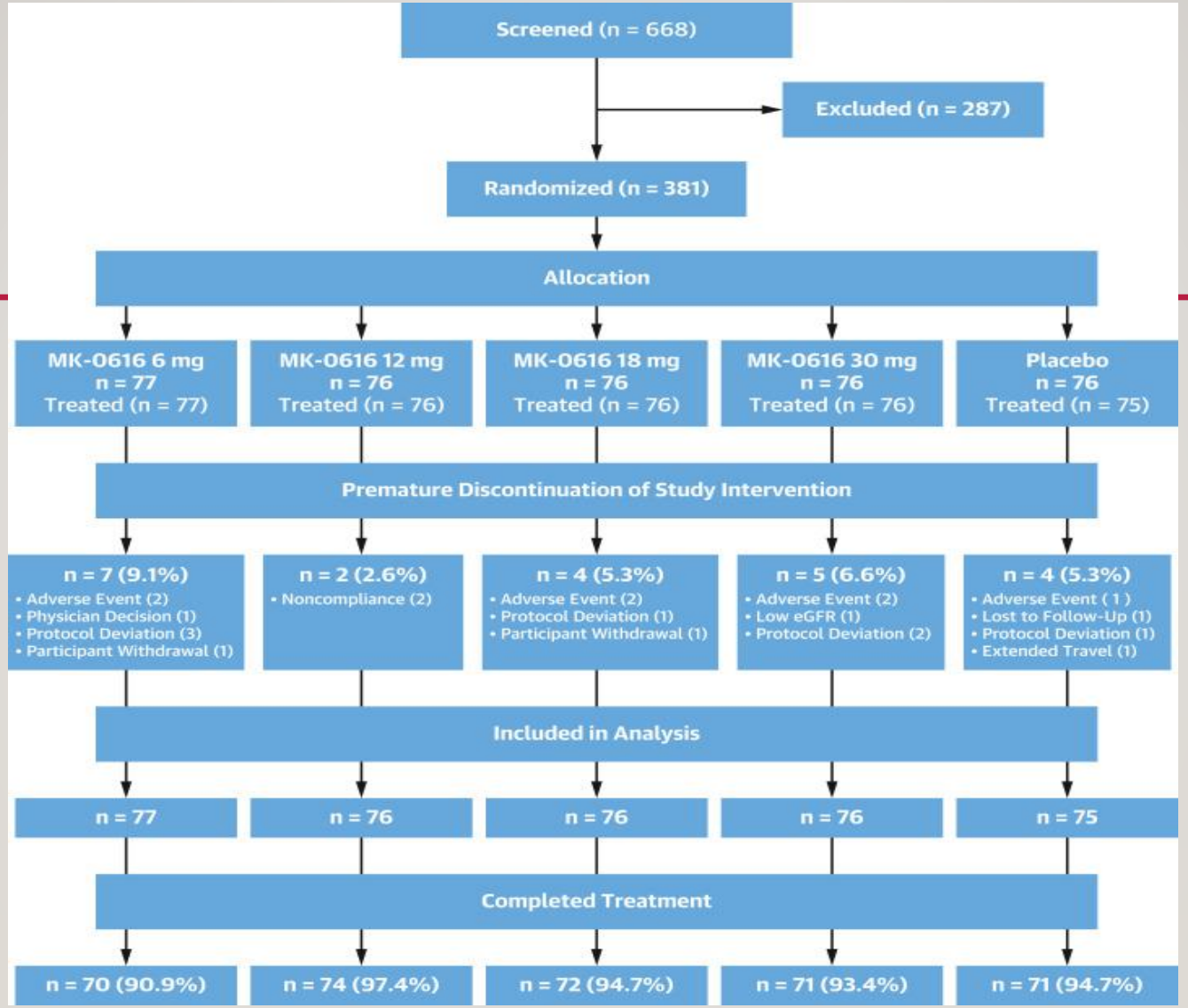
PCSK9 INHIBITOR

- MK-0616 is an oral macrocyclic peptide inhibitor of proprotein convertase subtilisin/kexin type 9 (PCSK9)
- Renally excreated



METHODS

- 375 adult participants
- Wide Range of Atherosclerotic Cardiovascular Disease Risk
- Randomly assigned 1:1:1:1 ratio of MK-0616 (6,12,18, or 30mg once daily) OR matching placebo
- Participants were monitored for 8 weeks for adverse events
- Endpoints: Percent change from baseline LDL-C at Week 8, Proportion of participants with adverse events and study intervention discontinuations due to adverse events

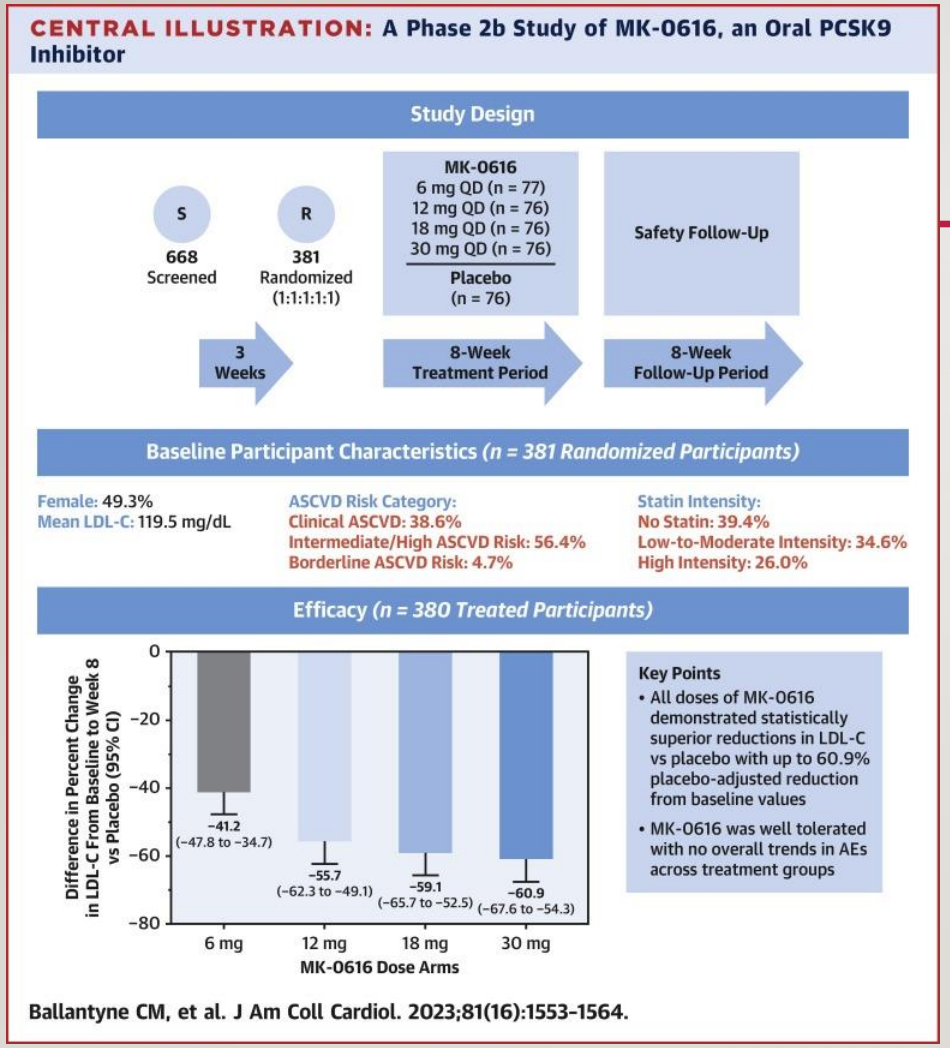

Screened (n = 668)
Excluded (n = 287)
Randomized (n = 381)
Allocation
MK-0616 6 mg
n = 77
Treated (n = 77)
MK-0616 12 mg
n = 76
Treated (n = 76)
MK-0616 18 mg
n = 76
Treated (n = 76)
MK-0616 30 mg
n = 76
Treated (n = 76)
Placebo
n = 76
Treated (n = 75)
Premature Discontinuation of Study Intervention
n = 7 (9.1%)
• Adverse Event (2)
• Physician Decision (1)
• Protocol Deviation (3)
• Participant Withdrawal (1)
n = 2 (2.6%)
• Noncompliance (2)
n = 4 (5.3%)
• Adverse Event (2)
• Protocol Deviation (1)
• Participant Withdrawal (1)
n = 5 (6.6%)
• Adverse Event (2)
• Low eGFR (1)
• Protocol Deviation (2)
n = 4 (5.3%)
• Adverse Event (1)
• Lost to Follow-Up (1)
• Protocol Deviation (1)
• Extended Travel (1)
Included in Analysis
n = 77
n = 76
n = 76
n = 76
n = 75
Completed Treatment
n = 70 (90.9%)
n = 74 (97.4%)
n = 72 (94.7%)
n = 71 (93.4%)
n = 71 (94.7%)

INCLUSION

- Both Genders. 51% men
- Ages ≥18 years and ≤80 years (average age 62) with one of the following risk categories with corresponding fasted LDL value:
- 1)Clinical ASCVD: LDL-C range = ≥70 and ≤160
- 2)Borderline risk for ASCVD: participants without clinical ASCVD with a 10-year risk of having an ASCVD event that is ≥5.0% and <7.5%; LDL-C range = ≥130 and ≤250
- 3)Intermediate or higher risk for ASCVD: participants without clinical ASCVD with a 10-year risk of having an ASCVD event that is ≥7.5% and/or an ASCVD-risk equivalent (eg, diabetes mellitus or heterozygous familial hypercholesterolemia); LDL-C range = ≥100 and ≤200 mg/dL (≥2.59 and ≤5.18 mmol/L); and
- Participants were also either on a stable dose of 1 or more lipid-lowering therapies for ≥30 days before the screening visit or had not received treatment with any lipid-lowering therapy for ≥30 days before the screening visit.

EXCLUSION

- At the screening visit, patients who had the following diagnosis:
- homozygous familial hypercholesterolemia
- unstable angina
- myocardial infarction
- transient ischemic attack
- Stroke
- a fasting triglyceride value ≥400
- A1c >9
- PCI within 3 months of the study or a planned PCI up to 3 months after the screening visit
- History of malignancy
- Nephrotic Syndrome
- Pregnant or breastfeeding females, or if they did not agree to abstain from heterosexual activity or use appropriate contraceptives
- Previous PCSK9 inhibitor use without adequate washout (6 months for monoclonal antibody or 1 year for a small interfering RNA PCSK9 inhibitor



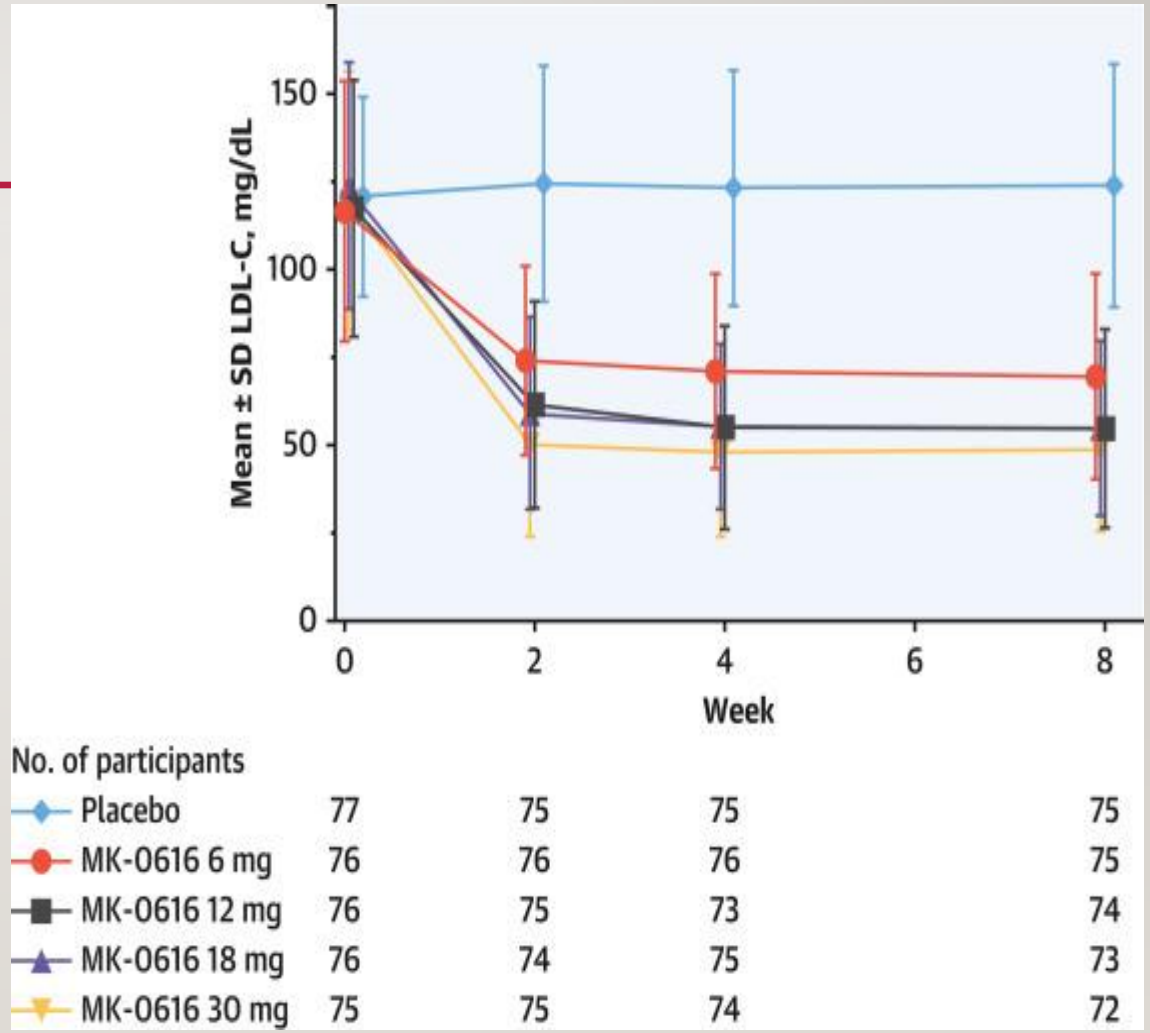
- Screening to Day 1: an up-to-21-day screening period
- Visit 2/Day 1 through Visit 5/Week 8: an 8-week treatment
- Follow up: Visit 5/Week 8 through Visit 7/Week 16:

an 8-week post-treatment follow-up period

RESULTS

- All doses of MK doses were demonstrated to statistically significant (P<0.001)
- Mean percentage change from baseline LDL-C at Week 8
  - -41.2% (6mg)
  - -55.7% (12mg)
  - -59.1% (18mg)
  - -60.9% (30mg)
  - Adverse events occurred in a similar proportion in the MK-0616 (39.5% - 43.4%) as placebo (44%). Discontinuations due to AEs occurred in 2 or fewer participants in either group

	MK-0616 6 mg QD	MK-0616 12 mg QD	MK-0616 18 mg QD	MK-0616 30 mg QD	Placebo
Primary endpoint					
LDL-C					
Participants evaluated	77	76	76	76	75
Baseline LDL, mg/dL	116.5 ± 37.0	117.3 ± 36.4	123.7 ± 35.1	119.4 ± 36.7	121.3 ± 28.0
Week 8 LDL, mg/dL	69.6 ± 29.2	54.9 ± 28.2	55.0 ± 24.9	48.8 ± 23.3	124.0 ± 34.6
LS mean percentage change from baseline (95% CI) in LDL-C at Week 8	−40.0 (−45.2 to −34.8)	−54.5 (−59.8 to −49.2)	−57.9 (−63.2 to −52.6)	−59.7 (−65.0 to −54.5)	1.2 (−4.1 to 6.5)
Difference in LS means vs placebo (95% CI)	−41.2 (−47.8 to −34.7)[a]	−55.7 (−62.3 to −49.1)[a]	−59.1 (−65.7 to −52.5)[a]	−60.9 (−67.6 to −54.3)[a]	—



CONCLUSIONS/LIMITATIONS

- MK-0616 showed statistically significant, dose-dependent reduction in LDL-C at Week 8 up to 60.9% from baseline and was well tolerated during 8 weeks of treatment and an additional 8 weeks of follow-up
- . Larger studies of longer duration will be needed to appropriately assess the efficacy, durability, and safety of MK-0616 in various subgroups in the context of available treatments

QUESTIONS

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