

**Discussant:
Lipid-Modulating Effects of
Evacetrapib,
a Novel CETP Inhibitor**

**AHA Scientific Sessions
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**Daniel J. Rader, MD
University of Pennsylvania**

Disclosure of Financial Relationships

Daniel J Rader, MD

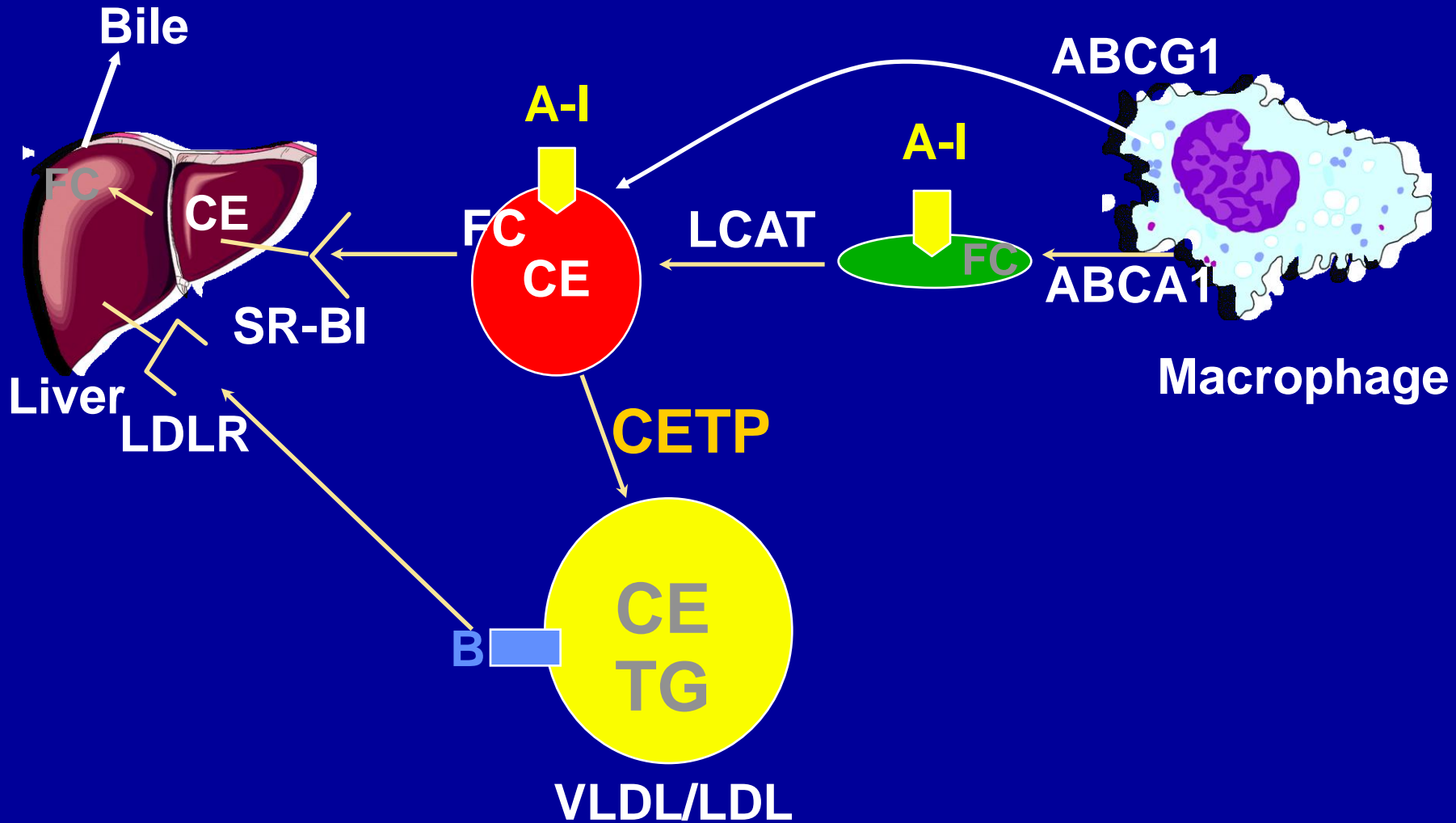
Consulting: AstraZeneca, Bristol-Myers Squibb, CSL Behring, Eli Lilly, Esperion, Johnson and Johnson, Pfizer, Merck, Novartis, Omthera, Sanofi-Aventis

Equity: Aegerion, VascularStrategies

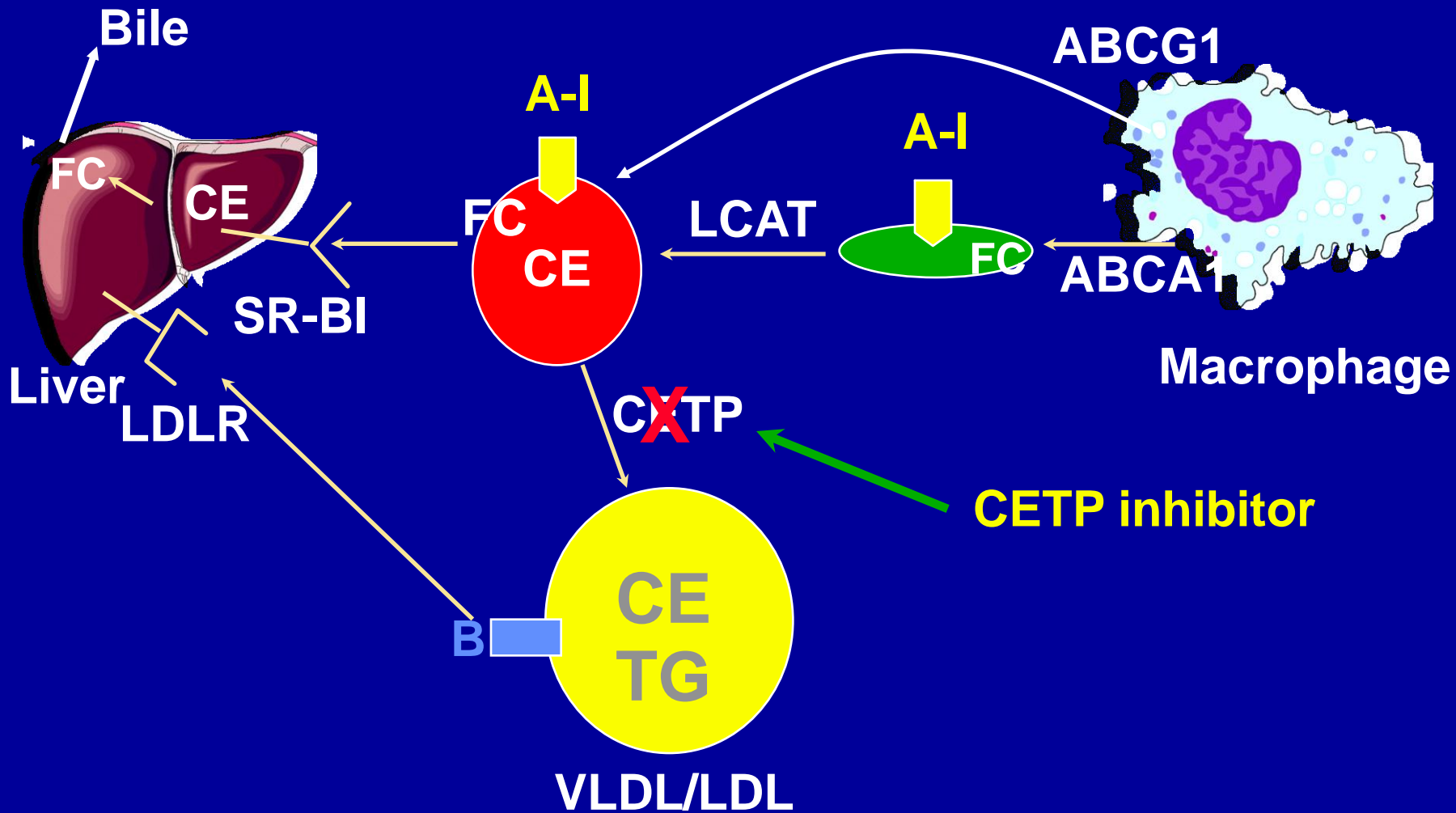
Lipoproteins and Atherosclerosis



Reverse Cholesterol Transport



CETP Inhibition as a Novel Strategy to Raise HDL Cholesterol



Lipid efficacy of CETP inhibitors (% change from baseline)

CETP inhibitor	Dose mg/d	HDL-C %	LDL-C %	TG %
Torcetrapib	60	61	-24	-9
Dalcetrapib	600	31	-2	-3
Anacetrapib	100	138	-40	-7

Adapted from Cannon C, JAMA 306:2154; 2011

Evacetrapib

1. No major adverse safety signals
2. Dose-dependent HDL increase and LDL reduction as monotherapy and in addition to statin

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Torcetrapib	60	61	-24	-9
Dalcetrapib	600	31	-2	-3
Anacetrapib	100	138	-40	-7
Evacetrapib	500	129	-36	-17

Adapted from Cannon C, JAMA 306:2154; 2011

CETP inhibitor outcome trials

CETPi	Dalcetrapib	Anacetrapib
Outcome Trial	dal-OUTCOMES	REVEAL
Dose	600 mg QD	100 mg QD
Trial Enrollment	15,600	30,000
Patient population	Acute coronary syndrome 4-12 weeks post index event	<ul style="list-style-type: none">• Stable CAD• History of ischemic stroke• PAD
Entry lipid criteria	<ul style="list-style-type: none">• LDL < 100 mg/dL• HDL any	<ul style="list-style-type: none">• LDL < 100 mg/dL• HDL any
Primary endpoint	<ul style="list-style-type: none">• Coronary death• Non-fatal MI• Hospitalization for UA• Ischemic stroke	<ul style="list-style-type: none">• Coronary death• Non-fatal MI• Coronary revasc.

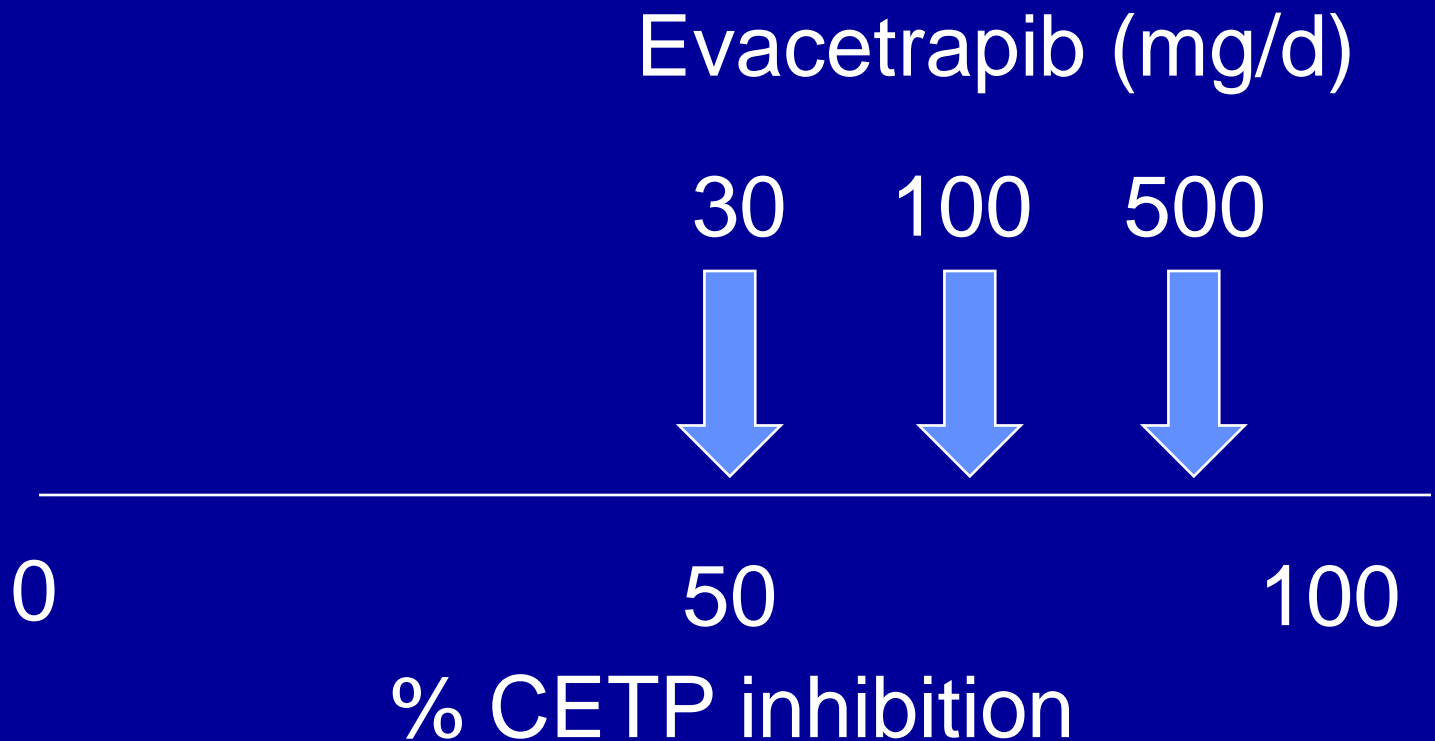
CETP inhibition and cardiovascular risk reduction

1. Optimal degree of CETP inhibition?

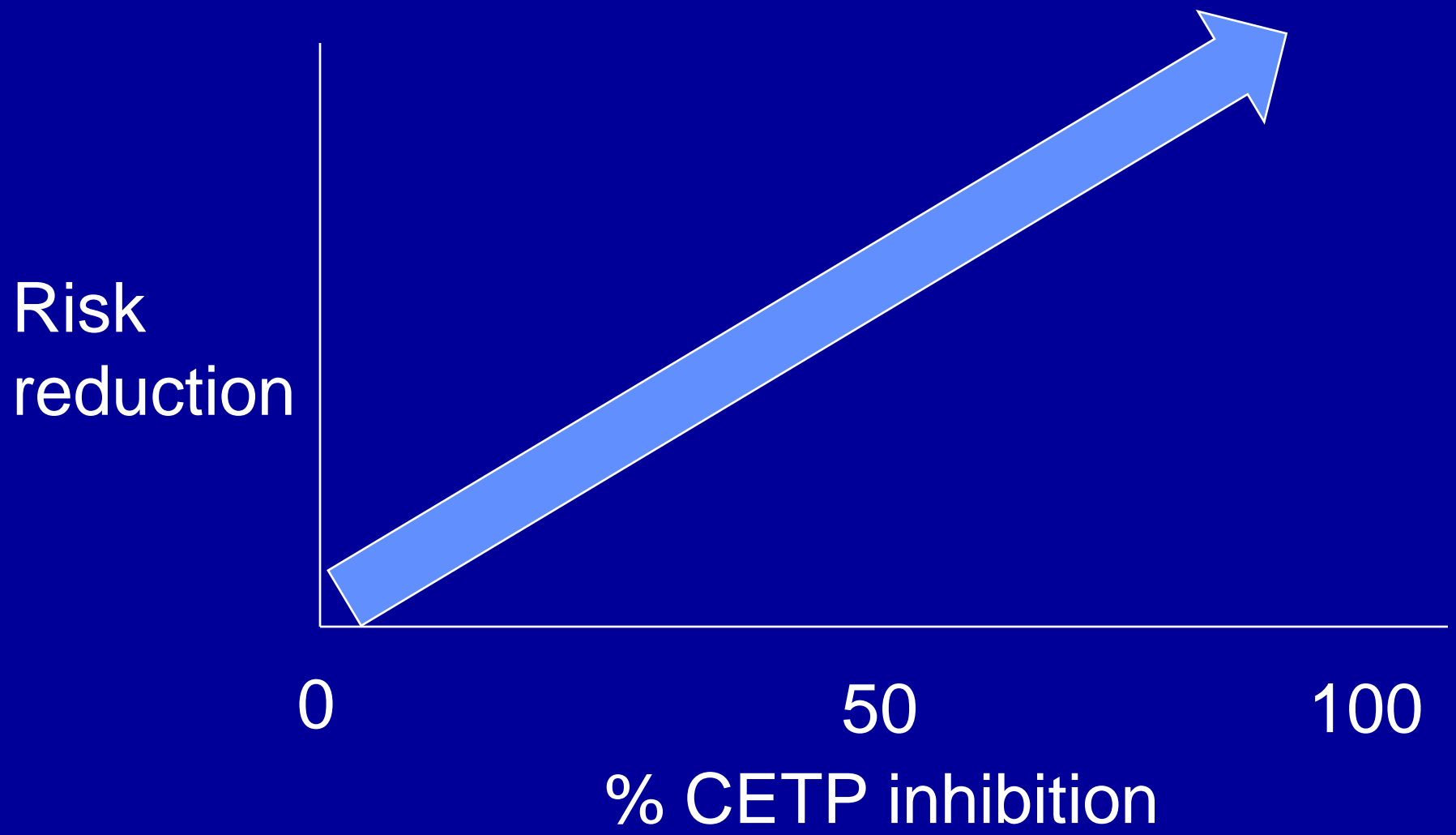
Degree of CETP inhibition



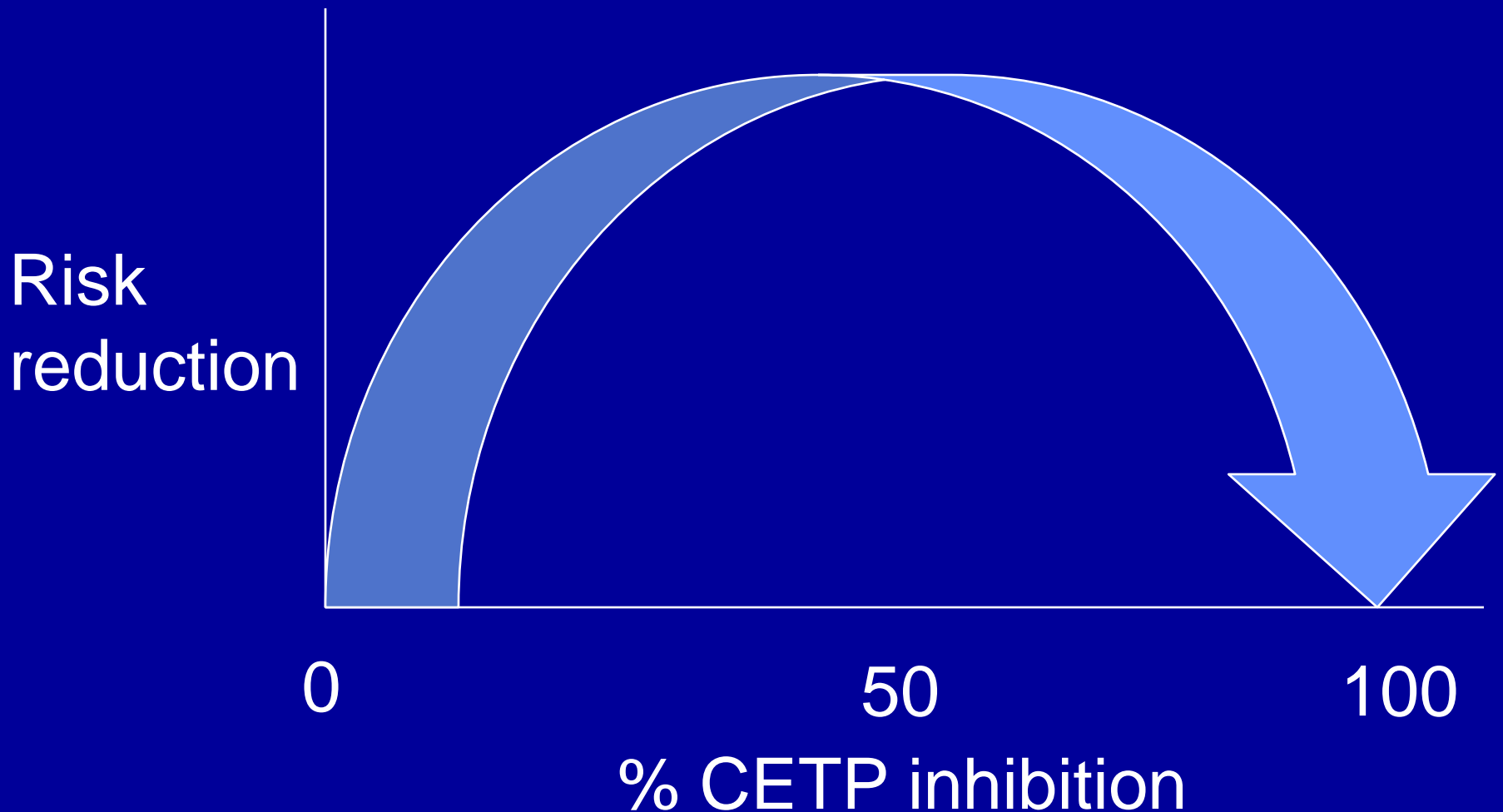
Degree of CETP inhibition: Evacetrapib



Relationship of CETP inhibition to relative risk reduction?



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CETP inhibition and cardiovascular risk reduction

1. Optimal degree of CETP inhibition?
2. Individuals most likely to benefit?

CETP inhibitor outcome trials

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CETP inhibition and cardiovascular risk reduction

One of the great experiments currently being carried out in medicine.