Statin differences
- Are they all the same?

서울의대 보라매병원 내과

김 상 현

LDL Cholesterol Goals and Cutpoints (2004)

Risk Category	LDL Goal (mg/dL)	LDL (mg/dL) - Therapeutic Lifestyle Changes (TLC)	LDL (mg/dL) - Drug Therapy
• CHD or CHD Risk Equivalents (10-year risk > 20 %)	<100 Optional < 70*	≥100	≥100 (<100 : drug optional)
• 2+ Risk Factors (10-year risk 10–20 %)	<130 Optional <100*	≥130	≥130 (100–129 : drug optional)
• 2+ Risk Factors (10-year risk <10 %)	<130	≥130	≥160
• 0–1 Risk Factor	<160	≥160	≥190 (160–189 : drug optional)

Primary target : LDL-lowering

reduction in total mortality, CHD mortality, major coronary events, coronary procedures (PTCA/CABG), and stroke

Secondary target : Metabolic syndrome
Non-HDL cholesterol

HMG CoA Reductase Inhibitors - Statins

Drug	Dose Range
Lovastatin	20–80 mg
Pravastatin	20–40 mg
Simvastatin	20–80 mg
Fluvastatin	20–80 mg
Atorvastatin	10–80 mg
Rosuvastatin	10–80 mg
Pitavastatin	1– 4 mg

Cerivastatin

Major actions on lipid profiles

↓	LDL-C	18 – 55 %
↑	HDL-C	5 – 15 %
↓	TG	7 – 30 %

Mechanism

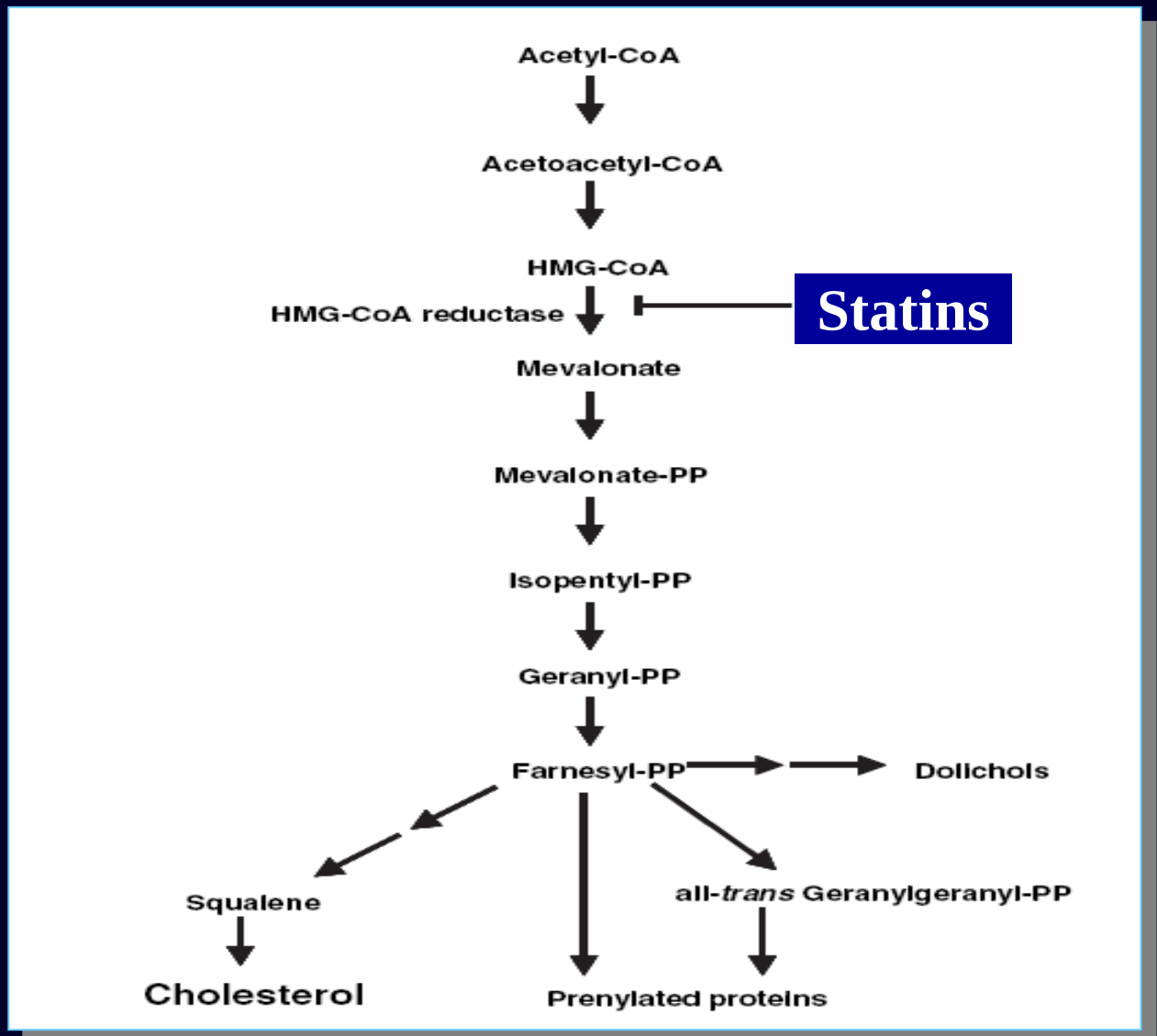
- Inhibition of HMG CoA reductase
  (rate-limiting step in cholesterol biosynthesis)

→ Increased LDL-receptor expression and activity

→ Enhanced removal of lipoprotein by LDL-receptor

- Reduced hepatic release of lipoprotein into the blood circulation
- Inhibition of lipoprotein assembly

Mammalian mevalonate pathway

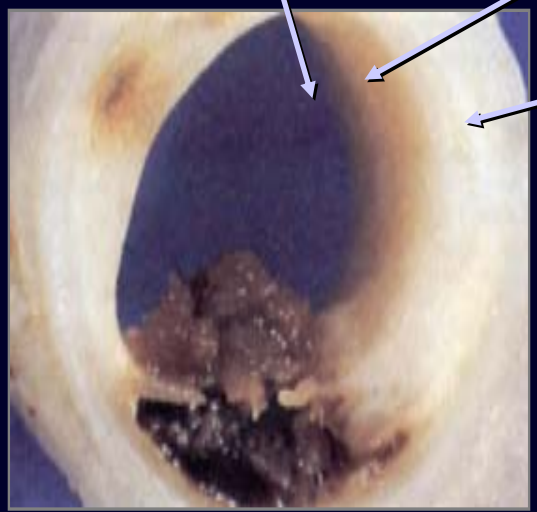


Potential Mechanisms of Benefit

statin

LDL Reduction

Reduction in lipoprotein remnants



- Decreased Thrombosis
- Restored Endothelial Function
- Maintained Smooth Muscle Cell Function
- Effects on fibrinogen
- Antioxidation
- Anti-inflammatory effects

Indications

most effective drugs in hypercholesterolemia

familial hypercholesterolemia

polygenic hypercholesterolemia

Combined hyperlipidemia

Hyperlipidemia of diabetes and renal failure

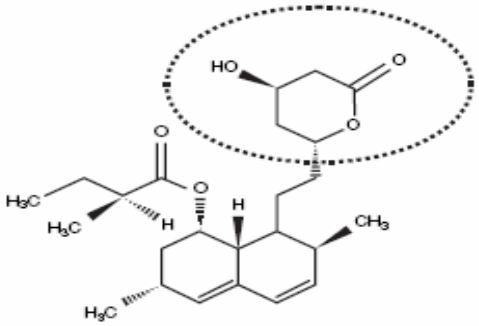
Contraindications

Active or chronic liver disease

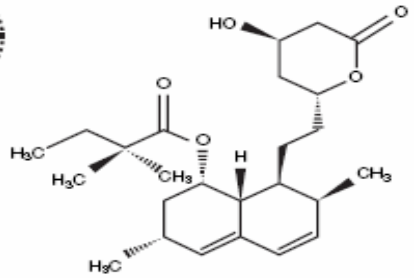
Concomitant use of certain drugs (relative)

: cyclosporine, macrolide antibiotics, antifungal agents, cytochrome P-450 inhibitors

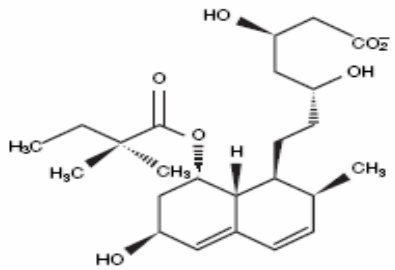
HMG-CoA analogue



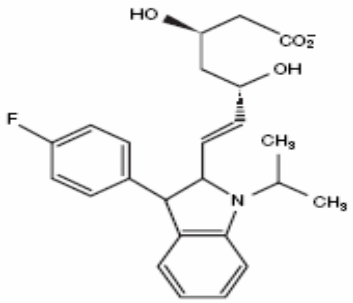
Lovastatin



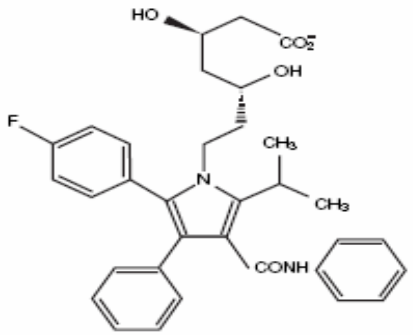
Simvastatin



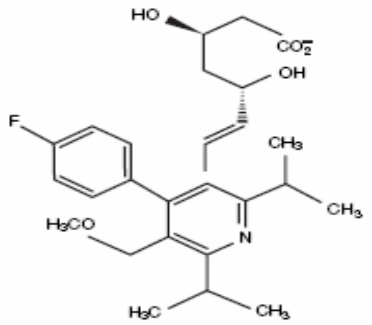
Pravastatin



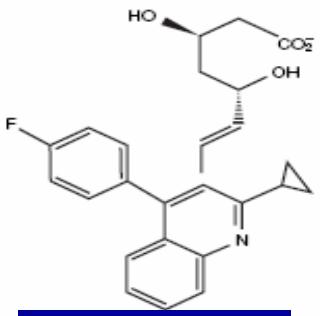
Fluvastatin



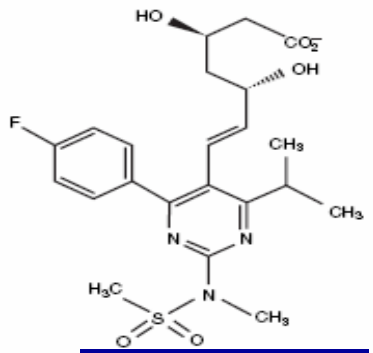
Atorvastatin



Cerivastatin

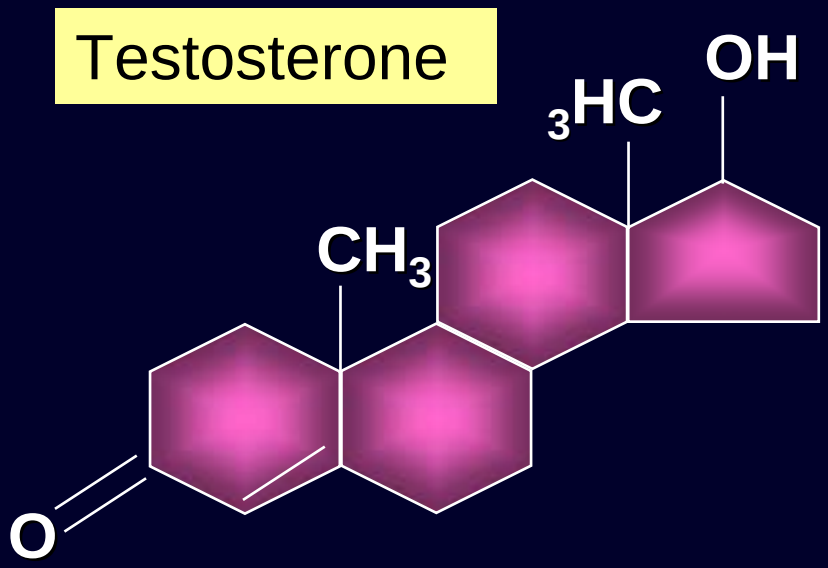


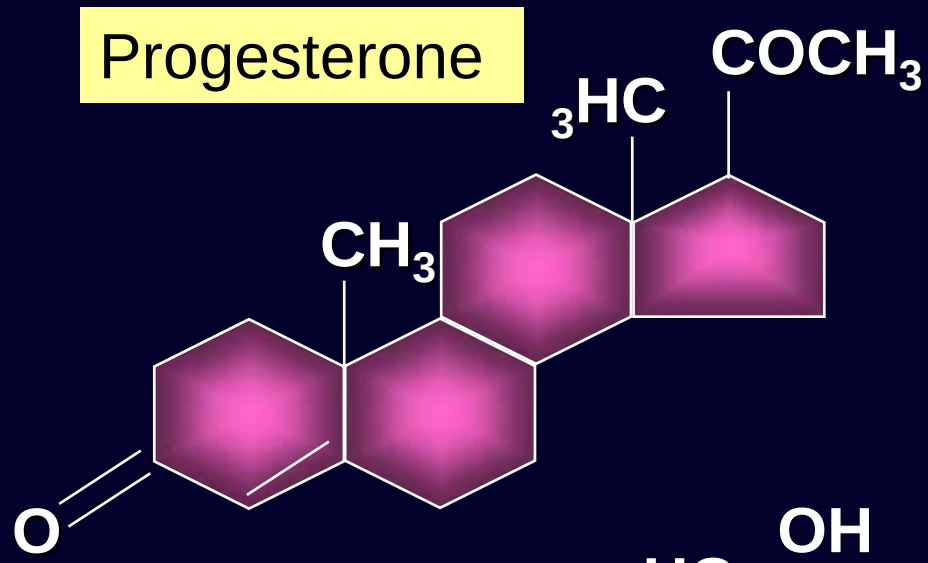
Pitavastatin

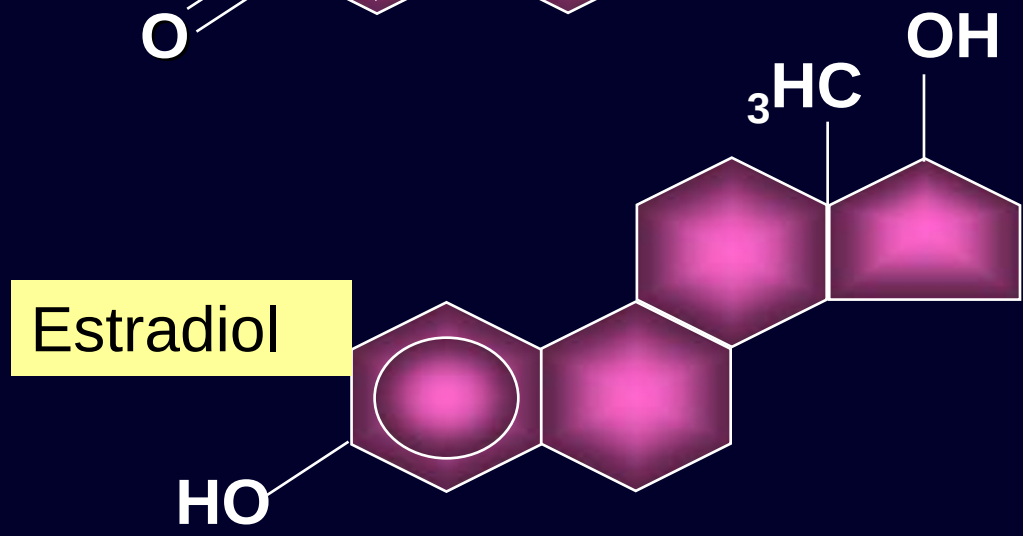


Rosuvastatin

Sometimes, Small Differences Can Have Profound Effects







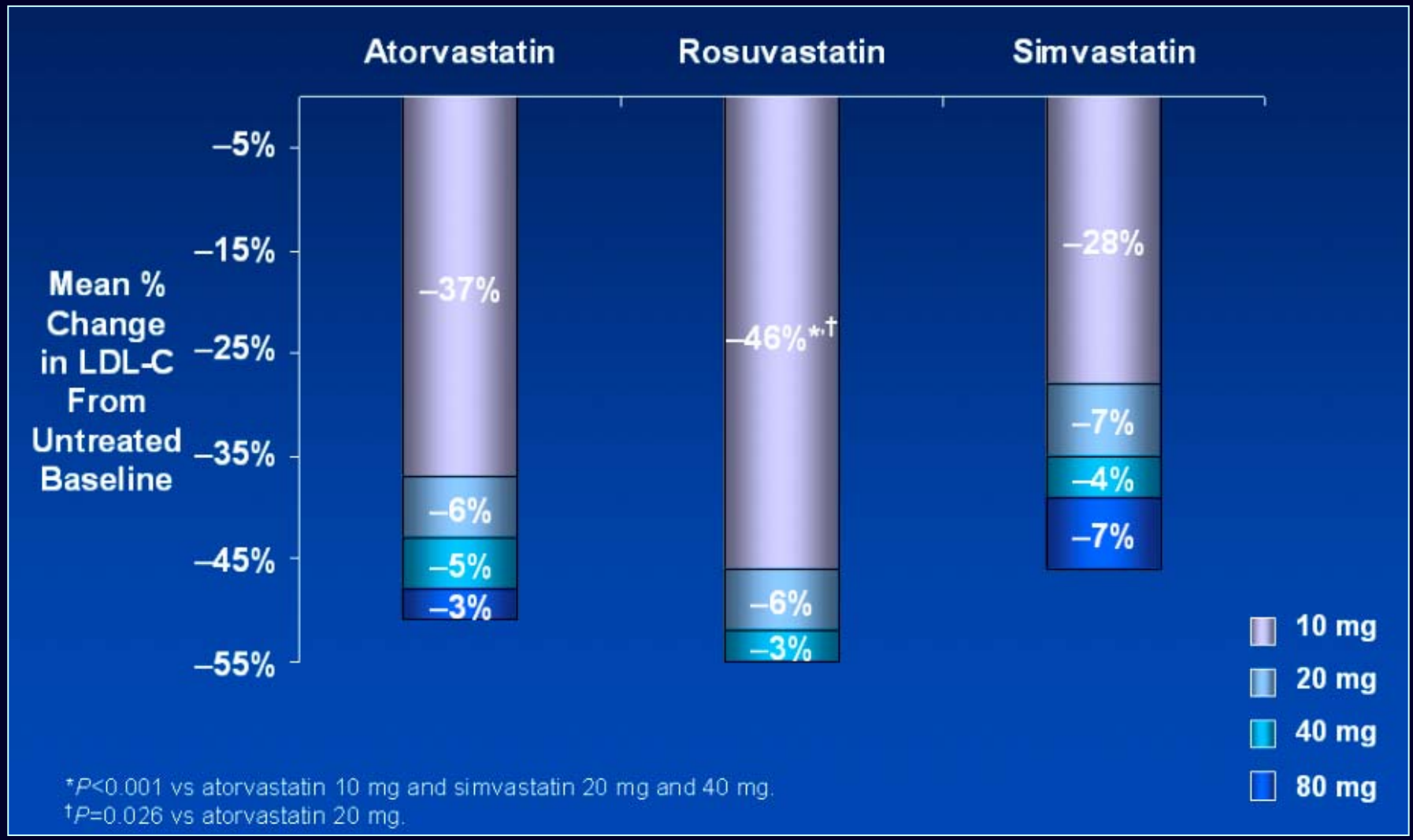
Statins - equivalent doses

Statin Drug, mg						Change in Lipid and Lipoprotein Levels			
AVS	SVS	LVS	PVS	FVS	CVS	Total	LDL	HDL	TG
....	10	20	20	40	0.2	-22%	-27%	4-8%	-10-15%
10	20	40	40	80	0.4	-27%	-34%	4-8%	-10-20%
20	40	80	80	….	….	-32%	-41%	4-8%	-15-25%
40	80	….	....	….	....	-37%	-48%	4-8%	-20-30%
80	….	….	....	….	....	-42%	-55%	4-8%	-25-35%

AVS : Atorvastatin, SVS : Simvastatin, LVS : Lovastatin,
PVS : Pravastatin, FVS : Fluvastatin, CVS : Cerivastatin

Maron DJ et al. Circulation 2000;101:207-213

STELLAR Trial

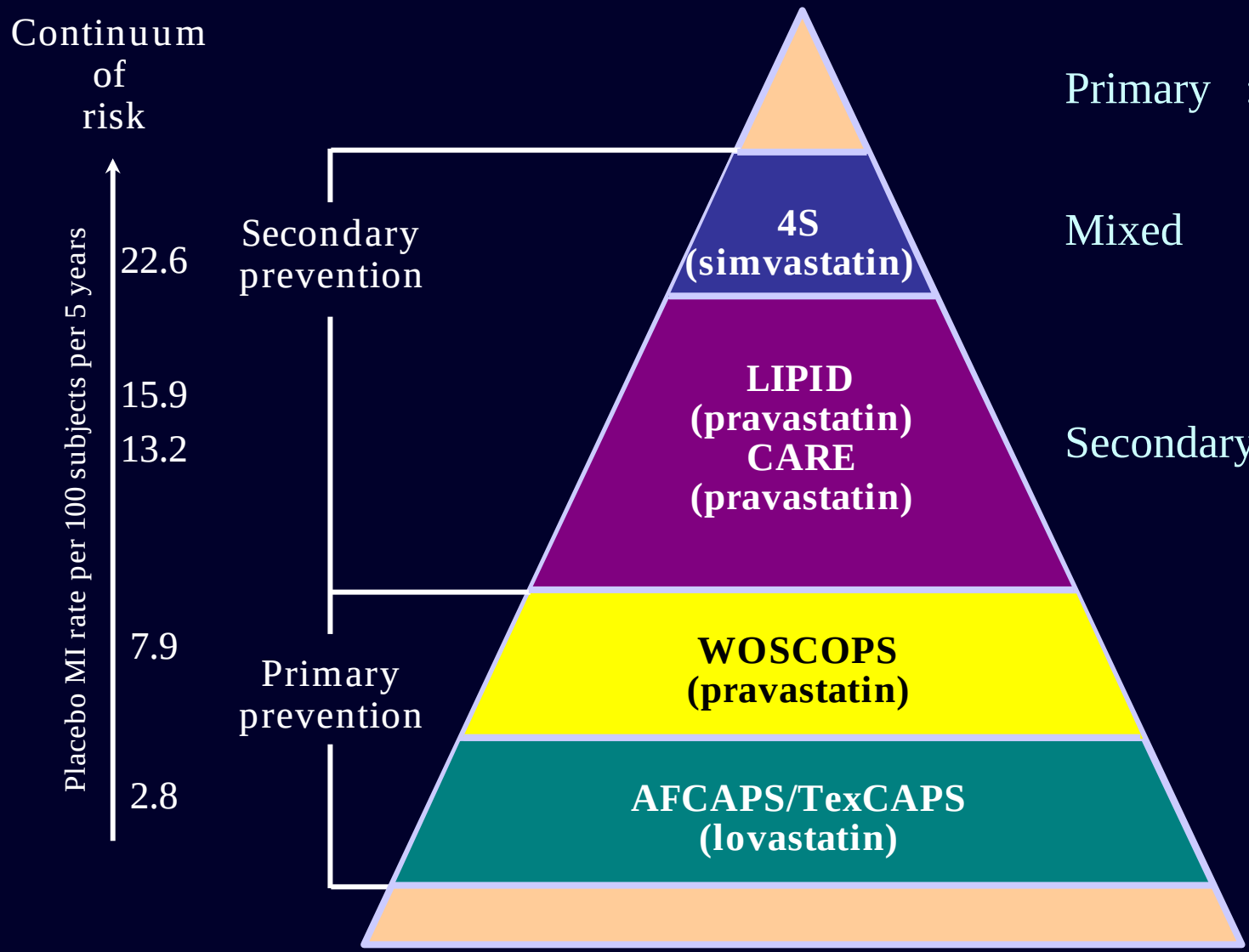


Jones PH et al. Am J Cardiol 2003;92(2):152-160

Comparative efficacy of Statins

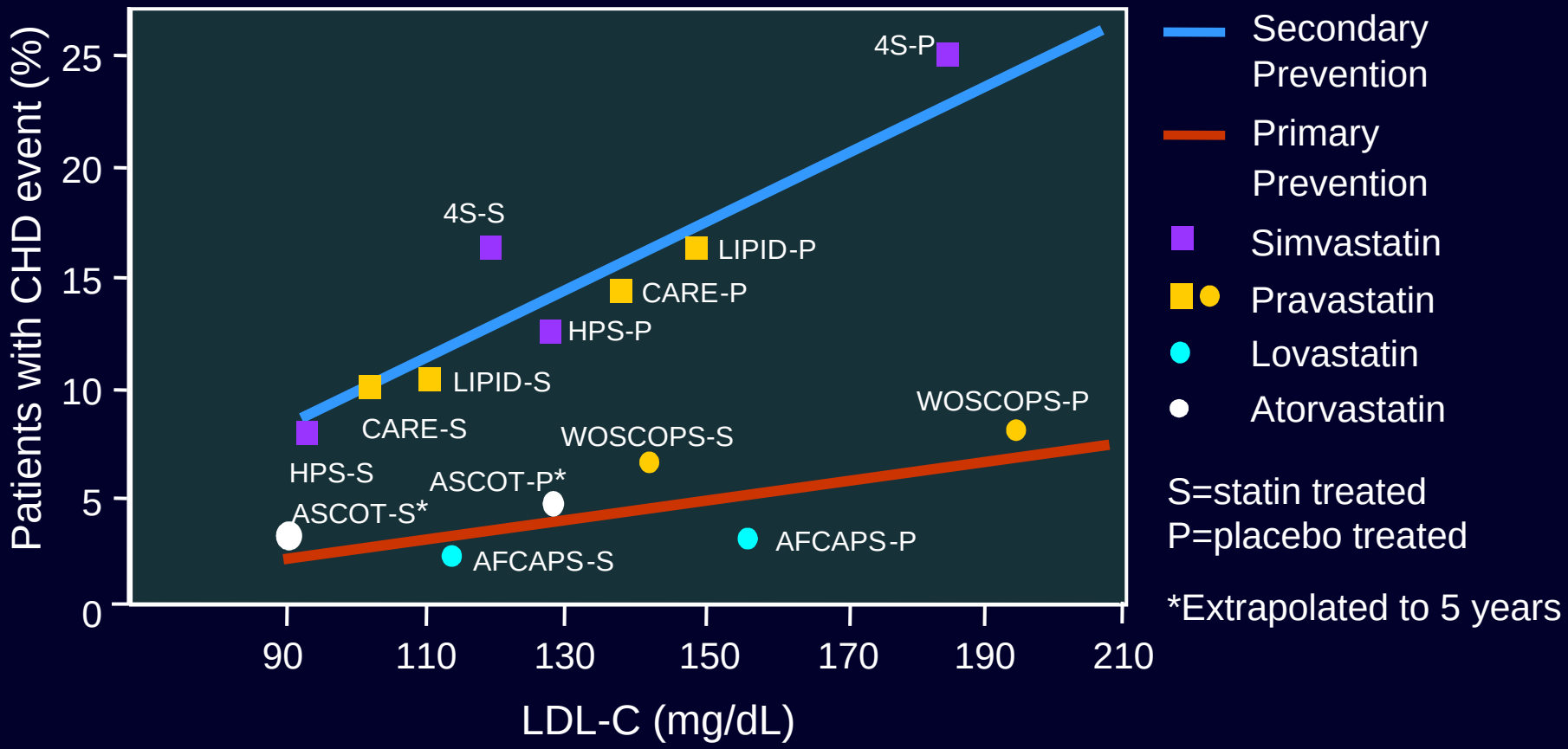
(%)	LDL-C ↓	HDL-C ↑	TG ↓
Rosuvastatin	-63	10	-28
Atorvastatin	-50	6	-29
Simvastatin	-41	12	-18
Pravastatin	-34	12	-8
Lovastatin	-34	9	-16
Fluvastatin	-24	8	-10
Cerivastatin	-28	10	-13
Pitavastatin	-48	-	-23

Relevance to Clinical Practice



Primary : ASCOT-LLA
CARDS
Mixed : HPS
PROSPER
ALLHAT-LLT
Secondary : PROVE-IT

Effects of lipid-lowering therapy on CHD events in statin trials



Modified from Kastelein JJP. *Atherosclerosis.* 1999;143(Suppl 1): S17-S21.

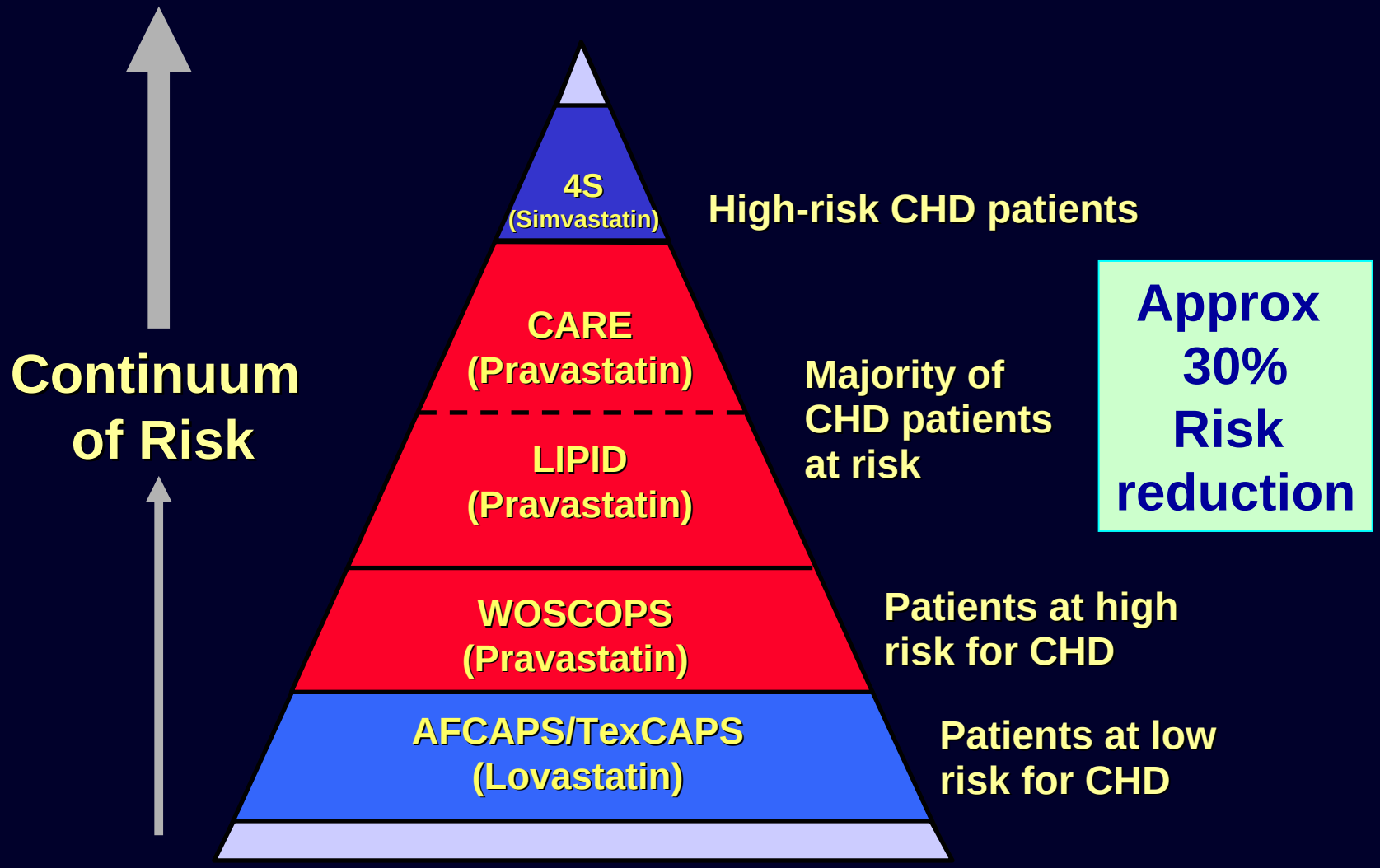
Primary Prevention Trials

Study	Persons	Duration	Statin Drug (dose/d)	Baseline LDL-C (mg/dL)	LDL-C Change	Major Coronary Events	Revascu-larization	Coronary Mortality	Total Mortality
WOSCOPS	6595 M/F (100/0)	4.9yrs	**Pravastatin** 40 mg	192	-26%	-31%	-37%	-33%	-22%
AFCAPS/ TexCAPS	6605 M/F (85/15)	5yrs	**Lovastatin** 20/40mg	150	-25%	-37%	-33%	NS	NS

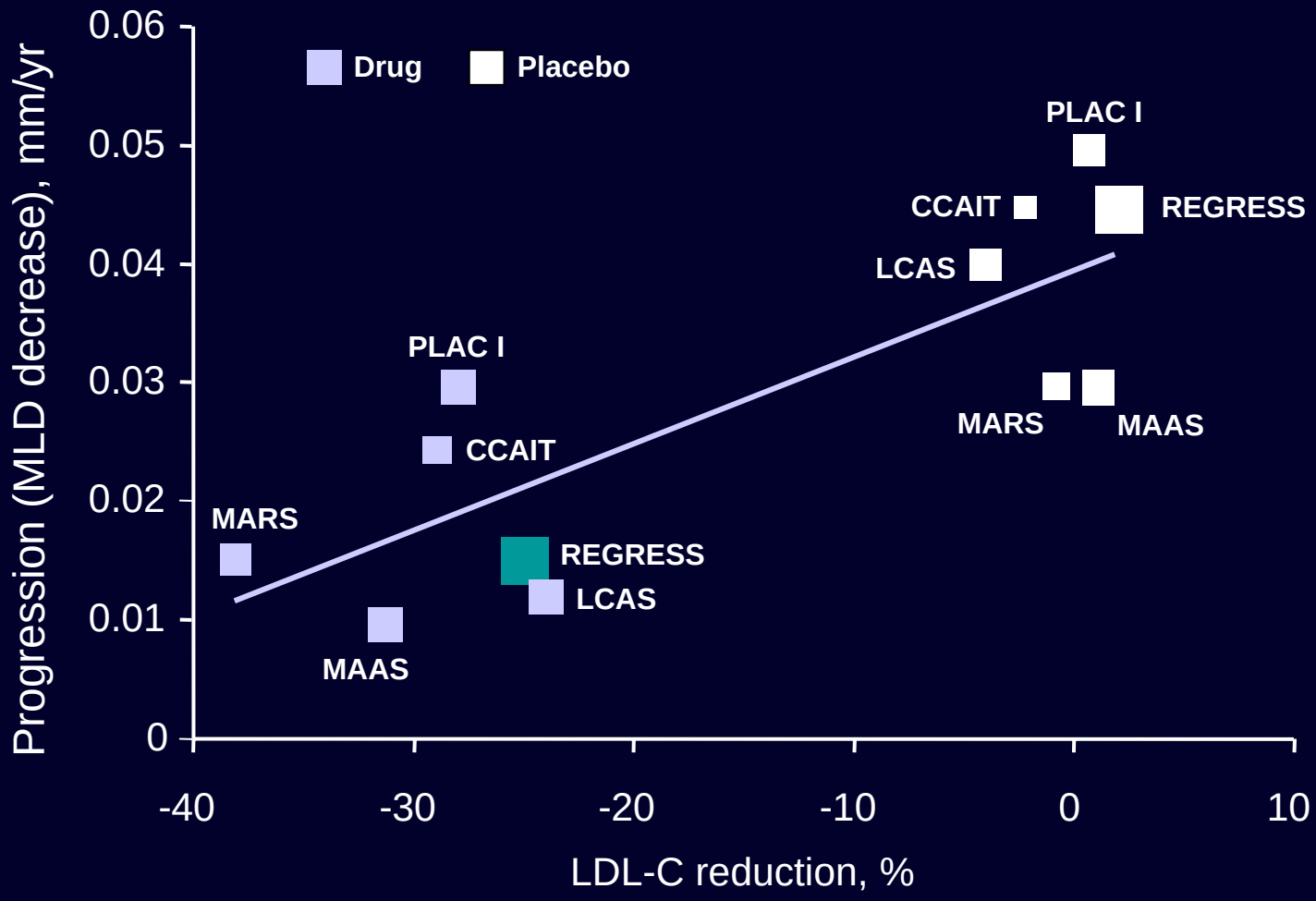
Major Secondary Prevention Trials

Study	Persons	Drug Duration	LDL-C (dose/d)	Baseline LDL-C (mg/dL)	Coronary Change	Major Revascu-Events	Coronary larization	Total Mortality	Mortality	Stroke
4S	4444	5.4 yrs	Simvastatin 10/40 mg	188	-35%	-35%	-37%	-42%	-30%	-27%
CARE	4159	5 yrs	Pravastatin 40 mg	139	-27%	-25%	-27%	-24%	-9%	-31%
LIPID	9014	5 yrs	Pravastatin 40 mg	150	-25%	-29%	-24%	-24%	-23%	-19%

Landmark Clinical Event Trials: Relevance to Clinical Practice



Effects of lipid-lowering with statins on progression of CHD



Ballantyne CM. *Am J Cardiol*. 1998:82:5M-11M.

The PROVE-IT Trial

PRavastatin Or atorVastatin Evaluation and Infection Therapy (TIMI 22)

Comparision of Intensive and Moderate Lipid Lowering with Statin after Acute Coronary syndrome

NEJM, April 8, 2004 350;15

Background

Statin therapy in long-term treatment of CHD

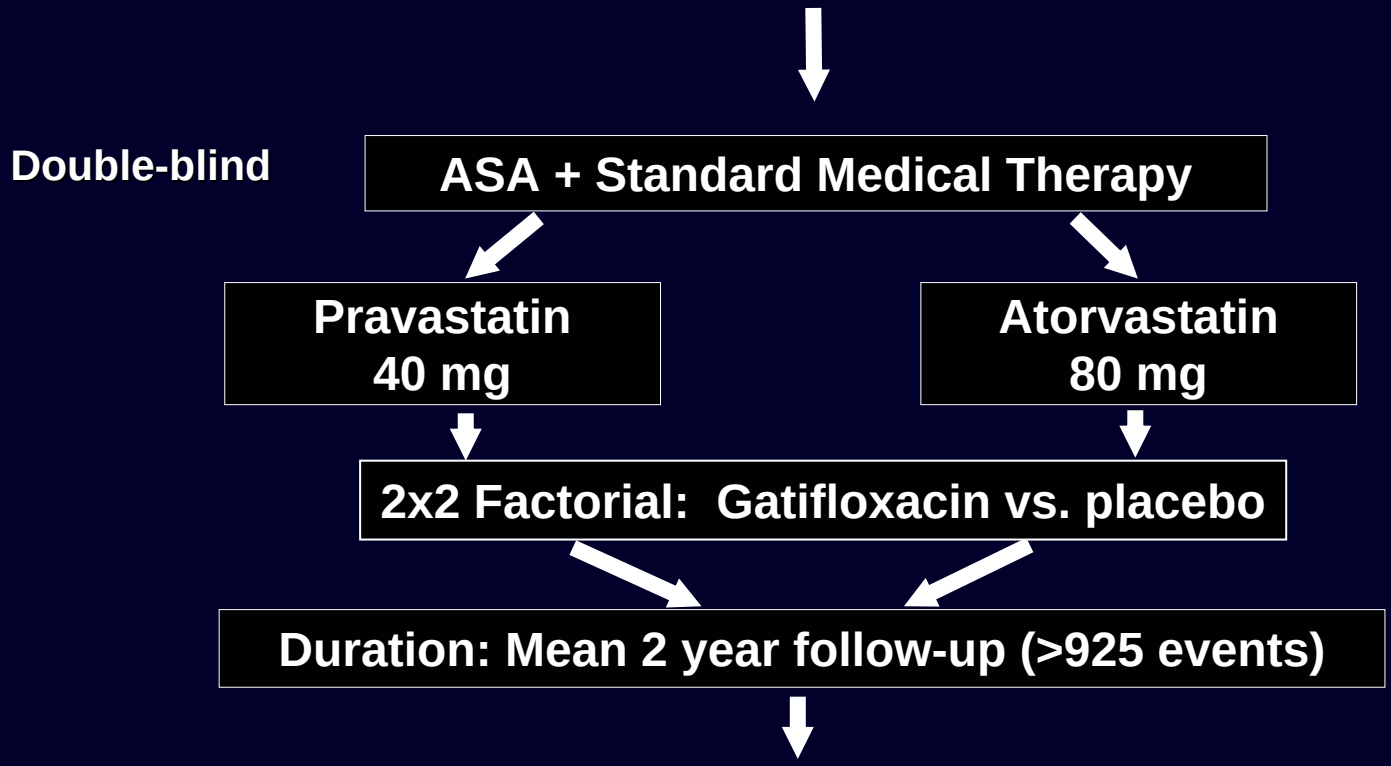
- statins in patients with an acute coronary syndrome (ACS)
- “intensive” LDL-C lowering to ~65 mg/dL

vs

“standard” LDL-C lowering to ~95 mg/dL

PROVE IT - TIMI 22: Study Design

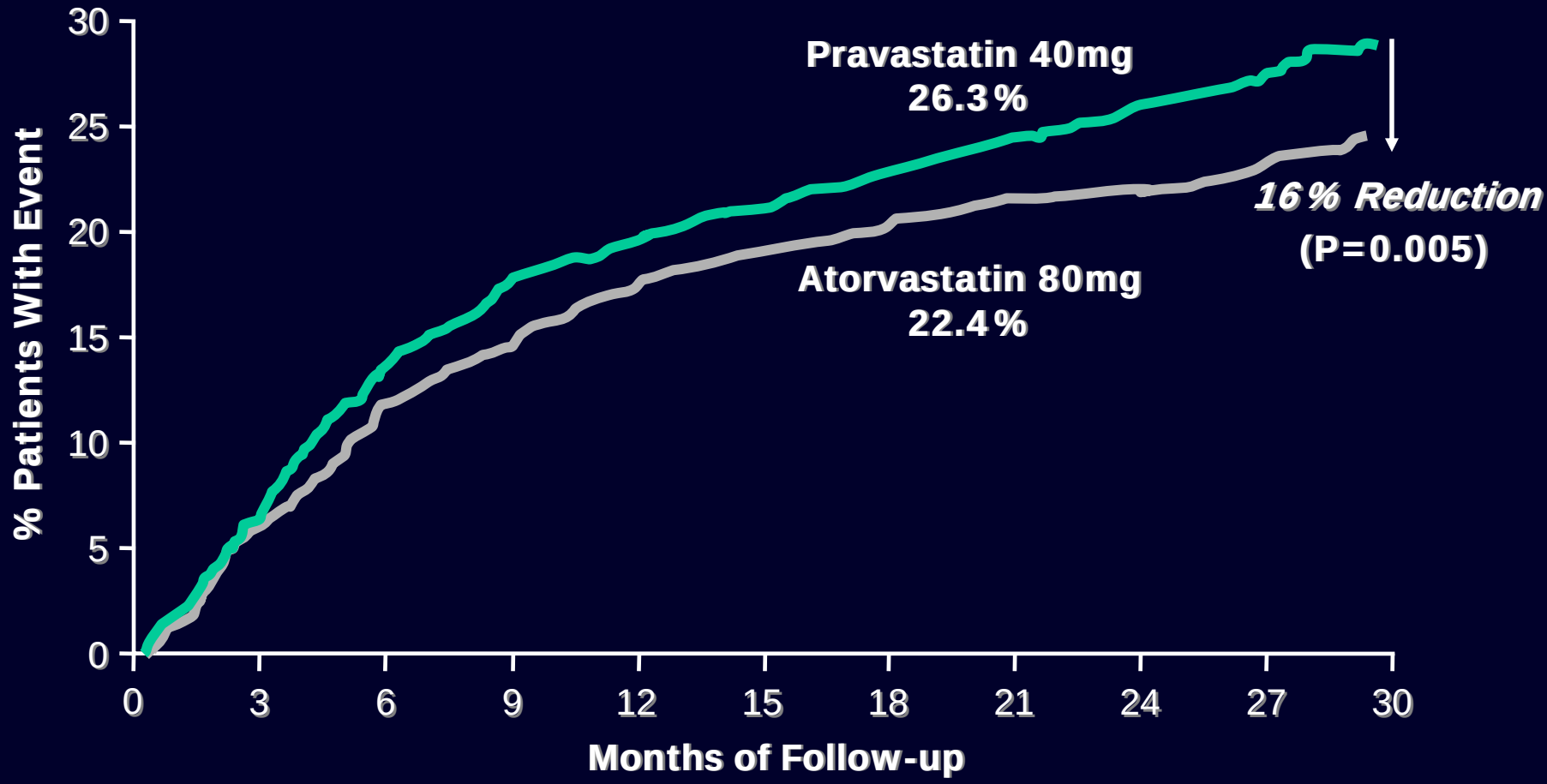
4,162 patients with an Acute Coronary Syndrome < 10 days



Primary Endpoint: Death, MI, Documented UA requiring hospitalization, revascularization (> 30 days after randomization), or Stroke

Primary Endpoint

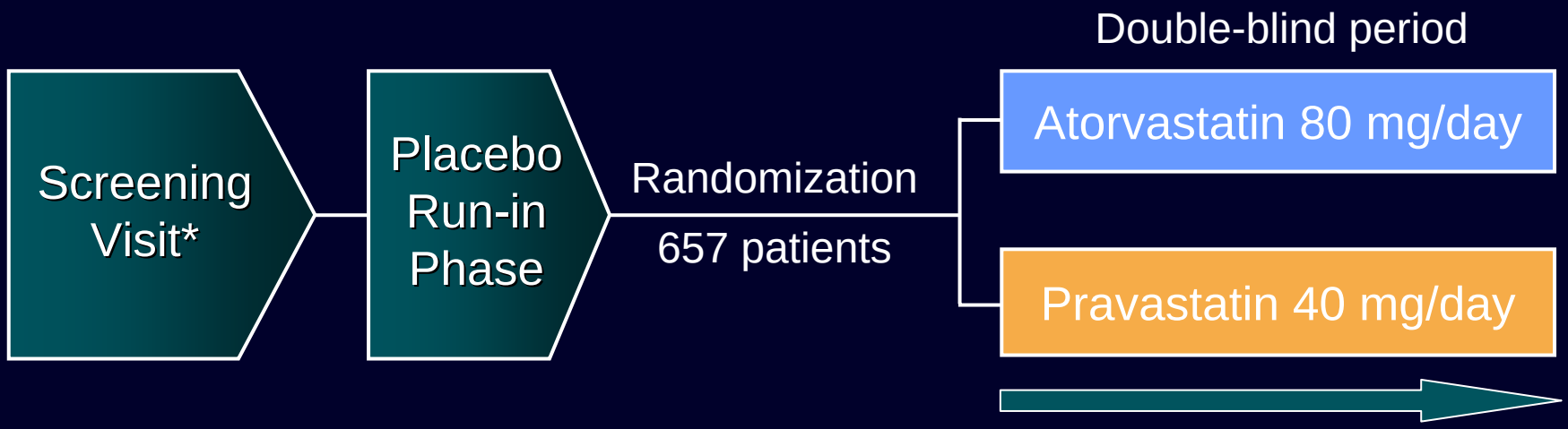
All-cause mortality or major CV event



The REVERSAL Trial

Reversing Atherosclerosis with Aggressive Lipid Lowering

REVERSAL: Study design



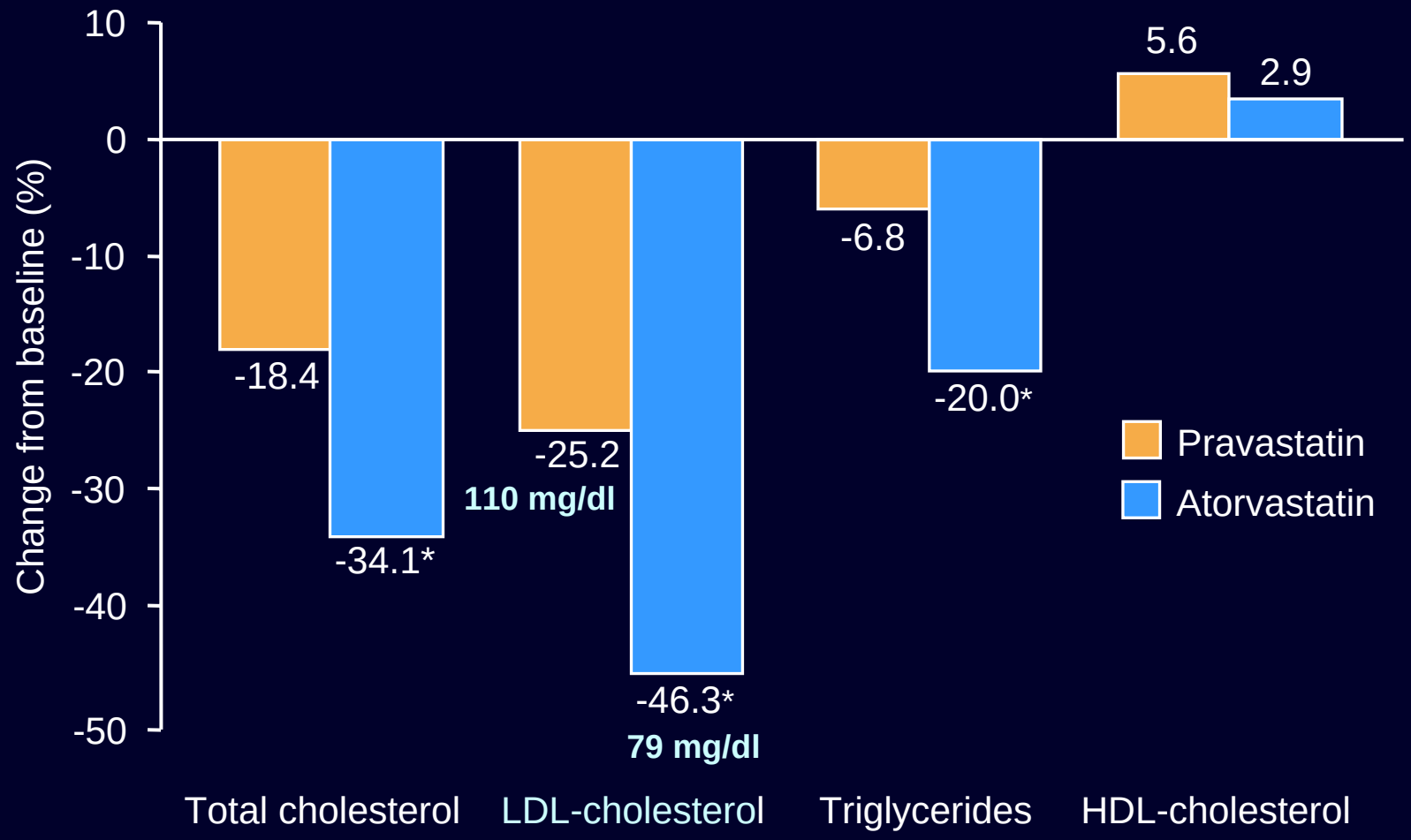
*Includes baseline intravascular ultrasound (IVUS)

18-month follow-up with IVUS

Design – Prospective, randomized, double-blind, multicenter trial

Setting – 34 community and tertiary care hospitals in the United States

Change from baseline in lipid parameters



**P*<0.001 vs pravastatin

Data are mean percent change from baseline to 18-month follow-up.

Pleiotropic effects

Lipid effects

inhibition of cholesterol biosynthesis (Endo, 1992)
Increased uptake and degradation of LDL(Goldstein & Brown, 1990)
Inhibition of LDL oxidation (Aviram et al., 1992; Giroux et al., 1993; Hussein et al., 1997)
Inhibition of scavenger receptor expression (Umetani et al., 1996)
Inhibition of lippprotein secretion (La Ville et al., 1984)
Inhibition of modified LDL endocytosis (Bernini et al., 1995)

Antiatherosclerotic effects

Inhibition of migration and proliferaiton of arterial myocytes (Corsini et al., 1993, 1996a, 1996b; Soma et al., 1993)
Inhibition of macrophage growth (Sakai et al., 1997)
Inhibition of cholesterol accumulation in macrophages (Bernini et al., 1993, 1995; Cignarella et al., 1998)
Inhibition of metalloproteinase secretion (Bellosta et al., 1998b)
Inhibition of cell adhesion (Masaaki et al., 1997)
Inhibition of tissue factor expression and activity (Colli et al., 1997)
Inhibition of superoxide generation (Giroux et al., 1993)
Inhibition of endothelin-1 synthesis and expression (Hernandez-Perera et al., 1998)
Increased expression and activity of eNOS (Endres et al., 1998; Kaesemeyer, 1999; Laufs et al., 1997, 1998)
Increased fibrinolytic activity (Essig et al., 1998)
Induction of myocyte apoptosis in proliferative lesions (Baetta et al., 1997a, 1997b; Guijarro et al., 1998)

Characteristics of Statins

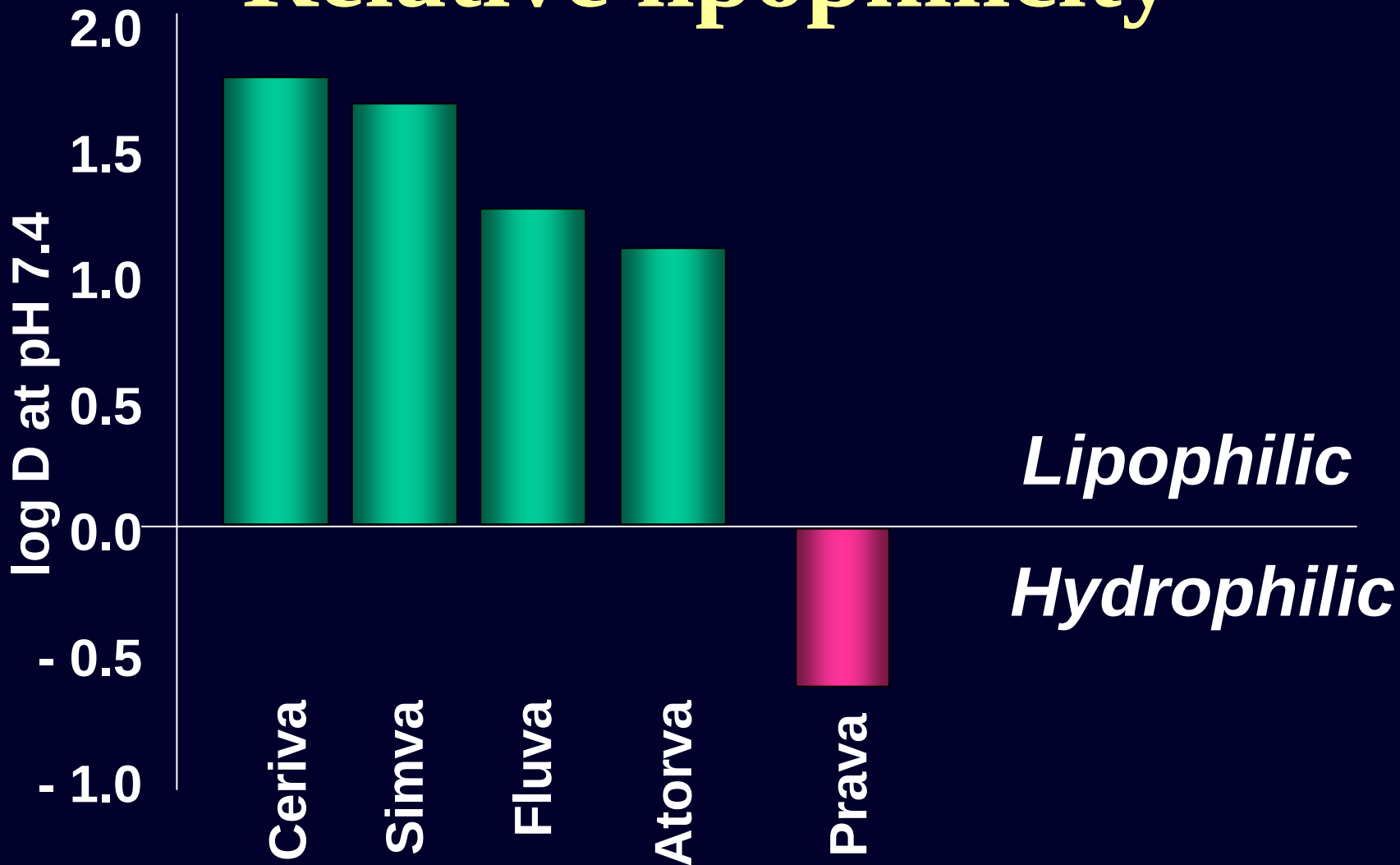
Characteristic	Lovastatin	Pravastatin	Simvtastin	Atorvastatin	Fluvastatin	Cerivastatin
Maximal dose (mg/day)	80	40	80	80	40	0.3
Maximal serum LDL cholesterol reduction produced (%)	40	34	47	60	24	28
Serum LDL cholesterol reduction produced (%)	34	34	41	50	24	28
Serum triglyceride reduction produced (%)	16	24	18	29	10	13
Serum HDL cholesterol increase	8.6	12	12	6	8	10
Plasma half-life(hr)	2	1-2	1-2	14	1.2	2-3
Effect of food on absorption of drug absorption absorption	Increased	Decreased	None	None	Negligible	None
Optimal time of administration	With meals (morning and evening)	Bedtime	Evening	Evening	Bedtime	Evening
Penetration of central nervous system	Yes	No	Yes	No	No	Yes
Renal excretion of absorbed dose	10	20	13	2	<6	33
Mechanism of hepatic metabo-lism	Cytochrome P-450 3A4	Sulfation	Cytochrome P-450 3A4	Cytochrome P-450 3A4	Cytochrome P-450 2C9	Cytochrome P-450 3A4, 2C8

Wood AJ. NEJM 1999;341(7):498-511

Pharmacokinetic properties of the statins

	Rosuvastatin	Pitavsatatin
Opitmal time of dosing	Any time of day	Not available
Bioavailability(%)	20	～80
Solubility	Hydrophilic	Lipophilic
Effect of food	No effect	Not available
Protein binding(%)	90	96
Active metabolites	Minor	Minor
Elimination half-life(h)	19	11
CYP450 metabolism and isoenzyme	Limited (2C9, 2C19, 1A2, 2D6, 2E1)	Limited
Renal excretion(%)	10	Not available

Relative lipophilicity

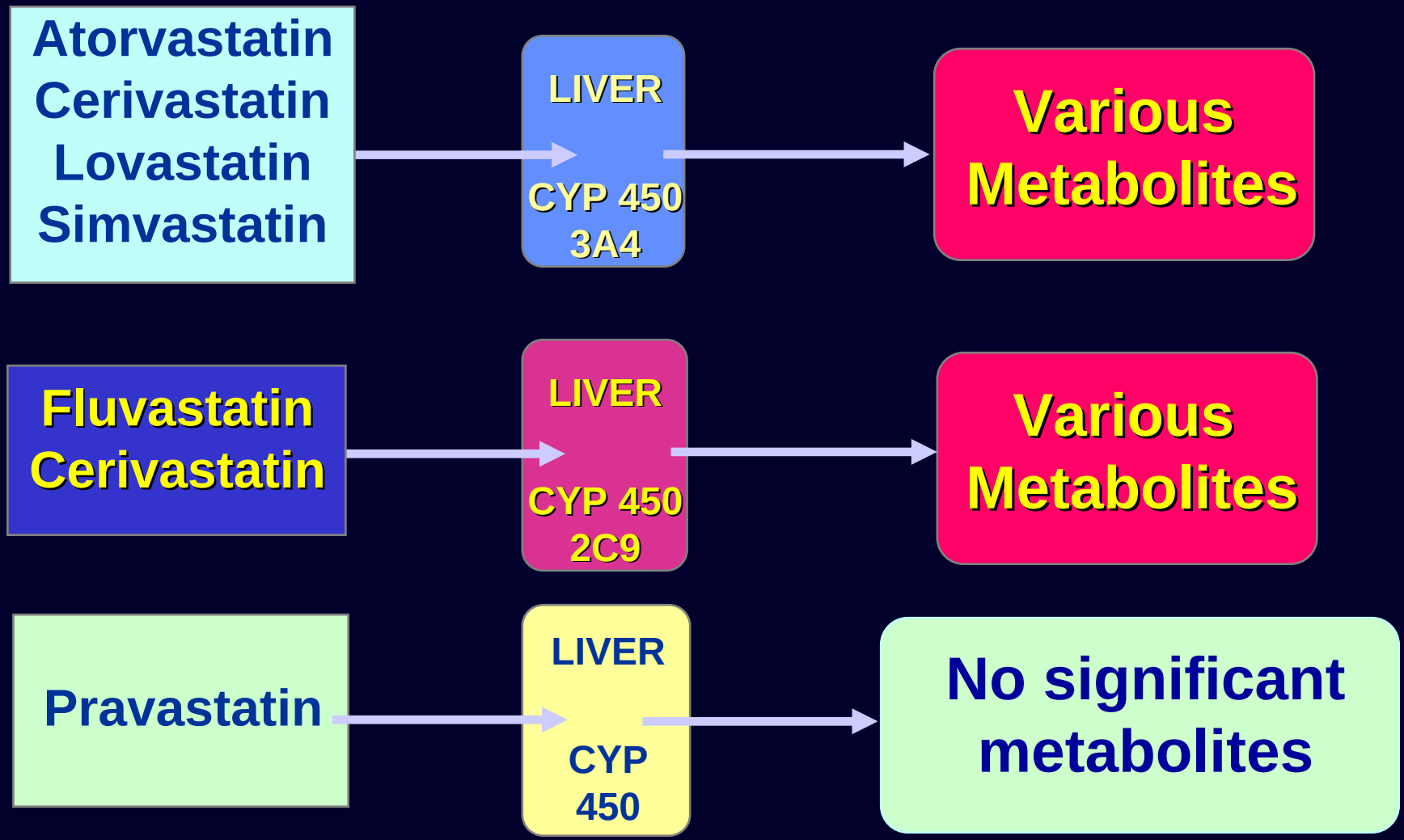


HMG CoA Reductase Inhibitors Pharmacokinetic Overview

Pharmacokinetic Parameter	Lova	Simva	Prava	Fluva	Atorva	Ceriva
Protein binding (%)	>95	95-98	50	>98	98	>99
Active metabolites	Yes	Yes	No	No	Yes	Yes
Elimination half-life (hrs)	3	2	1.8	1.2	14	2

White. *US Pharmacist.* 1998;19-27.
Cerivastatin Package Insert. Bayer/SKB 1998

Metabolism of Statins: Major Cytochrome P450 Isoenzymes



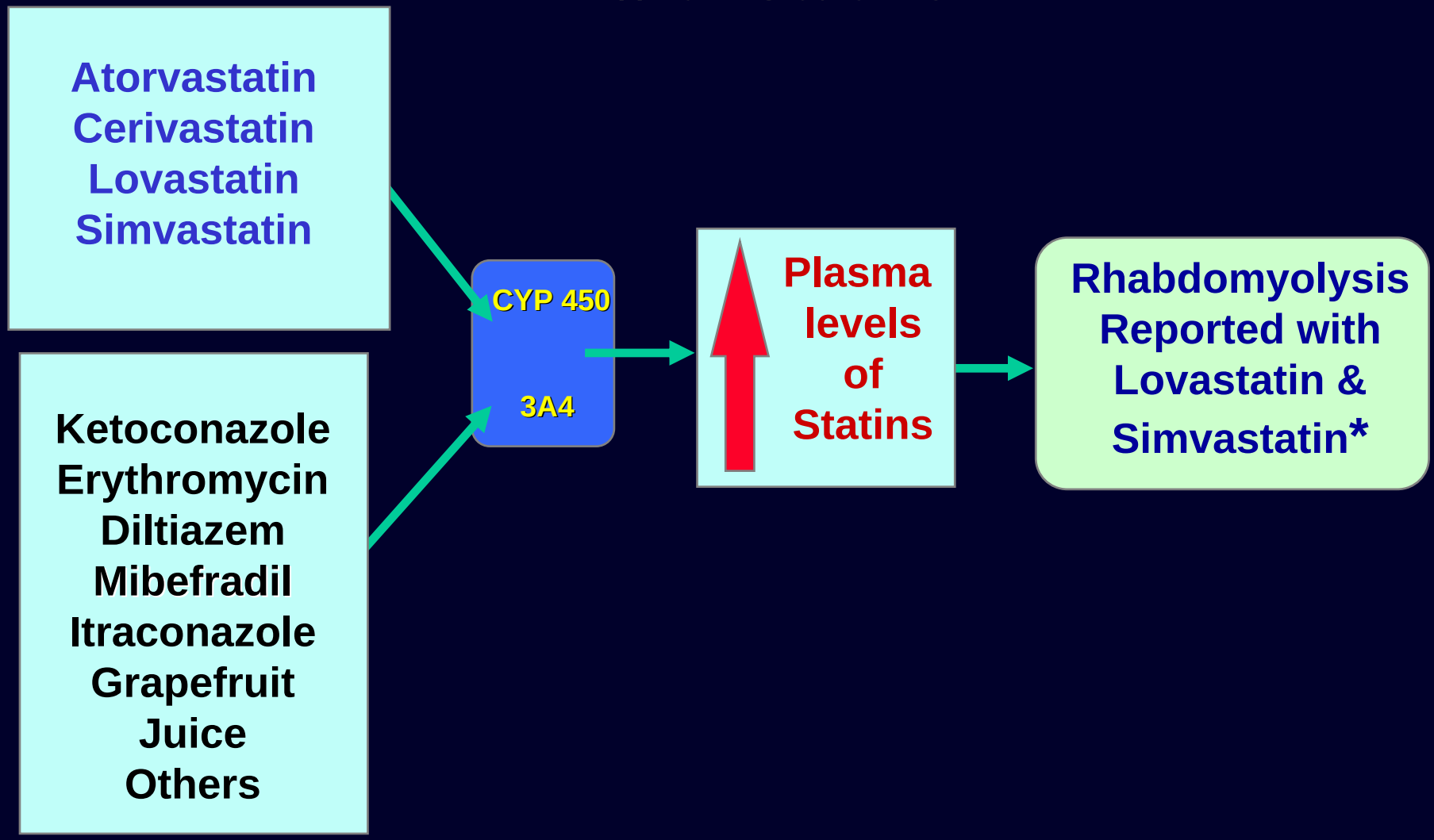
Statins

Drug Interaction : Cyt P-450

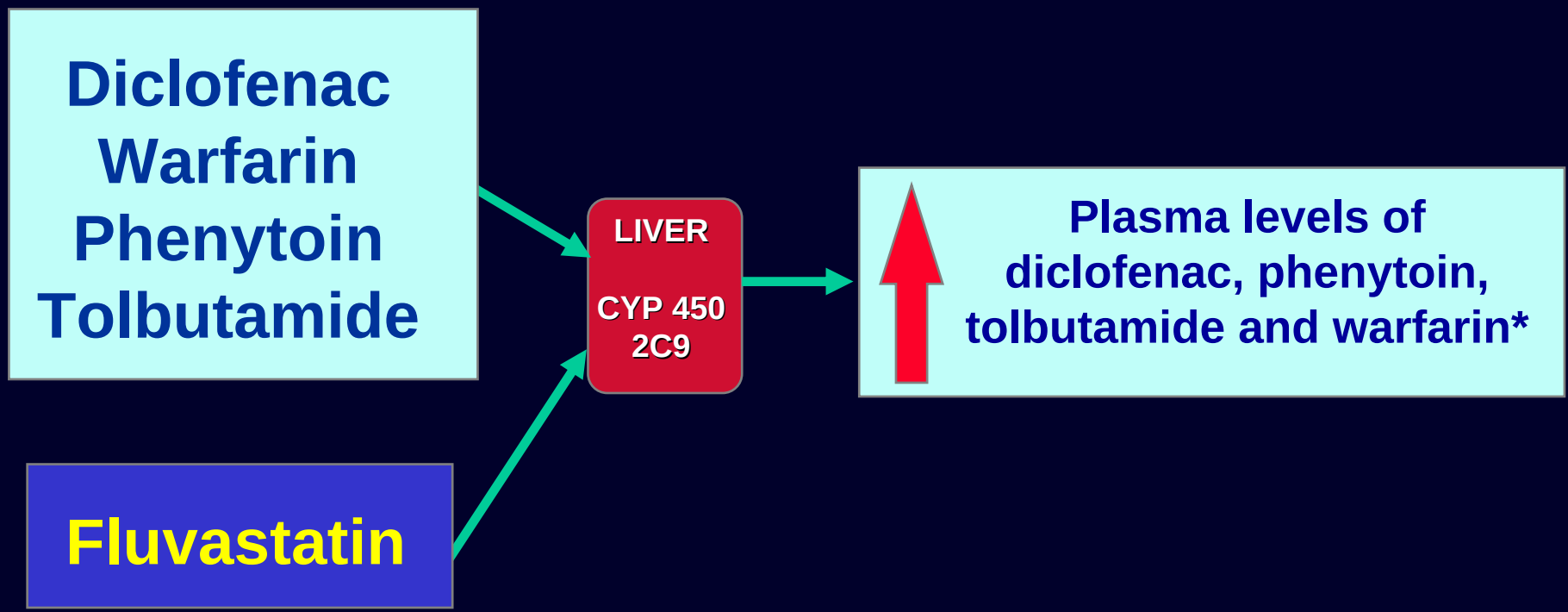
CYP1A2	CYP2C9	CYP2C19	CYP2D6	CYP2E1	CYP3A4
Acetaminophen	Alprenolol	Diazepam	Amitriptyline	Chloroxazone	Atorvastatin
Caffeine	Diclofenac	Ibuprofen	Bufaralol	Ethanol	Cerivastatin
Clozapine	Fluvastatin	Mephenytoin	Codeine	Halothane	Lovastatin
Phenacetin	*N*-Desmethyldiazepam	Methylphenobarbital	Debrisoquine	Paractamol	Simvastatin
Theophyline	Tolbutamide	Omeprazole	Desipramine		Erthromycin
	Warfarin	Proguanil	Dextromethorphan		Lidocaine
		Phenytoin	Encainide		Cyclosporine A
			Flecainide		Felodipine
			Impramine		Mibefradil
			Metoprolol		Nefazodone
			Mibefradil		Nifedipine
			Nortriptyline		Quinidine
			Perhexiline		Midazolam
			Perphenazine		Traizaolam
			Propafenone		Verapamil
			Propranolol		Warfarin
			Sparteine		
			Thioridazine		
			Timolol		

Corsini A et al. Pharmacology & Therapeutics 1999;84:413-428

CYP3-A4 Mediated Drug Interactions with Statins



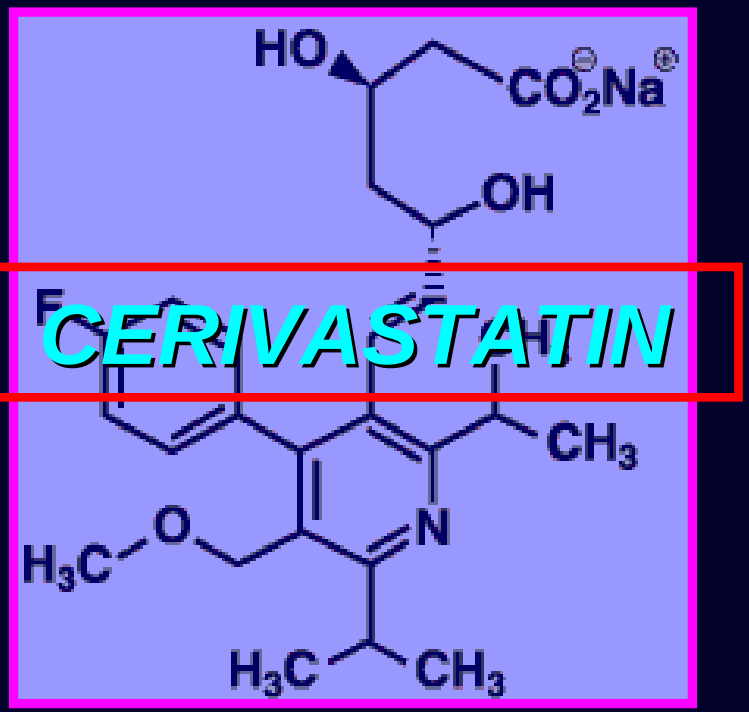
CYP2-C9 Mediated Drug Interactions with Fluvastatin



WHAT ABOUT THE SAFETY OF STATINS?

- Considered relatively ‘safe’ class of drugs
- Initial concerns are suicide, malignancy - evidence now does not support this…..
- Majority of side-effects mild and impact on the benefit-risk of treatment is small
- Concern are hepatic and muscle toxicity at high doses…..reversible, manageable, rare
- Some concerns are potential for drug interactions with some statins

CERIVASTATIN AND MYOPATHY



CERIVASTATIN → *MYOPATHY*

CERIVASTATIN

- Withdrawn from market on Aug 8, 2001 after reports of fatal cases of rhabdomyolysis.
- No serious safety concerns till the 800µg dose was marketed.
- Initial reports suggested the problem related to interaction with gemfibrozil.
- Further analysis revealed cases even with cerivastatin monotherapy.

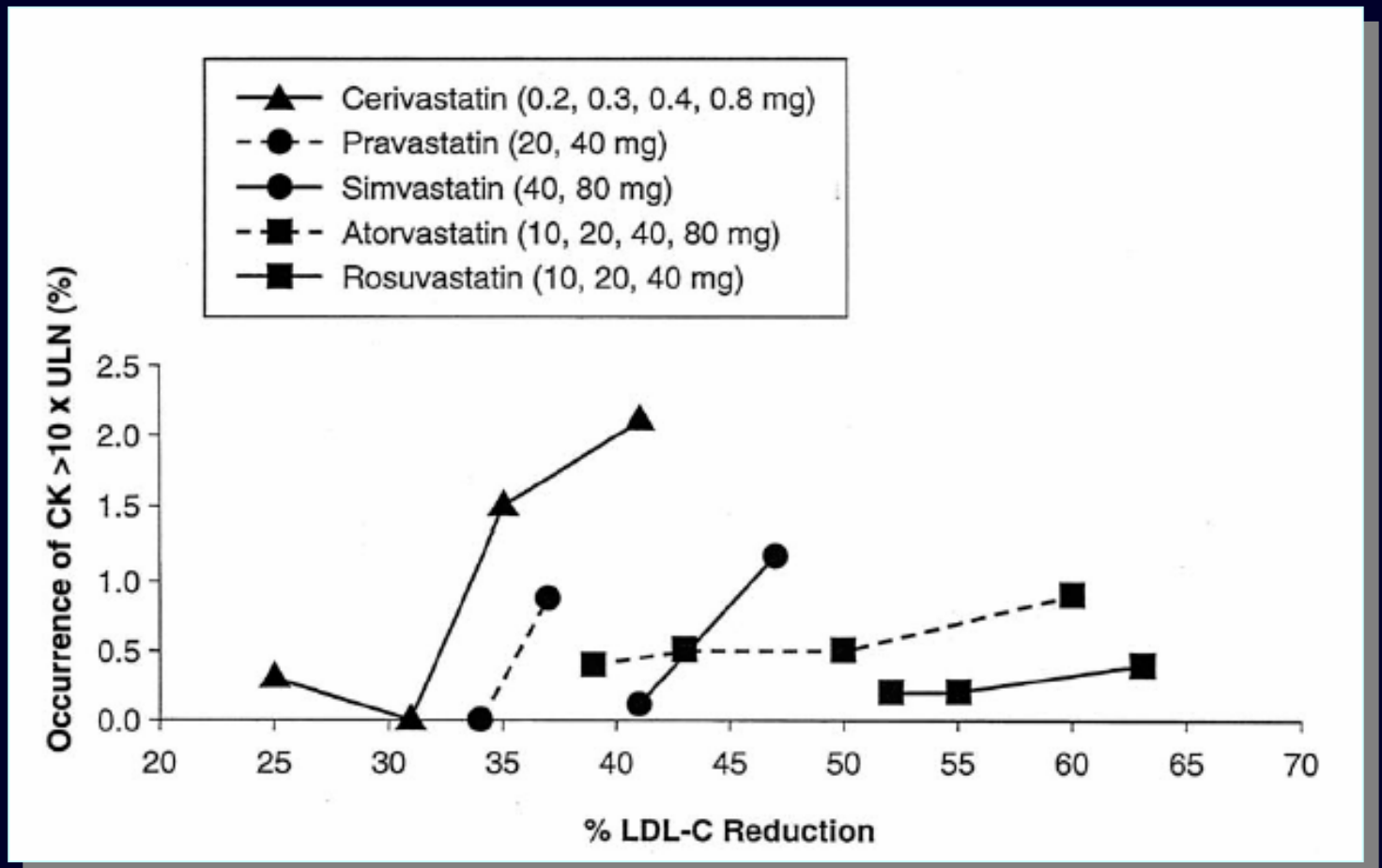
FATAL RHABDOMYOLYSIS AND STATIN TREATMENT IN THE USA

Reported Fatal Rhabdomyolysis and Numbers of Prescriptions for All Statins in U.S.A.

Variable	LOVA	PRAVA	SIMVA	FLUVA	ATORVA	CERIVA	TOTAL
Date approved	31/8/87	31/10/91	23/12/91	31/12/93	17/12/96	26/6/97	
Fatal cases of rhabdomyolysis	19	3	14	0	6	31	73
# of prescriptions since marketing began (x 1000)	99,197	81,364	116,145	37,392	140,360	9,815	484,273
Reporting rate per 10^9 prescriptions	0.19	0.04	0.12	0	0.04	3.16	0.15

Staffa JA et al. N Engl J Med 2002, 346: 539-540

CK elevation versus LDL-C reduction



Brewer et al. Am J Cardiol 2003;92:23k-29k

RHABDOMYOLYSIS PER 10,000 SUBJECT-YEARS OF EXPOSURE

		Combination Therapy	
Drug	MonoRx rate	Combination	Rate
Atorva	0.54	Atorva/Feno	22.45
Ceriva	5.34	Ceriva/Gem	1035
Prava	0	No cases	0
Simva	0.49	Simva/Gem	18.73
Fenofibrate	0	Feno/Atorva	16.86
Gemfibrozil	3.7	Gem/Ceriva	789

Graham et al. JAMA (2004); 292:2585 – 2590.

HOSPITALISED RHABDOMYOLYSIS DURING LIPID LOWERING DRUG THERAPY

CONCLUSIONS

1) **Rhabdomyolysis incidence/10 000 subject-years of exposure:**

   a) **For Atorva/Simva/Prava: 0.44**

   b) **For Ceriva: 5.34**

   c) **For Fibrates: 2.82**

   d) **For Atorva/Simva/Prava + Fibrate: 5.98**

   e) **For Ceriva + Fibrate: 1035**

2) **NNT to cause one case of rhabdomyolysis:**

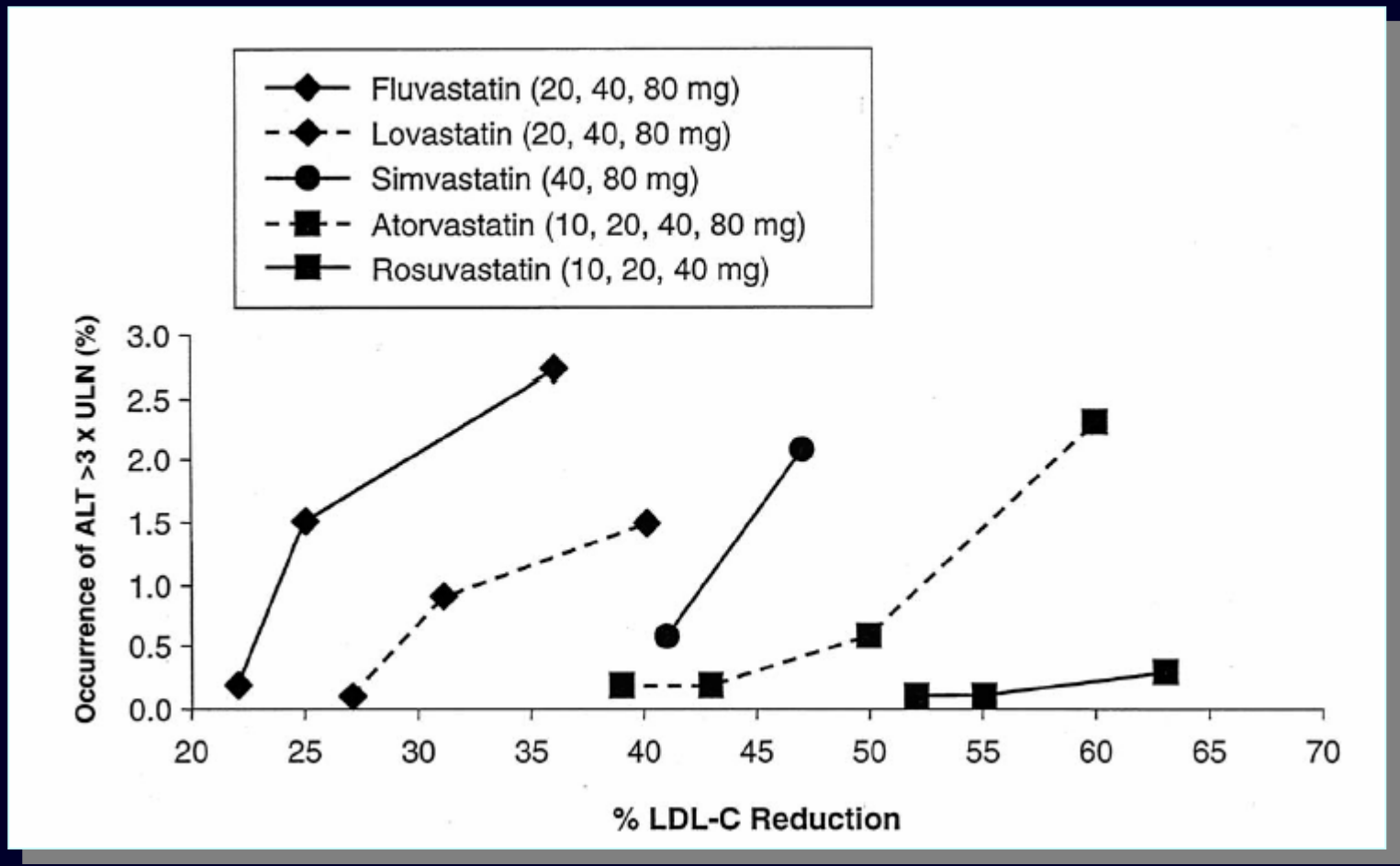
   a) **For statin monotherapy: 22 727**

   b) **For statin + fibrate (mostly in older diabetics): 484**

   c) **For Ceriva + fibrate: 10 - 13**

Graham et al. JAMA (2004); 292:2585 – 2590.

ALT elevation versus LDL-C reduction



Brewer et al. Am J Cardiol 2003;92:23k-29k

Pharmacogenetic aspect of statin therapy

Pharmacogenetic Study of Statin Therapy and Cholesterol Reduction

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THERAPY WITH 3-HYDROXY-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) lowers total and low-density lipoprotein (LDL) cholesterol and has proven to be highly effective for cardiovascular risk reduction. However, there is wide variation in interindividual response to statin therapy, and it has been hypothesized that genetic differences may contribute to this variation. While the implications of this hypothesis are broad in terms of "personalized medicine" and the use of genetic screening to guide selection of lipid-lowering therapy, clinical data addressing pharmacogenetic interactions with statins are limited and have largely focused on the lipid metabolism genes apolipoprotein E (*APOE*), apolipoprotein B (*APOB*), cholesteryl ester transfer protein (*CETP*), and the LDL receptor (*LDLR*).[1-4]

To explore this issue systematically, we genotyped 148 single-nucleotide

Context Polymorphisms in genes involved in cholesterol synthesis, absorption, and transport may affect statin efficacy.

Objective To evaluate systematically whether genetic variation influences response to pravastatin therapy.

Design, Setting, and Population The DNA of 1536 individuals treated with pravastatin, 40 mg/d, was analyzed for 148 single-nucleotide polymorphisms (SNPs) within 10 candidate genes related to lipid metabolism. Variation within these genes was then examined for associations with changes in lipid levels observed with pravastatin therapy during a 24-week period.

Main Outcome Measure Changes in lipid levels in response to pravastatin therapy.

Results Two common and tightly linked SNPs (linkage disequilibrium r^2=0.90; heterozygote prevalence=6.7% for both) were significantly associated with reduced efficacy of pravastatin therapy. Both of these SNPs were in the gene coding for 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, the target enzyme that is inhibited by pravastatin. For example, compared with individuals homozygous for the major allele of one of the SNPs, individuals with a single copy of the minor allele had a 22% smaller reduction in total cholesterol (–32.8 vs –42.0 mg/dL [–0.85 vs –1.09 mmol/L]; P=.001; absolute difference, 9.2 mg/dL [95% confidence interval (CI), 3.8-14.6 mg/dL]) and a 19% smaller reduction in low-density lipoprotein (LDL) cholesterol (–27.7 vs –34.1 mg/dL [–0.72 vs –0.88 mmol/L]; P=.005; absolute difference, 6.4 mg/dL [95% CI, 2.2-10.6 mg/dL]). The association for total cholesterol reduction persisted even after adjusting for multiple tests on all 33 SNPs evaluated in the HMG-CoA reductase gene as well as for all 148 SNPs evaluated was similar in magnitude and direction among men and women and was present in the ethnically diverse total cohort as well as in the majority subgroup of white participants. No association for either SNP was observed for the change in high-density lipoprotein (HDL) cholesterol (P>.80) and neither was associated with baseline lipid levels among those actively treated or among those who did not receive the drug. Among the remaining genes, less robust associations were found for squalene synthase and change in total cholesterol, apolipoprotein E and change in LDL cholesterol, and cholesteryl ester transfer protein and change in HDL cholesterol, although none of these met our conservative criteria for purely pharmacogenetic effects.

Conclusion Individuals heterozygous for a genetic variant in the HMG-CoA reductase gene may experience significantly smaller reductions in cholesterol when treated with pravastatin.

JAMA. 2004;291:2821-2827 www.jama.com

Cost-Effectiveness of Treatment with Statins

Drug/Dose (mg/day)	Annual Cost (US$/yr)	LDL-C Reduction (%)	Cost/LDL-C Reduction (US$/yr 1% LDL-C Reduction)
Fluvastatin			
20	439.20	23	19.09
40	489.60	26	16.83
Lovastatin			
20	610.00	24	33.75
40	1,548.00	30	48.60
80	2,916.00	40	72.90
Pravastatin			
20	709.20	25	28.37
40	1,195.20	27	44.27
Simvastatin			
10	730.80	28	26.10
20	1,274,40	35	36.41
40	1,324,80	40	33.12
Atorvastatin			
10	655.20	36	18.20
20	1.015.20	40	25.38
40	1.224.00	47	26.04

Statin의 용량, 가격비교

Brand	성분	Maker	용량	가격(원)
Zocor	Simvastatin	MSD	20mg	1226
			40mg	1251
Lipitor	Atorvastatin	Pfizer	10mg	1244
			20mg	1881
심바스트	Simvastin	한미	20mg	790
심바로드	Simvastin	종근당	20mg	950
심바스타	Simvastin	CJ	20mg	750
심바틴	Simvastin	동화	20mg	675

Treatment Gap between the Guideline and Real Practice

- L-TAP (Lipid Treatment Assessment Project) **38.4 %**

	Drug	Non-drug
Patient	84.6 %	15.4 %
Goal achievement	39 %	34 %

- ACCEPT (American College of Cardiology Evaluation of Preventive Therapeutics)
  - 59 % of patient : medication for hyperlipidemia
  - **24 %** of patients with medication : achieve target goal
- EUROASPIRE II (European Action on Secondary Prevention through Intervention to Reduce Events)
  - **50.6 %** of patients with medication : achieve target goal

REALITY & Ten Center Study

- Patients with risk factors in general [REALITY STUDY]
  - Overall only **41 %** patients attained LDL-C goal
    (37 % of CHD patients, 52 % of non-CHD patients)

- CAD patients at OPD of university hospitals [TEN CENTER STUDY]

  - 60 % of patients ; medication for hyperlipidemia
  - 55 % of patients with medication ; achieve target goal
  - **50 %** of whole patients at OPD ; achieve target goal

- Insufficient medication rate & dosage of statins
- Future requirements
  - Doctors' awareness of statin therapy for CAD patients
  - Initial adequate dose
  - Super statin or other drugs allowing the use of low dosage with safety
  - Problem of medical insurance

고지혈증 치료 보험기준

고시 제2001-28호

아래와 같은 기준으로 투여시 요양급여를 인정하며, 허가사항 범위이지만 동 인정기준 이외에 투여한 경우에는 약값의 100분의 100을 본인부담토록 함.

- 아 래 -

1. 순수 고콜레스테롤혈증의 경우

1) 위험요인이 없는 경우 : 혈중 총 콜레스테롤 수치가 250mg/dl 이상일때

2) 위험요인이 있는 경우 : 혈중 총 콜레스테롤 수치가 220mg/dl 이상일때

* 관상동맥질환이 확인된 경우는 혈중 총 콜레스테롤 수치가 220mg/dl 이상

3) 해당 약제 : HMG-CoA환원효소억제제, 담즙산제거제, Fibrate계열 약제 중 1종 인정

2. 순수 고트리글리세라이드혈증의 경우

1) 위험요인이 없는 경우 : 적절한 식이요법을 함에도 불구하고 TG검사에서 연속 2회 400mg/dL이상일 때

2) 위험요인이 있는 경우 : TG검사에서 연속 2회 200mg/dL이상일 때

3) 해당 약제 : Fibrate계열 또는 Niacin계열 약제중 1종 인정

3. 고콜레스테롤 및 고트리글리세라이드혈증의 복합형인 경우

1) 위험요인이 없는 경우 : - 혈중 총 콜레스테롤 250mg/dl 이상이고, 혈중 TG 320mg/dl 이상일때

2) 위험요인이 있는 경우 : - 혈중 총 콜레스테롤 220mg/dl 이상이고, 혈중 TG 200mg/dl 이상일때

3) 해당 약제 : 콜레스테롤 및 TG에 작용하는 약제별로 각각 1종씩 인정.

4. 동맥경화증 발생 유발 위험요인(심근경색증의 기왕력, 허혈성 심질환, 고혈압, 당뇨병이 있는 경우)이 있는 고지혈증 환자의 경우에는 상기 기준에 의해 투약하되, 가능한 한 저용량(1일 1 - 2정 또는 1 - 2 pack) 투여를 원칙으로 함.

고지혈증 치료 보험기준

- 2001-06-08
- 일련번호 1-1 관련근거 고시제2001-28호
- 고지혈증치료제의 요양급여기준(일반원칙)
- 아래와 같은 기준으로 투여시 요양급여를 인정하며, 허가사항 범위이지만 동 인정기준 이외에 투여한 경우에는 약값의 100분의 100을 본인부담토록 함.

1. 순수 고콜레스테롤혈증의 경우

1) 위험요인이 없는 경우

: 혈중 총 콜레스테롤 수치가 250mg/dl 이상일 때

2) 위험요인이 있는 경우 :

: 혈중 총 콜레스테롤 수치가 220mg/dl 이상일 때

* 관상동맥질환이 확인된 경우는 혈중 총 콜레스테롤 수치가 220mg/dl 이상

3) 해당 약제

: HMG-CoA환원효소억제제, 담즙산제거제, Fibrate 계열 약제 중 1종 인정

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기 타

4. 동맥경화증 발생 유발 위험요인(심근경색증의 기왕력, 허혈성 심질환, 고혈압, 당뇨병이 있는 경우)이 있는 고지혈증환자의 경우에는 상기 기준에 의해 투약하되, 가능한 한 저용량(1일 1 - 2정 또는 1 - 2 pack) 투여를 원칙으로 함.

LDL Cholesterol Goals and Cutpoints (2004)

Risk Category	LDL Goal (mg/dL)	LDL (mg/dL) - Therapeutic Lifestyle Changes (TLC)	LDL (mg/dL) - Drug Therapy
• CHD or CHD Risk Equivalents (10-year risk > 20 %)	<100 Optional < 70*	≥100	≥100 (<100 : drug optional)
• 2+ Risk Factors (10-year risk 10–20 %)	<130 Optional <100*	≥130	≥130 (100–129 : drug optional)
• 2+ Risk Factors (10-year risk <10 %)	<130	≥130	≥160
• 0–1 Risk Factor	<160	≥160	≥190 (160–189 : drug optional)