

The Prudent Prescriber

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Pharm Reps ≠ Rational Prescribing

(PR)



(RP)

Whither Vytorin?

Merck-Schering Plough (MSP) bought two full pages of the January 27, 2008 New York Times defending Vytorin against the media feeding frenzy that occurred when the ENHANCE trial data was made public. What's a doc to do?

ENHANCE

- Randomized, double blind study compared simvastatin 80mg/day vs. ezetimibe 10/simvastatin 80mg (Vytorin) in 720 patients with heterozygous familial hypercholesterolemia.
- Average LDL at the start of the study was 319mg% in both groups.
- Follow up was for two years.
- Primary outcome: carotid artery intimal thickness.
- Results:
 - Intimal thickness *increased* minimally in both groups, and there were no significant differences between the two groups.
 - No differences in deaths or non-fatal MIs (study not powered to assess CV events).
 - LDL decreased 58% in Vytorin group and 41% in simvastatin group.
 - No significant differences in side effects in the two groups.

What are the issues with ENHANCE?

- MSP delayed release of this study that was completed in 2004, citing the complexity of reviewing thousands of carotid ultrasounds.
- The primary endpoint of the trial was changed after the study was completed – an unusual step!
- Carotid intimal thickness is a surrogate marker (some data suggests a good one) and not a patient oriented outcome.
- The population studied (LDL average 319mg%) are very different than my patients.

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Antibiotics do NOT

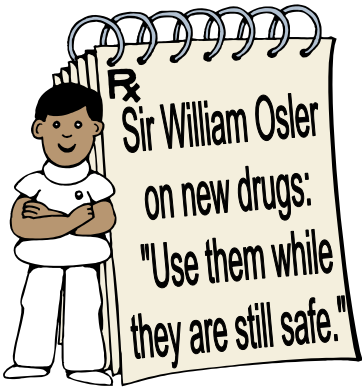


help acute bronchitis

β-blockers in post-MI save lives

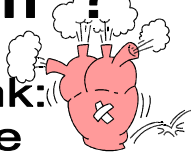


Pill splitters save big



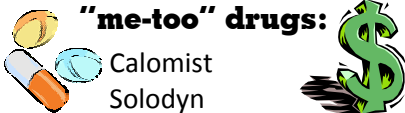
CHF?

Think:



**Ace
Aldactone
B-blocker
Dig
Diuretic**

Avoid these expensive "me-too" drugs:



Calomist
Solodyn
Soma 250
Amrix
Xyzal
Veramyst
Ultram ER
Ambien CR

**Treat diabetics
BP to 130/80**



now available
on the
Generic Marquee

Fosamax → alendronate
Altace → ramipril
Norvasc → amlodipine
Ambien → zolpidem
Flonase → fluticasone nasal
Zocor → simvastatin

Whither Vytorin, continued...

My Take:

- Reassure patients that they are not being harmed by Vytorin or Zetia.
- Restrict prescription of Vytorin to situations where you cannot get to target any other way or patients cannot tolerate high dose statins:
 - Add Niaspan 2gm: ↓LDL 14%, ↑HDL 24%.
 - Simvastatin 80mg: ↓LDL 45-50%.
 - Atorvastatin 80mg: ↓LDL 55%
- Await results of the 20,000 patient, clinically oriented trials that are underway.
- Remember the big picture: in primary prevention particularly, we expose large numbers of patients to side effects and expense for a limited return on investment. Think Number Needed to Treat (NNT)!

NNT

Condition	Intervention	NNT	Reference
Primary Prevention: High LDL	pravastatin vs. placebo	64 to prevent one stroke	Shepherd, <u>NEJM</u> 1995; 333:1301-7
Secondary Prevention: Older patients with a myocardial infarction	pravastatin vs. placebo	34 to prevent one stroke	<u>Ann Int.Med</u> 1998 Nov 1; 129(9) 681-9
		22 to prevent one death from coronary disease	

In the Shepherd study cited above, only 1 of 64 patients treated with pravastatin for 4.9 years would reap a stroke protection benefit!



Flash!!!

Fosamax went generic on February 6, 2008. Barr and Teva pharmaceutical companies will have 180 days of exclusivity on 35mg and 70mg tablets.

New Drugs: Where Not to Go



- ☆ **Xyzal** (levoisomer of Zyrtec)
 - 8 years of study, unable to show significantly less somnolence than Zyrtec.
 - Primary endpoint in clinical trials (Wheal and Flare) not clinically different than other non-sedating antihistamine.
 - Xyzal \$81/mo. vs. OTC Zyrtec or loratadine \$21/mo.
 - My Take: Novel name, worst sort of “me-too”.
- ☆ **Calomist** (vitamin B₁₂ nasal spray)
 - Still need to do initial B₁₂ replacement IM on new patients (you can do initial B₁₂ replacement orally).
 - Clinical trial with only 25 patients.
 - Calomist \$112/mo. vs. 100mcg B₁₂ per day orally for \$2.70.
 - My Take: Oral replacement works. I have had difficulty at times talking patients out of the magically cherry red intramuscular B₁₂. I'll go with oral B₁₂ at 2.5% of the cost of Calomist.
- ☆ **Solodyn** (minocycline extended release)
 - Approved for inflammatory, non-nodular acne.
 - Little evidence to suggest better compliance or fewer side effects.
 - Dosed by weight: 45mg, 90mg, 135mg tabs.
 - Solodyn: \$15/tab = \$450/mo. vs. 100mg minocycline at \$35/mo.
 - My Take: Egregiously priced pimple pill.



A big thank you and long overdue recognition to my two PharmD colleagues, Steve and Josh. They are an ongoing resource for new ideas, hard data and current pharma happenings. I appreciate very much their willingness to allow me to filch, appropriate, poach, mooch and just plain steal their work for this publication.

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