

S.A.M.: The Best “Natural” Pills for Patients Concerned about PCa?

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HOBBIES: None!



**What is the significance of the
numbers 27 and 10 for this
conference?**

??

Patriots 27 Broncos 10



**HEART HEALTHY=
PROSTATE HEALTHY
(2016 Update)**

Moyad MA, Vogelzang NJ. Asian J Androl 2015; February 3, epub ahead of print.

THE PROBLEM?

- SELECT +....=100+ Million U.S. Dollars
- ATBC + CARET=50+ Million U.S. Dollars
- Lycopene, Vitamin D....Rx....Heart Healthy?

WHAT WAS THE RESULT=???



MOYAD SAYS ALWAYS REMEMBER S.A.M.

- Natural, Generic (dirt cheap like me), Heart Healthy, Endpoints....
- Supplements in Cancer=Side Effects!

Statins for Primary Prevention

- “When used for primary prevention, statins are associated with lower rates of all-cause mortality, major vascular events, and revascularizations compared to placebo.”
- -18 Randomized trials, n=56,943, Age=57(28-97)
- -Toxicity?



Statins-Pca Meta-Analysis

- “Our meta-analysis suggests a potentially beneficial effect of statins on prostate cancer patients treated with RT but not among radical prostatectomy patients.”
- HR=0.68; (P=0.02)
- Not enough surgery data?



Korean, U.S. & U.K. Studies-RP Only-2014/2015

- KOREA=2137 BCR= -73%;P=0.001 for H-Grade
- U.S. 1146 RP patients. (SEARCH database)
- Post-RP statin use=HR=-36%; P=0.004
- U.K.=11,772. (3499 deaths & 1791=Pca)
- Pca Death=-45% & Overall= -34%



Statins-ASCO-GU-2015

ADT + Statins + Harvard/Canada

- “...statin use at the time of ADT initiation was associated with a sign increase in TTP on ADT even after adjusting for established prognostic factors.” (n=926)
- ADT following primary or salvage RT- “statin use was associated with improved overall and prostate cancer-specific survival & improved QL.” IAD-”more off trt intervals & longer off-trt.”(n=1364)

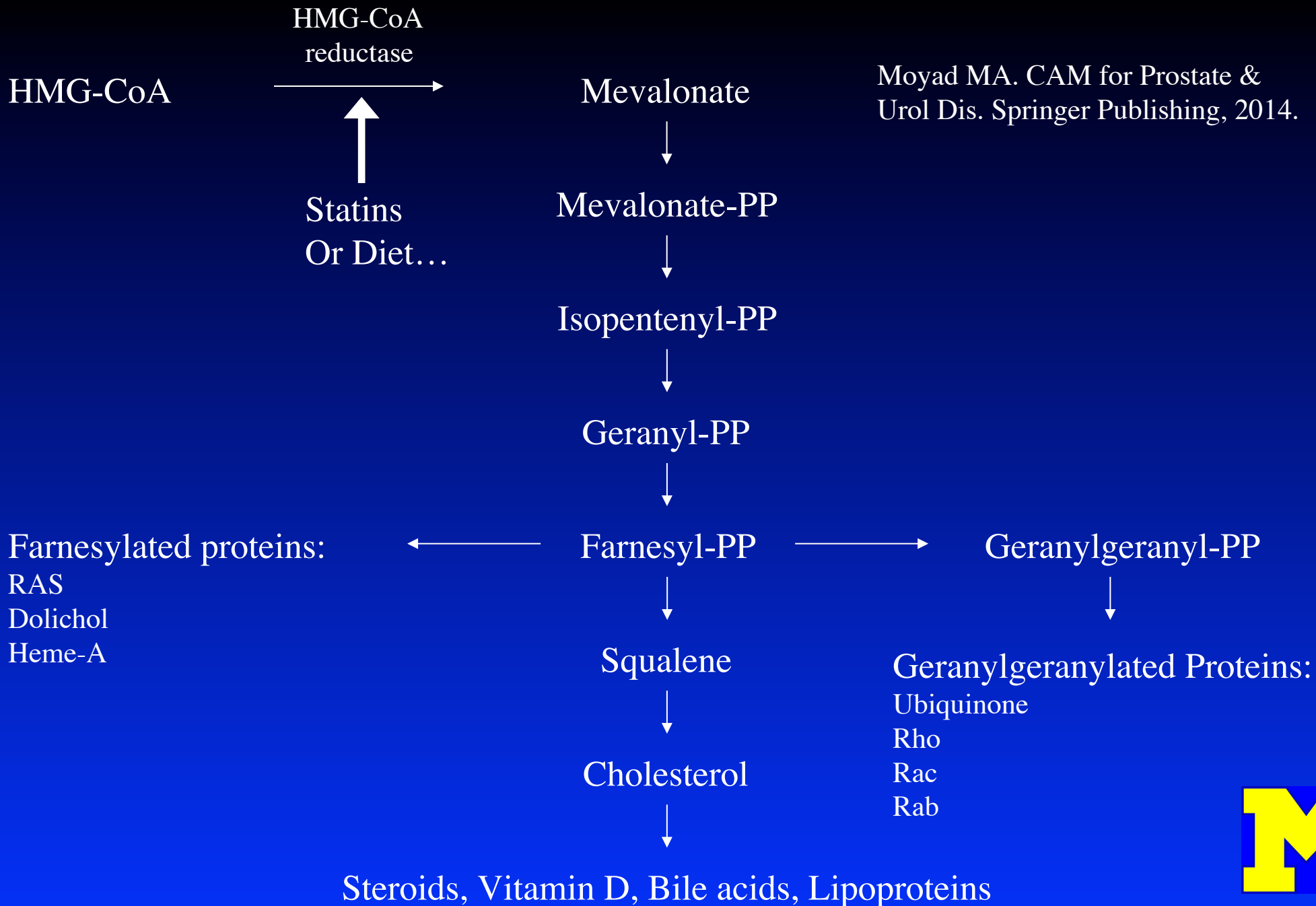


Pleiotropic Properties of Statins

- Inhibit thrombotic process (surgery?)
- Inhibit tumor cell proliferation
- Inhibit angiogenesis
- Modulate immune responses
- Reduce inflammation
- Improve vascular endothelium function
- Stimulate bone growth/ prevent bone loss
- Reduce oxidative stress
- Modulate smooth muscle cell proliferation
- Stabilize plaques
- Enhance fibrinolysis
- DHEA???

Stamm JA, Ornstein DL. *Oncology* 19(6):739-754, May, 2005.





Statins-Half-Life

Intolerance? Generic but 2!

ATORVASTATIN	<u>14 HOURS</u>
FLUVASTATIN	1.2 HOURS
LOVASTATIN	3 HOURS
PITAVASTATIN	<u>11 HOURS</u>
PRAVASTATIN	1.8 HOURS
SIMVASTATIN	2 HOURS
ROSUVASTATIN	<u>19 HOURS</u>

Schachter M. Fundam Clin Pharmacol 2005;19:117-125.



JUPITER SHOULD CHANGE YOUR LIFE (less is more)!

<u>LDL</u> <u>“bad cholesterol”</u>	<u>hs-CRP</u>	<u>WHAT</u> <u>HAPPENED?</u>
≥ 70 (1.81 mmol/L)	≥ 1 mg/L	-9% Reduction
≥ 70	≤ 1 mg/L	-35% Reduction
< 70	≥ 1 mg/L	-50% Reduction
< 70	≤ 1 mg/L	-79% Reduction!!!

Ridker PM, et al. Lancet 373:1175-1182, April 4, 2009. Justification for the Use of Statins in Prevention.



-DVT? CANCER MORTALITY RATE?

Red Yeast Rice-Components (Dose Range-1200-3400 mg/d)

Dihydromonacolin K
Monacolin J
Monacolin JA
Monacolin K (2.5 mg) (LOVASTATIN EQUIVALENT)
Monacolin KA
Monacolin L
Monacolin LA
Monacolin M
Monacolin X
Monacolin XA



Red Yeast Rice Vs. Placebo (n=4870, NNT=21)

Nonfatal MI	-62%*
CHD Death	-31%*
Fatal MI	-33% (p=0.19)
Fatal Stroke	-9%
Revascularization	-36%*
Death from CVD	-30%*
Death from Cancer	-56%*
Total Deaths	-33%*



Ezetimibe= Blocks GI Cholesterol Absorption

- IMPROVE-IT Trial=Statin + Ezetimibe
- Cholesterol=Increases Microvessel Density
- Ezetimibe reduces angiogenesis (Xenografts)

Bottom Line=Ezetimibe is another option!

PCSK9 inhib? EXERCISE & DIET=Lower LDL!



Aspirin & Cancer^{1,2}

Condition	Risk Reduction
Colorectal ^{1,2}	DEATHS = ? RISK = YES!
Esophageal ¹	???
Lung ¹	???
Pancreas ¹	???
Prostate ¹	??? Maybe = Meta Analyses

1. Rothwell PM, Fowkes FG, Belch JF, et al. *Lancet*. 2011;377(9759):31-41.

2. Cook NR, Lee IM, Zhang SM, et al. *Ann Intern Med*. 2013;159(2):77-85.



Aspirin- REDUCE TRIAL

- Dutasteride Prevention Trial (PSA=2.5-10)
- 3169 nonusers (50%), 1368 (21%) ASA
- Total Pca Reduced (OR=-19%, P=0.02)
- High-Grade Reduced (OR=-20%, P=0.04)
- “Among men with a negative biopsy, aspirin and/or NSAID use was associated with decreased prostate cancer risk.” (Obesity & Risk?!)



Pca & Aspirin- New 2014 Meta-Analysis

- 39 Studies (20 CC & 19 Cohort..>108,000 Cases)
- OR= -19% For Advanced PCa
- OR= -14% For Mortality
- 4+ years=Increased Association
- “The present meta-analysis provides support for the hypothesis that aspirin use is inversely related to Pca incidence and Pca-specific mortality.”



A=Aspirin (baby)=40,000 Women

CONDITION	RISK REDUCTION-ASA
Heart Attack-age 65+	34% Reduction
Ischemic Stroke-age 65+	30% Reduction
Hemorrhagic Stroke	24% Increase
Major GI Bleed	40% Increase
Peptic Ulcer	32% Increase

Colorectal Cancer=Yes!!!



REYNOLDS RISK SCORE

(www.reynoldsriskscore.org)

- AGE
- CURRENTLY SMOKE?
- SYSTOLIC BP
- TOTAL CHOLESTEROL (mg/dL)
- HDL
- Hs-CRP (Women>Men...No Supp Group)
- Family History (Mother or Father w/MI before age 60)

10-year Risk? No diabetes?

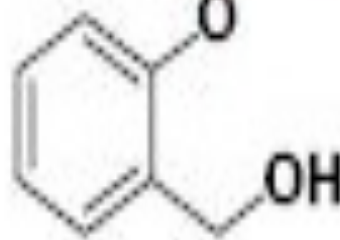


www.cvriskcalculator.com
(simple)



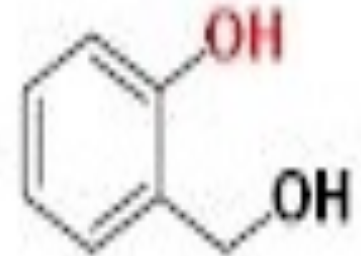


isolation
→
(1827)



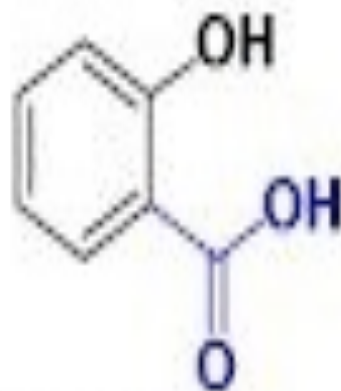
salicin

hydrolysis
→



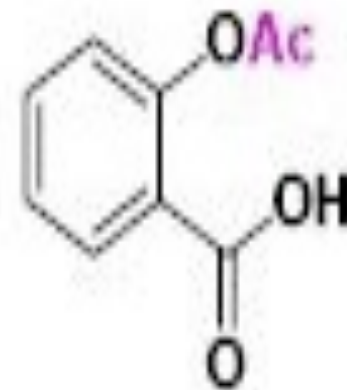
salicyl alcohol
(saligenin)

oxidation
→
(1938)



salicylic acid

acetylation
→



aspirin

Food? Herbs? Spices? Alcohol? Supplements? Tobacco/Screen....

Pca & Metformin- New 2014 Meta-Analysis

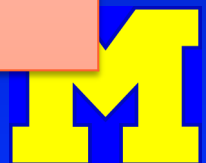
- 21 Studies
- HR=0.91 For Incidence
- HR=0.81 For BCR (n=2900)
- Not Significant=All-Cause=0.86
- “Results suggest that metformin use appears to be associated with a significant reduction in cancer risk and BCR of prostate cancer, but not in all-cause mortality of patients with prostate cancer.”



Metformin (850 mg bid + Low-Glycemic/Cal Diet + Exer)

PARAMETER (N=40, 6 months)	METFORMIN VS CONTROL RESULT (% Change from mean)
Waist Circumference (cm)	-0.58 vs. +2.15 (p=0.05)
BMI	-3.19 vs. +2.10 (p<0.001)
Weight (kg)	-3.19 vs. +2.18 (p<0.001)
Body fat (%)	-5.48 vs. +6.47 (p=0.08)
Systolic BP	-5.96% vs. +1.77 (p=0.01)
NO CHANGE IN LIPIDS	NO CHANGE IN LIPIDS (Hgb A1C reduced, p=0.07)

Nobes JP, Langley SE, Klopper T, et al. BJU Int 2012;109:1495-1502.



CRPC & Metformin- New 2014-Phase 2

- 10 Swiss Centers (1000 mg BID; n=44)
- Non-Diabetic
- 52% Prolongation DT
- 36% progression-free 12-wk (9% 24-weeks)
- IGF-1 (p=0.003) & IGFBP3 (p=0.03)

Bottom Line=Phase 3 Breast Ca Similar Results



METFORMIN- Final Thoughts

- 500-2000 mg (850 mg BID-Most Common)
- With meals & titrate! Hx. Of Weight loss in U.S.
- Soft Stool/Diarrhea/Wt Loss/Metallic Taste
- Contrast & Renal &/or Liver Insufficiency
- Deficiency of B12 & Magnesium
- Phase 3 Breast Ca. Trial? Others? (Acarbose...?)

Rothermundt C, et al. Eur Urol 2014;66:468-474. & Goodwin PJ, et al. J Natl Cancer Inst 2015; 107: epub March 4, 2015. & Moyad MA, Vogelzang NJ. Asian J Androl 2015; February 3, epub ahead of print.



Metformin (850 mg BID)-Final Slide

- Diabetes Prevention (n=3234 high-risk)
- 31%=Metformin & 58%=intensive lifestyle (7% wt loss & 150 min/wk-2.8 years.). Calories?

Bottom Line=10-years follow-up. Diabetes reduced 34% by lifestyle & 18% metformin vs. placebo!

(Diabetes Prevention Program Research Group. Lancet 2009;374:1677-1686. Knowler WC, Barrett-Connor E, Fowler SE, et al. N Engl J Med 2002;346:393-403.)





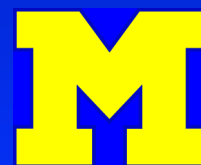
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www.cvriskcalculator.com

