Unproven Therapies in Prostate Cancer

Unproven Therapies in Prostate Cancer Overview

* Scientific approach to cancer treatment and drug development
* History and current status of Prostate Cancer treatment
* Dietary supplements defined
* Regulation of food, drugs and dietary supplements
* Alternative/integrative cancer treatments
* Concerns regarding dietary supplements
* PC-SPES
* Other unproven cancer treatments
* Recommendation for approach to alternative treatments
* Resources

Unproven Therapies in Prostate Cancer

* Cancer Drug Market
  - $100-175 Billion per year
* Supplement Market
  - $30-35 Billion per year
  - Hundreds of Companies
  - Thousands of products

Science

Science is a systematic enterprise that builds and organizes knowledge in the form of testable explanations and predictions about the universe.

http://global.britannica.com/topic/science

Characteristics of good science: measurable, reproducible, **peer reviewed**, systematically built on previous knowledge, follows logical progression and mechanistically plausible.

Psuedoscience is a claim, belief, or practice presented as scientific, but does not adhere to scientific method.

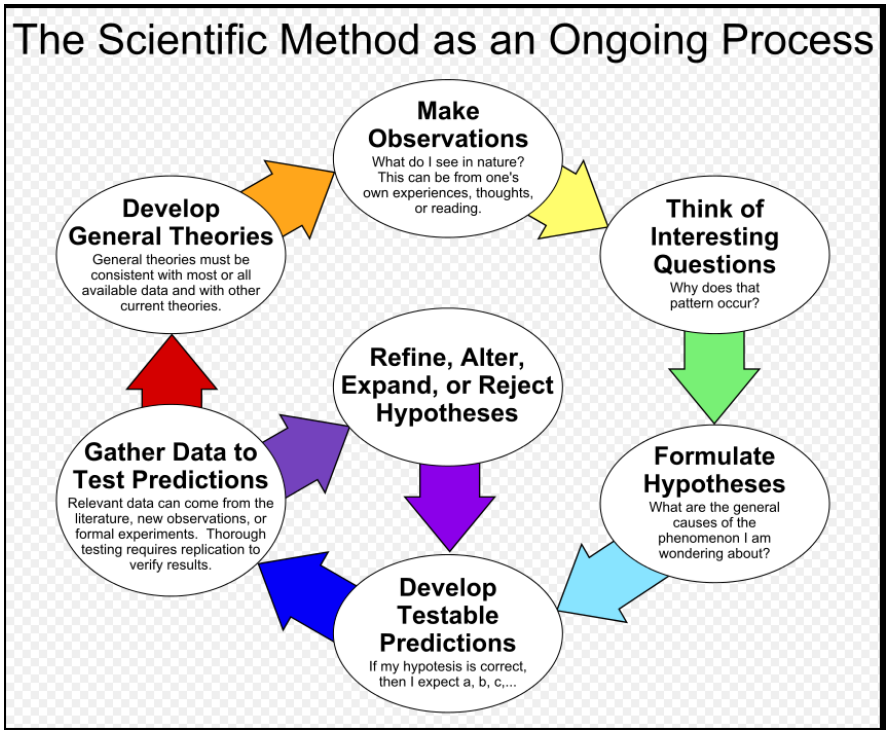
Wikipedia

Psuedoscience is often characterized by the following: contradictory, exaggerated or unproven claims; over-reliance on confirmation rather than rigorous attempts at refutation;

lack of openness to evaluation by other experts in the field; and absence of systematic practices when rationally developing theories

Wikipedia

https://en.wikipedia.org/wiki/Scientific_method



Clinical/Cancer Research – Historical Perspective

* Lind 1747 – first randomized trial
* 1937 – National Cancer Institute
* Hill 1948 – first published randomized trial
* 1955 – first medical meta-analysis published
* Zubrod 1955 – NCI-DTP
* 1995 - NCCN
* 1996 – Cochrane Library
* 2000 – GRADE
  * Grading Recommendation, Assessment, Development and Education
* 2005 – Stampede Trial
* "Basket Trials"

NCI Levels of Evidence

* Study Design
  * Randomized controlled clinical trials
    * Double blinded
    * Non-blinded
  * Nonrandomized controlled clinical trials
  * Case based series
    * Population based, consecutive case series
    * Consecutive case series
    * Nonconsecutive case series
  * Best case series

* End Points
  * Total mortality
  * Cause-specific mortality
  * Carefully assessed QOL
  * Indirect Surrogates
    * Disease-free survival
    * Progression free survival
    * Tumor response rates

Grading quality of evidence and strength of recommendations

GRADE Working Group, BMJ Vol 328. 19JUNE2004. bmj.com

* Quality of Evidence
  * Key Elements
    * Study design – Randomized v. Observational
    * Study quality
    * Consistency – effect across studies
    * Directness – Does evidence relate to population in question?
  * Grading
    * High = unlikely to change w/ further research
    * Moderate, Low and Very Low
* Strength of Recommendation
    * Net Benefits
    * Net benefits with trade offs
    * Net benefits with uncertain trade offs
    * No net benfits

Peer Review in Science

* Meeting Presentations
* Peer Reviewed Publication
* Meta-analysis
* Systemic Reviews
  * Cochrane Library
  * Professional Organizations
    * ASCO, AACR, ASTRO, AUA, EORTC, NCCN, NCI etc

… Theranos was performing tests on patients without having published peer-reviewed research – a cardinal science – and with minimal oversight

Lev Grossman

The fall of Theranos and the future of science in Silicon Valley. Time. May 26, 2016. pp 25-26

NCI Developmental Therapeutic Program

* 1955 Gordon Zubrod
* Branches
  * Molecular Pharmacology
  * Biological Testing
  * Toxicology and Pharmacology
  * Drug Synthesis
  * Natural Products
  * Biologic resources
  * Pharmaceutical Resources
  * Information Technology
  * Grants and Contract

NCI Developmental Therapeutic Program

* 1986 Natural Products Branch
  * 80,000 Plants
  * 20,000 Invertebrates
  * 16,000 microbes
  * Traditional Chinese Medicines
    * >200 Authenticated plant & fungal sources

Testing of Drug to Treat Cancer

* Preclinical
  * Cell culture screening
  * Animal model xenografts
* Human Subject
  * Phase 0
  * Phase 1
  * Phase 2
  * Phase 3
  * Phase 4

What does it take to get a cancer drug to market?

AstraZeneca - A Guide to Cancer Drug Development and Regulation

* 5,000 compounds tested for one new drug to come to market
* Currently 400 new cancer products are in development
* Time to development – 10-15 yrs
* Cost of development – approx $800 million

Future of Treatment Development

* Human Genome Project
* Cancer Genome Project
* Proteinomics
* Pharmacogenomics
* Pharmacoproteinomics

Prostate Cancer

238,590 New Case in 2013

29,720 Deaths per in 2013

8:1 Ratio of incidence to death in diagnosed patients

Estimated 70% of males >80 years of age have occult prostate Cancer

ASCO-SEP 4th Edition

Prostate cancer

Clinical Localized Disease →

Rising PSA →

Clinical Metastases: Noncastrate Resistent →

Clinical Metastases: Castrate Resistent →
-Pre-docetaxel
-Post-docetaxel

ASCO-SEP 4th Edition

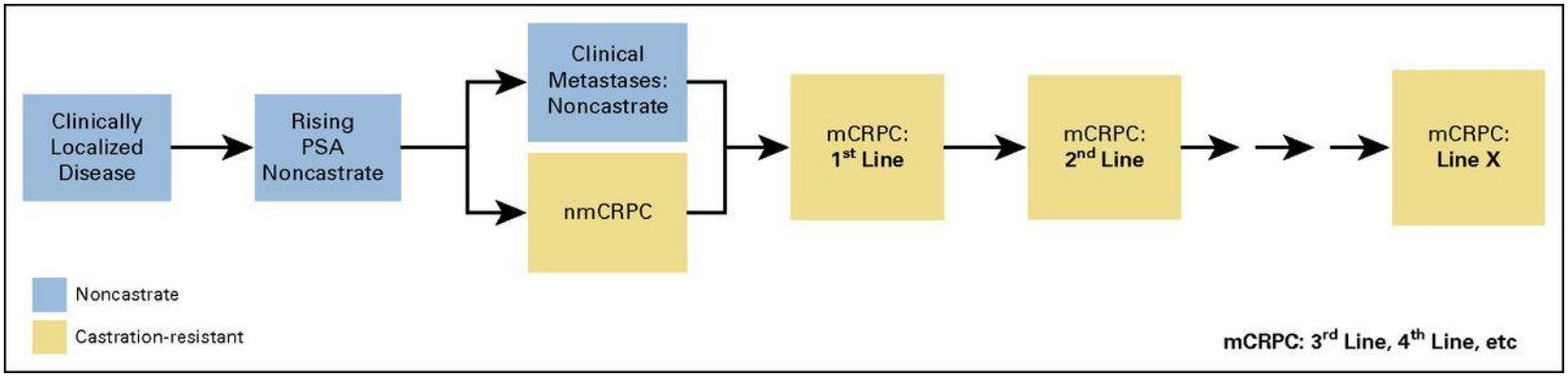
History of Metastatic Prostate Cancer Treatment

* 1947 Huggins – ADT
* 1999 -- PCCTWG
* 2004 – Tax 327 & SWOG 9916
* 2004 – Zometa
* 2008 -- PCCTWG 2
* April 2011 – Abiraterone
* August 2012 – Enzalutamide
* May 2013 – Alpharadin
* June 2014 – Adjuvant docetaxel
* 2016 – PCCTWG 3

Adjuvant Docetaxel

	Progression	P Value	OS	P Value
GETUG-AFU 15	22.9 v 12.9 M	0.0021	62.1 v 48.6 M	0.3
CHAARTED	20.2 v 11.7 M	<0.001	57.6 v 44.0 M	<0.001
STAMPEDE	44.4 v. 35.3	<0.000001	81 v. 71 M	0.006

Prostate cancer clinical states model, a framework for patient treatment and drug development, updated for the Prostate Cancer Clinical Trials Working Group 3.

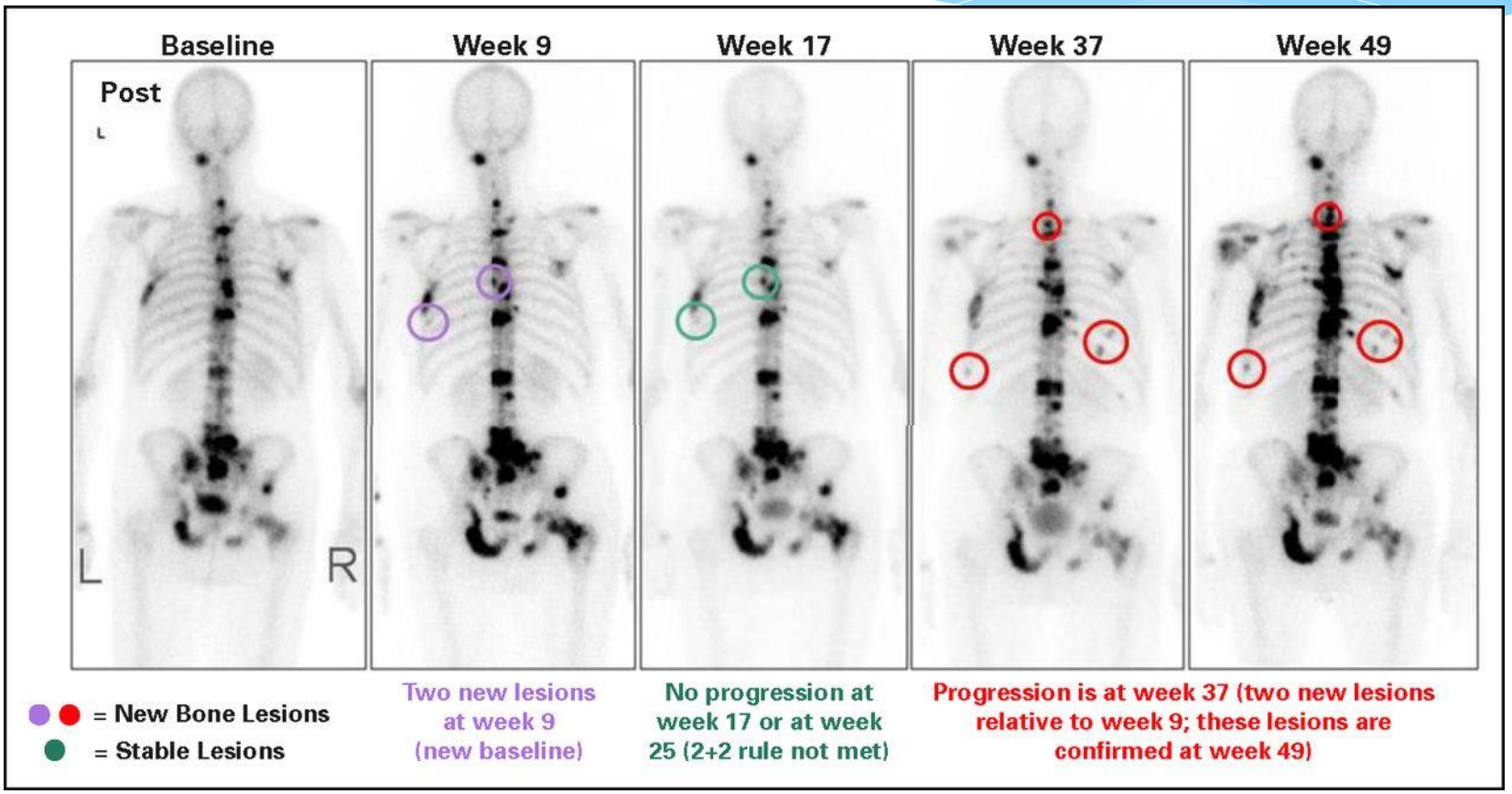


Howard I. Scher et al. JCO 2016;34:1402-1418

PCCTWG 2&3

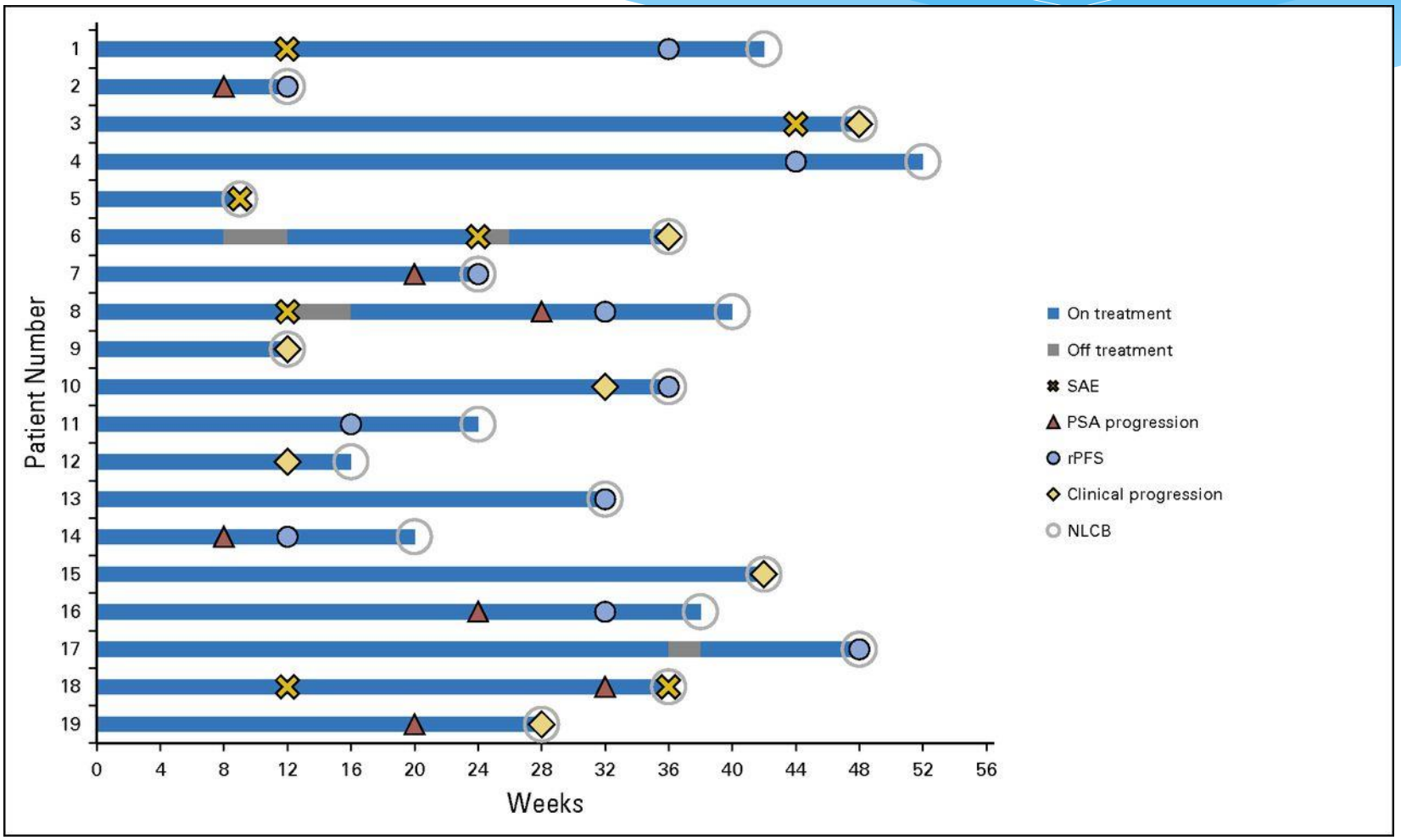
* PCCTWG 2
  * CT a/p, bone scan, PSA
  * 1st restaging at 12 weeks
  * Progression
    * Soft tissue – RECIST
    * Nodes >2cm
    * Bone Scan 2 or more new lesions
    * PSA >25% rise
* PCCTWG 3
  * 1st resting at 8 weeks and repeat in 8 weeks if progression
  * Mixed Response
  * PSA only progression in metastatic disease
  * NLCB
    * No longer clinically benefiting
  * Progression
    * Nodes >1.0cm short axis

Controlling for flare by applying the 2+2 rule using the first post-treatment scan as baseline.



Howard I. Scher et al. JCO 2016;34:1402-1418

Swim lanes illustrating the patient experience on a trial.



Howard I. Scher et al. JCO 2016;34:1402-1418

JOURNAL OF CLINICAL ONCOLOGY ASCO

What is a dietary supplement

* A dietary supplement is a product intended for ingestion that contains a "dietary ingredient" intended to add further nutritional value to (supplement) the diet. A "dietary ingredient" may be one, or any combination, of the following substances:
* •a vitamin
* •a mineral
* •an herb or other botanical
* •an amino acid
* •a dietary substance for use by people to supplement the diet by increasing the total dietary intake
* •a concentrate, metabolite, constituent, or extract
* Dietary supplements may be found in many forms such as tablets, capsules, softgels, gelcaps, liquids, or powders. Some dietary supplements can help ensure that you get an adequate dietary intake of essential nutrients; others may help you reduce your risk of disease.
    * FDA Website

Dietary Supplement Health and Education Act -1994

* Prohibits manufactures of dietary supplement from making products which are adulterated or misbranded
* Shifts burden of proof to FDA/USA for safety and labeling
* Does NOT require licensing of product or manufacturer
* Does NOT require proof of effectiveness

Dietary Supplement Health and Education Act -1994

* >50% US citizens use dietary supplements
* 600 manufactures
* 4,000 products
* $4 Billion industry

Pure Food and Drug Act - 1906

* "Any article of food or drug which is adulterated or misbranded."
  * Misdemeanor – 1 year prison or $500
* Drug strength, quality or purity must be plainly stated on the box

Federal Pure Food, Drug and Cosmetic Act - 1936

* Required safety testing before drug were sold
* Required manufacturing plants to be licensed and inspected
* Kefauver-Harris Amendment 1961
  * Added proof of effectiveness to drug licensure
* Rogers-Proxmire Amendment 1976
  * Prohibited FDA from classifying vitamins and mineral supplements as drugs, unless drug claims were made of said vitamins or supplements

Alternative Treatments on the Internet

Alkalinization – $NaHCO_3$; CeCl
Selenium
Vitamin D
Omega-3
Zinc
Antioxidants
Lycopene
Saw palmetto
Cannabis oil
Cayenne pepper

* Soy
* Cohosh
* Stinging nettle
* Nigella sativa (black cummin)
* Soursop
* Ginger extract
* Laetrile
* Proton therapy
* HiFu

Why Use Alternative and Complimentary Treatments

* Long history of ineffective and/or toxic cancer treatments
* Supplement Industry and Alternative Practitioners Claims
  * Conventional physicians use only: surgery, radiation and chemotherapy
  * PHARMA works with the FDA to prevent alternatives
  * Alternative treatments have a long history of curing cancer
  * Chemotherapy kills more than it cure
  * BIG PHARMA is a monopoly that excludes other players
* Natural remedies are safe
* Placebo Effect

NCI Complimentary and Alternative Medicine

* 1940's-1970's
  * Evaluated info on alternatives
* 1986 – Natural Products Branch of NCI
* 1991
  * Best Case Series Review Program
* 1998 – Office of Cancer Complimentary and Alternative Medicine
* 2010
  * 382 Projects
  * $105 million in Grants, Cooperative Agreement & Contracts
* Six Investigators/Administrators

What's in a name?

You call it a dietary supplement,

I call it a pharmaceutical drug

Chemotherapy in the Environment

Dietary element → Pharmaceutical → Toxin

Vitamin A

* Deficient state
  * Xerophthalmia
  * Poor bone growth
  * Skin changes
  * Immune deficiency
* Pharmaceutical
  * ATRA
  * Isotretinoin(Accutane)
  * Bexarotene(Targretin)
* Toxicity(10xRDA)
  * Cirrhosis
  * Hyperlipidemia
  * Pseudotumor Cerebri

Supplement Purity

* *What's in Those Supplements?*
  * Anahad O'Connor, New York Times Feb 3, 2015
  * New York State Attorney General's Office

  "The authorities said they had run tests on popular store brands of herbal supplements at the retailers – Walmart, Walgreens, Target and GNC – which showed that roughly **4/5** of the products **contained none of the herbs** listed on their labels."

* CHOP
  * Certificate of Analysis
    * Approx half didn't respond
    * 90% did not match labeling

* *DNA barcode identification of black cohosh herbal*
  * J AOAC Int. 2012 Jul-Aug; 95(4): 1023-34
  * 9/36 specimen matched

http://NCCIH.NIH.GOV/NEWS/ALERTS

Alerts and Advisories

Share:

Notices from government agencies, such as the Food and Drug Administration (FDA) and the Federal Trade Commission (FTC), to let consumers know about recalls, tainted products, and other alerts/advisories.

1 2 3 4 5 6 7 8 9 next ›

2016

- Ziyinzhuangyang contains hidden drug ingredient (FDA; 07/29/16)
- Ultimate Lean contains hidden drug ingredient (FDA; 07/28/16)
- Zi Xiu Tang Beauty Face and Figure Capsule contains hidden drug ingredients (FDA; 07/28/16)
- Weili (一炮到天亮 or Yi Pao Dao Tian Liang) contains hidden drug ingredient (FDA; 07/28/16)
- Slim Fit X contains hidden drug ingredients (FDA; 07/27/16)
- Mang Luk Power Slim contains hidden drug ingredient (FDA; 07/27/16)

Prostate Cancer and Supplementation of alpha-Tocopherol and beta-Carotene: Incidence and Mortality in a Controlled Trial

J Natl Cancer Inst 1998, Mar 18;90(6):440-6

* 29,133 male smokers, age 50-69 in SW Finland
* 2x2 design
* Median follow-up 6.1 yrs
* 246 new cases of prostate cancer
* 62 deaths

Prostate Cancer and Supplementation of alpha-Tocopherol and beta-Carotene: Incidence and Mortality in a Controlled Trial

J Natl Cancer Inst 1998, Mar 18;90(6):440-6

	New Prostate Cancer	Death
Alpha-Tocopherol	43	11
Alpha-Tocopherol and Beta-Carotene	56	12
Beta-Carotene	80	21
Placebo	67	18
Total	246	62

* Alpha v No Alpha
  * 41% decrease in mortality
  * 23% decrease in incidence
* Beta v No Beta
  * 15% increase in mortality

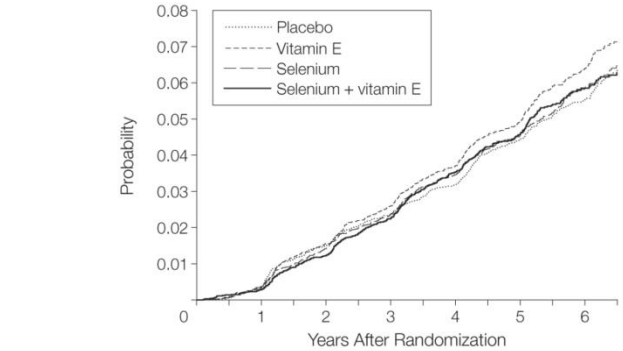
SELECT TRIAL

JAMA 2009 Jan 7;301(1):39-5

* 35,533 in US, Canada and PR
* 2001-2004
* 2x2 design
  * Vitamin E, Vitamin E & Selenium, Selenium, Placebo
* Age >50 AA; >55 all others
* Prescreened
  * PSA 4 or less and normal DRE
* 5.46 years of follow-up

From: **Effect of Selenium and Vitamin E on Risk of Prostate Cancer and Other Cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)**

JAMA. 2009;301(1):39-51. doi:10.1001/jama.2008.864



No. at risk

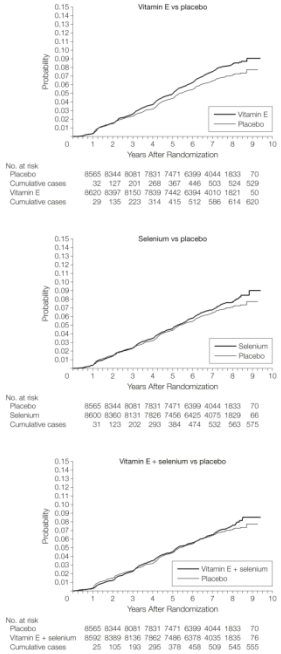
Placebo	8689	8553	8328	8039	7389	4892	2516
Vitamin E	8732	8610	8373	8098	7401	4867	2537
Selenium	8750	8597	8341	8083	7393	4848	2558
Selenium + vitamin E	8700	8585	8371	8097	7428	4894	2580

Figure Legend:

Compared with placebo, there was a statistically nonsignificant increase in prostate cancer in the vitamin E group (P=.06) and not in the selenium + vitamin E group (P=.52) or the selenium group (P=.62).

From: **Vitamin E and the Risk of Prostate Cancer: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)**

JAMA. 2011;306(14):1549-1556. doi:10.1001/jama.2011.1437



SELECT Trial Update

JAMA 2011 Oct 12;306(14): 1549-56

* Vitamin E
  * HR 1.17; 99% CI 1.004-1.36; P=.008
* Selenium
  * HR 1.05; 99% CI 0.89-1.22; P.46

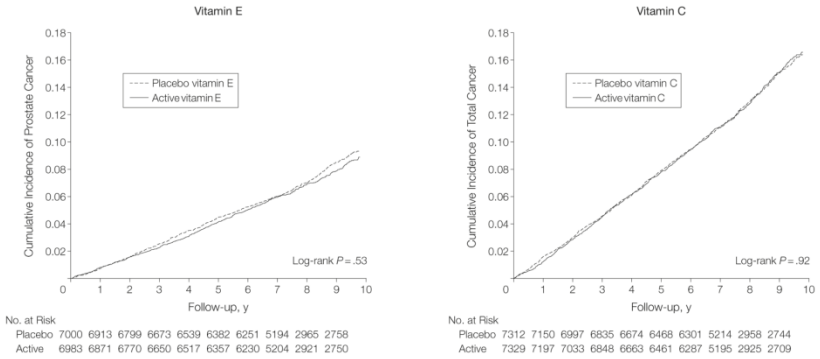
Physicians' Health Study II

JAMA 2009 Jan 7;301(1):52-62

* 1997-2007 w/ 8.0 yrs follow-up
* 14,641 Physicians > 50 yrs
* Randomized 2x2x2x2
  * Vit C, Vit E, Centrum Silver
* Endpoints
  * Total new cancers and cancer deaths
  * Total new prostate cancer and deaths
* 1008 new Prostate cancers (6.8%)

From: **Vitamins E and C in the Prevention of Prostate and Total Cancer in Men: The Physicians' Health Study II Randomized Controlled Trial**

JAMA. 2009;301(1):52-62. doi:10.1001/jama.2008.862



Prostate Cancer and Supplementation of alpha-Tocopherol and beta-Carotene: Incidence and Mortality in a Controlled Trial

J Natl Cancer Inst 1998, Mar 18;90(6):440-6

* Homogenous population
  * All were smokers
  * Dietary factors may have influence results
* Not prescreened for prostate cancer
* Case finding was through a registry
* Study was underpowered
    * Total # of new cancer was <1% of population
      * Likely represents late stage only cancers
      * Compare to SELECT where new cancer were 5%
    * 16 more deaths in non-alpha/29K lives

PC-SPES

http://www.cancer.gov/about-cancer/treatment/cam/hp/pc-spes-pdq, Last updated April 15, 2016

* Mixture of 8 herbs patented in US by Botanic Lab
  * Baikal skullcap, chrysanthemum(morifolium), gandoderma, isatis, licorice, panax ginseng, isodon rubescens, and saw palmetto
* Preclinical
  * Inhibited PSA expression in LNCaP cell line
    * Effect noted w/ PC-SPEC but when each element was tested separately only skullcap, serenoa repens and licorice lowered PSA
  * Inhibited clonal growth in LNCap, PC-3 & DU-145
* Reports of clinical success 1999-2003
  * 23 pt on respective analysis had PSA decline
  * BJ Uro Int 2000 Mar;85(4) 481-5
    * Prospective 16 pt w/ castrate resistant metastic Pca
    * 14/16 pain response; 13/16 PSA decline >50%

PC-SPES

http://www.cancer.gov/about-cancer/treatment/cam/hp/pc-spes-pdq, Last updated April 15, 2016

* Randomized Phase II v. DES w/ crossover
  * 90 pts, 85 evaluable
  * PSA response PC-SPES 40%; DES 24% n/s
  * TTP PC-SPES 5.5 M; DES 2.9 M
  * VTE PC-SPES 1; DES 4
  * Crossover results were non-conclussive
    * J Clin Oncol. 2004, Sept 15;22(18):3705-12
* Claims of DES contamination
  * 2001 Botanic Lab submitted specimens but no DES
  * Six random lots positive for DES
  * Rocky Mountain Labs found DES in three lots
  * Other lot found w/ varying amounts of DES, warfarin and indomethacin
  * All lot in JCO reported trial contained DES and/or Estradiol

Pomegranate Juice

Clin Cancer Res 2006;12:4018-4026

* Study
  * PSA Doubling time
  * N=48; 46 eval
  * Gleason 5-7, PSA 0.2-5
  * Planned crossover
  * Results
    * 16/46 w/ decreased PSA
    * 4/46 >50% decrease
* Critique
  * Variability of PSA as marker
  * Phase 2 data
  * Low to very low risk pts
  * Ongoing clinical trials

Saw Palmetto

* Beta-sitosterol
* Inhibits P3, LNKCaP Cell Lines
* BPH – multiple small studies
* Action
  * 5-a-reductase, cyclooxygenase
* Adverse reactions
  * GI, diarrhea, fatigue, HA. Bleeding complications reported
* Interactions
  * NSAIDs
  * Additive anticoagulant and antiplatelet effect
  * Inhibits UGT and CYP450
* BPH
  * Cochrane Review supports clinical effectiveness
  * Mechanism c/w other approved drugs
  * Efficacy v 5-a inhibitors is unknown
  * Safety v 5-ainhibitors is unknown
* Cancer Treatment
  * Data are primarily preclinical
  * Substantial risk of drug interaction
  * Data of PCa prevention w/ 5-a inhibitors is mixed

Ginger root is a miracle cure for prostate cancer
Natural News, December 05, 2012

* Ginger is the miracle cure
* The British Journal of Nutrition published the results of an American study recently in which ginger extract (zingiber officinale) actually killed human prostate cancer cells while healthy prostate cells did not die. The results occurred at a daily dose of 100 mg of ginger extract per kg of body weight (based on a man weighing 150 pounds this equals about 550 mg extract per day). In eight weeks, the ginger extract slashed prostate tumor growth in half. The researchers have estimated that 100 grams of fresh ginger eaten daily will offer the same results.

* As a cancer champion, ginger has anti-inflammatory, antioxidant and antiproliferative effects upon tumors making ginger a promising chemopreventive agent. Whole ginger extract holds significant growth-inhibitory and death-inductory effects in a spectrum of cancer cells by interrupting cancer cell-cycle progression, impairing cancer reproduction and modulating apoptosis. But most importantly, ginger does not have any toxicity in normal, rapidly dividing tissues such as gut and bone marrow.

* Ginger taken orally can prevent or relieve nausea resulting from chemotherapy, motion sickness, pregnancy, and surgery.

* Not only can ginger root cure cancer, but it is a natural remedy for travel sickness, nausea, indigestion, flatulence, colic, irritable bowel syndrome, loss of appetite, chills, poor circulation, menstrual cramps, dyspepsia, heartburn, indigestion and many other gastrointestinal problems. Ginger root is also a powerful anti-inflammatory for joint problems and is indicated for arthritis, fevers, headaches, toothaches, coughs, bronchitis, osteoarthritis, rheumatoid arthritis, tendonitis, high cholesterol and blood-pressure and can also prevent internal blood clots. Ginger is even anti-viral and makes a warming cold and flu remedy.

* Learn more: http://www.naturalnews.com/038215_ginger_root_miracle_cure_prostate_cancer.html#ixzz4D5FocVGQ

Ginger Continued

* Br J Nutr. 2012 Feb;107(4):473-84. doi: 10.1017/S0007114511003308. Epub 2011 Aug 18.
* Benefits of whole ginger extract in prostate cancer.
* Karna P1, Chagani S, Gundala SR, Rida PC, Asif G, Sharma V, Gupta MV, Aneja R.
* Author information
* Abstract
* It is appreciated far and wide that increased and regular consumption of fruits and vegetables is linked with noteworthy anticancer benefits. Extensively consumed as a spice in foods and beverages worldwide, ginger (Zingiber officinale Roscoe) is an excellent source of several bioactive phenolics, including non-volatile pungent compounds such as gingerols, paradols, shogaols and gingerones. Ginger has been known to display anti-inflammatory, antioxidant and antiproliferative activities, indicating its promising role as a chemopreventive agent. Here, we show that whole ginger extract (GE) exerts significant growth-inhibitory and death-inductory effects in a spectrum of prostate cancer cells. Comprehensive studies have confirmed that GE perturbed cell-cycle progression, impaired reproductive capacity, modulated cell-cycle and apoptosis regulatory molecules and induced a caspase-driven, mitochondrially mediated apoptosis in human prostate cancer cells. Remarkably, daily oral feeding of 100 mg/kg body weight of GE inhibited growth and progression of PC-3 xenografts by approximately 56 % in nude mice, as shown by measurements of tumour volume. Tumour tissue from GE-treated mice showed reduced proliferation index and widespread apoptosis compared with controls, as determined by immunoblotting and immunohistochemical methods. Most importantly, GE did not exert any detectable toxicity in normal, rapidly dividing tissues such as gut and bone marrow. To the best of our knowledge, this is the first report to demonstrate the in vitro and in vivo anticancer activity of whole GE for the management of prostate cancer.
* PMID: 21849094 PMCID: PMC3426621 DOI: 10.1017/S0007114511003308

Cesium Chloride

* Used in cardiovascular research for arrhythmogenesis
* Claims to raise pH in cancer cell environment
  * Warburg hypothesis(anaerobic)→tissue acid accumulation
* Some data in preclinical models
* All Clinical claims based on one article in 1984
* Hypomagnesemia, hypokalemia, prolonged QT
* Nausea, diarrhea, syncope, hypotension

Cesium Therapy in Cancer Patients

HE Sartori, MD Pharmacology, Biochemistry & Behavior. Vol. 21. Suppl. I. pp 11-13. 1984

* Lacked well defined/uniform patient population
  * 10 tumor types, proximity of previous treatments not noted
  * 3 pt comatose, 3 pt untreated, 14 considered terminal, 3 no mets
* Methodologic problems
  * No standard for tumor measurement or response
* Multiple variables in treatment
  * At least 3 dose levels of cesium used
  * Zinc, VitA, VitE, selenium, Amygdalin
  * Multiple variations of diets and dietary supplements
  * EDTA, DMSO, Magnesium, Potassium

Cesium Therapy in Cancer Patients

HE Sartori, MD Pharmacology, Biochemistry & Behavior. Vol. 21. Suppl. I. pp 11-13. 1984

* 5 best cases out of 50
  * Breast cancer – no staging info provided
  * Unknown primary – autopsy NED

    no tissue diagnosis or ante mortem staging

    Pt had previous chemo
  * Lymphoma – pt on chemo during Cs treatment
  * 4&5 Colon – palpable change in abdominal wall

Cesium Therapy in Cancer Patients

HE Sartori, MD Pharmacology, Biochemistry & Behavior. Vol. 21. Suppl. I. pp 11-13. 1984

* Peer reviewed journal but copy circulated by author has modified after publication by author
* Essentially a phase II trial
* Lacked well defined patient population
* Methodologic problems
* Multiple variables in treatment
* Give case reports of 5 best cases out of 50
* 14 day mortality of 26%
* Equates 1 yr survival to recovery from cancer
* Quotes unrelated study to support data
* Does not provide toxicity data

Amazing Cancer Therapy Wipes Out Prostate and Bone Cancer

Posted by ***Dr Sircus*** *on August 15, 2011 | Filed under* Cancer, Medicine

* Oral $NaHCO_3$ selectively increased the pH of tumors and reduced the formation of spontaneous metastases in mouse models of metastatic breast cancer. $NaHCO_3$ therapy also reduced the rate of lymph node involvement and significantly reduced the formation of hepatic metastases. Acid pH was shown to increase the release of active cathepsin B, an important matrix-remodeling protease.

* There has been work going on at the University of Arizona using bicarbonate (baking soda) as a potential treatment for cancer. Robert J. Gillies and his colleagues have demonstrated that pre-treatment of mice with sodium bicarbonate results in the alkalinization of the area around tumors (Raghunand 2003). This type of treatment has been found to "enhance the anti-tumor activity" of other anticancer drugs. This is very similar to the recently published research involving injecting O_2 directly into tumors and showing such direct administration of oxygen also facilitated the action of chemotherapy.
* This year these same researchers reported that bicarbonate increases tumor pH (i.e., makes it more alkaline) and also inhibits spontaneous metastases (Robey 2009). They showed that oral sodium bicarbonate increased the pH of tumors and also reduced the formation of spontaneous metastases in mice with breast cancer. It also reduced the rate of lymph node involvement.

Bicarbonate

* Biochem Pharmacol. 2003 Oct 1;66(7):1219-29.
* Tumor acidity, ion trapping and chemotherapeutics. II. pH-dependent partition coefficients predict importance of ion trapping on pharmacokinetics of weakly basic chemotherapeutic agents.
* Raghunand N1, Mahoney BP, Gillies RJ.
* Author information
* Abstract
* Ion-trapping theory predicts that alkalinization of tumor extracellular pH will enhance the anti-tumor activity of weak-base chemotherapeutics. We have previously demonstrated that chronic and acute treatment of tumor-bearing mice with sodium bicarbonate results in tumor-specific alkalinization of extracellular pH. Furthermore, bicarbonate pretreatment enhances the anti-tumor activity of doxorubicin and mitoxantrone in two different mouse tumor models. Previous work has indicated subtle, yet significant differences between the pH sensitivities of the biodistribution and anti-tumor efficacies of doxorubicin and mitoxantrone in vitro. The present study demonstrates that systemic alkalinization selectively enhances tumor uptake of radiolabeled mitoxantrone, but not doxorubicin. Results using these two drugs are quantitatively and qualitatively very different, and can be explained on the basis of differences in the octanol-water partition coefficients of their charged forms. These results suggest that inducing metabolic alkalosis in patients would have a positive effect on response to mitoxantrone therapy. However, the therapeutic index would not increase if sodium bicarbonate also caused increased retention of mitoxantrone in susceptible normal tissues in the host. The major dose-limiting organ systems for mitoxantrone are heart, liver, bone marrow, spleen and blood cells. Bicarbonate was found to have no significant effect on the distribution of mitoxantrone to any of these tissues except for spleen. However, neither spleen weights nor lymphocyte counts were adversely affected by NaHCO(3) pretreatment, indicating that this co-therapy does not enhance myelosuppression due to mitoxantrone therapy. These findings suggest that metabolic alkalosis would produce a net gain in mitoxantrone therapeutic index.

Bicarbonate

* Cancer Res. 2009 Mar 15;69(6):2260-8. doi: 10.1158/0008-5472.CAN-07-5575. Epub 2009 Mar 10.
* Bicarbonate increases tumor pH and inhibits spontaneous metastases.
* Robey IF1, Baggett BK, Kirkpatrick ND, Roe DJ, Dosescu J, Sloane BF, Hashim AI, Morse DL, Raghunand N, Gatenby RA, Gillies RJ.
* Author information
* Abstract
* The external pH of solid tumors is acidic as a consequence of increased metabolism of glucose and poor perfusion. Acid pH has been shown to stimulate tumor cell invasion and metastasis in vitro and in cells before tail vein injection in vivo. The present study investigates whether inhibition of this tumor acidity will reduce the incidence of in vivo metastases. Here, we show that oral NaHCO(3) selectively increased the pH of tumors and reduced the formation of spontaneous metastases in mouse models of metastatic breast cancer. This treatment regimen was shown to significantly increase the extracellular pH, but not the intracellular pH, of tumors by (31)P magnetic resonance spectroscopy and the export of acid from growing tumors by fluorescence microscopy of tumors grown in window chambers. NaHCO(3) therapy also reduced the rate of lymph node involvement, yet did not affect the levels of circulating tumor cells, suggesting that reduced organ metastases were not due to increased intravasation. In contrast, NaHCO(3) therapy significantly reduced the formation of hepatic metastases following intrasplenic injection, suggesting that it did inhibit extravasation and colonization. In tail vein injections of alternative cancer models, bicarbonate had mixed results, inhibiting the formation of metastases from PC3M prostate cancer cells, but not those of B16 melanoma. Although the mechanism of this therapy is not known with certainty, low pH was shown to increase the release of active cathepsin B, an important matrix remodeling protease.

Laetrile

PDQ Cancer Information summaries[Internet]. Bethesda (MD): National Cancer Institute (US); 2002-2015 Sept 29

* Amygdalin/Laetril – active metabolite – cyanide
* Other metabolites – prusasin & benzaldehyde
* 1970 IND denied due to lack of evidence in animal testing
* 1970's legal in 20 states
* 1980 federal ban on interstate shipping upheld by SCOTUS
* 1982 NCI Phase II 1 PR in 175 pt
* Side effects
  * Cyanide related
  * Oral > IV
  * Potentiated by fruit and vegetable high in beta-glucosidase, raw almonds or high dose Vitamin C

Treatment Alternatives for Early Stage Prostate Cancer

* Active Surveillance
* Surgery
* IMRT/SBRT/IGRT
* Proton Beam Therapy
* HiFU
* Cryotherapy

Proton Beam Therapy

* Studies
  * SEER 2002-2007
    * no difference in toxicity or effectiveness
  * Retrospective Medicare Database
    * Decreased 6 month toxicity
    * Equal 12 month toxicity
* Organizational Recommendations
  * ASTRO
    * Use only in context of a clinical trial
  * NCCN
    * "No clear evidence supports a benefit or decrement to proton therapy over IMRT for either treatment efficacy or long-term toxicity."

Prostate Cancer Treatment with Proton Therapy

Treatment for Prostate Cancer with a Low Risk of Serious Side Effects.

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*Last Name

*E-mail

*Address

Approach to Supplements and Alternative Treatments

* Question patients about use
* If outside of the biologic dose – view as a medication
* If not a standard treatment – view as experimental
* If possible, r/o interactions with current therapies
* Be aware the potentials for mislabeling and contamination
* Apply stepwise scientific approach when reviewing data.
  * "What phase of testing does this represent?"
  * Is there peer-review? Reproducibility?
* Recognize false/misleading claims.
  * Look for exaggerated or contradictory claims.
* Be aware of the placebo effect

Supplement Purity
Independent Testing

U.S. Pharmacopeial Convention
-Enforceable in the US by FDA

USP Verified Dietary Supplements

NSF International
-founded 1944 U of Michigan
-accredited by OSHA, SCC, ANSI, Int. Accred. Service

Claims made by Alternative Practitioners

* Conventional physicians use only: surgery, radiation and chemo
* Pharma works with the FDA to prevent alternatives
* Alternative treatment for cancer have a history of curing cancer
* Chemotherapy kills more than it cures
* Big Pharma is a monoply

Resources

- NIH
  - National Center for Complementary and Integrative Health
    - http://nccih.nih.gov/health
  - NCCIH Alerts and Advisories
    - http://nccih.nih.gov/news/alerts
- Micromedix
- NCI
  - Complimentary and Alternative Medicine
    - www.cancer/about-cancer/treatment/cam/hp
- MSKCC
    - https:www.mskcc.o/cancer-care/treatments/symptom-management/integrative-medicine/herbs/search
- ConsumerLab.com
    - Publishes independent testing of supplements purchased on the open market
- NSF International(National Sanitation Foundation)
    - www.nsf.org
- USP
    - www.usp.org/dietary-supplements/overview

Additional Resources

* GRADE Working Group
  * www.gradeworkinggroup.org
* Frontline, Jan 19, 2016
  * PBS.org/frontline
* Do You Believe in Magic? The sense and Nonsense of Alternative Medicine
  * By Paul Offit
* The Emperor of All Maladies: A Biography of Cancer
  * By Siddhartha Mukherjee

Is it even a good idea a for silicon valley start up to do medical research? Isn't that stuff supposed to be done by, you know, doctors…?

Lev Grossman

The fall of Theranos and the future of science in Silicon Valley. Time. May 26, 2016. pp 25-26