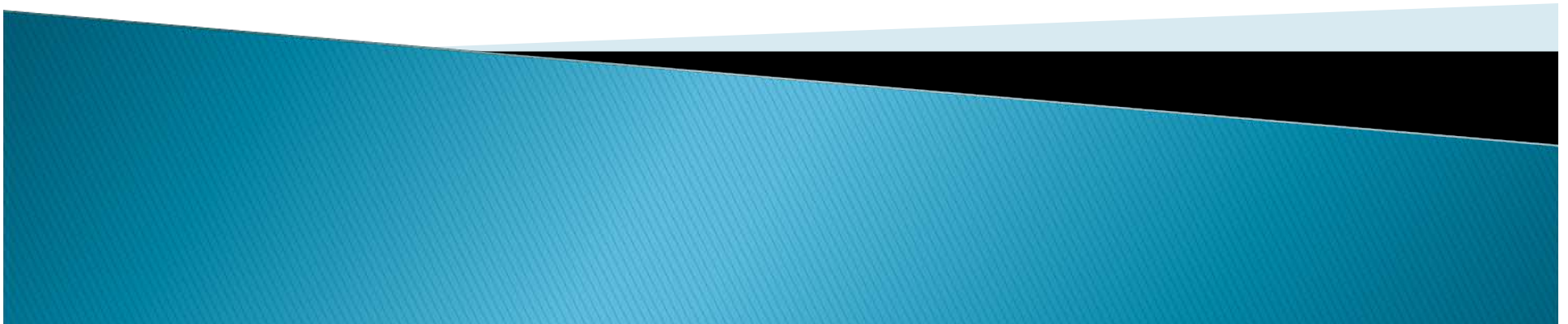


Second Line Hormonal Therapy

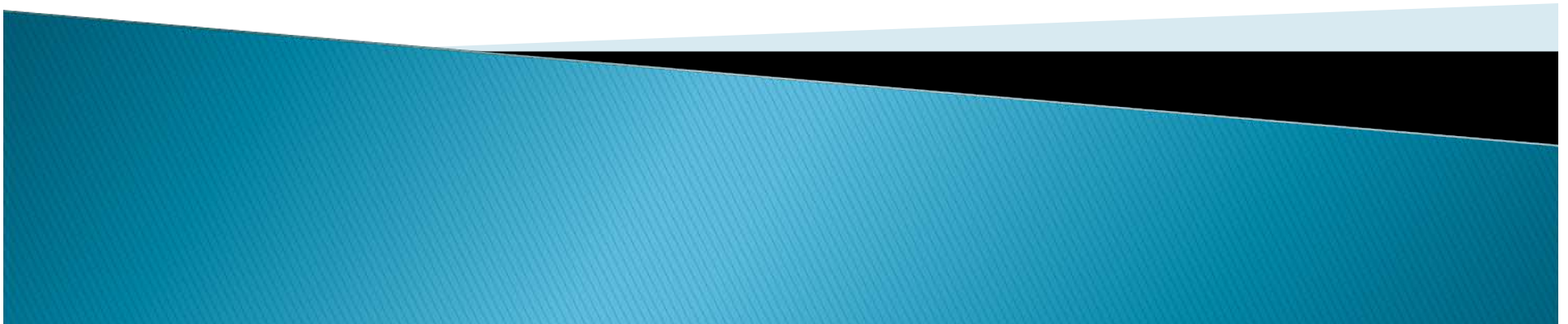
Charles E Myers, MD
FCRE & AIDP





AIDP and FCRE

- ▶ American Institute for Diseases of the Prostate (AIDP) - tailor treatment fit patient needs
- ▶ Foundation for Cancer Research and Education (FCRE): nonprofit that supports patient education and clinical research. FCRE strongly supports Us Too



Metastatic Prostate Cancer Standard Approach

- ▶ Start Treatment with an LHRH agonist
 - Lupron or equivalent
 - Casodex

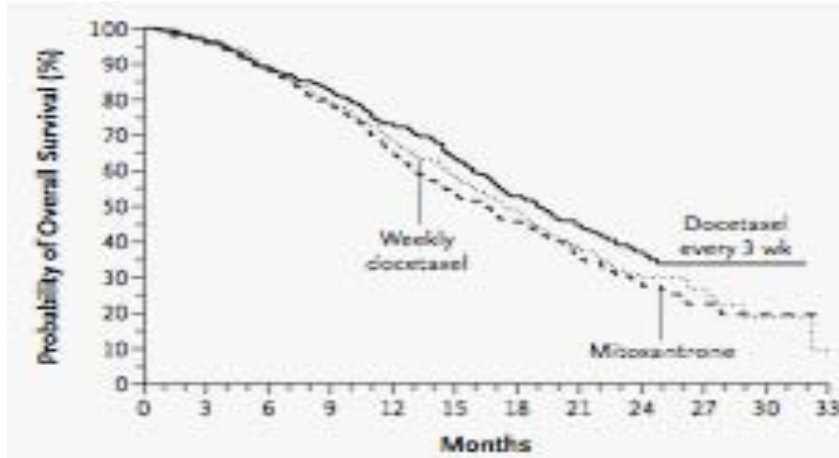
- ▶ Start Taxotere chemotherapy when pain appears or PSA is 20-100 ng/ml

- ▶ Go to Clinical Trials

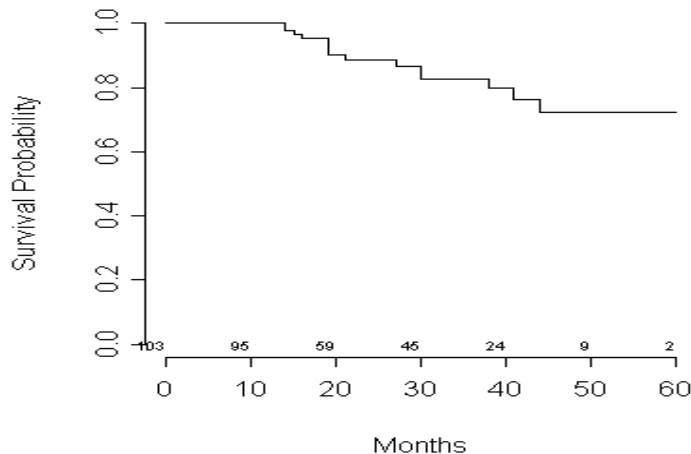
What is Wrong With This?

- ▶ You do not get second line hormonal Rx
 - Less toxic than chemotherapy
 - Responses can last years
 - Reduces cancer enough to help chemotherapy

After Lupron Fails



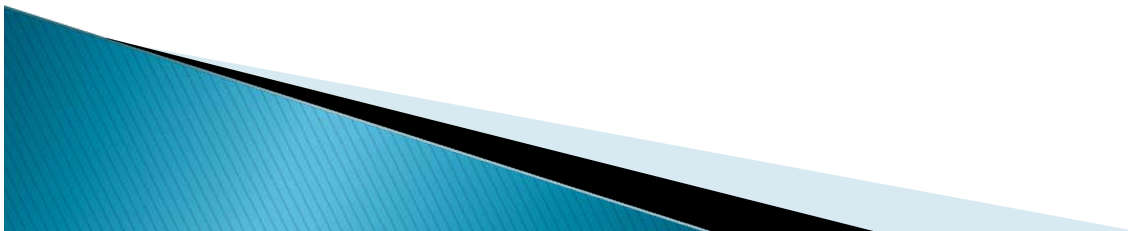
- ▶ The first panel shows typical results from chemotherapy. (NEJM 2004. 351;15)
- ▶ Note by 33 months, 20-30% survive.
- ▶ Second panel results at our clinic. Above 80% alive at 33 months



Treatment as a Two Act Play

- ▶ Act 1: Kill as much cancer as possible
 - Complete remission: PSA <0.01, healing of bone lesions
- ▶ Act 2: Slow cancer re-growth
 - Stop toxic treatment
 - Start nontoxic program to slow cancer
- ▶ If you relapse, start Act 1 again before cancer becomes too massive

Doing Your Part



Protect Your Health and Spirit

- Have a reason to live
- Treat blood pressure and cholesterol
- Watch for diabetes
- Mediterranean diet & exercise
- Reasonable optimism

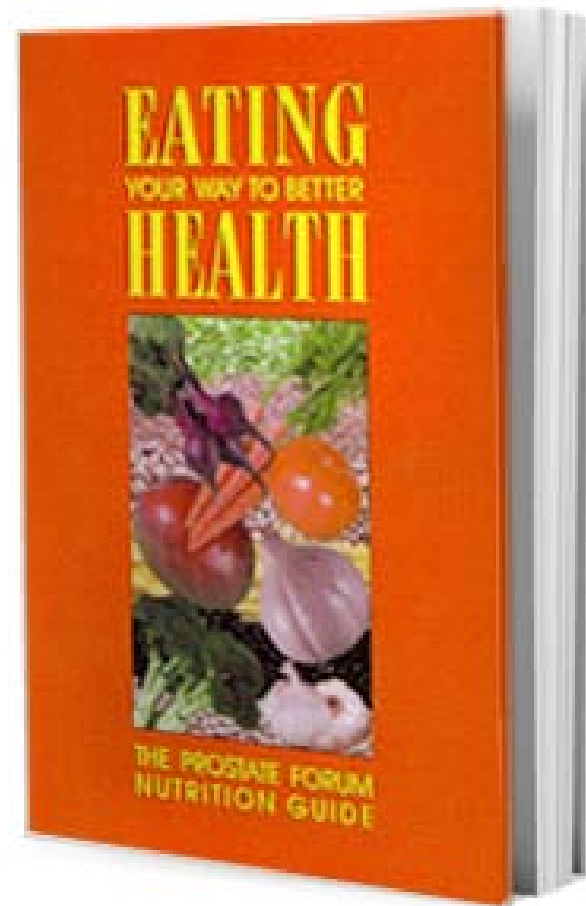


Mediterranean Ingredients



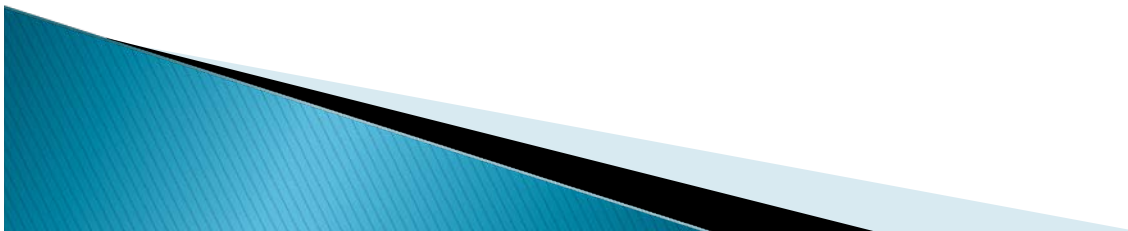
Eating Your Way to Better Health

- ▶ Science behind the Mediterranean diet
- ▶ Recipes designed for busy people
- ▶ Meal plans
- ▶ How to equip your kitchen



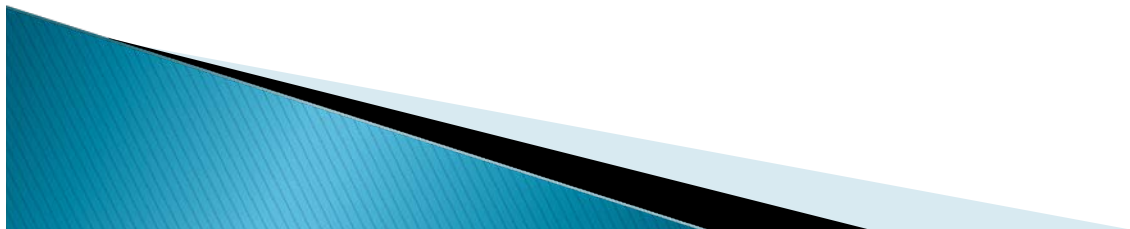
Exercise

- ▶ Lessens risk of obesity, diabetes, and hypertension
- ▶ Increases good cholesterol (HDL)
- ▶ Appears to reduce overall risk of cancer
- ▶ Minimum of 30 minutes of aerobic exercise a day. Further benefit to 60 and 90 minutes
- ▶ Three times a week, lift weights

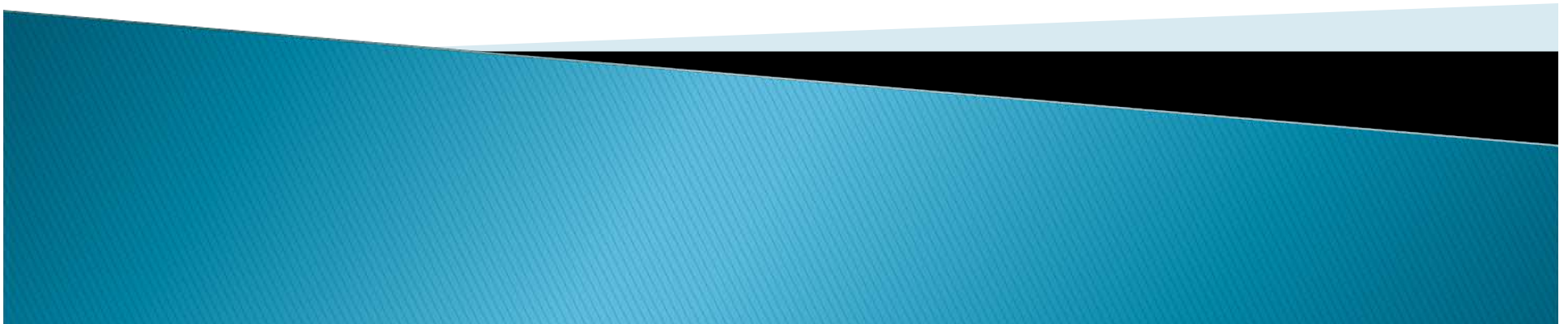


Your Spirit

- ▶ Pessimists have their worst fears confirmed, and are miserable waiting for bad things to happen
- ▶ Even with worst prostate cancer, some people do very well
- ▶ Stay away from pessimistic physicians
- ▶ Find a reason to live
- ▶ Support groups can save your life: companionship & information

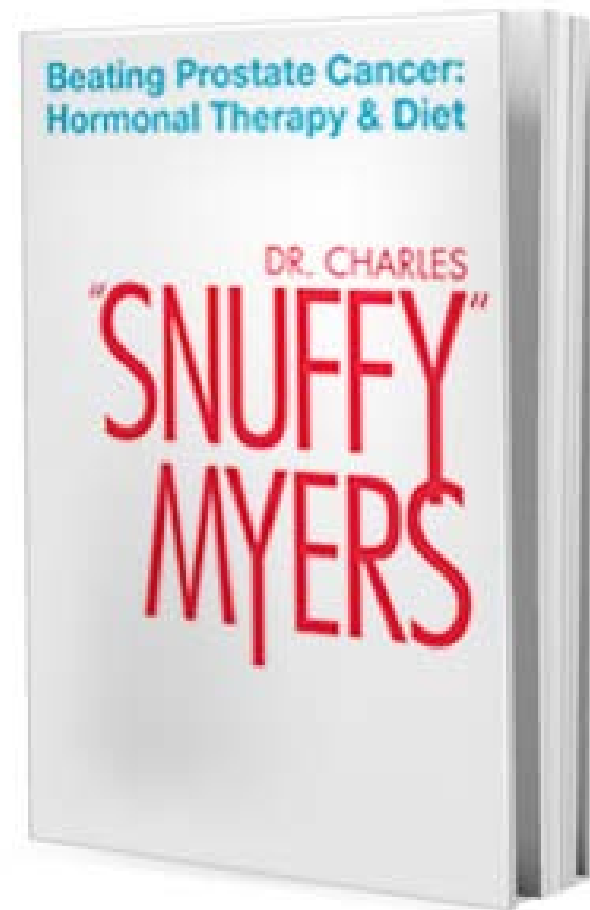


Elements of Second Line Rx Treatment Options



Beating Prostate Cancer

- ▶ Only guide to hormonal therapy
- ▶ Optimism key
- ▶ How to lessen side effects
- ▶ Second line hormonal therapy details



Ketoconazole

1982- activity against prostate cancer discovered

- ▶ Dramatically more active when PSA under 10 ng/ml.
- ▶ Greater the amount of cancer, the lower the response rate
- ▶ Published response rates equal to taxotere
- ▶ 90% reduction in cost compared to chemotherapy

Ketoconazole: Details Matter

- ▶ Every 8 hours or sooner.
- ▶ Take with soda, fruit juice, or vitamin C
- ▶ Interacts with a wide range of commonly used drugs

Ketoconazole Details Continued

- ▶ Drugs made more active by Keto
 - Statins
 - Erythromycin & related antibiotics
 - Calcium channel blocker
 - Xanax
 - Zoloft, Celexa, Lexapro, Prozac
 - Tylenol
 - Milk thistle extract

Ketoconazole Details Continued

- ▶ Dose must be individualized:
 - Option 1: measure blood levels and adjust
 - Option 2: increase dose to modest side effects
 - Maximally tolerated dose can range from 100 to 800 mg every 8 hours.

Estrogen

- ▶ Discovered more than 50 years ago.
- ▶ Kills cancer two ways:
 - Decreases testosterone
 - Triggers a death pathway independent of testosterone
- ▶ Several Different Estrogenic Drugs
 - DES, a synthetic chemical
 - Estradiol, the normal human estrogen

Patches vs DES

- ▶ DES: known to cause cancer in humans
- ▶ Estrogen patches less likely to cause blood clots
- may even reduce the risk caused by prostate cancer itself
- ▶ Thus, much higher estrogen levels possible
- ▶ We use Vivelle Dot from Novartis.

Estrogen Continued

- ▶ Disadvantages:

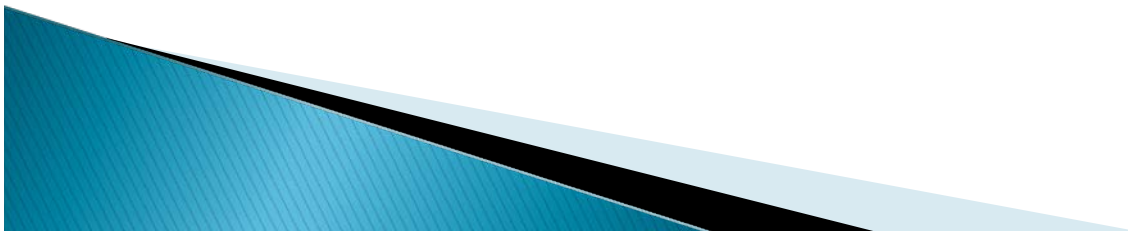
- Breast enlargement - 80%
- Leg edema - 20-30%
- Blood clots?

- ▶ Advantages:

- Least toxic form of hormonal therapy I know.
- Sex hormone levels above normal, **just not the sex hormone you grew up with!**
- Bone density better
- Better suppression of testosterone

Leukine

- ▶ Drug is the cloned human protein controlling immune system
- ▶ Extremely expensive: \$1,000/week
- ▶ Self injection every day for 90 days at total cost of \$12,000
- ▶ In USA, 30 days of taxotere greater than \$12,000
- ▶ While expensive, still less than 1/3 cost of taxotere chemotherapy



Leukine

- ▶ Stimulates immune function broadly
- ▶ Used to prepare cancer vaccines - Provenge
- ▶ Suppresses Melanoma, NonHodkin's lymphoma, breast and prostate cancer
- ▶ Activity against prostate cancer documented by Eric Small UCSF
 - Control of advanced disease for more than 5 years

Leukine Continued

- ▶ Leukine + ketoconazole response rate reported at 75%
- ▶ Taxotere response rate of 40-50%!
- ▶ Other benefits:
 - Repairs radiation damage
 - Crohn's disease 50% complete remission rate
 - Reverses angina by causing collaterals to form

Leukine Side Effects

- ▶ White blood count 20-30,000
- ▶ Leg edema
- ▶ Fatigue
- ▶ Histamine release
 - Hives
 - Increased gastric acidity
 - Sense of having to work to breath
 - Antihistamines work

Combined Therapy

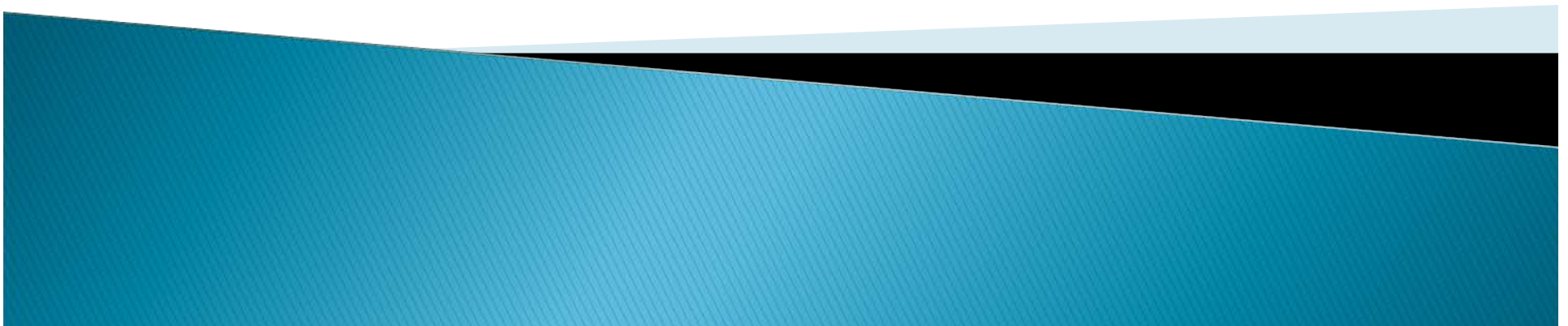
- ▶ Issue: How to improve effectiveness of Leukine + Ketoconazole?
- ▶ Solution: Add estradiol
 - Reduces ketoconazole fatigue
 - Reverses bone loss
 - As the cancer dies, speeds healing of the bone.

Combined Therapy

- ▶ PSA response rate = Leukine + ketoconazole
- ▶ Estrogen reduces fatigue of ketoconazole
- ▶ Estrogen rapidly reverses osteoporosis
- ▶ Estrogen reduces hot flashes
- ▶ Estrogen improves short term memory

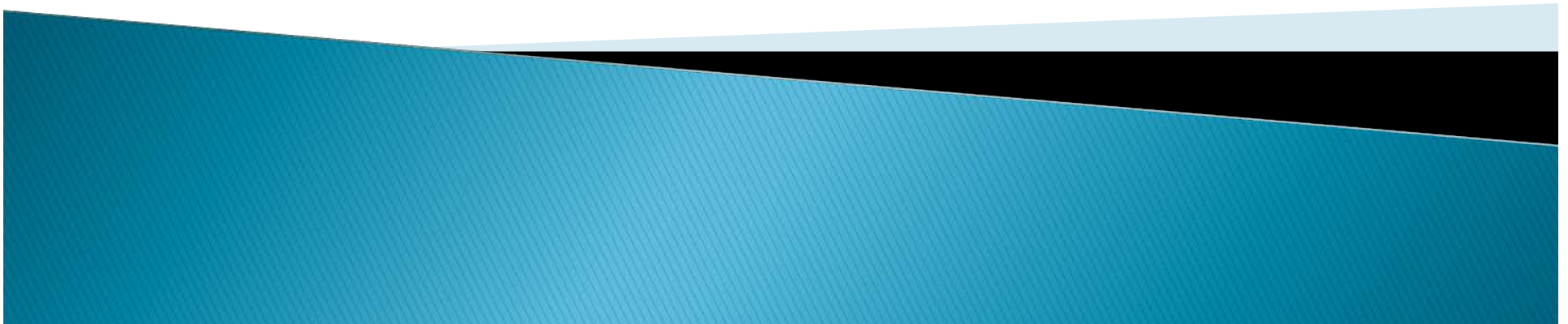
Growth Arrest

The idea is to stop or at least slow the growth and the spread of prostate cancer



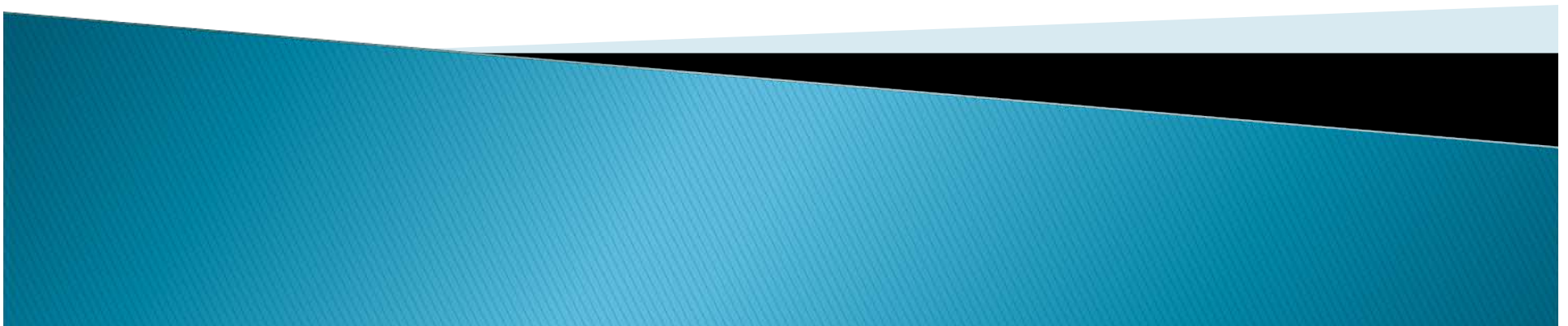
Block Cancer Blood Flow

- ▶ VEGF is the protein prostate cells produce
- ▶ VEGF also produced by normal tissues
 - Training effect on muscles
 - Wound repair
 - Repair of coronary artery blockade
- ▶ Block New Blood Vessel Formation
 - Avodart/Proscar, Celebrex, Sutent, Avastin



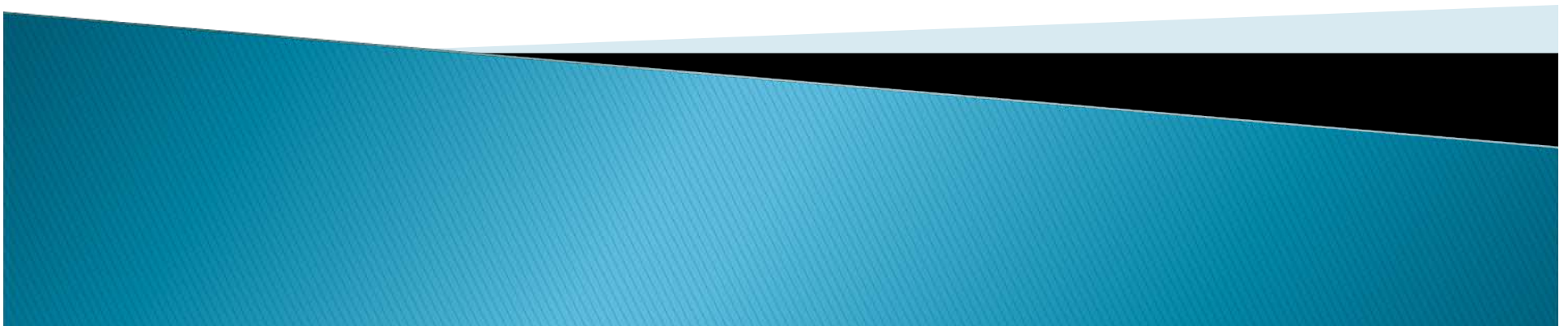
Immune response

- ▶ Leukine
- ▶ Provenge - special cases for now
- ▶ Excess stress reduces immune response



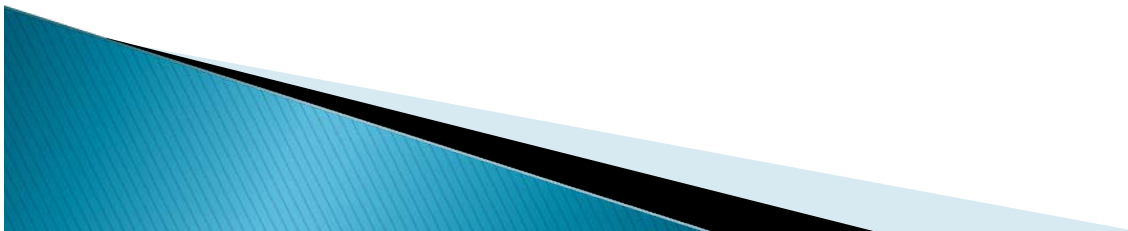
Differentiation Agents

- ▶ Vitamin D
- ▶ Retinoids
- ▶ Valproic Acid
- ▶ Phenylacetate
- ▶ Pomegranate
- ▶ Resveratrol
- ▶ Curcumin

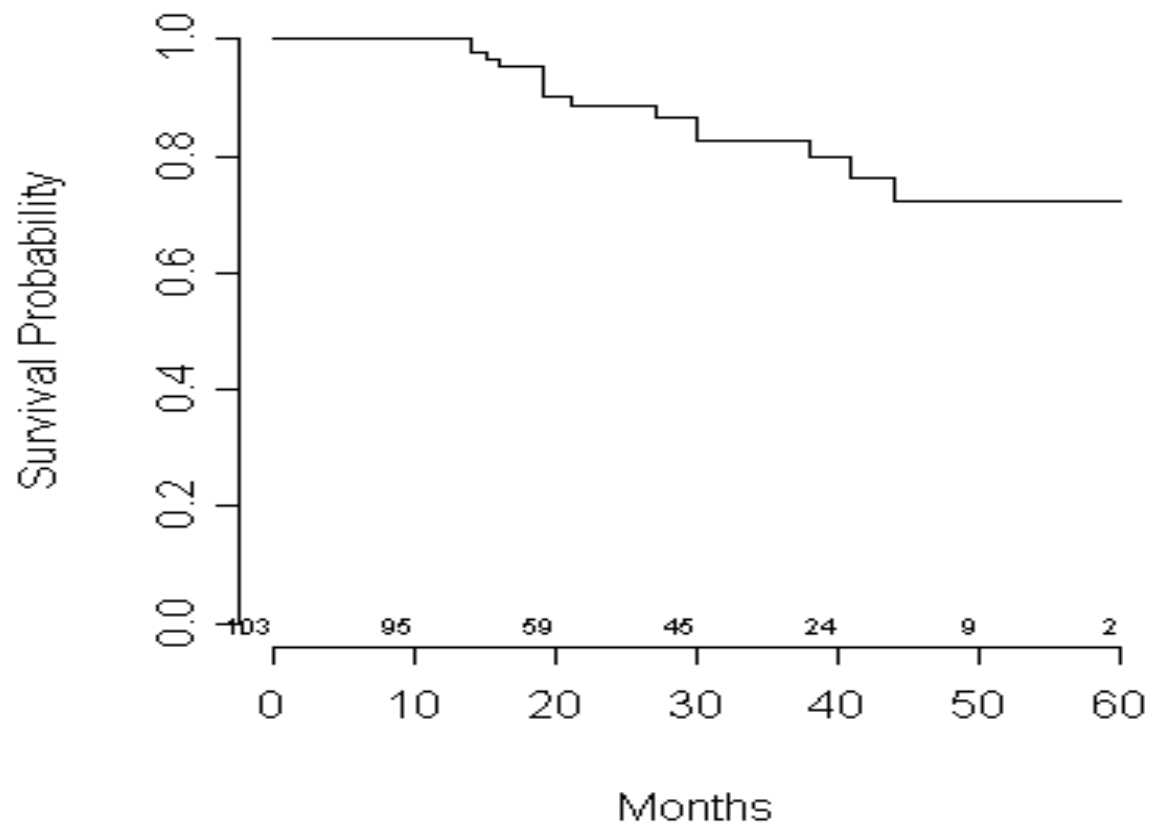


Putting It All Together

Supportive Care
Side Effect Reduction
Second Line Hormonal Therapy



Overall Survival

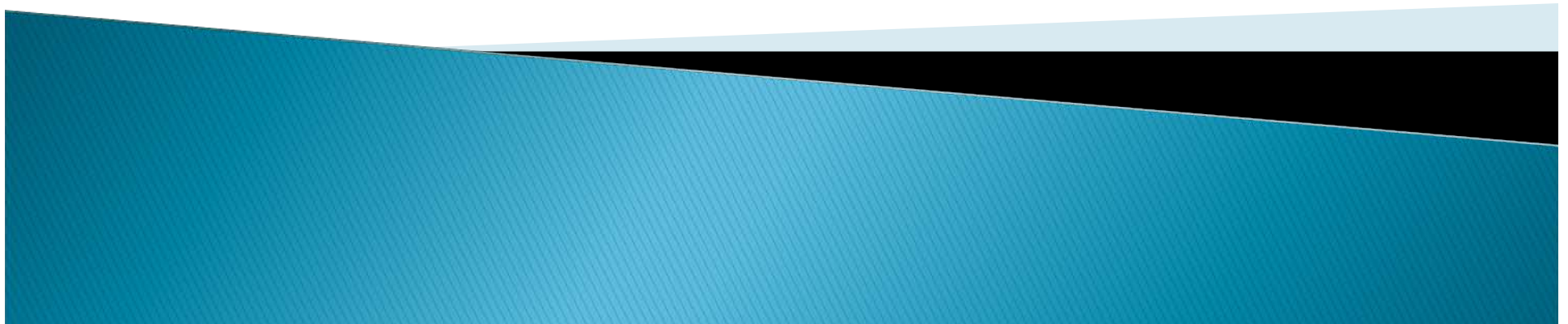


Conclusions

- ▶ Focus on comprehensive care makes a difference
- ▶ Second line hormonal therapy requires attention to the details
- ▶ Supportive care and side effect management an important contributor to our success

How to keep up to date

- ▶ Our newsletter & books available through www.prostateforum.com
- ▶ Ask Dr Myers video blog available through www.prostateforum.com or <http://askdrmyers.wordpress.com/>



American Institute Diseases of Prostate

- ▶ Information/appointments:
sherrieAIDP@yahoo.com
- ▶ Backup contact: maxinemed@aol.com

