Second Line Hormonal Therapy

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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

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

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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 \textit{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

![Survival Probability vs. Months Graph](image)

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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

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