

Highlights of the Presentations

By: Jim O'Hara – PCRI Educational Facilitator

Key topics in the talks were amplified in Dr. Moyad's short Q&A exchange following each talk. One attendee commented: "*Questions by Moyad were outstanding! Greatly expanding my understanding*". While most of the questions explored deeper into new concepts presented, one example I noted is that we learned from Dr. Myers where his nickname "*Snuffy*" originated.

Following each talk, the speaker adjourned to a corner of the Exhibit Hall to answer questions from interested attendees. This year, we recorded these "Meet the Speakers" sessions and over 3 hours of Q&A will be available on the conference DVDs.

Saturday's Gala Dinner featured:

- A keynote talk by Dr. Mark Moyad (see Lifestyle Modification below)
- The presentation of the Harry Pinchot Awards and the Catalyst Award (see separate article)
- An inspirational vocal presentation by "America's Tenor" Steve Amerson

Sunday, Dr. Mark Scholz began the program with a recap of key topics from Saturday's program. This was followed by six breakout sessions for Q&A with a number of experts that allowed direct interaction for attendees. Comments indicated that more of this type of session would be appreciated. Unfortunately, these simultaneous sessions could not be recorded for the DVDs. The conference concluded with a panel discussion involving many of the speakers sharing opinions relating to questions submitted from the attendees.

In addition to the educational sessions, many attendees took part in: the four support groups during lunch on Saturday; the "Women Against Prostate Cancer" Breakfast meeting on Sunday; the two Los Angeles Excursions and many casual opportunities to share feelings with others facing similar concerns. Attendees also took advantage of the wealth of



information available from the conference supporters in the Exhibit Hall. You can't get these experiences from the DVDs. To demonstrate the value some individuals place on attending the conference, I spoke with one man on Friday afternoon. He had just gotten off a plane from the Netherlands. He told me he was returning home after Sunday's session.

The information content from over 20 hours of presentations and Q&A sessions is enormous. I will not try to summarize each talk in this article. The DVDs will provide an opportunity for those interested to grasp the content. I will report some of the key comments made by the speakers that relate to several general topics covered. Please refer to prior issues of PCRI Insights or to the website for the agenda and a list of the faculty.

Lifestyle Modification

Both Drs. Ornish and Moyad cited the EPIC study (European Prospective Investigation into Cancer and Nutrition) published in 2008 for demonstrating the importance of healthy lifestyle. Exercise, not smoking, eating healthy and healthy weight (waist size) had prevention benefits for Diabetes 93%, heart attacks 81%, strokes 50% and all cancers 36%.

Dr. Ornish suggested an optimal diet as low in animal fats but also low in refined carbohydrates. He suggested supplements of Vitamin D3 and fish oil. He mentioned that fiber and bran can fill you up before eating too many calories. Dr. Moyad suggested chia seeds as a good source of fiber and omega-3.

Dr. Myers put special emphasis on this by saying that to optimize your treatment outcome *“You must do your part!”* He mentioned the importance diet and exercise to improve blood pressure, cholesterol and glucose levels. Patients should seek medications to control these if lifestyle changes are not sufficient. He also called for patients to maintain reasonable optimism, to avoid pessimistic physicians and to cultivate a *“reason to live”*.

In addition to monitoring cholesterol, Dr. Moyad suggested hs-CRP (High-sensitivity C-reactive protein) test be done with each cholesterol test. Less than 1 mg/L is considered low risk.

In his Active Surveillance talk, Dr. Strum emphasized the importance of life style monitoring and modification. In answer to a follow-up question from Dr. Moyad, he replied that he felt the most important (non-drug) factor is to restrict carbohydrates.

Active Surveillance

Dr. Strum said the major credit for the current emphasis on Active Surveillance goes to Laurence Klotz MD in Canada. Dr. Klotz has a 450 patient study with average follow-up 6.8 years, an overall survival 78.6% and a 10-year prostate cancer actuarial survival 97%. As of 2009, 6 active surveillance studies published all rely on PSA-kinetics and on rebiopsy findings.

- Total patients = 2,168
- Over 200 patients have > 10 years follow up
- Overall survival 93%
- CSS (cancer specific survival) 99.7%

Dr. Strum suggests additional testing be considered for men on Active Surveillance including:

- Color Doppler Ultrasound
- MRI & MR Spectroscopy
- DRE with formal report of findings including capsule and seminal vesicles
- Biomarkers PAP, CGA, NSE & CEA
- Bone Integrity

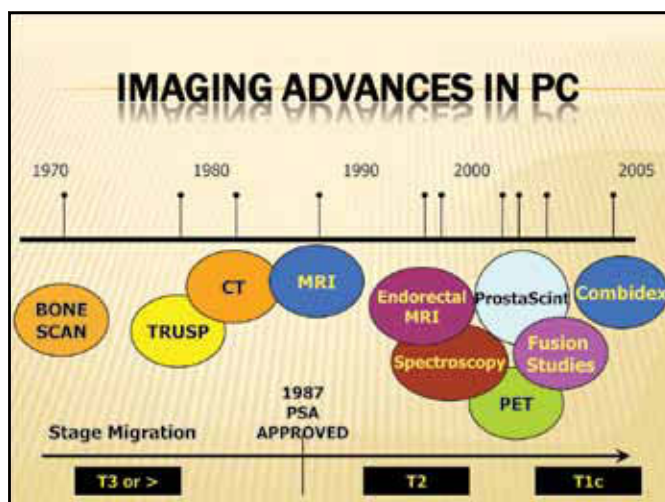
When asked if endorectal MRI was better than color Doppler ultrasound for monitoring A/S, he said each has value and may identify problems that the other does not. His advice, select an expert.

The following were comments by panel members to a question about using just PSA to monitor A/S.

- If there happens to be aggressive cancer present, PSA from prostate cancer may not be a large % of total PSA – a prostatic acid phosphatase PAP test may be beneficial
- Additional analysis of the biopsy samples using Aureon Prostate Px+ may be useful – also, Dr. Bonkhoff in Germany can produce a panel of 12 immunohistochemical tests to help determine the nature of the cancer

Staging Prostate Cancer

Dr. Strum described the evolution of our imaging tools. These have allowed for better staging and the concept of delayed treatment. There was a major setback with the FDA rejection of Combixel®. Several speakers mentioned the value of Combixel imaging done in the Netherlands for their patients. Unfortunately, the manufacturer has discontinued the product but a new product, ferumoxytol, is approved for iron deficiency. Dr. Roach said he expected UCSF would initiate a clinical trial using this with MRI in 2011.



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Local Treatment

Dr. Gil answered a question saying that there should not be a risk of lymphedema after prostatectomy because the lymph nodes removed are not the ones that drain from the legs.

Dr. Roach discussed “whole pelvic radiation” for selected high-risk patients. He said that 42% of the pelvic lymph nodes at risk are outside the area that a surgeon samples. He quoted research that suggests an improvement of progression free survival by 2 years without statistically significant increase in grade 3 toxicities.

He suggested that temporary implants might be better than permanent if the prostate is large or the tumor extends beyond the capsule.

When asked by Dr. Moyad if long-term ADT is required for high-risk patients, Dr. Roach replied that 2 years is the shortest duration of ADT that has shown a survival benefit in random clinical trials.

When asked about stereotactic radiation (like Cyberknife®), he expressed concern that the higher dose fractions might cause long-term risk of urethral strictures. He said longer follow-up was needed but questioned “Why choose this when there is 20 year data for brachytherapy?”

When asked to compare proton with IMRT, Dr. Roach said there is no reason to believe that proton is better if the dose is the same, also there is no good data that side-effects are less. To a similar question, Dr. Botnick said that image guidance and dose make the difference.

The following were comments to a panel question about high intensity focused ultrasound (HIFU)

- Potency outcomes about 60% – not as good as expected
- If prior prostatitis caused calcification, ultrasound is reflected leaving untreated areas

Radical prostatectomy, radiation and cryotherapy can all lead to erectile dysfunction. Dr. Mulhall discussed the four main factors that contribute to this condition: cavernous nerve injury, artery injury, erectile tissue damage and confidence erosion. He discussed several ways to address these factors. He stressed the importance of penile rehabilitation after local treatment for prostate cancer to preserve erectile tissue while normal erections are not occurring. Loss of erectile tissue leads to venous leak and permanent function loss.

Androgen Deprivation Therapy (ADT)

Dr. Myers commented that his goal with ADT is to drive the PSA to < 0.01 as quickly as possible and continue for 12 months. If he is not successful with the usual one to three drugs, he moves directly to second line with combinations of ketoconazole or estrogens. During off-cycles, he suggests options that could increase PSA Doubling Time like Proscar and Avodart, a Mediterranean diet, Celebrex (if medically appropriate), vitamin D3, pomegranate, resveratrol, curcumin. He cautioned when using supplements, it is important to monitor for blood levels and potential side-effects or drug interactions.

Dr. Mulhall discussed the risks of damage to erection tissue when testosterone is reduced. It appears that 4-6 months of ADT is enough to cause irreversible erectile damage. He suggests ¼ pill of Viagra® at night (as frequently as patient can afford) while on intermittent ADT.

Dr. Strum emphasized the importance of stopping the cycle of bone loss with exercise, diet, vitamin D3, boron, calcium and bisphosphonates (if necessary).

Castration-Resistant Prostate Cancer (CRPC)

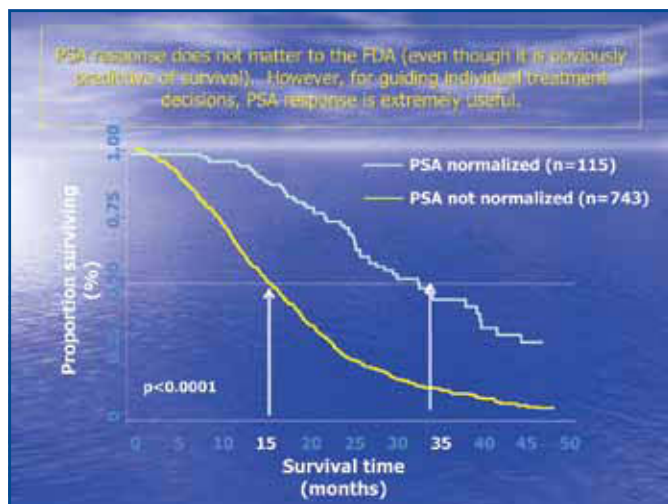
Dr. Vogelzang stated that 30,000 develop CRPC each year in this country.

Dr. Myers and Dr. Vogelzang both commented that patients should not start chemotherapy until all hormonal treatments (and possibly Provenge) have failed unless there is evidence of extremely aggressive or extensive metastatic cancer.

Dr. Myers updated his results with second-line hormonal therapy using ketoconazole, Leukine and estradiol. He reported a “75% reduction in PSA was seen in 78% of his patients with 49% reaching an undetectable PSA. The bad and good news: After 5 years, it is too early to measure the full benefit.”

Dr. Moyad asked why a patient should consider docetaxel when the overall survival advantage is just 2.5 months. Dr. Vogelzang answered that despite the chemo side-effects, quality of life was better and some have much longer survival. Dr. Scholz expanded on this in his summary showing that a

30% PSA decline within 3 months powerfully predicts improved survival. PSA response does not matter to the FDA (even though it is obviously predictive of survival). However, for guiding individual treatment decisions, PSA response is extremely useful. In the Taxotere® trials, the patients whose PSA normalized (less than 4.0) had a huge survival advantage over those that did not. (see slide)



Reprinted with permission of Dr. Scholz

Dr. Scholz also commented that there are keys to the management of CRPC patients which includes the need to monitor response to treatment closely and if a treatment is not working, move on to something else.

- Monitor for at least 60-90 days
 - PSA, PAP, LDH, ALP tests monthly
 - Circulating Tumor Cells (CTC) monthly
 - Bone scans, PET, CT, MRI (every 6 months?)
 - Pain
- Check for the “Small Cell” variant
 - Check CEA, NSE, CGA every 6 months
- Quality of life
 - Monitor side effects from treatment
 - Maintain fitness, diet and attitude (no tobacco)

Dr. Lam discussed some of the side-effects and stated that the most important concept is to take a break as soon as it is safe. Dr. Moyad mentioned a trial that suggests a benefit in taking ginger before Chemo to reduce nausea.

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PCRI and all of the conference attendees are especially indebted to the many supporters and volunteers who helped to make the 2010 Prostate Cancer Conference possible. These include:

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Harley Van DeLoo

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Mark Lichty
Joel Nowak
Erlinda Patterson

Finally, Thanks to the 67 attendees who made generous contributions in addition to their conference fees.

Update on Clinical Trials

Dr. Vogelzang reviewed the results of several recent and ongoing trials.

CALGB 90401:

- Addition of **bevacizumab (Avastin®)** to docetaxel/prednisone/ dexamethasone did not significantly increase overall survival for patients with CRPC
- Bevacizumab did significantly improve other clinical outcomes
 - Progression free survival, PSA decline, incidence of measurable disease
- Bevacizumab treatment was associated with more severe toxicities, including death from infections

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ASCENT 2:

- **Calcitriol** plus weekly docetaxel associated with significantly shorter survival times vs q3w docetaxel in patients with metastatic CRPC
 - Based on similarity of survival times to other studies of weekly docetaxel, survival effect may be due to weekly docetaxel schedule rather than to addition of calcitriol
- Neither protective effect nor reduced toxicity observed with calcitriol plus weekly docetaxel
- Weekly docetaxel is not recommended

TROPIC:

- **Cabazitaxel (Jevtana®) was approved by FDA 6/17/10** in combination with prednisone for patients with hormone-refractory prostate cancer previously treated with docetaxel
- Cabazitaxel/prednisone (CP) significantly improved overall survival vs. mitoxantrone/prednisone (MP) in metastatic CRPC
- Reduced risk of death: 28%
- CP also significantly improved Progression free survival, response rates, and time to progression
- Associated with acceptable safety profile
 - Febrile neutropenia and diarrhea more common with CP vs MP
- CP first treatment to demonstrate survival benefit in patients with metastatic CRPC who failed docetaxel-based therapy
- Warnings/precautions:
 - Neutropenic deaths and mortality related to gastrointestinal symptoms and renal failure reported
 - Elderly (≥ 65 years) at increased risk of toxicity
 - Not recommended if hepatic impairment present

Denosumab vs Zoledronic Acid:

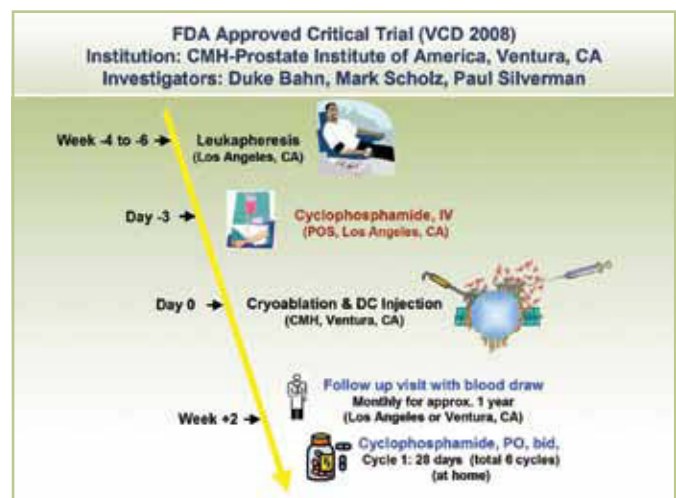
- Denosumab superior to zoledronic acid in delaying or preventing skeletal related events (**SRE**) in patients with CRPC and bone metastases
- No significant difference between treatments in survival or disease progression

- High incidence of adverse events in both arms
 - More patients who received zoledronic acid experienced acute phase reaction
 - More patients who received denosumab experienced hypocalcemia
 - Osteonecrosis of the jaw rare but occurred in approximately twice as many patients with denosumab vs zoledronic acid
- Denosumab potential treatment option for patients with CRPC and bone metastases

Immunotherapy

Several speakers discussed the FDA approval of Provenge® and its availability. Dr. Moyad discussed the current controversy about a delay in approval for payment by Medicare. A petition was circulated to present to the Centers for Medicare & Medicaid Services meeting on November 17th.

Dr. Bahn reviewed the “CRITICAL” trial for combined cryotherapy and immunotherapy which is now in process. The FDA approval for the trial is for men who: have proven recurrent cancer in the prostate after organ preserving therapy; are determined to be androgen –independent; with known metastasis limited to three sites and are chemo-naïve. The trial consists of cryoablation of the prostate, followed by injection of a known number of patients’ own immature dendritic cells into the cryoablated prostate with pre-and post-cryoablation low dose cyclophosphamide administration to reduce regulatory T cells temporarily. It is too early to report any findings.



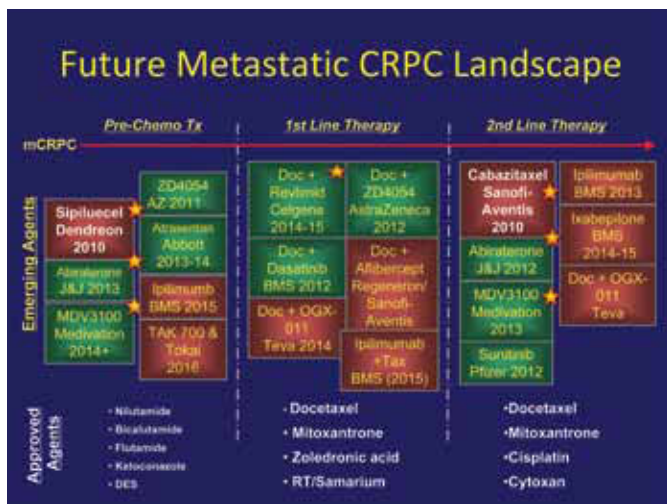
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Future Developments

The future looks brighter for prostate cancer patients. With the 2010 approvals of sipuleucel-t and cabazitaxel, physicians have two new weapons against the disease.

Dr. Vogelzang expressed optimism for the approval of abiraterone based on a recent news release stating that the Phase III study had been “unblinded” because “based on a pre-specified interim analysis, which demonstrated a statistically significant improvement in overall survival and an acceptable safety profile”. Based on these results, it was recommended that patients in the placebo arm be offered treatment with abiraterone acetate. Additionally, a program will provide early access to abiraterone acetate to patients who meet specified medical criteria is being initiated. [The study is not recruiting at the time of this writing but is listed as NCT01217697 at www.clinicaltrials.gov].

Dr. Vogelzang commented that prostate cancer now has two approved chemotherapies that have demonstrated improved survival. Breast cancer has five. He is enthusiastic about ten other agents are in Phase III trials (see slide). He stated that men must participate in the trials. The higher level of participation by breast cancer patients is one reason for higher funding to breast cancer trials and the larger number of approved treatments.



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Dr. Jonathan Simons of Prostate Cancer Foundation closed Saturday’s lecture session with a talk titled “Scientific Progress: Top Ten Reasons for Hope”. He listed 23 additional new agents in the pipeline. He

also described exciting PCF sponsored research at the University of Michigan that has identified 24 types of prostate cancer. This research may provide more effective screening for identifying the men who would likely benefit from treatment and additional ways to define targets for treatments. He also described research at UCLA that has identified four events that occur to turn a prostate cell into a prostate cancer stem cell. Other reasons for hope included the extended survival provided by the new treatments mentioned above and the many brilliant, young investigators dedicated to prostate cancer research. His final reason is the growing patient participation as evidenced by the attendance at the **2010 Prostate Cancer Conference**.

The Multi-Disc DVD Set of the 2010 PROSTATE CANCER CONFERENCE is expected to ship on December 14th. See coupon for details.

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The campaign has been a story of success after success, with buildings including the iconic Capitol Records Building, the Ramada Hotel in West Hollywood, the historic Roosevelt Hotel and the Paramount Studio’s Melrose Gate and Water Tower, all bathed in blue light throughout the month.

Other key partners to jump on board early include the Oakland Raiders, who dedicated their home season opener to the campaign, and Messenger Wines, who donated proceeds from their biggest selling wine towards the cause.

The philosophy behind Blue September is one of positivity and empowerment, using much loved famous faces, looking a little ridiculous in blue paint, and familiar landmarks, with a fun new ‘blue’ spin, to reach as many people as possible. But the message about prostate cancer is a serious one, with sobering statistics. Prostate cancer affects over 2 million Americans and is chronically underrepresented.

Ultimately, Blue September is about changing America’s attitudes and behaviors towards prostate cancer to save lives. For too long the issue has gone unattended, and together the PCRI and Blue September are going to change the face of prostate cancer in America.