May 2016 NEWSLETTER
P.O. Box 420142 San Diego, CA 92142
Phone: 619-890-8447 Web: http://ipcs.org
We Meet Every Third Saturday (except December)

Next Meeting
May 20, 2016
10:00AM to Noon

Meeting at
Sanford-Burnham-
Prebys Auditorium
10905 Road to the
Cure, San Diego CA
92121
SEE MAP ON THE
LAST PAGE

What We Are About
Our Group offers the complete spectrum of
information on prevention and treatment. We
provide a forum where you can get all your
questions answered in one place by men that
have lived through the experience. Prostate
cancer is very personal. Our goal is to make
you more aware of your options before you begin a treatment that has serious side effects
that were not properly explained. Impotence,
incontinence, and a high rate of recurrence are
very common side effects and may be for life.
Men who are newly diagnosed with PCa are of-
ten overwhelmed by the frightening magnitude
of their condition. Networking with our mem-
bers will help identify what options are best suit-
ed for your life style.

Be your own health manager!!

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Editor: Stephen Pendergast
3%. Due to PSA screening, there are 40% fewer deaths from prostate cancer than before. Many of the men now diagnosed with prostate cancer each year have "low risk disease," and never would die of it, but still undergo active treatment that is unnecessary. In May 2012, the U.S. Preventative Services Task Force recommended against PSA screening, due to frequent overdiagnosis and overtreatment. The PIVOT (prostate intervention vs observation trial) suggested that "observation" was as effective as surgery, in July 2012. But that applied only to low risk PCa, and there was a significant benefit for patients with high risk prostate cancer.

The Task Force recommendations were widely adopted, resulting in a 50% decline in PSA screening, and in turn resulting in fewer diagnoses of low risk PCa (as is desirable, since such cancers normally don’t need to be treated), but an increase in finding high risk PCa. This suggests that men are not being biopsied as early in their disease progression, due to the reduced frequency of PSA screening, and Dr. Gaylis and colleagues published a letter in the New England Journal of Medicine in February 2016 pointing this out, and warning that doctors may now be missing the window of curability for many men -- as was common in the pre-PSA era.

Just this month, the Task Force updated their recommendations to indicate that the decision whether or not to test for PSA must be "individualized" for men aged 55 - 69 years (including both men at average risk, as well as those who are at "increased risk," such as African American men, and those with a family history of prostate cancer). They still oppose testing of men aged 70 years and older, indicating their opinion that the benefits do not outweigh the harms. A major factor in the Task Force revision of their guidelines is the fact that whereas in 2012, very few men went on active surveillance, now almost 40% do after diagnosis (thus avoiding the harms of overtreatment). The American Urologic Association immediately issued a statement in favor of the revised guideline. Supporting evidence for the value of screening comes from the European Randomized Study of Screening for Prostate Cancer, which issued the prediction that 3 men out of 1000 will avoid metastatic prostate cancer because of screening.

Dr. Gaylis feels that men at "increased risk" (see above) should start PSA testing much earlier than age 55; as early as age 40. And he also believes that the age 70 cutoff is artificially rigid, and that each man’s situation should be considered individually. The popular term is "shared decision making." He has been doing this throughout his career, and notes that our support group helps men to be involved in the decision making.

Active surveillance can be considered to relate to "time of treatment," or "delayed treatment." The careful follow-up recommended by Genesis Healthcare includes an annual digital rectal exam (because very aggressive cancer may not produce PSA; Dr. Gaylis found a half-inch tumor in the prostate of a man with a PSA of only 0.7), regular PSA testing (useful for the vast majority), genomic testing (such as Oncotype Dx, Prolaris, and Decipher), multiparametric MRI, and biopsies.

About 33% of men on active surveillance will eventually require active treatment to prevent harm from the disease. Only 3% of men with favorable-risk PCas who go through active surveillance (with active treatment if and when needed) will die of the cancer within 10 years. The risk of dying from some other cause was 19 times higher than the risk of dying from PCa! (Source: J. Urol. Suppl., 2009,181:606 abstract 1682)

At Genesis Healthcare, for five years now, a "best practice" standard of care involving treatment both of "very low risk" men, as well as more liberal criteria for reasonable exceptions to the most strict criteria has been used and shared with other doctors and groups. Their data was published, with their guide-
lines, in the "Gold Journal," Urology, last year. Now about 70% of their "low risk" patients go on active surveillance, and more than 85% of "very low risk" patients likewise. The definition of "very low risk" is as follows: Stage T1c disease (identified only by needle biopsy; not palpable by DRE nor visible by imaging); Gleason Score = 6 or less; PSA less than 10 ng/ml; three or fewer biopsy cores positive, and less than 50% cancer in any core; PSA "density" less than 0.15 ng/ml/gram (density = PSA score divided by the estimated weight of the whole prostate). The more liberal criteria amount to the patient's request to go on active surveillance, with the risk estimated as low and approved by the physician.

Genetic testing discussion: Note that Genetics examines the function of a single gene, whereas "Genomics" examines groups of genes to identify their combined influence on an organism. The Oncotype DX prostate cancer assay was discussed as an example of genomic testing. It is suitable for newly-diagnosed men with very low, low, or low-intermediate risk PCa. It helps to improve assignment of the degree of risk, particularly to identify patients who may need immediate treatment.

One part of the Oncotype DX test evaluates the genes that affect the "health" of the interaction of the prostate cells with the surrounding stroma. Stroma is the scaffold or supporting structure around the cells. Proliferation genes are used to measure of how rapidly the cells turn over, or multiply. (Note that the Prolaris test only looks at proliferation.) Androgen signaling genes provide a measure of the cell's responsiveness to testosterone. And cellular organization is the fourth group of genes evaluated. All four groups of genes, 12 genes in all, are compared with 5 reference genes that serve to account for varying RNA quality and quantity in the test sample. The assay provides an overall "Genomic Prostate Score" on a scale of 100, with higher scores representing more aggressive cancer.

A study at UCSF showed, that whereas 10% of a group of 288 men were thought to be very low risk using the strict guidelines like Genesis Healthcare uses, after considering the Oncotype DX score, it was found that 26% of the men could be treated as very low risk. As might be expected, given the uncertainties of biopsy results, some individual men found their GP Score raised their predicted risk, while others found the opposite. Dr. Gaylis emphasized that these tests provide "additional information" that can be a valuable part of the overall assessment of risk and treatment options for each man.

Dynamic contrast enhanced (DCE) MRI detects the greater blood flow (more blood vessels) in prostate tumors as compared with healthy tissue. Along with two other parameters measured using MRI, a "PI-RADS" (Prostate Imaging Reporting and Data System) score is generated, on a scale of 1 to 5, with 5 being "highly suspicious of malignancy."

Fusion biopsies (combining prior MRI data with real-time ultrasound to guide the needles during the biopsy procedure) are now gaining acceptance, because they reportedly detect cancer two to three times as often as standard (i.e., "systematic" but blind, often referred to as random) biopsies, and are especially effective in finding cancer when the MRI images show a high level of suspicion. This new approach provides progress toward targeted, "pinpoint" biopsies.

A study published last year showed that only 5-11% of men on active surveillance after being diagnosed at age 66 or older during the years 2001-2009, received follow-up testing that met the strict guidelines of the prominent PCa research groups at Johns Hopkins and at Sunnybrook (Toronto, Canada), respectively. Hopefully, our group members are followed more closely!

At Genesis Healthcare, in collaboration with UCSD, three specific measures of the quality of active surveillance activities now are: adoption (currently, 70% of qualified candidates go on active surveillance), adherence (follow-up PSA testing; DRE annually; and "confirmatory biopsy" within 18 months), and patient satisfaction at their first consultation.
INFORMATION PRESENTED HEREIN REPRESENTS THE EXPERIENCE AND THOUGHTS OF OUR MEMBERSHIP, AND SHOULD NOT BE ANY SUBSTITUTE FOR MEDICAL COUNSEL.

Questions/discussion: Comments on drugs used for patients on active surveillance, such as Metformin, a statin, and Proscar? There is provocative info in the literature that says that statins help prevent growth of prostate cancer. Some doctors are using these drugs. Xtandi is being used in a trial at Genesis Healthcare, with patients on active surveillance. Also Casodex is being used by some. There is no data available yet that proves the benefits of any of these scientifically.

Are there oncologists at Genesis Healthcare? They have radiation oncologists, but there are “political problems” with adding medical oncologists, so they don’t have any.

A comment on economics: In the USA, we have an 18% inflation rate for medical expenses, and those expenses currently total 18% of GDP. That’s about twice the rate in other 1st world countries. The Task Force did a little good, trying to recommend against unnecessary expenses, but their recommendations also had some bad effects. The AUA (American Urologic Association) only recommends based on "scientific data," so they offer no recommendations for many issues.

Value of estradiol (an estrogen)? Estrogen slows prostate cancer, but can cause strokes.

Differences of other genomic tests compared to the Decipher test? Prolaris predicts 10-year survival, and is based only on “proliferation promoting” gene activity. The GenomeDX “Decipher” test is useful to predict if radiation would benefit a man who has adverse pathology (disease outside of the prostate and/or PSA rising after prior treatment). All are RNA based test. The microarray technology of the Decipher test looks at thousands of genes (others only look at hundreds), but shallowly (low, med, high); it is especially good at predicting recurrence after prostatectomy.

Dr. Gaylis is not in favor of MRI before biopsy, but wants 12-core first, then later a fusion biopsy and (for low risk patients) genomic testing to confirm the original biopsy findings.

A major factor in the Task Force revision of their guidelines is the fact that whereas in 2012, very few men went on active surveillance, now almost 40% do after diagnosis (thus avoiding the harms of overtreatment).

TURP effect on future treatment, for men on active surveillance? Depends on how aggressive the surgery was. A new technique is to vaporize the tissue, which he thinks may reduce introduction of cells into the bloodstream. He has tried green and red light laser, but didn’t like them. Now there is a technology using steam. Another new technology is the PlasmaButton from ACMI, which coagulates the tissue, and seems worthwhile.

DVD’s of the meeting will be available by the next meeting date via the website: www.ipcsg.org/shop or from the library at the next meeting. Slides are included in a file on the DVD.
FUTURE MEETINGS

May 20. Roundtable. A panel of members talk of their experiences followed by Q&A, then break-out sessions by treatment type for networking.

Jun 17. To Be Determined.

ON THE LIGHTER SIDE

...new miracle drug Mr. Poore. Extends survival by 6 to 12 months. But it costs $10,000 a month.

Spendy. How long will I survive if I don’t take it?

Uh, about 6 to 12 months.

Hmmmmmm

When someone asks “How can we help? You say: “We cheerfully accept all prayers, words of comfort, Paypal, MasterCard or Visa.”

(Warning this one is about death)

Three buddies were talking about death and dying. One asked, “When you’re in your casket and friends and family are mourning you, what would you like to hear them say about you?

The first guy says: “I would like to hear them say that I was a great doctor of my time and a great family man.

The second guy says: “I would like to hear that I was a wonderful husband and school teacher who made a huge difference in our children of tomorrow.

The last guy says: “I would like to hear them say: “LOOK! HE’S MOVING!!”
Study Sparks 'Cure' Talk for Metastatic Prostate Cancer
Multimodal approach shows promise in pilot trial
by Charles Bankhead
Senior Associate Editor, MedPage Today April 26, 2017

Action Points
• Note that this small, prospective study found that, for some men with metastatic prostate cancer, a multi-modality therapy approach comprising chemotherapy, surgery, radiation, and hormone therapy, can lead to prolonged suppression of PSA.
• This approach will need to be validated in larger studies.

A pilot study of multimodal therapy for noncastrate metastatic prostate cancer has urologic oncologists talking about a potential cure for a historically incurable disease.

The treatment -- consisting of sequential use of androgen deprivation (ADT), surgery, and radiotherapy -- led to undetectable PSA levels persisting for as long as 4 years in a handful of men. Although 19 of 20 men initially met the primary endpoint of an undetectable PSA level, the effect was often short-lived, as reported in Urology.

So why all the excitement about a study involving a small number of patients followed for a relatively short period of time, given prostate cancer’s long natural history?

"What's special is that in the past we have believed that we could never truly cure someone with metastatic prostate cancer," said Urology editor-in-chief Eric Klein, MD, of the Cleveland Clinic. "The patient with the longest follow-up is now 5 years out, has no evidence of prostate cancer, an undetectable PSA, and a normal testosterone, which means that all the effects of the androgen deprivation therapy that he's been on are gone. I have never seen that in my career before."

The patient has special meaning for Klein, who initially diagnosed the patient's "incurable" prostate cancer and recommended ADT as the standard of care. The patient sought a second opinion at Memorial Sloan Kettering Cancer Center (MSKCC) in New York City, where Howard Scher, MD, and colleagues were considering a dramatic departure from the conventional approach to treating metastatic prostate cancer.

"We know that surgery alone is not going to eliminate all of the metastatic disease, and the same is true of radiation," Scher told MedPage Today. "Our colleagues in radiation therapy have shown that patients who receive radiation and hormones do better than those who get radiation alone or hormones alone. We're just using surgery as the local treatment.

"We also know that if a patient has an established bone lesion, hormones alone don't eliminate all of the disease there, either. So we're using hormones and radiation for visible bone lesions."

'Pretty Exciting'

Klein acknowledged that the "proposed paradigm shift" requires testing and validation in larger clinical...
trials, but the results of the pilot study demonstrated the feasibility of the strategy.

"We rarely drive the PSA level to zero with androgen deprivation alone, but with a multimodal approach, we may be able to do that," said Klein. "Driving the PSA to zero and then having the patients' testosterone recover was the endpoint of the study. The paradigm shift is that if we can't get patients with metastatic disease to a PSA of zero with a multimodal approach, we're not going to cure anybody. The fact that they were able to get four patients to PSAs that were undetectable and normal testosterone, that's pretty exciting."

The 20 men selected for the pilot study had oligometastatic M1a (extrapelvic nodal involvement, n=5) or M1b (bone involvement, n=15) at diagnosis. All the patients started treatment with ADT, followed by surgery and stereotactic body radiation or radiotherapy then surgery. ADT stopped after a minimum of 6 months if a patient attained an undetectable PSA level after multimodal treatment. All others received ADT continuously.

The primary endpoint was an undetectable PSA level (<0.05 ng/dL) after testosterone recovery (>150 ng/mL), maintained at 20 months from the start of ADT. The endpoint allowed investigators to determine the safety and efficacy of the treatment with fewer patients followed for a shorter period of time, as compared with more conventional endpoints such as PSA recurrence, metastatic progression, and death, Scher noted.

None of the five patients with M1a disease achieved an undetectable PSA with ADT alone, but four did so after surgery. The fifth patient had undetectable PSA after radiation therapy. None of the patients met the primary endpoint, although one patient had a PSA level <0.05 ng/mL at 39 months, associated with a testosterone level of 47 ng/dL.

After a median follow-up of 34 months, two of the five patients progressed to castration-resistant prostate cancer at 18 and 32 months. Two patients had radiographic disease progression. One patient died of prostate cancer 24 months after the start of treatment.

In the M1b group, five patients attained undetectable PSA with ADT alone, six others after surgery, and three of the remaining four after radiation therapy. Four of the 15 patients met the primary endpoint. After a median follow-up of 47 months, eight patients had progression to CRPC, which occurred after a median follow-up of 23 months. One patient died of prostate cancer 59 months after the start of treatment.

"The results of this pilot study show that a multimodal treatment strategy can eliminate all detectable disease in patients with metastatic disease at presentation who are considered incurable with any single form of therapy," Scher's group concluded.

"Although longer follow-up is needed to assess durability, this binary endpoint [undetectable PSA/testosterone recovery] represents a first step toward establishing a paradigm of cure in patients with low-volume metastatic disease," they added.

**Looking Ahead**

Investigation of the approach will continue in a multi-arm, multistage study that will allow for incorporation of additional therapies, such as newer agents targeting the androgen receptor. Working with col-
laborators at other centers, the MSKCC group will conduct studies to learn more about the biology of the disease and its response to multimodal therapy, including so-called "super responders," patients whose response to treatment far exceeds the norm, Scher said.

The proportion of patients who might benefit from the multimodal strategy remains unclear, as most newly diagnosed prostate cancer is early-stage disease. However, several studies have suggested that the U.S. Preventive Services Task Force recommendation against routine PSA screening for prostate cancer has led to an increase in the diagnosis of more high-grade and later-stage disease, Klein noted.

Moreover, if the multimodal strategy pans out in additional studies of metastatic disease, the strategy might have a role in other clinical settings, such as localized disease at high risk of recurrence and progression.

The study was supported by The Sidney Kimmel Center for Prostate and Urologic Cancers, NIH/NCI, the Prostate Cancer Foundation, and the David H. Koch Fund for Prostate Cancer Research.

Scher and co-authors disclosed no relevant relationships with industry.

Reviewed by F. Perry Wilson, MD, MSCE Assistant Professor, Section of Nephrology, Yale School of Medicine and Dorothy Caputo, MA, BSN, RN, Nurse Planner

2017-04-26T16:15:00-0400

Primary Source

Urology


Objective - To evaluate a multimodal strategy aimed at treating all sites of disease that provides a rapid readout of success or failure in men presenting with non-castrate metastatic prostate cancers that are incurable with single modality therapy.

Materials and Methods - Twenty selected men with oligometastatic M1a (extrapelvic nodal disease) or M1b (bone disease) at diagnosis were treated using a multimodal approach that included androgen deprivation, radical prostatectomy plus pelvic lymphadenectomy (retroperitoneal lymphadenectomy in the presence of clinically positive retroperitoneal nodes), and stereotactic body radiotherapy to osseous disease or the primary site. Outcomes of each treatment were assessed sequentially. Androgen deprivation was discontinued in responding patients. The primary end point was an undetectable prostate-specific antigen (PSA) after testosterone recovery. The goal was to eliminate all detectable disease.

Results - Each treatment modality contributed to the outcome: 95% of the cohort achieved an undetectable PSA with multimodal treatment, including 25% of patients after androgen deprivation alone and an additional 50% and 20% after surgery and radiotherapy, respectively. Overall, 20% of patients (95% confidence interval: 3%-38%) achieved the primary end point, which persisted for 5, 6, 27+, and 46+ months. All patients meeting the primary end point had been classified with M1b disease at presentation.

Conclusion - A sequentially applied multimodal treatment strategy can eliminate detectable disease in selected patients with metastatic spread at diagnosis. The end point of undetectable PSA after testosterone recovery should be considered when evaluating new approaches to rapidly set priorities for large-scale testing in early metastatic disease states and to shift the paradigm from palliation to cure.
NETWORKING

The original and most valuable activity of the INFORMED PROSTATE CANCER SUPPORT GROUP is “networking”. We share our experiences and information about prevention and treatment. We offer our support to men recently diagnosed as well as survivors at any stage. Networking with others for the good of all. Many aspects of prostate cancer are complex and confusing. But by sharing our knowledge and experiences we learn the best means of prevention as well as the latest treatments for survival of this disease. So bring your concerns and join us.

Please help us in our outreach efforts. Our speakers bureau consisting of Lyle LaRosh, Gene Van Vleet and George Johnson are available to speak to organizations of which you might be a member. Contact Gene 619-890-8447 or gene@ipcsg.org to coordinate.

Member and Director, John Tassi is the webmaster of our website and welcomes any suggestions to make our website simple and easy to navigate. Check out the Personal Experiences page and send us your story. Go to: http://ipcsg.org

Our brochure provides the group philosophy and explains our goals. Copies may be obtained at our meetings. Please pass them along to friends and contacts.

Ads about our Group are in the Union Tribune 2-3 times prior to a meeting. Watch for them.

FINANCES

We want to thank those of you who have made special donations to IPCSG. Remember that your gifts are tax deductible because we are a 501(c)(3) non-profit organization.

We again are reminding our members and friends to consider giving a large financial contribution to the IPCSG. This can include estate giving as well as giving in memory of a loved one. You can also have a distribution from your IRA made to our account. We need your support. We will, in turn, make contributions from our group to Prostate Cancer researchers and other groups as appropriate for a non-profit organization. Our group ID number is 54-2141691. Corporate donors are welcome!

If you have the internet you can contribute easily by going to our website, http://ipcsg.org and clicking on “Donate” Follow the instructions on that page. OR just mail a check to: IPCSG, P. O. Box 4201042, San Diego CA 92142
Directions to Sanford-Burnham-Prebys Auditorium
10905 Road to the Cure, San Diego, CA 92121

Take I-5 (north or south) to the Genesee exit (west).
Follow Genesee up the hill, staying right.
Genesee rounds right onto North Torrey Pines Road.
Do not turn into the Sanford-Burnham-Prebys Medical Discovery Institute or Fishman Auditorium.

Turn right on Science Park Road. Watch for our sign here.
Turn Left on Torreyana Road. Watch for our sign here.
Turn Right on Road to the Cure (formerly Altman Row). Watch for our sign here.