Informed Prostate Cancer Support Group Inc.
"A 501 C 3 CORPORATION ID # 54-2141691"

FEBRUARY 2018 NEWSLETTER

P.O. Box 420142 San Diego, CA 92142
Phone: 619-890-8447 Web: http://ipcsg.org

We Meet Every Third Saturday (except December)

Thursday, February 08, 2018 Volume 11 Issue 2

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Next Meeting
February 17, 2017
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 often overwhelmed by the frightening magnitude of their condition. Networking with our members will help identify what options are best suited for your life style.

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Editor: Stephen Pendergast

PROSTATE CANCER IT'S ONLY 2 WORDS NOT A SENTENCE

From the Editor

This was a great way to kick off a new year!

Recap of January Meeting by Bill Lewis

Radiation Therapy for Prostate Cancer: The State of the Art in 2018

1. Dr. A. J. Mundt is Professor & Chair of Radiation Medicine and Applied Sciences at UCSC, and now also Senior Deputy Director of Moores Comprehensive Cancer Center. Besides bringing along three associates to provide presentations, he gave two brief **Radiation Oncology updates**.

A "**Halcyon**" machine, one of only two in the

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Video DVD's

DVD's of our meetings are available in our library for $10ea. Refer to the index available in the library. They can also be purchased through our website: http://ipcsg.org Click on the 'Purchase DVDs" button.

The DVD of each meeting is available by the next meeting date.

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world, has been just been installed at UCSD. It allows external beam radiation treatments in 5-7 minutes, and the moving parts (except the patient bed) are all concealed. The fast delivery improves accuracy (less internal organ and overall body movement), and is more comfortable.

The Proton Center has separated from Scripps, and has been "rebooted" as the **California Proton Center**. It's affiliated with UCSD and other local organizations. Two UCSD physicians have been placed there.

2. **Active Surveillance** presentation by Brent S. Rose, Radiation Oncologist at UCSD. There has been a consensus over recent years that many prostate cancer patients were overtreated in the past, resulting in unnecessary urinary incontinence, erectile dysfunction and/or bowel problems. The new goal is to identify men in whom the cancer is unlikely to metastasize or cause death from prostate cancer, and then NOT treat them – until/unless necessary.

Gleason scores have traditionally been used for risk stratification. See the video for scoring details. For those in the "very low risk" category, Active Surveillance is almost always the preferred option: Of 1,298 men with very low risk (71%) or low risk (29%) managed with AS, 50% did not undergo treatment by 10 years, and the 15-year cancer specific survival was 99.9%. The 15-year metastasis-free survival was a wonderfully high 99.4%.

The ProtecT trial studied men with "low risk" prostate cancer, showing very similar results no matter whether they received Surgery, Radiation, or were on Active Surveillance. There were a few more cases of metastases in the AS group, but it turns out that not all the participants were really "low risk." Also, note that 50% of the men on active surveillance did end up getting Surgery or Radiation within 8 years. But they avoided the side effects of those treatments for all those years! And it's my understanding that many of those who elected "treatment" did so simply out of fear of continuing to remain on AS – they couldn't stand to leave their disease untreated, despite its indolence.

For "intermediate risk" men, AS is considered to be appropriate only in carefully selected situations, in consultation with the physician. Most doctors are very reluctant to recommend AS to this group, so there is not a lot of data. In one study of 600 men, 28% of intermediate risk patients initially managed with AS had either metastases, or PSA recurrence after treatment, at 10 years. (But 72% didn't. That's a big group who avoided "treatment" side effects.)

The typical AS schedule includes a PSA test (looking especially at the rate of rise) and a DRE (digital rectal exam) every 3-6 months, and a confirmatory biopsy after 6-12 months. The repeat biopsy interval varies from yearly (ouch!) to every 3-4 years.

Triggers for initiating "treatment" are not well defined. But PSA rise >50% in one year or doubling in < 3 years usually triggers either re-biopsy or treatment. Gleason upgrading to 7 triggers treatment, unless there's just a tiny amount among the cores. An increase in the number of involved cores should trigger discussion of treatment.

The role of MRI: It's useful at diagnosis to rule out under-sampled high-grade disease that might be beyond the area reached by the biopsy needles. Dr. Rose also considers it can potentially be a useful adjunct to a repeat biopsy, although he considers that some repeat "random" biopsies will still be required.

The role of Genomic Testing: Biopsy core samples can be sent for genomic testing to assess the likelihood of low or intermediate risk PC becoming metastatic. "Decipher" and other tests are commercially available.

3. **The case for Brachytherapy boost for intermediate and high-risk prostate cancer**. By John Einck, Professor & Co-Director of Brachytherapy, and Chief of GU Radiation Oncology, at UCSD. See definitions of the risk categories in the video. As the volume of cancer within the prostate increases, the dose of radiation required to "cure" the cancer increases. ("Cure" means long-term stable/low PSA, to Dr. Einck.)

Data collected at UCSD, 2006-2015, from about 1000 men showed that patients with "unfavorable" High Risk disease fared significantly worse after EBRT (external beam radiation therapy) than those with "unfavorable" Intermediate Risk disease – about 10% less survival after 8 years. Somewhat surprisingly, men with Gleason 8 biopsy results, but no other risk factors (PSA was low, and volume of cancer was low, and confined to the prostate) fared very well. These men were all treated with "modern," targeted, high-dose radiation.

Combined therapy (EBRT + Brachytherapy "Boost") typically involves EBRT over 5 weeks, giving a dose of

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about 45 Gray (radiation units), followed after 2-4 weeks by either short-term, "High Dose" temporary insertion of highly radioactive seeds, or "permanent" seed implants that give a "Low Dose." It's crucial to understand that the dose designations refer to the dose rate, not the total dose. So the temporary seeds give about 20 Gray, whereas the permanent seeds actually deliver a much higher overall dose, of about 100 Gray.

The way the radiation is given, and especially the rate at which it is given, determines how much "biological effect" that radiation has (faster deliver means a lower dose is needed) and how much overall dose can be given without unacceptable side effects. So a method for harmonizing the potential biological effect from different EBRT fractionation schemes (how many sessions are used to deliver the radiation, i.e., using more radiation per session for "hypofractionated" – 5 week or less – vs. conventional 8 weeks of treatment, or only about 5 treatments for "Cyberknife" EBRT), or different Brachytherapy rates, or combinations has been worked out. This "BED" (biologically effective dose) is expressed in Gray units, and in EBRT with a Brachytherapy boost will ideally be about 200 Gray. However, note that with Brachytherapy, there will be an area within the treatment zone where the dose from the seeds (either permanent or temporary) will be as much as 50% higher than the nominal dose. This higher-dose region coincidentally and beneficially is the same region in the prostate where most tumors occur, and this is probably why Brachytherapy is especially efficacious.

Historically, permanent Brachytherapy implants were first used only with the lowest risk patients. Gradually, combination therapy with EBRT came to be used for Gleason 7-10 / PSA > 10 / palpable-disease patients. Brachtherapy "believers" like Dr. Einck consider Brachytherapy first for all localized prostate cancer, and just add EBRT if they are higher risk.

Numerous trials have been published, supporting the combination therapy. See the video. There is a "cost" for the combined therapy. Side effects are somewhat worse, especially urethral strictures. Those with existing urinary problems may not be good candidates for the Brachytherapy. There is some evidence that hormone therapy may not be necessary, when combined EBRT and Brachytherapy is administered.

SpaceOAR is a hydrogel that can be injected in the space between the prostate and the rectum. It breaks down and disappears in about three months. It provides a buffer zone between the irradiated area in the prostate, and the rectum, to avoid bowel problems, from either seeds or EBRT.

4. **The Physics Direct Patient Care Initiative**. By Todd Atwood, Ph.D, Medical Physicist, UCSD Radiation Medicine and Applied Sciences. There are 16 Faculty Medical Physicists at UCSD, working alongside 21 Faculty Radiation Oncologists. What they do: a. Calibrate and maintain treatment equipment, including external beam radiation therapy (linear accelerators) and Brachytherapy (afterloaders). b. Establish a quality assurance program, determine and perform tests to prevent errors, and "evolve" as new technologies become available. c. Oversee treatment planning and delivery, create the highest quality treatment plan possible, and ensure that it is delivered correctly to the patient.

They've asked how else they can improve patient care. They went out and learned from colleagues, and learned from patients. Radiation oncologists faced a dilemma of clinical practice in latter half of last century: They were often viewed merely as technicians that treated referrals, but gradually began to participate in tumor boards, multidisciplinary clinics, etc. They transformed from radiotherapists to radiation oncologists.

Regarding patients, they found these factors: Access to the internet is increasing – 88% of adults by 2015 (which means that both good and bad information is widely available). Patient-related distress can negatively impact outcomes following RT (according to Habboush, Y. et al. Adv Radiat Oncol, 2017). Online patient information is too complex for the general population (see Rosenburg, S. et al. Pract Radiat Oncol, 2017).

So, it was concluded at UCSD that medical physicists should expand their roles to help patients better understand their therapy. The Physics Direct Patient Care Initiative has these goals: a. Establish an independent professional relationship with patients. b. Take ownership of all technical aspects related to treatment. c. Meet with the patient at regularly scheduled appointments. d. Allow physicians to focus on other aspects of patient care.

A pilot program has begun, to explore clinical implementation, learn from patients, and provide personalized information for the patients including computer-graphic simulations to illustrate the treatment planning and deliv-

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ery. They have found that medical physicists are easily integrated into the patient-care team, and are able to help a wide variety of patient "types" (e.g., anxious, distrusting, scared and confused about radiation OR calm, thankful, and fascinated by the therapy), and that most patients want their questions heard and answered, want to be a part of the decision-making and want personalized information to review and share. Furthermore, this has been a very rewarding experience for the medical physicists involved in the program.

Question/Answer Roundtable:

Is EBRT possible after a hip replacement? Yes, though trickier with a bilateral replacement, especially if considering proton therapy.

Should most patients get an MRI during the early stages of their diagnosis, especially to be sure that significant cancer hasn't been missed (with or without a biopsy)? Dr. Rose noted that he is in favor of the use of MRI, but that it's expensive to screen everyone, just to look for the small percentage of cases where serious disease was missed in the biopsy. However, if he were the patient, he would want it! (This writer felt this same way, and paid out-of-savings / out-of-insurance-plan for an MRI, then again for an MRI-guided, targeted biopsy, which was almost without pain, and gave perfect confidence in the resulting diagnosis. Let those who will, accept "poke and hope!"). Dr. Rose noted that an MRI after biopsy does not add much information if the Gleason score is high, since some form of aggressive treatment is likely anyway, except that it provides useful information on the exact location of the disease, and the specific prostate anatomy, if brachytherapy is being considered.

For high-risk patients who have bone metastases, do they still qualify for the combination therapy? No. It won't cure the cancer that has already escaped the prostate, and there is a downside of urinary side effects.

Does the size of the prostate matter? Yes. If the prostate is large, the needle path used to introduce the seeds may be blocked by bone. So Dr. Einck prefers to limit his use of seeds to prostates under 50 cc's, or to men with prostates up to about 70 cc's who are willing to use hormone therapy for 3 months, to reduce their prostate size by about 30%. Note: Measurement units of cc's, milliliters and grams are all essentially equivalent, since human tissue has a density equal to water.

What about larger prostates producing more PSA? For patients without cancer, it's relevant. But prostate cancer produces a lot more PSA than healthy prostate tissue, so in practice, a prostate cancer patient's PSA can be considered a relevant measure of cancer "volume." A large prostate can produce a PSA as high as 12-14, but the key is to look at the whole picture, such as whether an MRI was done, the rate of PSA rise, etc.

Role and value of "simulating" with a CT scanner? This is a CT scan used to determine anatomy, and is necessary for treatment planning. The resulting images can be fused with other images, such as C-11 PET scans, or MRI images, giving additional useful information by combining anatomy with biological function.

Data on surgery vs. radiation? The available data wasn't directly comparable for many years, but now the ProtecT trial (see above) has shown in a randomized trial, that the results are equivalent.

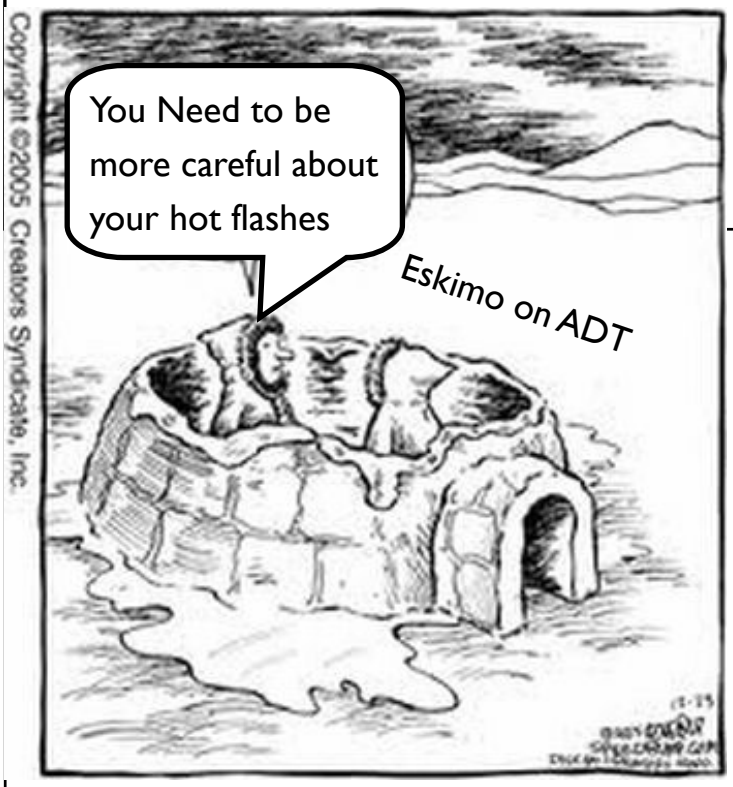
Combination treatment with EBRT + seeds, versus Proton + seeds? Dr. Einck considers EBRT and proton therapy to be equivalent to each other, with or without seeds. In either case, the seed boost improves the cure, but also has side effects (especially urinary) that need to be considered.

What PSA is indicative of "cure?" Dr. Einck: Less than 0.2 after seeds – but it might take three to five years to get to that point. A broader indicator/definition is that the PSA never rises more than two points above its nadir.

UCLA use of high dose rate Brachytherapy, and a report that Dr. Steinberg "abandoned" use of low dose rate seeds? Dr. Einck said that they never really used seeds. They hired Dr. Demanes, who spearheaded the high dose rate technique, so that's what they do. Dr. Einck trained in Seattle with the group that developed the permanent (low dose rate) seed implantation, so that's what he favors. He considers the results equivalent for control of cancer. However, he notes that the high dose rate approach is better-reimbursed by insurance plans. The possibility of putting a high-dose-rate facility into the new California Proton Center is being considered.

A video of the January IPCSG meeting, including the four presentations (with copies of the slides) and the roundtable Q&A session, will be available via the website shortly before the next meeting, or at the February meeting.

ON THE LIGHTER SIDE



"First we're going to run some tests to help pay off the machine."

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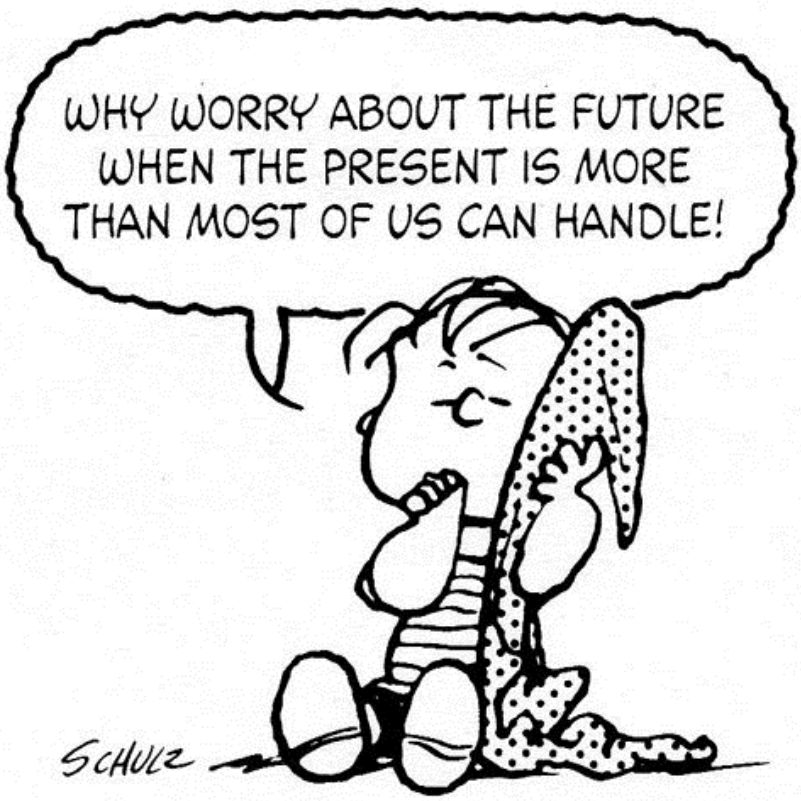

FUTURE MEETINGS

February 17, 2018 Meeting - A panel of members talk of their experiences. Then the group will break-out into sessions by treatment type (Active Servaliance, Surgery, ADT, Radiation, Chemo) for networking. This is when you can get all your questions answered by other members who are currently going through treatment, or have had treatment. All areas related to PcA are also discussed

INTERESTING ARTICLES

www.medscape.com

'Finally, Real Promise' for Non Metastatic Castrate Resistant Prostate Cancer 20+-Month Improvement in Metastasis-Free Survival

Nick Mulcahy

February 05, 2018

Long-needed change appears to be coming to the management of a group of prostate cancer patients for whom there is no apparent standard of care — men with early-stage disease whose prostate-specific antigen (PSA) score is rapidly rising after surgery or radiotherapy despite androgen-deprivation therapy (ADT).

There are currently no approved treatments for these men, who are destined to develop metastatic disease and are at increased risk for death. There are currently about 100,000 such patients in the United States.

Now, two phase 3, placebo-controlled clinical trials have shown that there are drugs that significantly delay the onset of metastasis in these patients.

The trials, which will be fully presented later this week at the Genitourinary Cancers Symposium (GUCS) 2018, in San Francisco, feature two different androgen-receptor inhibitors that are orally administered.

The SPARTAN trial employed the next-generation investigational agent **apalutamide** (Janssen Biotech). The PROSPER trial employed the earlier-generation enzalutamide (**Xtandi,** Astellas/Pfizer), which is already approved for men who have metastatic prostate cancer.

Both trials showed that in the treatment of men with nonmetastatic castrate-resistant prostate cancer, daily administration of the respective agents *reduced the relative risk for metastasis or death by more than 70% and prolonged metastasis-free survival (MFS) by more than 20 months* compared to placebo. All patients, in both the treatment and placebo arms, also received ADT.

Both trials enrolled men who had undergone definitive treatment, either surgery or radiotherapy, for prostate cancer but whose PSA scores subsequently double within 10 months or less, despite ADT. For each trial, MFS was the primary endpoint. Each trial showed a trend toward improved overall survival in

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an early interim analysis.

"These trials are addressing a great clinical need for these patients, who currently generally only receive observation," said Alexander Kutikov, MD, chief of urologic oncology at Fox Chase Cancer Center in Philadelphia, Pennsylvania, who was not involved in the research.

"The reported results will undoubtedly disrupt the treatment paradigms for these patients, delay the time to metastatic disease, and, ultimately, hopefully prove to extend survival," he told Medscape Medical News.

In the 1207-patient SPARTAN trial, which was discussed during a presscast today before the GUCS, which will be held later this week, apalutamide decreased the risk for distant metastasis or death by 72% (hazard ratio [HR] = 0.28; 95% confidence interval [CI], 0.23 - 0.35; P < .0001), with a median MFS of 40.5 vs 16.2 months in the placebo group (an improvement of 24.3 months).

Median follow-up was 20.3 months.

"These data suggest that apalutamide should be considered as a new standard of care for men with high-risk nonmetastatic castrate-resistant prostate cancer," lead study author Eric J. Small, MD, professor of medicine at the University of California, San Francisco, said at the presscast.

"Currently, there is no obvious standard of care for these patients," commented Sumanta K. Pal, MD, urologic oncologist at City of Hope in Duarte, California. He was moderating the presscast as an American Society of Clinical Oncology expert.

"These findings suggest there may finally be a treatment that holds real promise for extending their health and their lives," he added.

In the 1401-patient PROSPER trial, enzalutamide decreased the risk for distant metastasis or death by 71% (HR = 0.29; 95% CI, 0.24 - 0.35; P < .0001), with a median MFS of 36.6 vs 14.7 months in the placebo group (an improvement of 21.9 months).

"In the PROSPER trial, treatment with enzalutamide plus ADT delayed the development of metastases compared to standard-of-care ADT alone and, if approved, may provide men with nonmetastatic, castrate-resistant prostate cancer an important new treatment option," said lead author Maha Hussain, MD, professor of medicine, Northwestern University, Chicago, Illinois, in a press statement.

Both apalutamide and enzalutamide were well tolerated, with only about 10% of patients discontinuing treatment, compared to roughly 6% and 8%, respectively, of patients who received placebo in the trials.

Which therapy looks better? Dr Kutikov was cautious in answering.

He agreed that apalutamide appeared more effective. But he emphasized that "the results are similar" and advised "great caution in making comparisons between the two trials with regard to superiority or equivalency of one agent vs another."

Only a direct, prospective, randomized comparison can establish the superiority of one agent over another, he reminded.

Dr Pal suggested that enzalutamide might be favored by clinicians because of the "familiarity that oncologists already have" with the drug, "which may help with clinical adoption."

He also asserted that the nonmetastatic, castrate-resistant prostate cancer patient population may be "shrinking."

That's because newer and improved imaging modalities are detecting metastatic spread earlier than the current standards of CT and conventional bone scanning, which were used in the SPARTAN trial, Dr Pal observed. In short, the spread of disease may become apparent in conjunction with the rapid rise of PSA, he suggested.

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More Details on Both Trials

The SPARTAN study was conducted at 332 institutions internationally. Patients were randomly assigned in a 2:1 ratio to receive either apalutamide 240 mg QD or placebo. Baseline PSA doubling time was <5 months in both groups.

The primary endpoint of MFS was defined as the time from randomization to first radiographic evidence of distant metastasis (determined on the basis of blinded central review) or death.

Patients were eligible to receive study-provided abiraterone acetate plus prednisone after developing distant metastases.

At the median follow-up of 20.3 months, 61% of patients who received apalutamide and 30% of patients who received placebo were still on treatment.

Mean baseline health-related quality-of-life scores were maintained in both study groups. There was "no decrement in quality of life on apalutamide," reported Dr Small. There was also no difference in serious adverse events between the two groups, he said.

Of those whose disease progressed, 80% of patients who were given placebo and 56% of patients who were given apalutamide received open-label abiraterone (Zytiga, Janssen-Cilag) for metastatic castrate-resistant prostate cancer.

In the PROSPER study, eligible men were also randomly assigned in a 2:1 ratio to receive either enzalutamide 160 mg or placebo.

Enzalutamide, compared to placebo, also significantly prolonged time to first use of new antineoplastic therapy (39.6 vs 17.7 months; P < .0001) and time to PSA progression (37.2 vs 3.9 months; P < .0001), the study authors report in their abstract.

However, adverse events were higher with enzalutamide than with placebo (any grade: 87% vs 77%; grades ≥3: 31% vs 23%; serious: 24% vs 18%).

The SPARTAN trial was funded by Aragon Pharmaceuticals, Inc, a wholly owned subsidiary of Johnson & Johnson. The PROSPER trial was funded by Medivation, a Pfizer company, and Astellas, the codevelopers of enzalutamide. Mutliple investigators with both trials have ties to industry and include employees of the sponsoring companies. Dr Kutikov is the cofounder and a shareholder of Visible Health, Inc. Dr Pal has financial ties to Eisai, Ipsen, Astellas, Medivation, Bristol-Myers Squibb, Exelixis, Genentech, Myriad Pharmaceuticals, Aveo, Novartis, and Pfizer.

Genitourinary Cancers Symposium (GUCS) 2017. Abstracts 3 and 161, to be presented February 8, 2018.

Follow Medscape senior journalist Nick Mulcahy on Twitter: @MulcahyNick

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For further reading:

http://spendergast.blogspot.com/2018/02/prostatecancer-news-2018-02.html

For Comments, Ideas and Questions, email to Newsletter@ipcsg.org

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.

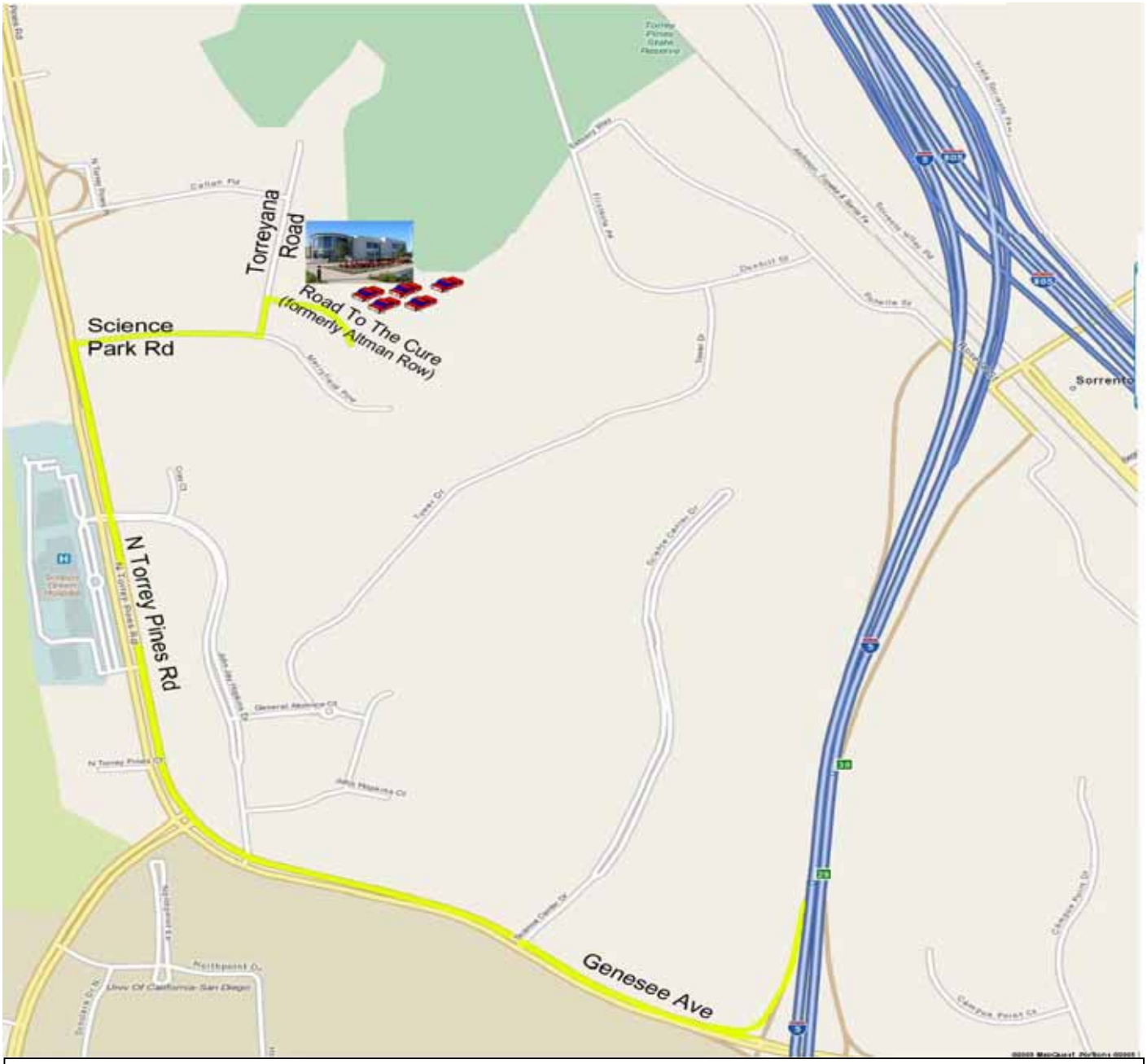
Ads about our Group are in the Union Tribune 2 times prior to a meeting. Watch for them.

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.