



# Informed Prostate Cancer Support Group Inc.

"A 501 C 3 CORPORATION ID # 54-2141691"



## January 2019 NEWSLETTER

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We Meet Every Third Saturday (except December)



<p><b>Officers</b></p> <p>Lyle LaRosh President</p> <p><b>Additional Directors</b></p> <p>Gene Van Vleet George Johnson John Tassi Bill Manning</p> <hr/> <p><b>Honorary Directors</b></p> <p>Dr. Dick Gilbert Judge Robert Coates</p> <hr/> <p>George Johnson, Facilitator Bill Manning, Videographer John Tassi, Webmaster Bill Bailey, Librarian Jim Kilduff, Greeter Chuck Grim, Meeting Set-up</p>	<p><b>Next Meeting</b></p> <p><b>Jan 19, 2019</b></p> <p><b>10:00AM to Noon</b></p> <p><b>Meeting at</b></p> <p><b>Sanford-Burnham- Prebys Auditorium</b></p> <p><b>10905 Road to the Cure, San Diego CA 92121</b></p> <p><b>SEE MAP PAGE 10</b></p> <hr/> <p><b>PROSTATE CANCER</b></p> <p><b>2 WORDS, NOT A SENTENCE</b></p>	<p>Tuesday, January 15, 2019</p> <p><b>What We Are About</b></p>	<p>Volume 12 Issue 01</p>
<p><b>Table of Contents</b></p> <p>Pg.</p> <p>#1 What We Are About</p> <p>#1 Video DVD's</p> <p>#1-4 Recruiting -Last Meeting Recap</p> <p>#5 On the Lighter Side</p> <p>#4 Future Meetings</p> <p>#6-9 Noteworthy Articles</p> <p>#10 Networking, Finances</p> <p>#10 Directions and Map to Meeting Place</p> <hr/> <p>Editor: Stephen Pendergast</p>	<p><b>WE ARE SEEKING REPLACEMENT FOR SOME OF OUR IPCSG TEAM</b></p> <p>Serving in this team can be rewarding and is a way to pay it forward to the group. To offer your services and/or ask questions about functions, Contact any of the individuals at their listed phone number.</p> <p><b>FUNCTIONS NEEDED:</b></p> <ol style="list-style-type: none"> <li><b>President:</b> IPCSG public relations, research and advice. Lyle LaRosh has performed for 18 years. 619-892-3888</li> <li><b>Vice President:</b> Support all team members, assist in monthly planning and speaker acquisition. <i>currently vacant</i> Gene Van Vleet has performed Functions 2, 4, 5 for 11 years. 619-890-8447.</li> <li><b>Meeting facilitator:</b> Monthly planning and speaker acquisition. George Johnson has performed for 8 years. 858-456-2492</li> <li><b>Treasurer/Secretary:</b> Handle banking, accounting, government reporting (see 2)</li> <li><b>Hot Line:</b> Communicate directly with newcomers and handle phone inquiries. (see 2)</li> </ol> <p style="text-align: right;"><i>(Continued on page 2)</i></p>	<p><b>Video DVD's</b></p> <p>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: <a href="http://ipcs.org">http://ipcs.org</a> Click on the 'Purchase DVDs' tab.</p> <p>The DVD of each meeting is available by the next meeting date.</p>	

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## November 2018 Meeting Summary by Bill Lewis

November 2018 meeting summary, by Bill Lewis

Dr. Richard Lam, of Prostate Oncology Specialists in Marina del Rey, gave his annual Prostate Cancer Update. He provided new information relating to the various stages of prostate cancer, including low/intermediate/high risk, relapsed disease and metastatic disease. He introduced a scheme for categorizing the various stages, which is discussed in detail in Dr. Mark Scholz' new book, *The Key to Prostate Cancer*. Sky, Teal, Azure, Indigo and Royal Blue "shades" each have low, medium and high subgroups, as discussed in the book.

Dr. Lam asserted that knowing the stage (or shade) of the cancer helps men appreciate that there are very different "kinds" of prostate cancer, understand the severity of their own disease, and know that there is a pathway for them to optimal therapy. They can limit their research to their particular stage, base decisions on facts, and interact with their doctor on a more equal playing field. You can take a quiz to find your stage, at [prostatecancerstaging.org](http://prostatecancerstaging.org).

On the flip side, the barriers to optimal treatment include having the wrong assumption that prostate cancer is just like other cancers, going to doctors who limit themselves to just one type of therapy, having the onus for choice resting on the patient, having information overload, dealing with the complex staging system used prior to this new system, patient inability to estimate the risk of micro-metastases, and a lack of a clear perspective.

Cancer metastases consist of growing prostate cancer cells located outside the prostate. These metastases are still prostate cancer, though located in bones or the liver or elsewhere. They are not the same as "bone" cancer or "liver" cancer. The reason that metastases are so dangerous is that enlarging tumors can cause organ malfunction leading to failure of the bone marrow, kidney or liver. This is the essence of the danger of prostate cancer.

He explained the concept of micro-metastases, which are individual or small clumps of cells outside the prostate. They are not as serious as visible mets. They are too small to be seen on scans, and are asymptomatic. Their presence can only be estimated by knowing the stage of the cancer (in particular, the shade of blue and its subtype). If they are present, surgery or radiation to the prostate alone will not be curative, but they are potentially treatable with systemic therapy or regional radiation therapy. The risk that they are present increases with each stage. Here are the stages:

1. "Sky." Low risk prostate cancer (defined as PSA < 10, no or small nodules in rectal exam, Gleason 3+3 or certain 3+4, <25% of cores involved, a favorable genetic profile, and small or no lesions seen on MRI or Ultrasound) has a low risk of "invisible disease" (micro-mets) elsewhere in the body, and Active Surveillance may be appropriate, or some local treatment of the "mother ship" may be chosen in hopes of a "cure." Systemic therapies such as ADT (androgen deprivation by blocking testosterone production), Chemotherapy, Radiopharmaceuticals or Immunotherapy are only rarely used.

2. "Teal." Intermediate risk prostate cancer is defined as Gleason score = 7, "moderate" nodule on rectal exam, PSA between 10 and 20, more than 50% of biopsy cores involved, imaging shows the cancer is confined to the prostate -- not extracapsular nor in seminal vesicles, and "intermediate" genetic panel results. Recommended treatments depend on the subgroup: Active Surveillance for the low group, Seed implants or hypofractionated Irradiation for the mid group, and Radiation with 4-6 months ADT, with or without Seeds, or a Prostatectomy for the high group.

Dr. Lam gave an update on "hypofractionated" Radiation Therapy, using a higher dose of radiation per visit, with a reduced number of visits (5 or 20 vs. 39 or more). This is more convenient, and less expensive. The PROFIT trial published in 2017 investigated the efficacy and safety of this approach for 4 weeks vs. 8 weeks of radiation, and found practically identical results, including side effects. This year, Hoffman et al reported in JCO that hypofractionated RT has a slightly lower relapse rate, and Katz, et al reported at ASTRO 2018 that 5-visit treatment gave a 93% cure rate for low risk cancer and 81% for intermediate risk cancer.

3. "Azure." High risk prostate cancer (defined as Gleason score = 8 to 10, a large nodule on rectal exam, PSA > 20, more than 50% of cores involved, and imaging showing extracapsular extension and/or seminal vesicle involvement) has as main treatment recommendations Seeds + Radiation Therapy + ADT (for low and mid subgroups, lasting 4-6 months or 12-18 months, respectively), or for the high subgroup, expanding the Radiation Therapy to the pelvis, prolonging the ADT to 18-36 months, and adding Zytiga.

In JAMA this year, it was reported that survival over 7.5 years was better for Seeds + Radiation Therapy + ADT (12 months) than with Surgery or Radiation Therapy + ADT (20 months).

The ASCENDE-RT trial showed that EBRT (external beam radiation therapy) + Seeds gave better results than EBRT alone for high risk prostate cancer, with 6.5 years of followup.

4. "Indigo." Relapsed disease: Relapse after surgery or other local treatment is manifested by rising PSA or the appearance of tumors in pelvic nodes (but not yet elsewhere). Recommended therapies: After prostatectomy, radiation to the prostate bed, and perhaps the pelvis, plus ADT. After Radiation Therapy, Cryotherapy, HIFU, or Surgery, Zytiga may be added. If the PSA doubling time is very slow, observation instead of immediate treatment may be appropriate. If high volume, then 4-6 cycles of Taxotere may be appropriate. Intermittent ADT is another option to be considered.

5. "Royal." Metastatic disease (defined as metastases beyond the pelvic nodes and/or castrate resistance (a rising PSA with Testosterone < 50). If no metastases visible, but castrate resistance, Earleada or Xtandi is recommended. Earleada was shown to delay metastases by 24 months, in a Feb 2018 NEJM report, with low levels of serious side effects. Similar outcomes were reported for Xtandi in June in the NEJM, but with possibly more side effects.

If only a few mets (without castrate resistance), Dr. Lam recommends ADT + Zytiga, and/or radiation to all sites of disease (including the prostate). If the patient is castrate-resistant, he recommends Provenge for 6 weeks, then Zytiga or Xtandi, and consideration of radiation

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therapy to all sites of the disease. In his experience, Radiation Therapy allows the patient to stop ADT sooner, and prolongs the time until ADT is needed again.

If more than 4 mets, without castrate resistance, he recommends ADT + Taxotere and/or Zytiga (especially if the patient cannot tolerate Chemo). If the patient is castrate-resistant, he recommends adding Zytiga or Xtandi to the ongoing ADT, with backup options of Radiopharmaceuticals, Chemotherapy or Immunotherapy.

An update on Lutetium-177 radiopharmaceutical: UCLA reports a 40 – 50% success rate with heavily pretreated patients. Hoffman et al (of Australia) reported similar results in Lancet this year.

Keytruda was shown to be of benefit to only a minor proportion of about 250 men (heavily pretreated) in the KEYNOTE-199 study. Prostate Oncology Specialists is getting somewhat better results by giving the drug earlier in the course of the disease. A new study combining Keytruda with Opdivo will be reported in 2019.

Olaparib (a PARP inhibitor) was shown in 2015 in the NEJM to work for men with certain gene mutations. A UK study of 142 men was reported at ASCO this year to provide 14 months vs. 8 months of time to disease progression when combined with Zytiga, as opposed to Zytiga alone. The TRITON study reported at ESMO 2018 showed that Rucaparib gave cancer shrinkage in 44% of 25 men with BRCA mutations, and > 50% PSA drop in 51% of 45 men.

A study of random biopsy vs. MRI-targeted biopsy was reported in NEJM in March 2018, and showed very positive results for the targeted biopsies. More significant cancers were identified. Fewer insignificant cancers were identified. And 28% of the MRI group were found to not need any biopsy at all. Side effects, such as bleeding, pain or erectile dysfunction were cut in half. Other suggestions for avoiding or minimizing the need for a biopsy are Ultrasound, Urine-based genetic tests (Exosome DX, Select MDX, or PCA-3), or a blood-based test such as the 4K score.

Recapping the benefits of the new staging and sub-staging scheme, Dr. Lam asserted that it provides the patient with a tailored list of reasonable treatment options. Armed with this knowledge, you can pick the right doctor by ascertaining the doctor's knowledge level, and discover which doctors are willing to co-partner with you in the decision-making process.

Questions:

How about radiation therapy with protons vs photons? Proton therapy is much more expensive, and in Dr. Lam's experience, is not significantly more effective. So he recommends the commonly used X-ray based Radiation Therapies.

For younger men with aggressive prostate cancer, what to do? He recommends being more aggressive, and using systemic therapy to knock down any micro-mets.

For metastatic disease, when to stop treatment? As a guideline, he would stop when the PSA is below 0.1 (then start again if it rises).

When start Chemo on relapse? Normally only used if the disease has metastasized, and it would be used right away. If ADT + Zytiga were already being given, and the cancer was progressing, chemo would be recommended (possibly with Xtandi beforehand).

What about a high percentage of cores that have 3 + 3 Gleason? Only about 1 out of 1000 men will end up with metastases in this case, so he treats them as low risk disease.

When is Surgery a recommended treatment option? He feels Brachytherapy is often effective (i.e., a better choice), but that surgery may be appropriate in the high subgroup of intermediate-risk cancer.

Guidelines for metastatic disease, as to how long to stay on ADT + Zytiga? If many metastases, stay on it until resistance occurs (usually after about 3 years). If few metastases, about a year – or up to 18 months if tolerated well – if the PSA goes to < 0.1 (and preferably with Radiation Therapy). Restarting depends on a PSA rise, but could be done when the PSA is anywhere between 1 and 6.

Genomic testing value? Dr. Lam uses it often as a “tiebreaker” to decide on treatment or not. If BRCA mutations are found, that higher risk would indicate the cancer needs to be watched more closely and treated more aggressively.

What can we do to delay castrate resistance? Use Zytiga early. Chemotherapy does that as well. It's not yet known whether “zapping” a hot spot with radiation will delay castrate resistance. A recently reported result from the STAMPEDE trial regarding relapsed metastatic disease indicated, surprisingly, that zapping the prostate (while continuing ADT) delayed castrate resistance. This is an example of “debulking” – knocking down the volume of cancer cells so that there are fewer cells to mutate.

What does a pathology report of T3b mean? This means that there was cancer in the seminal vesicles. There is a 50% probability that there are micro-mets in such cases – and that the surgery did not get all the cancer out.

Is there a benefit to getting a biopsy if MRI already shows a lesion? If growing or large, or near to breaking through the capsule or near the neurovascular bundle, Dr. Lam would recommend (targeted) biopsy to get the Gleason score.

A member reported that repeated biopsies over 8 years of active surveillance gave Gleason scores rising from 6 to 7 to 8. What treatment would have the least side effects? In general, radiation will have fewer side effects and equal or better outcome compared to surgery. Including sexual function? Yes.

How do Zytiga and Xtandi compare in his experience? There is good, strong data from the STAMPEDE trial that Zytiga with ADT is effective for newly-diagnosed (not previously treated with ADT) metastatic disease. Corresponding data for Xtandi is yet to be published, but is expected. In the case of castrate resistance, published data supports the use of either, but Xtandi has more troublesome cognitive and fatigue side effects. If Prednisone (which is administered with Zytiga) is contraindicated due to diabetes and congestive heart failure, then Xtandi would preferentially be used. Typically, both would be used sequentially, in one order or the other, for metastatic disease.

If Gleason score is 3+3, what other factors would make it advisable to begin treatment? If high volume 3+3 (high percentage of disease in the cores or large nodule), if some 3+4 is somehow suspected but the patient doesn't want more testing to confirm that, or if the patient is relatively young.

If metastatic, having had Chemo, then a year of ongoing ADT, with PSA rising from 0.18 to above 0.4, when would you add Zytiga? He would do scans, then do 5 weeks of Provenge, then Xtandi or Zytiga right afterwards.

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When would you test for BRCA mutations? If family history, Gleason > 7, if relapsed, if metastatic disease, he would check. The test is only \$100 now, even without insurance.

How important is it to have “the right doctor” if you choose Seeds? Very important – as much as in choosing a robotic surgery doctor. How to choose? Ask your oncologist, your radiation doctor, look on PubMed for his publishing activity.

Starting and stopping ADT – does intermittent therapy delay castrate resistance? No. But you do still get treatment “holidays” with the intermittent approach.

What’s good imaging to look for systemic cancer in the face of a rising PSA? PET scans are better than MRI’s. Medicare covers Axumin. The PSA should be at least 2.0 for a good image. Carbon-11 (done by Dr. Almeida in Phoenix for about \$3000) is very good, and works for a PSA as low as 0.8 or 0.9. Gallium-68 PSMA PET scans (done at UCSF and UCLA at \$1000 to \$3000) can detect cancer when the PSA is as low as 0.5. The Mayo Clinic in Minnesota also has Carbon-11 (less than \$1000 if you have Medicare) and it is very good.

4K blood test info? It’s a “super-PSA” test. It measures total PSA, and in addition, free PSA, pro-PSA (Intact PSA), and Human Kallikrein 2 (hK2). The higher the combined score, the greater likelihood of clinically significant cancer.

When is Erleada used? When rising PSA despite ADT, with no visible mets. You add it to ADT to delay the appearance of mets – for an extra 2 years.

What to do if your PSA keeps rising over years, but biopsies continue to give Gleason = 6? The prostate could be growing or the tumor could be growing (but Gleason = 6 would almost never spread). It’s important to consider whether there is a Gleason = 7 tumor that was missed by the biopsies – but targeted biopsies would effectively rule that out.

The video of this presentation, including the PowerPoint slides, will be available via the website shortly before the next meeting, or at that meeting, which will be held on January 19<sup>th</sup>, 2019.

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## UPCOMING MEETINGS

January 19, 2019

Dr. A.J. Mundt and Dr. Tyler Siebert

Advances in Radiation Therapy

Dr. Mundt is an internationally-recognized academic radiation oncologist and educator whose career has focused on the development and implementation of novel radiation technologies in a wide number of malignancies. He is the founding Chair of the UC San Diego (UCSD) Department of Radiation Medicine and Applied Sciences and serves as Senior Deputy Director of the UCSD Moores NCI-Designated Comprehensive Cancer Center.

An author of over 180 journal articles and book chapters, predominantly focused on advanced radiation technologies, Dr. Mundt has edited 3 academic textbooks, two devoted to intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) with over 100 contributors from the United States, Canada, Europe and Asia. He has delivered over 250 invited lectures at cancer symposia and conferences throughout the United States, Europe, South America and Asia, and has been a Visiting Professor at over 20 Universities and Cancer Centers.

Dr. Mundt last briefed us in January 2018 on Radiation Therapy for Prostate Cancer: The State of the Art in 2018. Topics discussed were “Halcyon” machine, Active Surveillance, Brachytherapy and the “Physics Direct Patient Care Initiative”.and are described in the Feb 2018 Newsletter.

What a great way to start off the new year with a presentation of the advances in the field of radiation oncology.

**For further reading**

<https://spendergast.blogspot.com/2019/01/prostatecancernews-for-1218-to-january.html>

**For Comments, Ideas and Questions**

Send email to [Newsletter@ipcs.org](mailto:Newsletter@ipcs.org)

ON THE LIGHTER SIDE



"You've got only 12 more years 'til retirement."



"I've crunched the numbers in your retirement account. It's time to figure out who will be wearing the mask and who will be driving the getaway car."



Since more and more seniors are texting and tweeting there appears to be a need for a STC (Senior Texting Code).

- ATD: At The Doctor's
- BTW: Bring The Wheelchair
- BYOT: Bring Your Own Teeth
- CBM: Covered By Medicare
- SCGU: Shit! Can't Get Up
- CUATSC: See You At The Senior Center
- DWI: Driving While Incontinent
- FWIW: Forgot Where I Was
- FYI: Found Your Insulin
- GGPBL: Gotta Go, Pacemaker Battery Low!
- GHA: Got Heartburn Again
- HGBM: Had Good Bowel Movement
- IMHO: Is My Hearing-Aid On?
- LMDO: Laughing My Dentures Out
- LOL: Living On Lipitor
- LWO: Lawrence Welk's on
- OMMR: On My Massage Recliner
- OMSG: Oh Migawd! Sorry, Gas.
- ROFL... CGU: Rolling On The Floor Laughing... And Can't Get Up
- SGGP: Sorry, Gotta Go Poop
- TTYL: Talk To You Louder
- WAITT: Who Am I Talking To?
- WTFA: Wet The Furniture Again



## Notable Articles

www.medscape.com

### **Combination Strategy Improves Identification of Clinically Significant Prostate Cancers**

By Reuters Staff, January 05, 2019

NEW YORK (Reuters Health) - Combining visual-registration and image-fusion biopsy targeting strategies provides the highest rate of detecting clinically significant prostate cancers, according to results from the SmartTarget biopsy trial.

Multiparametric MRI improves the diagnostic sensitivity for clinically significant prostate cancer while reducing the over-detection of clinically insignificant cancer, but it remains unclear which MRI-targeted biopsy method is best.

Dr. Hashim U. Ahmed of the Faculty of Medicine at University College London and colleagues sought to determine whether visual registration (mentally translating MRI targets onto real-time ultrasound images) is sufficient or whether it needs augmentation with image-fusion software.

Among 129 men who underwent both visual-registration and image-fusion biopsies, 93 (72%) had clinically significant prostate cancer (Gleason pattern of 3 or higher + 4 = 7) using both biopsy strategies.

Each strategy alone detected 80 of these significant cancers, with each method identifying 13 cancers that the other missed, so that the combination of the methods resulted in a 14% improvement in the detection of clinically significant prostate cancer.

Results were similar using an alternative definition of clinically significant prostate cancer (Gleason pattern of 4 or higher + 3 = 7), the researchers report in *European Urology*, online December 6.

The safety profiles were similar with the two biopsy strategies, and there were no significant differences in patient-reported outcome scores.

"Both strategies missed clinically significant cancers detected by the other strategy and so should be used in combination to optimize cancer detection," the researchers conclude.

"A cost-benefit analysis is a complex question beyond this study's scope," they add. "However, our results suggest potential benefits of a faster learning curve and higher repeatability that may enable less experienced centers to increase throughput and achieve cancer detection rates equivalent to those of highly experienced centers."

Several of the authors report financial ties to SmartTarget Ltd., which is commercializing the image guidance device used in this study.

Dr. Ahmed did not respond to a request for comments.

SOURCE: <https://bit.ly/2Ts4EXO>

Eur Urol 2018.

Reuters Health Information © 2019

Cite this article: Combination Strategy Improves Identification of Clinically Significant Prostate Cancers - Medscape - Jan 03, 2019.

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### **Surgery and Adjuvant RT Show Superiority in Locally Advanced Prostate Cancer**

<https://www.onclive.com/web-exclusives/surgery-and-adjuvant-rt-show-superiority-in-locally-advanced-prostate-cancer?log=f>

Caroline Seymour

Grace Lu-Yao, PhD

Higher survival rates were observed with radical prostatectomy (RP) and adjuvant radiotherapy (RT) compared with radiotherapy and androgen deprivation therapy (ADT) in men with locally advanced prostate cancer, according to a comparative analysis published in *Cancer*.<sup>1,2</sup>

Results showed that 10 years after treatment, 89% of men who received radical prostatectomy and RT were

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still alive, compared with 74% of those who received RT and ADT, demonstrating a 15% survival benefit in the prostatectomy arm. The coprimary endpoints were prostate cancer–specific survival and overall survival (OS), both of which were improved in the prostatectomy/RT arm, regardless of tumor stage or Gleason score.

“There is a lot of debate about whether to remove the whole prostate and follow up with radiation therapy,” senior author Grace Lu-Yao, PhD, associate director of Population Science at the Sidney Kimmel Cancer Center, said in a statement. “Or, as a second option, to spare the prostate and treat it using radiation therapy plus hormone -blocking therapy. Our study suggests that removing the prostate followed by adjuvant radiotherapy is associated with greater overall survival in men with prostate cancer.”

The analysis compiled data from the SEER database from 1992 to 2009 of men older than 65 years old who were diagnosed with locally or regionally advanced prostate cancer and had received either radical prostatectomy/RT or RT/ADT. Additional exclusion criteria included a history of previous malignancy; stage T1/T2, in situ, or M1 disease; distant lymph node involvement; Health Maintenance Organization coverage during the 6 months following diagnosis; no Part A or B Medicare coverage during the 6 months after diagnosis; indiscernible treatment; and primary chemotherapy.

Men who had received surgery that was not considered curative were excluded from the prostatectomy/RT group. This included cryotherapy, subtotal prostatectomy, and transurethral resection of the prostate. The study defined adjuvant RT as RT received within 6 months after RP. RT/ADT was defined as ADT given 2 months prior to receiving RT until anytime 3 years after RT.

Among men who received prostatectomy/RT, >55.7% were aged 65 to 69, 9.6% were aged 75 to 79, and <1.3% were aged 80 or older, whereas >26.7% of men who received RT/ADT were aged 65 to 69, 26.1% were 75 to 79, and 13.5% were aged 80 or older ( $P < .0001$ ).

Of the 13,856 men eligible for evaluation, 6.1% ( $n = 848$ ) received prostatectomy/RT versus 23.6% ( $n = 3272$ ) who received RT/ADT. Among men who received RT after prostatectomy, 29.8% ( $n = 253$ ) also received concurrent ADT.

Comorbidity index scores of 0 (90.1% and 79.2%), 1 (7.8% and 13.7%), and  $\geq 2$  (2.1% and 7.1%) were attributed to patients who received prostatectomy/RT as opposed to RT/ADT ( $P < .0001$ ).

Patients were staged according to the American Joint Committee on Cancer criteria, and comparison groups were matched by age, race, and comorbidity. Propensity score methods were used to account for differences between treatment arms. The 10-year survival analyses were conducted with the Kaplan-Meier method and Cox proportional hazards models. Prostate-specific antigen data were excluded from all analyses.

The adjusted 10-year survival advantage seemed to favor those without lymph node metastasis, though men with high-risk disease that was not localized still seemed to derive benefit from prostatectomy/RT (T3a/bN0M0, 88.9%; T3a/bN1M0, 75.7%; T4N0M0, 72%) over RT/ADT (T3a/bN0M0, 74.2%; T3a/bN1M0, 58.6%; T4N0M0, 60.5%).

The prevalence of treatment-associated adverse events served as a secondary endpoint of the study. Higher rates of erectile dysfunction (28.3% vs 20.4%;  $P = .0212$ ) and urinary incontinence (49.1% vs 19.4%;  $P < .001$ ) were seen with prostatectomy/RT versus RT/ADT, respectively. Additionally, men on the prostatectomy arm were more likely to undergo procedures to address urinary incontinence (12.4% vs 1.6%;  $P = .0007$ ) and erectile dysfunction

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(8.4% vs 3.7%;  $P = .0186$ ). Higher rates of bladder neck contractures (37.6% vs 18.3%;  $P < .0001$ ) and corrective procedures (34.3% vs 12.8%;  $P < .0001$ ) were also observed in men who received prostatectomy/RT compared with RT/ADT.

Rates of acute myocardial infarction, sudden cardiac death, coronary artery disease, thromboembolic events, skeletal fractures, and osteoporosis were similar between groups.

“Prostatectomy is an unpopular treatment,” said Lu-Yao. “Our study showed that only 6% of men with high-risk cancer were treated with it. It’s not just the risk of side effects. For some men, especially those who are not fit enough for the surgery, prostatectomy is not an option. However, this may be an option for some patients to re-consider.”

Moving forward, the authors noted there should be a surgical arm in future clinical trials for men with high-risk prostate cancer in addition to prospective trial data to confirm these findings.

#### References

Jefferson University Hospitals (2018). Combination therapy of prostatectomy plus radiotherapy may improve survival in patients with locally advanced prostate cancer. Published September 25, 2018. <https://bit.ly/2PIDoxt>. Accessed 4 Oct. 2018.

Jang TL, Patel N, Faiena I, et al. Comparative effectiveness of radical prostatectomy with adjuvant radiotherapy versus radiotherapy plus androgen deprivation therapy for men with advanced prostate cancer [published online September 25, 2018]. *Cancer*. doi: 10.1002/cncr.31726.

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## **Radiotherapy Shows Benefit in Select Patients With Metastatic Prostate Cancer**

Brandon Scalea

Chris Parker, MD

<https://www.onclive.com/web-exclusives/radiotherapy-shows-benefit-in-select-patients-with-metastatic-prostate-cancer>

Radiotherapy should be a standard treatment option for patients with newly diagnosed metastatic prostate cancer who have a low metastatic burden, said Chris Parker, MD.

In the multi-arm, phase III STAMPEDE trial, one arm of which was presented at the 2018 ESMO Congress, patients were randomized to receive either the standard of care or the standard of care plus radiotherapy. Standard treatment consisted of lifelong androgen deprivation therapy or docetaxel, and radiotherapy began  $\leq 8$  weeks after randomization or the introduction of docetaxel. The primary endpoints of the trial were failure-free survival (FFS) and overall survival (OS).

In the general cohort, radiotherapy improved FFS (HR, 0.68; 95% CI, 0.68-0.84), but not OS (HR, 0.92; 95% CI, 0.80-1.06). However, in a subgroup analysis of patients with low metastatic burden ( $n = 819$ ), OS was improved by 32% (HR, 0.68; 95% CI, 0.52-0.90).

Additionally, there was no benefit observed in patients with high metastatic burden (HR, 1.07; 95% CI, 0.90-1.28).



In an interview with OncoLive, Parker, who is the lead author of the study and a consultant clinical oncologist at The Royal Marsden NHS Foundation Trust in the United Kingdom, discussed the clinical implications of STAMPEDE and how radiotherapy fits into the treatment paradigm for these patients.

OncoLive: Please provide some background to this study.

Parker: Men with metastatic prostate cancer have always been managed with systemic treatment only. They have not had specific treatment of the prostate unless they had symptoms of progressive disease. In terms of radiation therapy and surgery, it was palliation only. In some preclinical models, it looks like when you treat the primary cancer, the metastases actually slow down and you can improve survival. That was the hypothesis we wanted to test in this trial of men with newly diagnosed metastatic prostate cancer. Metastatic disease is, sadly, incurable and the average survival is around 4 years. There is clearly scope to improve that considerably. Radiotherapy is a very simple treatment and it is very well tolerated, so if it works, it is an important addition to treatment.

What were the findings?

The trial included just over 2000 patients and they were randomized to receive drug therapy alone or drug therapy plus radiation to the prostate. The primary endpoint was OS, and it was significantly improved by radiotherapy. The hazard ratio was 0.9. However, we did a prespecified subgroup analysis according to metastatic disease burden. In patients with high metastatic disease burden, the trial was completely negative. In patients with low metastases, we saw a benefit—about a 30% improvement in OS.

What is your take-home message from these data?

I should perhaps start by saying some people are skeptical about subgroup analyses in general, but this particular subgroup finding is robust, and one can be confident about it. Our group meets the standard criteria in evaluating subgroup effects. In the future, prostate radiotherapy should be a standard treatment option for men with newly diagnosed metastatic prostate cancer and a low metastatic burden.

There is a second interesting message as well, and that includes men with pelvic node-positive prostate cancer. They were not included in the trial, but if you think about it, prostate radiotherapy improved survival in men with distant metastases; it should surely improve survival in men with regional metastases.

There is a third, more speculative message. That is, we have proven the principle that radiotherapy to the primary tumor improves survival. It is quite possible that this approach will be applicable to metastatic disease in other cancers.

Our findings are sufficient to change clinical practice. When patients come to the clinic with newly diagnosed metastatic prostate cancer with low metastatic burden, they should receive radiotherapy. Going forward, there are a couple of other questions we should ask. Is there potential for radiotherapy to oligometastases? Also, can we expand this to other solid tumors?

Parker CC, ND James, C Brawley, et al. Radiotherapy (RT) to the primary tumour for men with newly diagnosed metastatic prostate cancer (PCa): survival results from STAMPEDE (NCT00268476). In: Proceedings from the 2018 ESMO Congress; October 19-23, 2018; Munich, Germany. Abstract LBA5.

## NETWORKING

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](mailto: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: <https://ipcsg.org/personal-experience>

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.

## 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.