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

SEPTEMBER 2024 NEWSLETTER

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Monday, September 16,

Volume 17 Issue 09

Next IPCSG Meeting *3rd* Saturday, 10am September 21, 2024

- Jonathan J Chen, M.D, PhD. Is Medical Director of Division of Radiation Oncology, and Assistant Professor, Fred Hutch Cancer Center, University of Washington. He is a board-certified radiation oncologist who specializes in caring for patients with ocular melanoma, the most common type of eye tumor, and genitourinary cancers, which affect the urinary tract and the male reproductive system. His expertise includes using proton therapy that minimizes radiation exposure to healthy tissue. He will be discussing the latest radiation treatments including "Flash Radiation" as well as other related topics.
- **The will be a light lunch provided after the meeting**
- **For links to further Reading: https://ipcsg.blogspot.com/**
- **If you have Comments, Ideas or Questions,** email to Newsletter@ipcsg.org
- **For more information, please send email to bill@ipcsg.org or call Bill at (619) 591-8670**

Informed Prostate Cancer Support Group August 17, 2024

Telix - Future of Precision Medicine for Prostate Cancer

Denise Guilbault from Telix pharmaceuticals gave a presentation on their new Lutetium based therapy and their current diagnostic tools. Telix, based in Australia, is a commercial-stage biopharmaceutical company focused on the development and commercialization of therapeutic and diagnostic ('theranostic') radiopharmaceuticals. For more information, visit their website: https://telixpharma.com/ We unfortunately did not have permission to video this presentation, but I will summarize it here, and provide my detailed notes online.

Short Simplified Summary

Here's a short summary tailored for advanced mCRPC patients:

Telix Pharmaceuticals is developing a new treatment called TLX591 for men with advanced prostate cancer, specifically metastatic castration-resistant prostate cancer (mCRPC). Here's what you should know:

How it works: TLX591 targets a protein called PSMA, which is found in high amounts on prostate cancer

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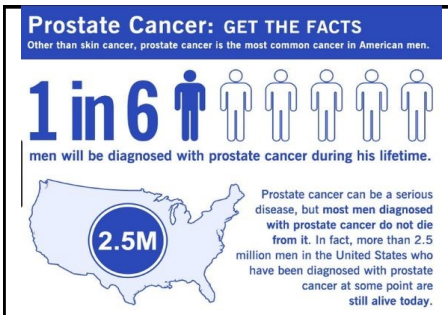

Organization

a 501c3 non-profit organization - all positions are performed gratis

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Stephen Pendergast ..... Editor

NEWSLETTER
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PROSTATE CANCER—*2 WORDS, NOT A SENTENCE*

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.

Join the IPCSG TEAM

If you consider the IPCSG to be valuable in your cancer journey, realize that we need people to step up and HELP. Call **President** Bill Lewis @ (619) 591-8670 "bill@ipcsg.org"; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor (SLP)

In this issue:

For original articles see the blog at https://ipcsg.blogspot.com/ . First, we have a claude.AI generated summary of my detailed notes from the Telix presentation. These notes are published online on the blogsite, since we were not permitted to video this presentation. The Phase 3 Clinical Trial of TLX591 for radiotheranostics looks very promising for advanced mCRPC.

This month, we include a couple items of interest:

1. Cryotherapy versus radical prostatectomy as a salvage treatment for radio-recurrent prostate cancer—if you had radiation and it came back, these therapies might give you a good chance.
2. Liquid Biopsy in Progressing Prostate Cancer Patients Starting Docetaxel with or Without Enzalutamide: A Biomarker Study of the PRESIDE Phase 3b Trial—Early ctDNA testing during docetaxel treatment might indicate treatment futility.

(Continued from page 1)

cells. It uses a radioactive substance (lutetium-177) attached to an antibody to deliver targeted radiation to cancer cells.

Treatment schedule: Unlike some other treatments that require multiple doses over several months, TLX591 is given as just two doses, two weeks apart. This means less time spent receiving treatment.

Potential benefits:

Early studies show it may be effective in slowing cancer progression.

It appears to have less impact on salivary glands and kidneys compared to similar treatments.

The treatment stays in tumor sites for a long time (up to 2 weeks), which may improve its effectiveness.

Side effects: The most common side effects in early studies were:

Fatigue

Temporary decreases in blood cell counts

Mild nausea and loss of appetite

Current status: TLX591 is being tested in a large clinical trial (called ProstACT GLOBAL) for patients whose cancer has progressed after treatment with hormonal therapy or chemotherapy.

Quality of life: The study is also looking at how the treatment affects patients' overall well-being and pain levels.

If you're interested in learning more or potentially participating in the clinical trial, you should discuss this option with your oncologist to see if it might be appropriate for your specific situation.

Prospective Clinical Impact

The clinical impact of a successful TLX591 trial could be significant for advanced mCRPC patients and the field of prostate cancer treatment. Here's an analysis of the potential impact:

New treatment option: A successful trial would provide a new therapy for mCRPC patients who have progressed on current standard treatments like ARPIs (e.g., abiraterone, enzalutamide) or docetaxel. This is crucial as mCRPC patients often have limited options after initial treatments fail.

Improved efficacy: If TLX591 demonstrates superior radiographic progression-free survival (rPFS) and overall survival (OS) compared to standard of care, it could become a preferred treatment option. The early data showing a median rPFS of 8.8 months is promising, but the Phase 3 results will be critical.

Better tolerability profile: The dosimetry data suggests lower radiation exposure to critical organs like salivary glands and kidneys compared to other PSMA-targeted radiotherapies. This could result in fewer side effects and better quality of life for patients.

Simplified treatment regimen: The two-dose regimen of TLX591 (given 14 days apart) is more convenient than the typical six-dose regimen of other radiopharmaceuticals. This could improve patient compliance and reduce the burden of treatment.

Personalized medicine approach: The use of PSMA PET imaging to select patients ensures that the treatment is targeted to those most likely to benefit, aligning with the trend towards precision medicine in oncology.

Potential for earlier use: If the safety profile is favorable, there might be potential to study TLX591 in earlier disease stages or in combination with other therapies, possibly expanding its clinical utility.

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Impact on treatment sequencing: A successful trial could lead to changes in treatment guidelines, potentially positioning TLX591 as a preferred option after first-line ARPI or chemotherapy failure.

Economic considerations: While pricing is unknown, if TLX591 proves more effective or has a better safety profile than current options, it could potentially reduce overall healthcare costs by decreasing hospitalizations or the need for supportive care.

Advancement in radioligand therapy: Success would further validate the antibody-based approach to radioligand therapy, potentially inspiring more research in this area for prostate and other cancers.

Quality of life improvements: If the treatment leads to better pain control and maintains or improves overall quality of life (as measured by the study's QoL questionnaires), it could significantly impact patient well-being.

In conclusion, a successful trial could position TLX591 as an important new option in the mCRPC treatment landscape, potentially offering improved outcomes, better tolerability, and a more convenient dosing schedule. However, the full impact will depend on the magnitude of benefit shown in the Phase 3 trial and how it compares to other emerging therapies in this space.

Q&A

As an advanced mCRPC patient, here are some key questions to ask your oncologist about the TLX591 trial, along with the types of answers you might expect:

1. Q: Am I eligible for this clinical trial?

   A: Your oncologist will likely review your specific case, considering factors like:

   - Confirmation of PSMA-positive mCRPC
   - Prior treatments (especially ARPI use in mCSPC or 1L mCRPC)
   - Current disease burden and metastases
   - Overall health status (ECOG 0-2)

   They may need to order additional tests, like a PSMA PET scan, to determine eligibility.

2. Q: How does TLX591 compare to other available treatments for my condition?

   A: The oncologist might explain that TLX591 is still experimental but potentially offers:

   - A more targeted approach to delivering radiation to cancer cells
   - Possibly fewer side effects on salivary glands and kidneys compared to similar treatments
   - A convenient two-dose regimen

   They'll likely emphasize that while early results are promising, the Phase 3 trial aims to confirm these benefits.

3. Q: What are the potential side effects of TLX591?

   A: Your doctor may discuss:

   - Common side effects like fatigue, nausea, and loss of appetite
   - Potential for temporary decreases in blood cell counts
   - How these compare to side effects of other treatments you've had or are considering

4. Q: If I join the trial, what's the chance I'll receive TLX591 versus standard care?

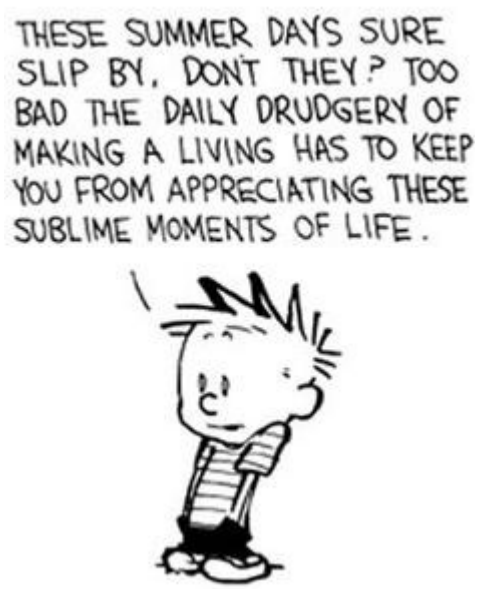
   A: They should explain the 2:1 randomization, meaning you have a 2 in 3 chance of receiving TLX591 plus standard of care, and a 1 in 3 chance of receiving only standard of care.

5. Q: How will participating in this trial affect my future treatment options?

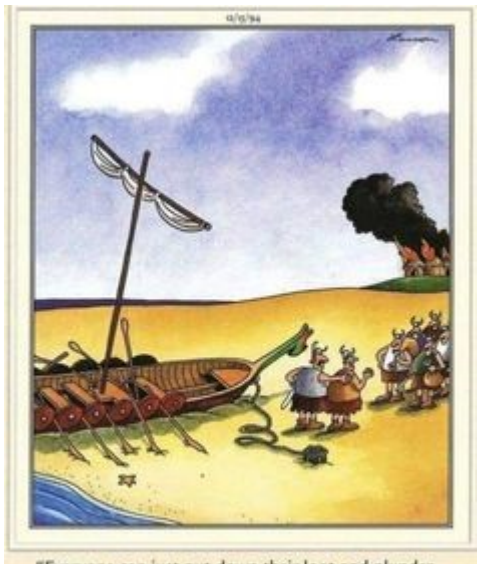
A: Your oncologist should explain that participating shouldn't negatively impact future options. They might add that if TLX591 proves effective, you could potentially continue receiving it after the trial ends.

Remember, your oncologist's answers will be tailored to your specific medical history and current condition. They should be open to discussing any concerns you have about the trial or your treatment options in general.

On The Lighter Side



"Never mind my name. You just tell your boss some *thing* is here to see him!"



"Everyone can just put down their loot and plunder, and Sven here—yes, old Sven, who was in charge of reading the tide chart—has something to say to us all."

Items of Interest

Cryotherapy versus radical prostatectomy as a salvage treatment for radio-recurrent prostate cancer | World Journal of Urology

Simplified Summary

"This study looked at two treatments for prostate cancer that has come back after radiation therapy. The treatments are:

1. Salvage radical prostatectomy (SRP): Surgery to remove the entire prostate

2. Salvage cryoablation of the prostate (SCAP): Freezing the prostate to kill cancer cells

The researchers compared how well these treatments worked in 96 men (25 had SRP, 71 had SCAP). They followed the patients for about 2 years on average. Here's what they found:

- Both treatments were effective at controlling the cancer in the short term.

- After 5 years:

  - About half the men in both groups were still free of cancer signs.

  - Around 90% of men in both groups were still alive.

  - Very few men died from prostate cancer in either group.

- There wasn't a big difference in side effects between the two treatments.

The study suggests that both treatments can work well for prostate cancer that comes back after radiation. SCAP might have fewer complications, but it's not certain.

The researchers say we need longer studies with more patients to be sure about the long-term results. For now, both treatments seem to be good options for patients in this situation."

Remember, this is just one study. It's always best to discuss your specific case and options with your doctor, who knows your full medical history and can give personalized advice.

Citation

Rivas, J.G., Taratkin, M., Azilgareeva, C. *et al.* Cryotherapy versus radical prostatectomy as a salvage treatment for radio-recurrent prostate cancer. *World J Urol* **42**, 515 (2024). https://doi.org/10.1007/s00345-024-05199-4

- Research
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Cite this articleWorld Journal of Urology Aims and scope

Juan Gomez Rivas, Mark Taratkin, Camilla Azilgareeva, Andrey Morozov, Silvia Laso, Dmitry Enikeev, Jesús Moreno Sierra, Ksenia Schelkunova, Francesco Sanguedolce, Alberto Breda, Alexander Govorov, Alexander Vasilyev, Marcos Cepeda, Lukas Lusuardi, Maximilian Pallauf, Antonio Celia, Tommaso Silvestri, Cristian Fiori, Esaú Fernández, Juan

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Ignacio Martínez-Salamanca & Eric Barret

Abstract

Introduction

The aim of this study is to compare outcomes of SRP (salvage radical prostatectomy) with SCAP (salvage cryoablation of the prostate) in local radio-recurrent PCa (prostate cancer) patients.

Materials and methods

A retrospective analysis of a multicentric European Society of Uro-technology (ESUT) database was performed. Data on patients with local recurrent PCa after radiotherapy who underwent salvage treatment were collected. Patients and their respective disease characteristics, perioperative complications as well as oncological outcomes were then described. The treatment success rate was defined as PSA nadir < 0,4 ng/ml. Any complications were graded according to the modified Clavien system. A descriptive and comparative analysis was performed using SPSS software.

Results

25 patients underwent SRP and 71 patients received SCAP. The mean follow-up was 24 months. The median PSA level before initial treatment was 8.3 (range 7-127) ng/ml. The success rates of SRP and SCAP were largely comparable (88% (22 patients) vs. 67.7% (48 patients), respectively, $p = 0.216$). The mean serum PSA levels at 12 months after salvage treatment were 1.2 ± 0.2 ng/mL vs. 0.25 ± 0.5 ng/mL, $p > 0.05$). During the follow-up period, only 3 (12%) patients in the SRP group had PSA recurrence compared with 21 patients (29.6%) in the SCAP group. The 5-year BRFS was similar (51,6% and 48,2%, $p = 0,08$) for SRP and SCAP respectively. The 5-year overall survival rate was 91.7%, and 89,7% ($p = 0.669$) and the 5-year cancer-specific survival was 91.7%, and 97,1% ($p = 0.077$), after SRP and SCAP respectively. No difference was found regarding the complications.

Conclusions

Both SRP and SCAP should be considered as valid treatment options for patients with local recurrence of PCa after radiotherapy. SCAP has a potentially lower risk of morbidity and acceptable intermediate-term oncological efficacy, but a longer follow up and a higher number of patients is ideally needed to draw any long-term conclusions regarding the oncological data

Liquid Biopsy in Progressing Prostate Cancer Patients Starting Docetaxel with or Without Enzalutamide: A Biomarker Study of the PRESIDE Phase 3b Trial - ScienceDirect

sciencedirect.com

K. Desai, J.M. McManus, N. Sharifi

Simple Summary

Here's a simplified summary for prostate cancer patients. The PRESIDE study looked at how to better treat advanced prostate cancer. Here are the main points:

The study tested whether continuing a drug called enzalutamide along with chemotherapy (docetaxel) would help patients more than just chemotherapy alone.

Researchers used blood tests (called liquid biopsies) to look for cancer markers.

Key findings:

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Patients with cancer DNA in their blood before starting chemotherapy didn't do as well.
A special blood test could show which patients might benefit from continuing enzalutamide with chemotherapy.
Patients who tested negative on this special test and continued enzalutamide lived about 2.5 months longer without their cancer getting worse.

The study also found that:

Testing for cancer DNA early in chemotherapy might show if the treatment is working.
Some genes related to cancer growth become more common after chemotherapy, which might lead to new treatment ideas.

What this means for patients:

In the future, doctors might use these blood tests to choose the best treatment for each patient.
This could help some patients get more benefit from their medications.

Remember, these findings still need more research before they change how doctors treat prostate cancer. Always discuss your specific situation with your doctor.

Summary

This document describes a biomarker study conducted as part of the PRESIDE phase 3b clinical trial for patients with metastatic prostate cancer. Here are the key points:

Study Design:

- PRESIDE trial tested continuing enzalutamide with docetaxel vs. placebo with docetaxel in patients who progressed on enzalutamide alone.
- The biomarker study analyzed liquid biopsies (blood samples) to identify patients who might benefit most from continuing enzalutamide.

Main Findings:

- Patients with detectable circulating tumor DNA (ctDNA) at baseline had shorter progression-free survival (PFS) on docetaxel.
- Patients who remained or became ctDNA-positive after starting docetaxel had worse outcomes.
- A liquid biopsy "resistance biomarker" (AR gene amplification and/or AR-V7 in circulating tumor cells) identified patients who did not benefit from continuing enzalutamide.
- Patients negative for this biomarker had significantly longer PFS when continuing enzalutamide (11.2 vs 8.7 months).

Other Observations:

- TP53 and AR alterations were independently associated with worse outcomes.
- At progression on docetaxel, there was an increase in copy number gains of cell cycle-related genes (e.g., CDK4, CDK6).

Implications:

- Early ctDNA testing during docetaxel treatment might indicate treatment futility.
- The AR-based liquid biopsy biomarker could help select patients for continuing enzalutamide with docetaxel.
- Targeting cell cycle pathways might overcome docetaxel resistance.

Limitations:

- Sample size was not predetermined for biomarker analysis.
- Results are considered hypothesis-generating and require further validation.

The study provides evidence for using liquid biopsies to guide treatment decisions in metastatic prostate cancer, particularly for continuing enzalutamide with docetaxel in selected patients.

Clinical Impact

Based on the study results, the potential clinical impacts for prostate cancer treatment are significant. Here's a breakdown of the key clinical implications:

Early treatment response assessment:

Doctors might use ctDNA testing after the first cycle of docetaxel to quickly identify patients who are not responding well to treatment.

This could allow for earlier changes in treatment strategy, potentially improving outcomes and quality of life.

Personalized treatment decisions:

The liquid biopsy "resistance biomarker" (AR alterations) could help identify patients who are likely to benefit from continuing enzalutamide along with docetaxel.

This personalized approach could lead to improved progression-free survival for some patients while avoiding unnecessary treatment for others.

Improved patient selection:

Patients without the resistance biomarker showed a 51% improvement in progression-free survival when continuing enzalutamide.

This significant benefit could justify the continued use of enzalutamide in selected patients, potentially changing current practice.

Monitoring disease progression:

Regular liquid biopsies could provide a non-invasive way to monitor cancer progression and treatment response.

This could reduce the need for more invasive tests or imaging studies.

New therapeutic targets:

The identification of cell cycle gene alterations (like CDK4 and CDK6) at disease progression suggests potential new treatment targets.

This could lead to clinical trials testing CDK inhibitors in combination with or after docetaxel.

Refinement of treatment sequencing:

Understanding which patients benefit from continued enzalutamide could help optimize the sequencing of treatments in advanced prostate cancer.

Cost-effectiveness:

By identifying patients who are most likely to benefit from continuing enzalutamide, healthcare systems could potentially reduce costs associated with ineffective treatments.

Future clinical trial design:

These findings may influence the design of future clinical trials, incorporating biomarker testing to stratify patients or as inclusion/exclusion criteria.

It's important to note that while these results are promising, they are considered hypothesis-generating and require further validation in larger, prospective studies before being widely implemented in clinical practice. Nonetheless, they provide a strong foundation for future research and potential improvements in prostate cancer treatment.

Q&A

Here are some questions you could ask your oncologist based on these study results, along with potential answers you might receive:

1. Q: "Is liquid biopsy testing available for my cancer? Could it help guide my treatment decisions?"

   A: Your oncologist might say: "Yes, liquid biopsy testing is becoming more available. While it's not yet standard practice for all patients, it could provide valuable information about your cancer. However, we'd need to consider if it would change our treatment approach in your specific case."

2. Q: "Can we test my blood for circulating tumor DNA (ctDNA) to get more information about my cancer?"

   A: "ctDNA testing is possible, but it's not routinely done for all patients yet. It could give us insights into your cancer's genetic makeup and how it's responding to treatment. We'd need to discuss the potential benefits and limitations for your situation."

3. Q: "If I'm starting docetaxel, could we do a blood test after the first cycle to see how well it's working?"

   A: "This study suggests early ctDNA testing might indicate treatment response. While intriguing, it's not yet standard practice. We typically assess response through PSA levels, scans, and how you're feeling. But I'll keep an eye on research in this area."

4. Q: "Based on my current treatment, would continuing enzalutamide along with chemotherapy be an option for me?"

   A: "The PRESIDE study looked at this approach. Whether it's right for you depends on several factors, including your previous treatments and how you've responded. This study suggests it might benefit some patients, but it's not yet a standard approach. We'd need to carefully consider the potential benefits and risks for you."

NETWORKING

Please help us in our outreach efforts. Our speakers bureau consisting of Gene Van Vleet and Bill Lewis is available to speak to organizations of which you might be a member. Contact Bill 619-591-8670 (bill@ipcsg.org) to coordinate.

Member 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

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!

DIRECTIONS TO MEETINGS

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.