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

Friday, August 18, 2023

AUGUST 2023 NEWSLETTER

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

Volume 16 Issue 08

Next Meeting Saturday, August19, 2023 IPCSG—10:00am PT.

- Members of the IPCSG group will share stories about their journey with Prostate Cancer. This is a great time to ask your questions from men who have gone through different treatments, their successes', difficulties and lessons learned. A combined Q&A session will occur after all 3 have spoken. This is your chance to get all your questions answered by men who have "been there, done that"...
- As always, spouses/partners and caregivers are welcome and encouraged to attend!
- *After the meeting a light lunch will be served in the foyer outside the meeting room*
- **For links to further Reading: https://ipcsg.blogspot.com/ (includes member suggested links)**
- **If you have Comments, Ideas or Questions,** email Newsletter@ipcsg.org
- **For more information, please send email to bill@ipcsg.org or call Bill at (619) 591-8670 or Gene at (619) 890-8447**

Future of Precision Medicine: Prostate Cancers

July 2023 IPCSG Presentation - Summary by Bill Lewis

Note: "Intended for US members and their caregivers only"

Mary Hames, PhD, MBA, Telix Pharmaceuticals – US Medical Affairs and Dr. Simon Chowdhury from the UK spoke to us about the Telix pipeline of s**mall molecules and antibodies for imaging and therapy for Prostate Cancer, Kidney, Brain, and BMC/RD (Bone marrow conditioning/rare diseases). TLX591-CDx (68Ga-PSMA-11, Illuccix®) is already commercially available, and is usually covered by insurance.**

ILLUCCIX, after radiolabeling with Ga-68, is a radioactive diagnostic agent indicated for use with positron emission tomography (PET) imaging combined with Computerized Tomography (CT) in patients

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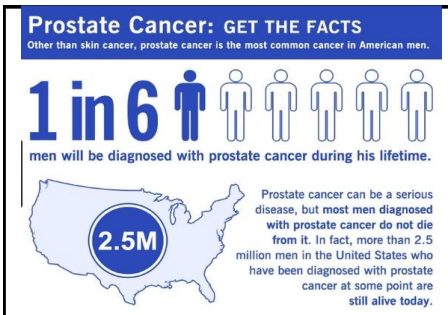

Organization

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

IPCSG

Officers

Bill Lewis President

Additional Directors

Gene Van Vleet

Aaron Lamb

Bill Manning

Honorary Directors

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Bill Manning, ...Videographer
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Bill Bailey, ...Librarian
Mike Corless,.....Greeter
Aaron Lamb, ...Meeting Set-up
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@prostatecancerhelp.info"; or **Director** Gene Van Vleet @ 619-890-8447.

From the Editor

In this issue:

Bill Lewis produced a summary of the Telix talk last meeting. For further articles see the blog at https://ipcsg.blogspot.com/ . Many new advanced topics are covered in articles linked in the blog for further reading. Some apparently important optimistic items of interest this month:

1. UCSD Health Breakfast of Champions—an event to help fight prostate cancer
2. Potential cancer breakthrough as 'groundbreaking' pill annihilates ALL types of solid tumors in early study | Daily Mail Online
3. Resistant Prostate Cancer Patients Undergoing Prostate-Specific Membrane Antigen–Targeted Radioligand Therapy
4. The role of nuclear medicine tracers for prostate cancer surgery: from preoperative to intraoperative setting

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with prostate cancer:

- who are at risk of metastasis and who are suitable for initial definitive therapy.
- who have suspected recurrence based on elevated serum prostate specific antigen (PSA) level.

68Ga-PSMA-11 (Illuccix) is well supported by real-world experience and ongoing clinical trials. Recent, large, multinational, prospective studies have been conducted to support the use of 68Ga-PSMA-11 in the staging of patients with: Suspected metastatic PCa, BCR (biochemical recurrence), or for selection of patients with mCRPC (metastatic, castrate resistant PCa) for radioligand therapy.

Clinical studies of Illuccix before radical prostatectomy and of biochemical recurrence after surgery showed good results. No serious AEs (adverse events) were attributed to 68Ga-PSMA-11, and low rates of grade 1 AEs were reported.

Detection of metastatic disease is improved using Illuccix vs. conventional imaging with CT and bone scan. 68Ga-PSMA-11 revealed metastases in 10% of patients classified as M0 (i.e., no metastases found) on bone scan. In randomized studies of biopsy-proven, high-risk PCa, 68Ga-PSMA-11 was found to influence management changes by up to 43% of patients at primary staging. Management changes were implemented almost 2X more often with 68Ga-PSMA-11 vs. conventional imaging. In randomized studies of patients with metastatic PCa, 68Ga-PSMA-11 PET/CT was found to influence staging and management very frequently. SNMMI, EANM and NCCN guidelines now recognize the value of PET/CT including 68Ga-PSMA-11 (e.g., Illuccix).

177Lu-DOTA-TLX591 therapy characteristics:

The cell surface prostate-specific member antigen (PSMA) has proven to be an ideal therapeutic target in prostate cancer. 177Lu-DOTA-TLX591-CHO (**TLX591;** 177Lu-rosopatamab) is a radioimmunoconjugate comprised of the humanized IgG1 monoclonal antibody rosopatamab, linked to lutetium-177 via the chelating agent, DOTA.

TXL591 as a potential radioimmunotherapy (RIT) for the treatment of prostate cancer is supported by clinical evidence on the conjugate safety and tumor specificity. TLX591 has been evaluated in approximately 200 patients over five Phase 1 and Phase 2 studies.

PSMA competitive landscape: the Telix approach is highly differentiated – see image below. TLX591 is cleared via the liver, then through fecal excretion. The competitive small molecule approach (Pluvicto) binds to lacrimal, parotic and submandibular (salivary) glands, and is taken up by the liver, spleen, kidneys and small bowel, with urinary excretion through the bladder.

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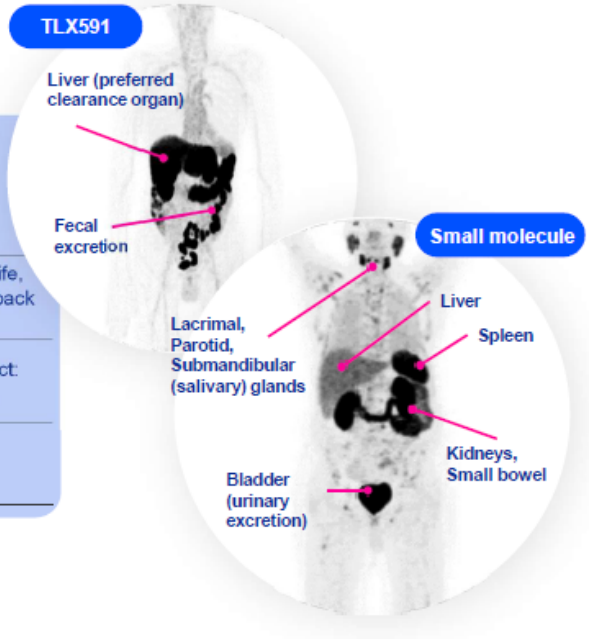
PSMA competitive landscape

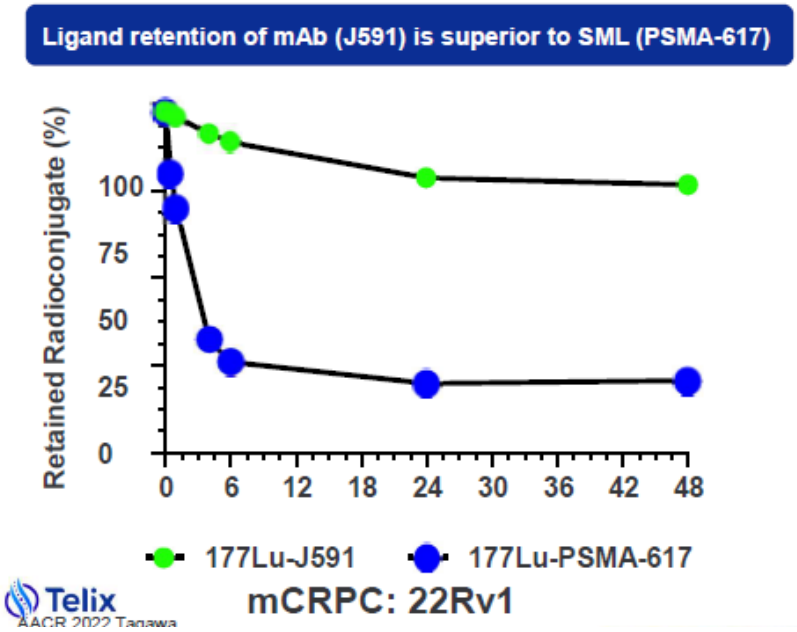
Telix approach is highly differentiated

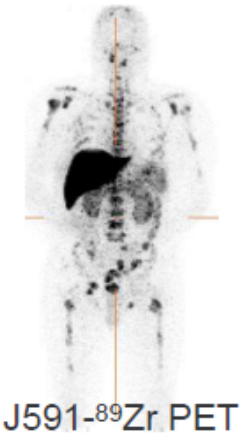
ANTIBODY (TLX591)	SMALL MOLECULES
Functionally specific for tumor-expressed PSMA, does not "hit" most endogenous PSMA	Taken up by endogenous PSMA
Reduced off-target radiation, reduced potential for undesirable side-effects[1]	Off-target effects impact quality of life, including dry eye, xerostomia and back pain from ganglia irradiation
Longer circulation time and tumor retention, cleared in the liver and excreted, allowing for fewer doses[2]	Rapidly excreted via the urinary tract: approx. 70% activity lost by 12 hrs
Shortest dosing regimen of all PSMA therapies, two x 76 mCi doses, 14 days apart	Dosing regimens range up to 36 weeks, at up to 200 mCi per dose



Product	TLX591 (^{177}Lu-rosopatomab)	177Lu-PSMA-617
Recommended Adult Dose	76 mCi	200 mCi
Recommended Doses	2 Doses (14 days apart)	4 Doses (6 weeks apart) up to 6 doses
Total Treatment Activity	152 mCi	800 mCi up to 1200 mCi
Critical Organ	Liver	Kidneys
MOA	Monoclonal antibody	Small Molecule PSMA Ligand
PSMA Extracellular Target	Apical Region	Enzymatic pocket of the catalytic domain
PSMA Ligand	N/A	PSMA-617
Excretion	Hepatic	Renal

J591: Humanized Monoclonal Anti-PSMA Antibody

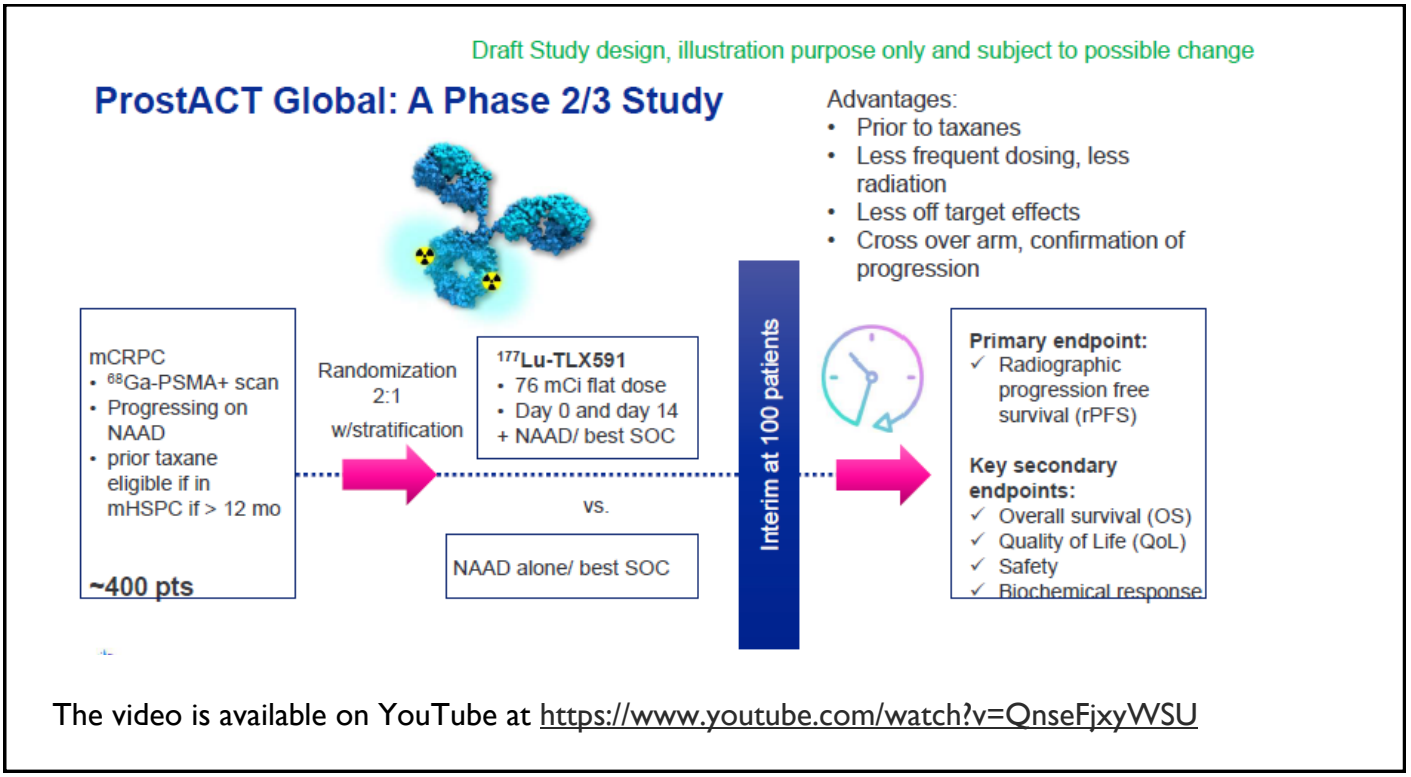




TLX591 (177Lu-DOTA-rosopatamab) has clear evidence of anti-tumor effect and a dose-response of key measures of activity: PSA and CTC (circulating tumor cells) response, as well as overall survival. It is highly tolerated by patients with predictable and transient reductions in hematological (blood) parameters with subsequent recovery. Fractionated (reduced / split) dosing addresses hematologic safety while delivering a targeted and potent radiation dose to metastatic prostate cancer.

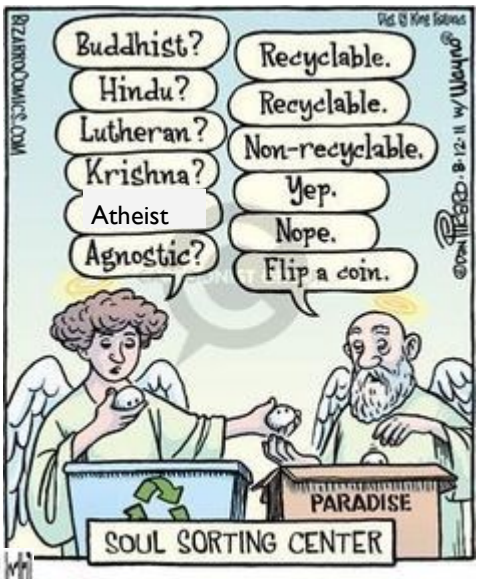
Biodistribution data indicates TLX591 antibody is retained in the tumor with high activity remaining at two weeks and beyond – see graph. Longer-term retention of TLX591 in the tumor (and metastases) may maximize the cell-killing effect of the 177Lu radioisotope at the cancer sites and allow optimized dosing.

TLX591 Summary: Antibody vs small molecule. Promising overall survival seen in early phase studies. Reduced potential for undesirable side-effects; dry eye, xerostomia (salivary gland ablation), back pain (ganglia irradiation). Short treatment duration / significantly fewer hospital visits – two weeks total vs. 36 weeks; supports close supervision by medical oncology. >60% less radiation per dose and >80% less radiation exposure for entire treatment compared to 6 cycles of Pluvicto. Reduced 177Lu isotope requirement via more targeted dosing / less waste.



The video is available on YouTube at https://www.youtube.com/watch?v=QnseFjxyWSU

On the Lighter Side



On Memorial Day ->

UCSD Health Breakfast of Champions— an event to help fight prostate cancer

Christopher J. Kane, MD, dean of Clinical Affairs at UC San Diego School of Medicine, cordially invites you to attend the 10th Anniversary Breakfast with Champions event benefiting prostate cancer research in the Department of Urology and Moores Cancer Center at UC San Diego Health.

Thursday, September 21, 2023 8 –10 a.m. at the La Jolla Country Club 7301 High Avenue La Jolla, California

Together, we will celebrate our patients, highlight our clinical and research programs, and hear from Pro Football Hall of Famer Mike Haynes about his NFL career and prostate cancer advocacy. Register Here https://one.bidpal.net/breakfast2023/welcome

Potential cancer breakthrough as 'groundbreaking' pill annihilates ALL types of solid tumors in early study | Daily Mail Online

dailymail.co.uk

Caitlin Tilley

Scientists have developed a holy grail cancer drug that kills all solid cancer tumors while leaving other cells unharmed.

The new molecule targets a protein present in most cancers that helps tumors grow and multiply in the body.

It is significant because this protein - the proliferating cell nuclear antigen (PCNA) - was previously thought to be 'undruggable'.

The drug was tested on 70 different cancer cells in the lab - including those derived from breast, prostate, brain, ovarian, cervical, skin, and lung cancer - and was effective against them all.

The pill is the culmination of 20 years of research and development by the City of Hope Hospital in Los Angeles, one of America's largest cancer centers.

The medicine is codenamed AOH1996 after Anna Olivia Healy, who died in 2005 from a deadly childhood cancer aged nine. Dr Linda Malkas, who leads the research team, met Anna's father just before she died and was inspired to find a cure in her memory.

It comes amid excitement that cancer will be curable within the coming decade, a claim that has been made by the scientists who invented the Pfizer Covid vaccine.

For more, see https://www.news-medical.net/news/20230804/New-PCNA-inhibitor-AOH1996-shows-selective-cancer-cell-killings-and-tumor-suppression-potential.aspx

Conclusions

In sum, the study reported two AOH1160-based inhibitor analogs, and the lead candidate, AOH1996, was more metabolically stable with drug-like characteristics. AOH1996 enhanced PCNA-RPB1 interactions, leading to the overall degradation of RPB1 and the collapse of replication forks in actively transcribed regions.

Specifically, these enhanced interactions prevent TRC resolution, leading to lethal double-strand breaks and the disruption of the transcription machinery by the degradation of RPB1.

CaPCNA disrupts the PCNA-TRC interface in cancer cells, allowing AOH1996 to exert selective and potent anti-cancer effects with a remarkable safety profile.

Overall, the study underscores the therapeutic potential of AOH1996 and its utility in characterizing TRC in cancer cells. Given its multi-functionality, further studies are required to understand the effects of AOH1996 on other aspects of PCNA

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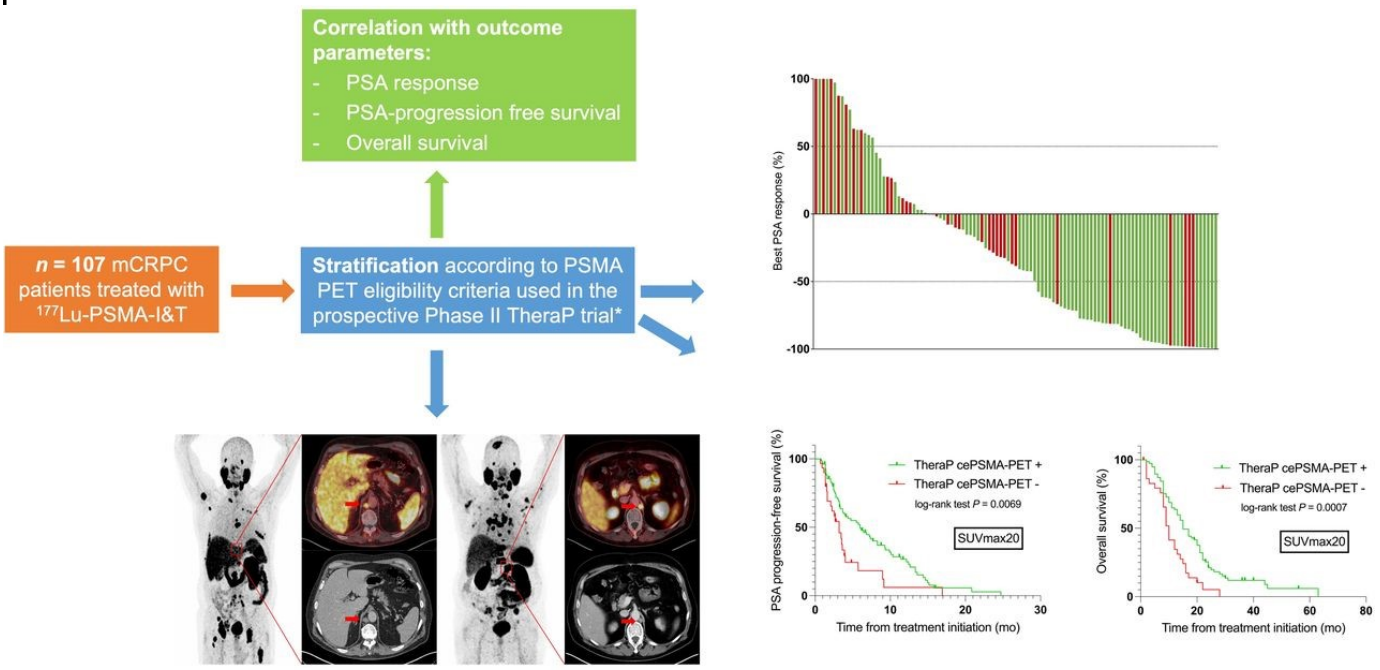

*Notably, in comparison to the TheraP trial our patients did not undergo ^{18}F-FDG PET prior to ^{177}Lu-PSMA RLT

The Impact of PSMA PET–Based Eligibility Criteria Used in the Prospective Phase II TheraP Trial in Metastatic Castration-Resistant Prostate Cancer Patients Undergoing Prostate-Specific Membrane Antigen–Targeted Radioligand Therapy

Amir Karimzadeh, Matthias Heck, Robert Tauber, Esteban Solaris, Stephan Nekolla, Karina Knorr, Bernhard Haller, Calogero D'Alessandria, Wolfgang A. Weber, Matthias Eiber and Isabel Rauscher

Journal of Nuclear Medicine August 2023, 64 (8) 1252-1258; DOI: https://doi.org/10.2967/jnumed.122.265346

Abstract

Prostate-specific membrane antigen (PSMA) radioligand therapy (RLT) has shown encouraging results for treatment of metastatic castration-resistant prostate cancer (mCRPC) in the prospective, multicenter, randomized phase II TheraP study. The inclusion criteria for that study comprised a pretherapeutic ^{68}Ga-PSMA-11 PET scan showing sufficient tumor uptake using a predefined threshold and the absence of ^{18}F-FDG–positive, PSMA ligand–negative tumor lesions. However, the prognostic value of these PET-based inclusion criteria remains unclear. Therefore, we evaluated the outcome of mCRPC patients treated with PSMA RLT using TheraP as well as other TheraP-based PET inclusion criteria.

Methods: First, patients were dichotomized into 2 groups whose PSMA PET scans did (TheraP contrast-enhanced PSMA [cePSMA] PET–positive) or did not (TheraP cePSMA PET–negative) fulfill the inclusion criteria of TheraP. Notably, unlike in TheraP, ^{18}F-FDG PET was not performed on our patients. Prostate-specific antigen (PSA) response (PSA decline ≥ 50% from baseline), PSA progression-free survival,

and overall survival (OS) were compared. Additionally, patients were further dichotomized according to predefined SUV_{max} thresholds different from those used in TheraP to analyze their potential impact on outcome as well.

Results: In total, 107 mCRPC patients were included in this analysis (TheraP cePSMA PET–positive, *n* = 77; TheraP cePSMA PET–negative, *n* = 30). PSA response rates were higher in TheraP cePSMA PET–positive patients than in TheraP cePSMA PET–negative patients (54.5% vs. 20%, respectively; *P* = 0.0012). The median PSA progression-free survival (*P* = 0.007) and OS (*P* = 0.0007) of patients were significantly longer in the TheraP cePSMA PET–positive group than in the TheraP cePSMA PET–negative group. Moreover, being in the TheraP cePSMA PET–positive group was identified as a significant prognosticator of longer OS (*P* = 0.003). The application of different SUV_{max} thresholds for a single hottest lesion demonstrated no influence on outcome in patients eligible for PSMA RLT.

Conclusion: Patient selection for PSMA RLT according to the inclusion criteria of TheraP led to a better treatment response and outcome in our preselected patient cohort. However, a relevant number of patients not fulfilling these criteria also showed substantial rates of response.

The role of nuclear medicine tracers for prostate cancer surgery: from preoperative to intraoperative setting

The role of nuclear medicine tracers for prostate cancer sur... : Current Opinion in Urology
journals.lww.com

Barletta, Francesco; Ceci, Francesco; van den Bergh, Roderick C.N.; Rajwa, Pawel; Montorsi,

Abstract

Purpose of review

There has been a growing interest in the use of novel molecular imaging modalities for the management of prostate cancer (PCa), spanning from diagnostic to therapeutic settings. The aim of this review is to provide a comprehensive overview of recently published studies investigating the use of novel nuclear medicine tracers across different stages of PCa management.

Recent findings

Emerging evidence supports the use of molecular imaging for preoperative staging of PCa, where prostate-specific membrane antigen (PSMA) PET has shown superior accuracy compared to conventional imaging for the detection of nodal and distant metastases, which needs to be translated to new risk stratification. A role for PSMA PET has been proposed for PCa diagnosis, with local activity associated with histology. Surgical guidance, using either visual feedback or gamma-ray detectors to identify tissues with accumulated radio-labeled tracers, may improve the ability to resect locoregional diseases and thus maximize oncological control. PSMA targeted therapy (Lu-PSMA) has been mainly investigated in the castration-resistant setting, but might have a role in earlier settings such as neoadjuvant treatment.

Summary

Novel molecular imaging using PSMA-based tracers could significantly improve PCa management in the diagnosis, staging, and intraoperative guidance settings, potentially leading to personalized and effective treatment decisions.

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 Gene 619-890-8447 or gene@ipcsg.org or Bill 619-591-8670 (bill@prostatecancerhelp.info) 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.