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

MAY 2024 NEWSLETTER

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Wednesday, May 15, 2024

Volume 17 Issue 05

Next Meeting *3rd* Saturday, June 15, 2024 IPCSG—10:00am—Noon PDT.

- **May meeting cancelled due to construction in meeting hall.**
- June meeting presentation by Ze'ev Ronai, PhD., head cancer researcher at SBP who studies how cells respond to stress and how these responses contribute to PCa development and progression. His talk will be followed by a talk by Bill Manning on his journey with Active Surveillance:

- 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/**
- **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 or Gene at (619) 890-8447**

IPCSG Meeting Summary, April 27, 2024

Here is a summary of Dr. Michael S Kipper's presentation on "A Patient's Journey with Prostate Cancer":

Introduction:

Dr. Kipper is presenting to a prostate cancer support group, focusing on a patient's perspective from diagnosis through treatment options. His experience is primarily in prostate cancer imaging, and he worked at the Advanced Prostate Cancer Center in Mesa for 8 years. He emphasizes the importance of quality of life in addition to quantity of life.

Background:

Prostate cancer treatment has advanced significantly in the past 20 years, with the introduction of chemotherapy and over 40 new treatments. However, there is still no single "magic bullet" cure. Dr. Kipper will discuss the many aspects and complexities of prostate cancer, while highlighting reasons for optimism.

Diagnosis:

Prostate cancer diagnosis typically begins with an elevated PSA level, which is prostate-specific but can also rise for benign reasons. A PSA above 4 is concerning but must be interpreted in the context of an individual patient's history, followed by a repeat PSA, digital rectal exam (DRE), and biopsy.

The biopsy procedure involves placing an ultrasound probe in the rectum, taking 12 or more tissue cores, and

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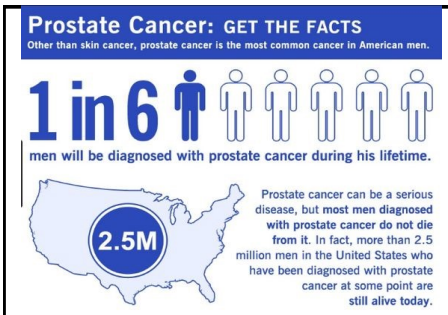

Organization

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

IPCSG

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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 last months very enlightening talk by Dr. Kipper. This month, we're trying a new format using AI to summarize each article in layman's terms so you can hopefully understand it, and then describe impact on clinical practice and questions to ask you physician. Links are still provided to original articles. Some important items of interest this month:

1. Cancer Research by Dr. Ze'ev Ronai's team at SBP Medical Discovery Institute.—*our June Speaker*
2. Extraperitoneal robot assisted laparoscopic prostatectomy with Versius system: single centre experience | Prostate Cancer and Prostatic Diseases—*new robotic surgery tool, easily learned*.
3. Characterising the contribution of rare protein-coding germline variants to prostate cancer risk and severity in 37,184 cases | medRxiv—*extensive germline study finds genes tied to PCa*
4. Defining oligometastatic state in uro-oncological cancers : Current Opinion in Urology—*some metastatic disease may be treatable.*
5. .

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giving antibiotics to prevent infection. Targeted biopsies using combined MRI/ultrasound images are becoming more common. The biopsy report provides the Gleason score, which grades the aggressiveness of the cancer based on the two most common cell patterns seen. In modern practice, Gleason scores range from 6 to 10, with 6 being the least aggressive.

Receiving a cancer diagnosis is highly stressful for patients and families. Dr. Kipper humorously describes how the DRE technique was perfected and marketed using animals and celebrity athletes.

Staging and Treatment Planning:

After diagnosis, staging determines the extent and location of the cancer. Modern imaging techniques like MRI, CT, bone scan, and PET/CT have revolutionized staging, allowing detection of metastases even at very low PSA levels. Staging helps guide treatment decisions.

The newly diagnosed patient must process a large amount of information and deal with the reality of having cancer. He will need to decide between surgery and radiation, consider androgen deprivation therapy, and confront potential side effects and impacts on quality of life. Having a spouse or partner present can help with information processing and decision-making.

Androgen Deprivation Therapy (ADT):

ADT, using medications like Lupron, Firmagon, and Orgovyx, is a mainstay of prostate cancer treatment. It lowers testosterone levels to slow cancer growth. While not curative alone, it can control the disease for many years. Side effects include impotence, fatigue, cognitive issues, lipid abnormalities, muscle loss, fat gain, bone density loss, and others. Bone density loss is a significant risk, as 20% of men who suffer a hip fracture die within a year due to complications.

Surgery and Radiation:

Mr. Jones chooses robotic prostatectomy. At surgery, lymph node involvement is found, so radiation is added to his treatment plan along with ADT. Common side effects include incontinence and impotence.

After treatment, he experiences low energy, weakness, uncertainty about the future, and worries about mortality and family impact. This is a vulnerable time when support is especially important.

Follow-up and Recurrence:

Prostate cancer requires lifelong surveillance, as it can recur years or decades later. Monitoring involves regular PSAs, imaging, and sometimes genetic testing. Treatment options for recurrence include additional radiation, immunotherapy, chemotherapy, novel agents like Lu-PSMA, and clinical trials.

Mr. Jones' cancer becomes castration-resistant, meaning it progresses despite low testosterone. He receives additional therapies but ultimately exhausts treatment options. At this stage, the focus shifts to palliative care and support.

Conclusion:

A prostate cancer patient's journey is complex and can involve many treatment modalities and decision points. While rapidly advancing, current treatments are still not curative for all patients. However, there are always reasons for optimism and hope. The importance of a multidisciplinary care team, support network, and empowering the patient with knowledge cannot be overstated. Dr. Kipper emphasizes that even when treatments are exhausted, patients should never be abandoned, and palliative/hospice teams provide essential support and guidance.

The presentation highlights the many facets and challenges of a prostate cancer diagnosis, the critical role of the patient's perspective and quality of life considerations, and the reassuring message that manifold treatment options and support resources exist for patients throughout their journey. Dr. Kipper's engaging presentation style, incorporation of humor and relatable analogies, and obvious passion for patient care and advocacy shine through in this informative talk.

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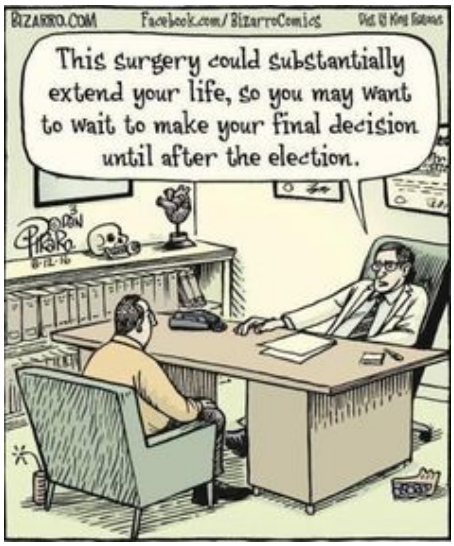
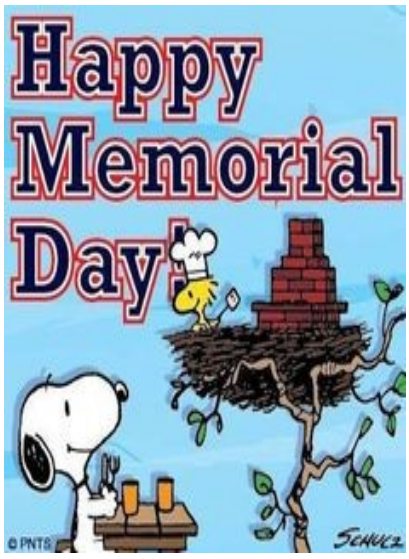
On the Lighter Side



"I'll give you something to ease the pain."

"Repeat after me: 'Hypnotherapy is worth $60 an hour.'"

"I remembered the Alamo … but forgot everything else!"



Cancer Research by Dr. Ze'ev Ronai's team at SBP Medical Discovery Institute.

Dr. Ronai's team identified a protein named Siah2 and its associated pathway that plays a crucial role in converting non-malignant prostate tumors into aggressive, metastatic neuroendocrine tumors. Targeting this pathway could provide new diagnostic markers and therapeutic targets for aggressive prostate cancers.

The researchers also studied the roles of various ubiquitin ligases, such as Siah1/2, RNF5, and RNF125, in melanoma development, progression, and treatment resistance. Some of these findings could potentially be applicable to prostate cancer as well.

Two different strategies for starving cancer cells of vital nutrients were investigated. One study focused on blocking glutamine uptake in melanoma cells, while the other targeted macropinocytosis (A form of endocytosis in which a large fluid-filled vesicle, or macropinosome, is pinched off from the cell membrane and brought into the interior of the cell.) in pancreatic cancer-associated fibroblasts. Both approaches showed promising results in slowing tumor growth.

Dr. Ronai received a prestigious NCI Outstanding Investigator Award, providing $7.9 million over seven years to support his research on understanding how tumors adapt to harsh conditions and develop resistance to therapy. His work aims to establish new paradigms and therapeutic modalities for cancer treatment.

Overall, these studies provide valuable insights into the molecular mechanisms driving aggressive tumor behavior and treatment resistance, particularly in prostate cancer and melanoma. The findings could lead to the development of new diagnostic tools and targeted therapies for these challenging cancers.

Extraperitoneal robot assisted laparoscopic prostatectomy with Versius system: single centre experience | Prostate Cancer and Prostatic Diseases

F. Dibitetto, C. Fede Spicchiale, R. Castellucci, S. Sansalone, A. Akhundov, L. Defidio & M. De Dominicis

Prostate Cancer and Prostatic Diseases (2024)Cite this article

Abstract

Introduction

Versius Surgical System (CMR Surgical, Cambridge, UK) is a novel tele-operated robotic surgical system designed to assist surgeons for minimally invasive surgery which is gaining momentum in the world of robotic surgery. We describe our single centre experience with Versius and report the advantages and challenges posed by this new robotic system in a series of 53 extraperitoneal robotic assisted laparoscopic prostatectomies (eRALP) for prostate cancer (PCa).

Materials and methods

Data of 53 eRALP performed with Versius in our centre were collected and analysed, Descriptive statistics were used to report our results.

Results

In 16 months we performed 53 eRALP: 18 (34%) with PLND, 33 (62%) nerve sparing cases. Mean setup time was 15 min, mean console time was 100 min and mean operative time was 130 min. We observed a substantial reduction of console time and set-up time after only 5 procedures. In the first 4 procedures, the dissection of the neurovascular bundle was performed laparoscopically, to switch back to robotic assisted approach afterwards. No major system failures were observed. No major intra-operative and post-operative complications occurred. Mean follow-up time was 9 months (range 3–15 months); no patients experienced biochemical recurrence or metastatic progression over this period, 8 (15%) patients had adjuvant radiotherapy based on unfavourable pathology report (positive surgical margins or positive limphnodes).

Conclusion

This represents to our knowledge the largest extraperitoneal RALP case series with Versius, and it aims to provide solid clinical proof of the safety, effectiveness and versatility of this innovative system. In our experience, this plat-

form represents a good option for every urologic surgeon who wants to start a robotic programme and it appears particularly suitable for urologists with a large laparoscopic expertise.

May 11, 2024

Characterising the contribution of rare protein-coding germline variants to prostate cancer risk and severity in 37,184 cases | medRxiv

Summary

This research article characterizes the contribution of rare protein-coding germline variants to prostate cancer risk and severity through a large-scale meta-analysis of sequencing and genotyping data from 37,184 prostate cancer cases and 331,329 male controls across multiple cohorts.

Key findings:

1. Gene-level analysis revealed that rare damaging variants in SAMHD1 and DNA damage response (DDR) genes like BRCA2, ATM, and CHEK2 are associated with increased prostate cancer risk.
2. Rare damaging variants in AOX1 and BRCA2 were associated with increased prostate cancer severity in a case-only analysis of aggressive vs non-aggressive disease.
3. Single variant-level analysis identified rare non-synonymous variants in HOXB13, CHEK2, and BIK significantly associated with increased prostate cancer risk, while variants in ANO7, SPDL1, AR, and TERT were associated with decreased risk.
4. Different rare germline variants appear to influence prostate cancer risk vs severity, with BRCA2 and ATM associated with both, SAMHD1 and CHEK2 associated only with risk, and AOX1 only with severity.
5. Identification of these risk and severity genes provides insight into prostate cancer pathogenesis and potential therapeutic targets.

In summary, this large multi-cohort meta-analysis provides the most comprehensive characterization to date of rare coding germline variants influencing prostate cancer risk and severity. The findings have implications for genetic risk stratification, screening, and treatment strategies in prostate cancer.

Impact

The results of this study could potentially have significant implications for the clinical care of prostate cancer patients who carry the identified germline variants:

1. Screening and early detection: Men with variants that increase prostate cancer risk, such as those in HOXB13, CHEK2, and SAMHD1, may benefit from earlier and/or more frequent screening for prostate cancer. This could lead to detection of the disease at an earlier, more treatable stage.
2. Risk stratification: Genetic information could be incorporated into risk stratification tools along with other factors like family history, allowing for more personalized prostate cancer risk assessment. This could inform decisions about when to start screening and how frequently to screen.
3. Treatment decisions: Patients with variants associated with more aggressive prostate cancer, such as those in BRCA2 and AOX1, may benefit from more intensive treatment upfront. For example, knowing a patient has a BRCA2 mutation may guide treatment towards PARP inhibitors or platinum chemotherapy, which have shown efficacy in this population.
4. Precision medicine: Identifying specific gene variants can help guide targeted therapies. For instance, the association of rare AR variants with decreased prostate cancer risk suggests that these variants may disrupt normal AR signaling. This could potentially inform the use of AR-targeted therapies.
5. Genetic counseling: Patients found to carry risk variants may benefit from genetic counseling to understand their risks, screening and prevention options, and implications for family members.
6. Clinical trials: Patients with specific germline variants may be candidates for clinical trials testing targeted therapies or novel screening/prevention strategies.

However, it's important to note that translating these research findings into changes in clinical practice will require

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further studies to validate the associations and determine the most effective ways to use this genetic information to improve patient outcomes. Guidelines from professional organizations will also be needed to direct implementation.

Questions

As a prostate cancer patient, you can engage your doctor in a discussion about the potential role of genetic testing and how it might impact your care. Here are some questions you could consider asking:

1. Based on my personal and family history, do you think I could benefit from genetic testing to look for inherited variants associated with prostate cancer risk or aggressiveness?
2. If I were to undergo genetic testing and a risk variant is identified, how would that information potentially change my treatment plan?
3. Are there any specific genes or variants that you would recommend testing for based on my particular situation (e.g., family history, age at diagnosis, disease characteristics)?
4. If a genetic test identifies a variant associated with more aggressive prostate cancer, such as in BRCA2 or ATM, would you recommend any changes to my treatment, such as considering additional therapies or clinical trials?
5. If I am found to have an inherited prostate cancer risk variant, what screening or prevention options would you recommend for my male family members?
6. How would you interpret and use the results of a genetic test in the context of other clinical factors, such as my Gleason score, PSA levels, and imaging results?
7. Can you refer me to a genetic counselor who can help me understand more about the potential risks, benefits, and implications of genetic testing for prostate cancer?

Remember, while this study identifies some potential genetic factors in prostate cancer, the science is still evolving, and not all of these findings may be ready for use in routine clinical care. Your doctor can help you understand what role, if any, genetic testing should play in your specific situation and how to interpret and act on the results in the context of your overall care plan.

May 10, 2024

Defining oligometastatic state in uro-oncological cancers : Current Opinion in Urology

journals.lww.com

Summary

Oligometastatic prostate cancer is a stage of prostate cancer where the cancer has spread beyond the prostate gland to a limited number of other sites in the body, typically four or fewer detectable metastatic lesions. This is an intermediate stage between localized prostate cancer (confined to the prostate) and widespread metastatic disease. Key points about oligometastatic prostate cancer:

1. Definition: It is characterized by a limited metastatic burden, often defined as ≤3-5 metastatic lesions.
2. Prognosis: Patients with oligometastatic disease generally have a better prognosis than those with extensive metastatic disease.
3. Imaging: Advances in imaging techniques, such as prostate-specific membrane antigen (PSMA) PET/CT, have improved the detection of oligometastatic disease.
4. Treatment: The management of oligometastatic prostate cancer is evolving. Treatment options may include:
   - Systemic therapy (hormonal therapy, chemotherapy)
   - Local therapy to the prostate (surgery, radiation)
   - Metastasis-directed therapy (stereotactic body radiation therapy, surgery)

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5. Clinical trials: There is ongoing research to determine the optimal treatment strategies for oligometastatic prostate cancer.

Recognition of the oligometastatic state in prostate cancer is important because these patients may benefit from more aggressive, metastasis-directed therapies in addition to systemic treatments. The goal is to delay the progression to more extensive metastatic disease and potentially improve survival outcomes.

This article from Current Opinion in Urology reviews the current definitions of the oligometastatic state in prostate, bladder, and kidney cancers. Key takeaways include:

- Oligometastatic tumors represent a distinct state between localized and systemic disease, potentially harboring unique biological features. They may be amenable to long-term disease control or even cure.
- For prostate cancer, most experts define oligometastatic disease as a maximum of 3-5 lesions involving no more than 2 organs, excluding visceral metastases. However, there is no firm consensus currently.
- Data on oligometastatic bladder cancer is limited. A consensus of experts defined it as a maximum of 3 metastatic lesions, either resectable or suitable for stereotactic therapy, with no restrictions on the number of organs involved.
- In kidney cancer, oligometastatic disease is defined as a maximum of 5 metastases without limitations on location. The timing of developing metastases since primary tumor diagnosis is considered important.
- Establishing clear definitions of the oligometastatic state in urological cancers is crucial for designing future clinical trials and developing guidelines to improve patient care.

Advances in molecular imaging are expected to transform the understanding and management of oligometastatic urologic tumors moving forward.

In summary, this review highlights the importance of defining oligometastatic disease as a distinct entity in prostate, bladder and kidney cancers, while acknowledging the current lack of firm consensus criteria, especially in prostate cancer. More research is needed to refine these definitions and optimize treatment approaches for patients with limited metastatic disease.

Clinical Impact

The report on defining the oligometastatic state in uro-oncological cancers is likely to impact clinical care in several ways:

1. Treatment strategies: By clearly defining the oligometastatic state, clinicians can better identify patients who may benefit from more aggressive, localized therapies in addition to systemic treatments. This could lead to more personalized treatment plans tailored to the patient's specific disease state.

2. Clinical trial design: A standardized definition of oligometastatic disease will help in designing future clinical trials to evaluate the efficacy of various treatment approaches. This will ensure that the studied patient populations are more homogeneous, leading to more reliable and applicable results.

3. Prognosis and patient counseling: Recognizing the oligometastatic state as a distinct entity with a potentially better prognosis than widespread metastatic disease can help clinicians provide more accurate information to patients about their expected outcomes and treatment options.

4. Surveillance and monitoring: Understanding the oligometastatic state may influence the frequency and type of imaging studies used to monitor patients after initial treatment, as earlier detection of limited metastatic disease could prompt timely intervention.

5. Multidisciplinary collaboration: As the oligometastatic state often involves a limited number of metastatic sites, it may encourage greater collaboration among different specialists (e.g., urologists, radiation oncologists, medical oncologists) to deliver targeted therapies to specific metastatic lesions.

6. Guidelines and policy: As more evidence emerges, the definition of oligometastatic disease in uro-oncological cancers may be incorporated into clinical practice guidelines and influence health policy decisions regarding insurance coverage for specific treatments.

In conclusion, by providing a clearer framework for defining and understanding the oligometastatic state in uro-oncological cancers, this report has the potential to significantly impact various aspects of clinical care, ultimately leading to improved patient outcomes. However, further research is needed to validate and refine these definitions and to determine the optimal management strategies for patients with oligometastatic disease.

Questions

As a patient diagnosed with metastatic prostate cancer, this article provides a basis for several important questions you can discuss with your oncologist:

1. Assessment of your metastatic burden:
- - How many metastatic lesions have been detected in my case?
- - Which organs or sites are involved?
- Based on this, would my cancer be considered oligometastatic?

2. Prognosis:
- - Given my metastatic burden, what is my expected prognosis?
- How does having oligometastatic disease (if applicable) affect my prognosis compared to more widespread metastatic disease?

3. Treatment options:
- What are the recommended treatment options for my specific metastatic state?
- In addition to systemic therapies (like hormone therapy or chemotherapy), are there any localized treatments (such as surgery or radiation) that could be beneficial in my case?
- Are there any clinical trials investigating new treatments for patients with my metastatic status that I could participate in?

4. Imaging and monitoring:
- What imaging studies will be used to monitor my cancer during and after treatment?
- How often will I need to undergo these imaging studies?
- Are there any newer molecular imaging techniques (like PSMA PET/CT) that could provide a more accurate assessment of my disease?

5. Multidisciplinary care:
- Will I be referred to other specialists (such as a radiation oncologist or medical oncologist) for additional treatments or opinions?
- How will my care be coordinated among these different specialists?

6. Impact on quality of life:
- How might the proposed treatments affect my quality of life?
- Are there any side effects I should be particularly aware of?
- What supportive care measures are available to help manage any side effects or symptoms?

Remember, every patient's case is unique, and the answers to these questions may vary depending on your specific situation. Open communication with your oncologist is key to ensuring you receive the most appropriate care tailored to your individual needs.

Food for Thought

Here are some one-liners and epigrams about medicine, doctors, nurses and hospitals in the humorous styles of Bob Hope, Mark Twain and Oscar Wilde:

"I told my doctor I broke my leg in two places. He told me to quit going to those places." (Henny Youngman-style)

"Nurses dispense comfort, compassion, and caring without even a prescription." (Val Saintsbury)

"The art of medicine consists of amusing the patient while nature cures the disease. If nature fails, then at least he enjoyed himself in passing" (Voltaire)

"A hospital bed is a parked taxi with the meter running." (Groucho Marx)

"My doctor gave me six months to live. When I couldn't pay the bill, he gave me six more months." (Walter Matthau-esque)

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@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.