Newsletter

Prostate Cancer 101, Inc.

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The Prostate Cancer Information and Support Group of the Mid-Hudson

FDA Grants Olaparib Breakthrough Designation in mCRPC

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Olaparib (Lynparza) has received an FDA breakthrough therapy designation as a treatment for patients with BRCA1/2 or ATM-mutated metastatic castration-resistant prostate cancer (mCRPC) in those who have received a prior taxane-based chemotherapy and at least either hormonal agent enzalutamide (Xtandi) or abiraterone acetate (Zytiga).

The designation, which will accelerate the development and review of the first-in-class oral PARP inhibitor, is based on data from the phase II TOPARP-A trial that demonstrated that olaparib monotherapy had an overall response rate (ORR) of nearly 90% in a biomarker-defined subgroup of patients who had DNA-repair defects.1

"More than 27,000 men died of prostate cancer last year in the US alone," said Antoine Yver, head of Oncology, Global Medicines Department, AstraZeneca, in a statement. "The Breakthrough Therapy designation for Lynparza is encouraging news for patients, and their families, as there are currently very limited treatment options for metastatic castration-resistant prostate cancer. We will work closely with the FDA to introduce Lynparza as a new treatment option as soon as possible."

Results from the TOPARP-A trial were presented at the 2015 American Association for Cancer Research Annual Meeting.

The open-label, single-group, two-stage, multicenter study examined olaparib in 50 patients with mCRPC whose disease had progressed following 1 or 2 chemotherapy regimens. Patients had an ECOG performance status of 0 to 2 and all had received prior docetaxel. Ninety-eight percent (n = 49) of patients received prior abiraterone acetate or enzalutamide, and 58% (n = 29) had received cabazitaxel (Jevtana).

Olaparib was administered at a dose of 400 mg twice daily until radiologic progression, unequivocal clinical progression, unacceptable side effects, withdrawal of consent, or death. Next-generation sequencing (NGS) was conducted on biopsied tumor specimens. The primary endpoint was ORR, while secondary endpoints included radiologic progression–free survival (rPFS), progression-free survival, overall survival (OS), time to PSA progression, proportion of patients with con-

version of circulating tumor cell count, and adverse events.

In the 49 evaluable patients who received at least one dose of olaparib, ORR was 33% (n = 16). At a median follow-up of 14.4 months, median OS was 10.1 months. The median duration of treatment was 40 weeks, with 12 patients receiving olaparib for >6 months and 4 patients receiving the agent for >12 months. Twenty-two percent of patients had reductions in PSA of 50% or more.

Using NGS, the researchers discovered that 16 of 49 (33%) patients had homozygous deletions, deleterious mutations, or both in DNA-repair genes. Fourteen of these 16 (88%) patients (labeled as "biomarker-positive") responded to olaparib.

Of these 14 patients, 7 harbored BRCA2 mutations, 5 had ATM aberrations, and 2 had ATM mutations with no germline events. Homozygous somatic deletions of BRCA1 or CHEK2 occurred with FANCA deletion in 3 patients, while a somatic frameshift mutation in PALB2 was also detected in a patient with a heterozygous PALB2 deletion. Moreover, biallelic somatic aberrations in histone deacetylase 2 (HDAC2) were identified in 1 patient.

Radiographic progression-free survival (rPFS) was significantly longer in the biomarker-positive group than in those who were biomarker negative (median, 9.8 vs 2.7 months; P <.001). OS was also prolonged in the biomarker-positive group (median, 13.8 months, vs 7.5 months in the biomarker-negative group; P = .05). Established prognostic factors were balanced between the two groups.

Grade 3/4 treatment-related adverse events included anemia (20%), fatigue (12%), leukopenia (6%), thrombocytopenia (4%), and neutropenia (4%). Twenty-six percent of patients required a dose reduction to 300 mg twice daily. Of these 13 patients, 3 required a second dose reduction to 200 mg twice daily. Treatment was permanently discontinued in 6% of patients due to adverse events.

Under the breakthrough therapy designation, the FDA will expedite review of submission data within 60 days of receiving it.

"Our trial marks a significant step forward in the treatment of prostate cancer, showing that olaparib is highly effective at treating men with DNA repair defects in their tumors. It also proves the principle that we can detect prostate cancers with specific targetable mutations using genomic sequencing to deliver more precise cancer care by matching treatment to those men most likely to benefit," said Johann de Bono, MD, professor, head of Drug Development at the Institute of Cancer Research and The Royal Marsden, in a statement following publication of the phase II data. "I hope it won't be long before we are using olaparib in the clinic to treat prostate cancer, or before genomic stratification of cancers becomes a standard in this and other cancers."

Olaparib is currently approved as a maintenance therapy for patients with BRCA-mutated ovarian cancer. AstraZeneca is currently examining the PARP inhibitor's potential in other PARP-dependent tumors, including gastric cancer, pancreatic cancer, and adjuvant and metastatic BRCA-mutated breast cancer.

1. Mateo J, Carreira S, Sandhu S, et al. DNA-repair defects and olaparib in metastatic prostate cancer. N Eng J Med. 2015;373:1697-1708.

Source: http://www.onclive.com/web-exclusives/fda-grants-olaparib-breakthrough-designation-in-mcrpc?msource=JAN16NPSP&tr=y&auid=16417056

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Radium-223 linked to longer overall survival in patients with castration-resistant prostate cancer with bone metastases

Author reporterPublished on June 3, 2015

June 3, 2015. Radium-223, brand name Xofigo (formerly Alpharadin), is an FDA approved intravenous injectable treatment for painful bone metastases in men with castration-resistant prostate cancer (CRPC). The drug Radium-223 dichloride (radium-223), an alpha emitter, selectively targets bone metastases with alpha particles. Radium-223 is taken by intravenous injection once a month (every four weeks) for up to six months. Radium-223 received priority review two years ago based on its ability to extend Overall Survival as shown in its Phase 3 trial.

This June 1 at the ASCO meeting in Chicago, Fred Saad MD FRCS from CHUM Centre Hospitalier Universitaire de Montreal, Canada reported on followup to the original Phase 3 trial. This latest study confirms and possibly strengthens improvement in Overall Survival and finds no new safety concerns. Designed as a Phase 3b international multicenter trial, this followup was part of an early access program (EAP). It enrolled prostate cancer patients with metastatic castrate-resistant prostate cancer (mCRPC) from a dozen countries in Europe plus Canada and Israel.

Unsurprisingly, the followup finds that Overall Survival is longer for healthier patients and also for patients who at the start are taking additional drugs to protect bone and attack the cancer.

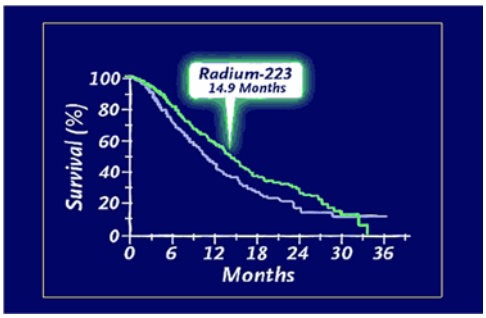
Overall Survival is defined as length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive. Measuring Overall Survival is one way to see how well a new treatment works.

In the original Phase 3 study, called ALSYMPCA, patients with symptomatic bone metastases received Radium-223 and best standard of care, versus best standard of care and placebo. Treatment with the combination resulted in significantly improved Overall Survival (see slide below) at a median of 14.9 vs 11.3 months and delayed time to first symptomatic skeletal event (e.g. bone pain, measurable bone tumor, or cancer-related fracture).

Skeletal-related events (SREs), a common complication of bone metastases, have serious negative consequences for patients with advanced prostate cancer. SREs can lead to severe pain; reduced quality of life; patient, family and caregiver distress; increased need for specialized medical care, and increased risk of death.

Overall survival advantage of Radium-223 (Xofigo) compared with standard treatment, 2013

The multinational followup study, Saad explained, enrolled 839 patients from 113 sites and 14 countries. Of these, 696 patients were treated with one or more doses of Radium-223. Some 58% received all 6 injections. Median patient age was



72 years; 88% of patients were high performance status (able to pursue normal or close to normal daily activities).

Baseline characteristics of study subjects were similar to the ALSYMPCA trial, with the exception of pain at baseline and prior and concomitant treatment. Pain was reported as: no pain 21%, mild-moderate 52%, and severe in 27% respectively. Some 60% of patients had already received prior therapy with docetaxel (Taxotere). At the start of and during the trial patients were also taking a variety of recently-approved drugs for advanced prostate cancer: 22% were taking abiraterone (Zytiga); 20% denosumab (Xgeva); 18% bisphosphonates (e.g. Zometa) and 4% enzalutamide (Xtandi).

At 16 months, median Overall Survival was comparable with ALSYMPCA OS results. Saad described at ASCO how the study's other preplanned goals related to its final analysis. The researchers set out to measure time to first skeletal-related event (SRE), and changes in ALP/PSA blood test levels indicating disease progression. Final analysis focused on Overall Survival in subgroup populations based on:
use of other medication at baseline (i.e., abiraterone, enzalutamide, docetaxel, denosumab, and bisphosphonates)
baseline total ALP Opens in a new window values (a blood test for assessing bone turnover)
baseline ECOG PS Opens in a new window i.e. measure of patient's illness-related "performance status" from Fully Active to Disabled
baseline pain.

Patients in different countries and from differently treated local populations may bring different levels of factors such as performance status, prior use of other medical drugs, and so on. Some may have had less intensive treatment than available in the USA. Others may be taking more advanced drugs. Between a current trial and its precursors, more patients may have access to newly approved medical drugs. Such is the case with e.g. abiraterone (Zytiga) and enzalutamide (Xtandi), which were unavailable at the start of the US-based Phase 3 Radium-223 (Xofigo) trial.

In comparison with the U.S. trial, the new data are stronger, said co-investigator Joe O'Sullivan, MD, from Queens University, Belfast. "Survival and toxicity data are more robust by virtue of the numbers of patients. This study also shows that the good safety profile of the drug was maintained, thereby supporting the good safety profile that was shown in the randomized trial."

Overall Survival was slightly longer than in the ALSYMCA trial, possibly because patients were treated at a slightly earlier stage. Dr. O'Sullivan said. Still, a median survival of 16 months compared very favorably to the 14-month survival data in the ALSYMCA trial O'Sullivan pointed out. This international trial also produced some "hypothesis-generating" analyses, O'Sullivan said.

"It would appear -- and again this is hypothesis-generating because patients were not randomized," Dr. O'Sullivan said, "that patients receiving abiraterone or enzalutamide along with radium had better survivals. Whether that's a synergistic effect or not is very hard to tell. But there is something – a separation of the survival curves which certainly merits further study."

Some ongoing large, randomized trials are testing the hypothesis of combining abiraterone or enzalutamide with Radium-223. Based on the data so far (albeit unrandomized). O'Sullivan said, "there would appear that there would

be some effect." See link to active trials below.
"To me," Sullivan said, "the most reassuring thing, as a clinician treating patients, is that the toxicity profile remains good, and acceptable. And in real-world patients, it looks like the survival is in the range of – or slightly better than – what was seen in the ALSYMCA trial, at a median of 16 months."

Serious adverse events (Grade 3/4) occurred in 38% of patients. Of these, 21% of patients (1 out of 5) discontinued Radium-223 due to adverse event. A grade 3 event is categorized as "Severe but not life-threatening; hospitalization required; limitation of patient's ability to care for him/herself." A Grade 4 event is categorized as "Life-threatening; urgent intervention required." To put these events in perspective we need to compare them with 1) adverse events in patients not receiving treatment 2) adverse events in the earlier trial where fewer patients were taking other advanced drugs like abiraterone. Beyond this, of course, oncologists must compare adverse events for the other drugs taken alone.

In the earlier trial, as reported in The New England Journal of Medicine, "The number of patients who had adverse events after they received the study drug was consistently lower in the radium-223 group than in the placebo group for all adverse events. . . . Overall, no clinically meaningful differences in the frequency of grade 3 or 4 adverse events were observed between the study groups." This lessening of adverse events went along with a higher percentage of patients experiencing "a meaningful improvement in the quality of life" (notably through pain reduction) and prolonged survival.
Dr. O' Sullivan, reviewing the new trial, agreed that the additional Overall Survival benefit could simply arise from the new hormonal agents (abiraterone or enzalutamide) which didn't exist or weren't widely available at the time of the ALSYMCA trial.

"It's interesting how the goal posts are shifting in the castrate-resistant prostate cancer patient," he said. "We're seeing better survivals, and I guess we're trying to figure out where all the new therapies fit in a sequence. These data, although they don't answer the question, at least help us think about this and help us to understand that it's reasonably safe to combine these agents, without encountering any significant additional toxicity."
For current or planned clinical trials using Radium-322 alone or with drugs such as abiraterone or enzalutamide see Clinical trials of radium ra 223 dichloride Opens in a new window active as of June 3, 2015.

Reported by Jacqueline Strax from ASCO-15 session highlights and resources below.
Sources and Links
Radium-223 in an international early access program (EAP): Effects of concomitant medication on overall survival in metastatic castration-resistant prostate cancer (mCRCP) patients. Fred Saad et al.
Saad F, Carles J, Gillessan S, et al. Radium-223 in an international early access program (EAP): Effects of concomitant medication on overall survival in metastatic castrate-resistant prostate cancer (mCRPC) patients Opens in a new window. ASCO 2015

Dr. Fred Saad is a Professor and Chief of Urology and Director of G-U Oncology, University of Montreal Hospital Centers. He is Chair at the National Cancer Institute of Canada G-U Group and Canadian Urologic Oncology Group.

• Dr. Fred Saad holds the University of Montreal Endowed Chair in Prostate Cancer and is Director of the molecular oncology research lab in Prostate Cancer.
Saad, O'Sullivan and other trial investigators' ASCO disclosures of payments from Bayer (Radium 223 / Xofigo manufacturer) and other drug companies Opens in a new window.
Report on the trial that established Rad-223's safety and power to improve overall survival: Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer Opens in a new window N Engl J Med 2013; 369:213-223July 18, 2013

Source: http://www.psa-rising.com/2015/06/radium-223-linked-to-longer-overall-survival-in-mcrpc-prostate-cancer-patients-with-bone-metastases/

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Simpler Prostate Cancer Grading System Proposed

Tumors fall into 1 of 5 grade groups based on what pathologic findings indicate about prognosis.

A consensus panel of experts has proposed a new and simpler prostate cancer grading system that could help clinicians give patients a better understanding of their prognosis.

The system, initially proposed by Jonathan I. Epstein, MD, Professor of Pathology, Urology, and Oncology at Johns Hopkins Medical Institutions in Baltimore, and supported by the International Society of Urological Pathology (ISUP), is based largely on the 1967 to 1973 Gleason scoring system, but more accurately reflects PCa biology than the Gleason system. It incorporates the latest understanding of the pathologic and clinical aspects of PCa.

Jonathan I. Epstein, MD, Professor of Pathology, Urology, and Oncology at Johns Hopkins Medical Institutions in Baltimore

The new grading system, first described in BJU International in 2013 and recently verified in a large multi-institutional study described in the upcoming March issue of European Urology (2016;69:428-435), consists of 5 "grade groups," with Grade Group 1 indicating the most favorable prognosis and Grade Group 5 the least favorable. In the Gleason scoring system, 25 grading combinations are possible.

In an interview with Renal & Urology News, Dr. Epstein said the proposed system distills pathologic findings into the key differences in prognosis "that can be intuitive to both patients and clinicians," he said.

"Clinicians will be forced to look at the grades appropriately in terms of different prognoses," Dr. Epstein said.

The original Gleason system used PCa-related death as an outcome, whereas the new system uses biochemical recurrence as an outcome, although recent studies have verified that the new system also predict death due to PCa.

A noteworthy aspect of new grading system is the distinction it makes between Gleason score 3 + 4 and 4 + 3 cancers, which often are simply called Gleason score 7 disease in discussions with patients. Dr. Epstein emphasized that Gleason 3 + 4 tumors are associated with substantially better prognoses than Gleason 4 + 3 tumors. The new grading system separates these cancers into Grade Group 2 and 3, respectively.

This distinction could affect patient decisions whether to be placed on active surveillance if their doctors recommend it. Patients may feel more comfortable with this approach if they are told their cancer is a grade 2 out of 5 instead of a Gleason 7 out of 10, Dr. Epstein said.

Another important feature of the new system is the placement of Gleason score 6 cancers into Grade Group 1. Dr. Epstein pointed out that patients with Gleason score 6 disease often believe their prognosis is worse than it is because Gleason score 6 is half way along the Gleason scoring scale of 2 to 10, when, in fact, a Gleason score 6 tumor is the lowest-grade cancer currently assigned with an excellent prognosis. The new system reflects this.

The new grading system has been in use at Johns Hopkins since 2013, with biopsy reports including both Gleason scores and grade groups, and clinicians at the institution have embraced it, Dr. Epstein said. "It helps them to explain to patients in simple terms the relative prognosis of their tumors," he said.

The consensus panel was convened in 2014 by ISUP and included 65 PCa pathology experts as well as 17 clinicians, including urologists, radiation oncologists, and medical oncologists from 19 countries.

The new grading system and terminology of Grade Groups 1 through 5 have been accepted by the World Health Organization for the 2016 edition of Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs.

As for how quickly the new system will be adopted by U.S. clinicians, Dr. Epstein noted that this depends largely on its adoption by the College of American Pathologists checklists, to which every medical institution adheres. This often follows what the Union for International Cancer Control (UICC) and the American Joint Committee on Cancer (AJCC) do with respect to the TNM Classification of Malignant Tumors, which both groups maintain.

David F. Penson, MD, Chair of the Department of Urologic Surgery and Director of the Center for Surgical Quality and Outcomes Research at Vanderbilt University Medical Center in Nashville, Tenn.

"The new grading system has some significant advantages over the Gleason grading system," said David F. Penson, MD, Chair of the Department of Urologic Surgery and Director of the Center for Surgical Quality and Outcomes Research at Vanderbilt University Medical Center in Nashville, Tenn. "The Gleason system can be quite confusing to patients. Patients often misinterpret the news of a Gleason 3 + 3 = 6 tumor as bad news, as the scale runs from 2 to 10 and 6 is in the middle, implying intermediate-risk disease. Resetting the grading system so the lowest risk cancers are a Grade Group 1 will be very helpful for patient counseling and will aid in the further uptake of active surveillance in appropriate men with low-risk disease."

The differentiation between Gleason 3 + 4 and 4 + 3 as Grade Groups 2 and 3 is also an important advance that will improve patient education and future studies of PCa, Dr. Penson said. "Specifically, many administrative and institutional databases fail to differentiate between 3 + 4 and 4 + 3 disease, reporting both as Gleason score 7, he said. "This is probably not the optimal approach given that studies show that there are differences in outcomes between the 2 groups."

Although the proposed Grade Group system is an advance, some questions still remain, Dr. Penson said. The validation data presented by Dr. Epstein uses biochemical recurrence-free survival as the endpoint, Dr. Penson pointed out. "As we know, not all biochemical recurrences result in a clinical event such as metastasis or death and, of course, the definition of a biochemical recurrence differs between surgery and radiation. It's also not entirely clear to me how patients who have a tertiary Gleason pattern on prostatectomy will be graded in the new system."

Given these and other remaining questions, further study of the new system is needed. "That being said, however, it is definitely time for us to take a critical look at the Gleason grading system and develop better approaches to pathologic grading of prostate cancer," Dr. Penson said. "Gleason developed his scoring system roughly 50 years ago. Our understanding of prostate cancer has obviously advanced exponentially since then. The new grading system is definitely a big step forward in the care of this disease."

Source: http://www.renalandurologynews.com/prostate-cancer/prostate-cancer-new-gleason-grading-system-proposed/article/470952/?_ga=1.118740302.611357903.1454440878

Caution Urged With High Intensity Focused Ultrasound Therapy in Prostate Cancer

The U.S. Food and Drug Administration has approved 2 types of minimally invasive, high intensity focused ultrasound therapy for treating prostate cancer.

The U.S. Food and Drug Administration (FDA) has approved 2 types of minimally invasive, high intensity focused ultrasound (HIFU) therapy for treating prostate cancer. However, this advanced revolutionary technology requires significant urologic training as the technology is complex and caution is being urged.

"Well-selected prostate cancer patients can benefit by maintaining their quality of life and still treating their prostate cancer. However, due to training requirements, I believe that the technology should roll out slowly over 12 to 24 months. Patients should be cautioned that excellent outcomes are only consistently obtained by highly trained users of the technology," said Stephen Scionti, MD, who is medical director of Vituro Health and founder of the Scionti Prostate Center in Sarasota, FL.

Dr Scionti has been involved in the treatment of approximately 1000 patients over the last decade at the International HIFU Prostate Cancer Centers in the Caribbean and Mexico and as lead proctor for the FDA trials in the United States. He said patients should carefully inquire about the skill level and the experience of the HIFU surgeon and should seek out only highly experienced physicians as this technology rolls out into the US market.

He noted that the FDA has granted regulatory approval to both the Sonablate and the Ablatherm devices via the 510 K pathway. The FDA approved indication is for prostate tissue ablation. "Skilled physicians can employ this technology to ablate prostate tissue in a variety of conditions. However I believe that the technology will be most commonly used to ablate prostate cancer tissue," Dr Scionti told Cancer Therapy Advisor. "HIFU treatment offers an alternative approach to treating localized prostate cancer. Tissue ablation with HIFU is an option to traditional treatments such as surgery or radiation. The technology allows for focal targeted therapy and allows MRI images to be fused to ultrasound images to allow for targeted ablation in the prostate. The best candidates are men who have localized prostate cancer, a normal sized prostate, and a desire to preserve sexual and urinary function."

He said HIFU for prostate cancer is not new. The technology has been available in Europe and Asia for more than 15 years. Dr Scionti said long-term studies out beyond 10 years have documented comparable efficacy to other treatments for localized prostate cancer. "The side-effect profiles are favorable with excellent preservation of both urinary and sexual function," said Dr Scionti.

He said he became an early adopter of HIFU because of the promise of an outpatient, non-invasive procedure where it was possible to customize treatment to the patient through proper understanding of where the tumor was in their prostate. Dr Scionti said HIFU offers an opportunity in properly selected patients to treat cancer with a much reduced side-effect profile that preserves quality of life, including less chance of urinary leakage and sexual issues.

On Dec. 4, 2015, 61-year-old Graceville, FL resident Daniel Hazell was the first patient of Dr Scionti's to be treated with HIFU on American soil. Dr Scionti said what is so remarkable with this approach is that within a week most of the patients won't even notice that they had a procedure done.

The use of HIFU is now offering considerable promise. However, just how widely it is adopted will be determined as more patients are treated and long-term outcomes are validated. Gerald Andriole, MD, who is Chief of Urologic Surgery at Washington

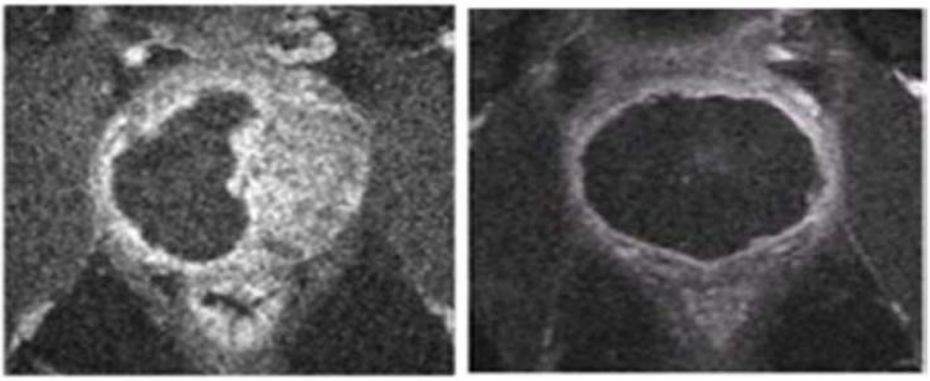
University School of Medicine in St. Louis, MO, said ablation of the entire prostate or targeted ablation of only the malignant parts of the prostate, are possible by a variety of technologies.

“HIFU is now an option to consider in addition to cryoablation, radiofrequency, microwave, laser, vascular targeted, and electroporation devices among others. The side-effect profile, cost, and the length of the learning curve for effective use of the modality will determine which will be most widely used,” Dr Andriole told Cancer Therapy Advisor. “Most urologists are more conversant with transperineal needle ablation approaches, while HIFU represents a new approach with a completely new learning curve without, at this time, a demonstrated superiority over the other modalities. Time will tell whether it will emerge as a commonly used modality."

Source: http://www.cancertherapyadvisor.com/prostate-cancer/prostate-cancer-pca-high-intensity-focused-ultrasound-therapy/article/462389/?_ga=1.159697467.70210372.1441220924

TOOKAD Soluble approved for prostate cancer therapy in Mexico

January 4, 2016



Magnetic resonance images of the prostate gland after treatment with Tookad Soluble. The black regions show the portions of the prostate that have been eliminated to remove the previously detected cancerous tissue. Credit: Weizmann Institute of Science

A therapy invented at the Weizmann Institute of Science and clinically developed in collaboration with Steba Biotech (Luxembourg) has been approved by Cofepris, Mexico's health authority, for the focal treatment of early-stage prostate cancer.

The therapy involves a laser and a novel drug, TOOKAD Soluble. A successful Phase III clinical trial in Latin America (Mexico, Peru and Panama), involving 80 patients, confirmed the high rate of local cures and minimal side effects already reported in Phase II clinical trials, as evidenced by negative biopsies and maintenance of patients' potency, continence and overall quality of life.

The marketing approval in Mexico comes in the wake of the recent completion of a second Phase III clinical trial in Europe. This randomized pivot study compared disease progression, cancer-free rate and urinary and erectile functions in patients treated with TOOKAD Soluble and those undergoing active surveillance with a follow-up of two years. It involved more than 400 patients at 43 hospitals in 11 European countries and is currently under evaluation by the European Medicines Agency (EMA).

The approved therapy follows a new paradigm developed by Prof. Yoram Salomon of the Biological Regulation Department and Prof. Avigdor Scherz of the Plant and Environmental Sciences Department in the framework of photodynamic therapy. It comprises an intravenous infusion of TOOKAD Soluble, immediately followed by near-infrared laser illumination through thin optic fibers that are inserted into the cancer prostatic tissue, under ultrasound control. Tookad Soluble

was first synthesized in Scherz's lab from bacteriochlorophyll, the photosynthetic pigment of certain aquatic bacteria that draw their energy supply from sunlight. The drug stays in the patient's blood circulation until it totally clears 3-4 hours later, and it shows no toxicity. Confined illumination of the diseased tissue activates the circulating drug locally, resulting in the extensive generation of short-lived toxic molecules: oxygen and nitric oxide radicals. These highly reactive molecules initiate rapid occlusion and destruction of the tumor blood vessels, followed by necrotic death of the entire tumor while sparing nearby structures and their functions. The use of near-infrared illumination, together with the rapid clearance of the drug from the body and the unique non-thermal mechanism of action, makes it possible to safely treat large, deeply embedded cancerous tissue using a minimally invasive procedure. The recent marketing approval was provided to both the drug (TOOKAD Soluble) and the laser illumination device (Laser), together designated Vascular Targeted Photodynamic Therapy (VTP) with TOOKAD Soluble.

In the currently approved focal therapy setting, TOOKAD Soluble VTP (TS-VTP) is a day-case procedure lasting approximately 90 minutes. Patients are released a few hours later and can return to normal activities within a few days, with none of the side effects frequently associated with prostate removal by surgery or radiotherapy. This new minimally invasive technology offers a good alternative to patients diagnosed with early-stage prostate cancer. The number of these patients has dramatically increased in the last two decades due to widespread screening relying on levels of prostate specific antigen (PSA). This population faces the dilemma of undergoing the radical treatment of prostate removal with the risk of high morbidity, or remaining under active surveillance with increased risk of further cancer progression.

Tookad Soluble answers an unmet need in providing this category of patients with an appropriate treatment, which combines good efficacy with a preservation of the quality of life.

Weizmann institute and Steba Biotech are currently pursuing an extensive oncological research program in collaboration with several clinical groups at Memorial Sloan Kettering Cancer Center in New York City. Four clinical studies for more advanced prostate cancer and other oncological indications stemming from this research are scheduled to start in 2016.

Yeda Research and Development Company, the Weizmann Institute's technology transfer arm, has licensed the drug to Steba Biotech, which manufactures Tookad Soluble. Amir Naiberg, CEO of Yeda: "Our cooperation with Steba covers 20 years of fruitful collaboration. The commitment made by the shareholders of Steba and their personal relationship and effective collaboration with Weizmann Institute scientists and Yeda, have enabled this tremendous accomplishment."

Source: http://medicalxpress.com/news/2016-01-tookad-soluble-prostate-cancer-therapy.html?_ga=1.197337513.70210372.1441220924

African American men with prostate cancer have significantly lower PSA density than Caucasian men

Published on January 5, 2016 at 12:00 AM.

A new study published in The Journal of Urology® revealed that African American men with Gleason score 3+3=6 prostate cancer (PCa) produce less prostate specific antigen (PSA) and have significantly lower PSA density (PSAD) than Caucasian men. These findings could have important implications when selecting patients for inclusion in active PCa surveillance programs.

Prostate cancer remains the second leading cause of cancer death among men in the U.S., with nearly 30,000 deaths annually. According to the latest recommendations by the American Urological Association, PSA re-

mains the only screening test to select men with unremarkable digital rectal examination in whom prostate biopsy should be considered. Deaths from prostate cancer have declined by about 40% since the advent of PSA screening in the late 1980s, and 40-70% of that decline may be attributable to screening. For early stage low grade disease, active surveillance, commonly called watchful waiting, is considered appropriate.

Although prior studies have identified race as a contributing risk factor for PCa, lead investigator Oleksandr N. Kryvenko, MD, Assistant Professor of Pathology and Urology at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine, explained that "active surveillance criteria that were predictive in Caucasian men were not accurate in African American men. Despite this finding, active surveillance criteria do not include race as a variable."

In this study the investigators measured tumor volume from consecutive radical prostatectomies in 414 men with National Comprehensive Cancer Network low risk prostate cancer (348 Caucasians, 66 African Americans). They compared clinical presentation, pathological findings, PSA, PSAD, and PSA mass (PSAM), which is an absolute amount of PSA in a patient's circulation, between African American and Caucasian men.

This study revealed that African American men with Gleason score 3+3=6 PCa produce less PSA than Caucasian men. African American and Caucasian men had equal serum PSA and PSAM despite significantly larger prostates in African American men (approximately 10 gm larger) with all other parameters, particularly total tumor volume, being the same. PSAD was approximately 20% lower in African American men compared to Caucasian men, even when tumor volume was the same.

"When low volume and low grade cancer is detected, especially in older individuals, the decision between active surveillance and definitive therapy must be made. Because PSAD was about 20% lower in African American men even with the same tumor volume as in Caucasians, this finding could be one of the factors why current active surveillance criteria in African Americans are not as accurate as those for Caucasians. A lower PSAD threshold for active surveillance inclusion criteria in African American men may account for these differences," commented Dr. Kryvenko.

Dr. Kryvenko added that this new discovery complements his prior observations published in The Journal of Urology (J Urol. 2014 Jan;191(1):60-7.). "African Americans overall not only have a higher grade cancer at radical prostatectomy, but also their spatial distribution of cancer in prostate is such that standard prostate biopsy may undersample more aggressive tumor nodules. Thus, there could be a constellation of factors explaining why contemporary surveillance criteria do not work well in African American men."

Source: http://www.news-medical.net/news/20160105/African-American-men-with-prostate-cancer-have-significantly-lower-PSA-density-than-Caucasian-men.aspx?_ga=1.97152409.70210372.1441220924

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