US TOO® PROSTATE CANCER EDUCATION & SUPPORT

HOTSHEET

JULY 2012

BREAK FROM PROSTATE THERAPY LOWERS SURVIVAL ODDS

Interrupting androgen blockade in men with hormone-sensitive metastatic prostate cancer could shorten their lives. In a long-running clinical trial, survival among men given intermittent androgen deprivation (IADT) was inferior to survival in men treated continuously, according to Maha Hussain, MD, of the University of Michigan Comprehensive Cancer Center in Ann Arbor, MI. Moreover, the survival inferiority was most marked among men with less widespread disease – the very patients most likely to be offered IADT, Hussain told reporters at the annual meeting of the American Society of Clinical Oncology.

"Continuous therapy continues to be the standard of care," she said.

Despite that, IADT is widely used in the US, commented Bruce Roth, MD, of Washington University School of Medicine in St. Louis, who was not part of the study but who moderated a media conference at which details were presented. That's because the available evidence seemed to show the two approaches had the same efficacy, he said. "Doctors didn't have any specific reason (for men) not to come off therapy," he said. "It looked like survival was equivalent."

"If you can give less treatment while maintaining or improving efficacy and potentially improving the side-effect

(Continued on page 4)

ENZALUTAMIDE IS A GAME CHANGER IN PROSTATE CANCER

A first-in-class drug, the androgen-receptor signaling inhibitor enzalutamide (MDV3100), has shown a survival benefit in men with postdocetaxel prostate cancer. The risk for death decreased by 37% vs. placebo, extending survival by more than 4 months, according to findings from the phase 3 AFFIRM study. Neal Shore, MD, from the Carolina Urologic Research Center, in Myrtle Beach, SC, and colleagues presented the findings in an oral podium poster session at the American Urological Association (AUA) 2012 Annual Scientific Meeting.

According to the researchers, enzalutamide competitively inhibits the binding of androgens to the androgen receptor. It also inhibits androgen receptor nuclear translocation and the association of the receptor with DNA. Enzalutamide displayed activity during phase 1 and 2 trials in pre- and postchemotherapy patients with progressive castration-resistant prostate cancer (CRPC).

In this double-blind placebo-controlled multinational study, researchers randomized patients with CRPC who had received at least 1 regimen of docetaxel-based chemotherapy to enzalutamide 160 mg/day or placebo (2:1 ratio). Patients were stratified according to baseline Eastern Cooperative Oncology Group (ECOG) performance status and Brief Pain Inventory scores.

(Continued on page 3)

UNTREATED PROSTATE CANCER RESPONDS TO ZYTIGA

Men with metastatic castration-resistant prostate cancer (CRPC) had significant improvement in radiographic progression-free survival (rPFS) when treated with abiraterone before chemotherapy, a randomized clinical trial showed. After a median follow-up of almost 2 years, median radiographically assessed rPFS was 8.3 months with placebo, whereas the median had yet to be reached in the abiraterone (Zytiga) group. The results suggested an overall survival (OS) benefit with abiraterone, but the data failed to meet the prespecified definition of statistical significance, as reported at the 2012 American Society of Clinical Oncology (ASCO) meeting.

"The point estimates for overall survival favored abiraterone in all patient subgroups," said Charles J. Ryan, MD, of the University of California San Francisco. "We observed statistically significant improvement in all secondary endpoints," he added.

In contrast to traditional hormonal therapies for advanced prostate cancer, abiraterone disrupts androgen biosynthesis by inhibiting CYP17 lyase, a key enzyme in the steroidogenic pathway. Treatment with the drug improved overall survival in patients with metastatic CRPC that had progressed after chemo-

(Continued on page 4)

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POSTPROSTATECTOMY TEST IDENTIFIES RISK FOR CLINICAL RECURRENCE

A newly available diagnostic test that uses immuno-polymerase chain reaction (IPCR) technology can detect serum PSA at concentrations in picograms per mL in men after radical prostatectomy (RP) to help identify men at a low risk of clinical recurrence. Jonathan E. McDermed, PharmD, Director of Scientific and Clinical Affairs at Iris Molecular Diagnostics in Carlsbad, CA, and colleagues conducted a study using this test. The results were published in the April issue of Clinical Chemistry (*Clin Chem* 58: 732-40, 2012).

Increasing levels of PSA in men with prostate cancer treated by RP can signify a risk for biochemical recurrence. According to the researchers, this new post-RP prognostic test differs from standard PSA tests because it identifies risk for clinical recurrence. This can help clinicians identify men who might be able to avoid follow-up treatment.

The test, developed using the nucleic acid detection immunoassay (NADiA) platform and sold under the name ProsVue, combines sandwich immunoassay technology with quantitative PCR (qPCR) to quantify very low levels of PSA. The immunoassay uses 2 monoclonal antibodies to capture PSA, and the label antibody is conjugated to a short strand of double-stranded DNA. After several washing steps, the immuno complex is subjected to qPCR, and the amount of PSA can be determined from the levels of amplified DNA.

The assay proved to be robust, with a limit of quantification of 0.000065 ng/mL (0.65 pg/mL). Imprecision was determined using low (3.8), medium (24.1), and high (69.1) pg/mL PSA samples and was 5.2, 9.4, and 10.6%, respectively.

"The analytical characteristics of the assay support its use for sensitive and precise measurement of serum PSA," even at concentrations measured in picograms per milliliter, Dr. McDermed and colleagues note. According to the researchers, studies investigating the prognostic clinical utility of ProsVue PSA slope in men after RP are completed and will be reported separately.

(Continued on page 6)

CLASSIFYING PROSTATE CANCER MALIGNANCY BY QUANTITATIVE HISTOMORPHOMETRY

Loeffler M, Greulich L, Scheibe P, et al

J Urol 187: 1867-75, 2012

Purpose: Prostate cancer is routinely graded according to the Gleason grading scheme. This scheme is predominantly based on the textural appearance of aberrant glandular structures. Gleason grade is difficult to standardize and often leads to discussion due to inter-rater and intra-rater disagreement. Thus, we investigated whether digital image based automated quantitative histomorphometry could be used to achieve a more standardized, reproducible classification outcome.

Materials and methods: In a proof of principle study we developed a method to evaluate digitized histological images of single prostate cancer regions in hematoxylin and eosin stained sections. Preprocessed color images were subjected to color deconvolution followed by the binarization of obtained hematoxylin related image channels. Highlighted neoplastic epithelial gland related objects were morphometrically assessed by a classifier based on 2 calculated quantitative and objective geometric measures, that is, inverse solidity and inverse compactness. The procedure was then applied to the prostate cancer probes of 125 patients. Each probe was independently classified for Gleason grade 3, 4 or 5 by an experienced pathologist blinded to image analysis outcome.

Results: Together inverse compactness and inverse solidity were adequate discriminatory features for a powerful classifier that distinguished Gleason grade 3 from grade 4/5 histology. The classifier was robust on sensitivity analysis.

Conclusions: Results suggest that quantitative and interpretable measures can be obtained from image based analysis, permitting algorithmic differentiation of prostate Gleason grades. The method must be validated in a large independent series of specimens.

ENZALUTAMIDE IS A GAME-CHANGER *(Continued from page 1)*

The study involved 1199 men from 15 countries, recruited from September 2009 to November 2010. About three quarters of the men had received docetaxel and 37.8% had more than 20 bone lesions. The primary end point was overall survival (OS); secondary end points included radiographic progression-free survival, time to first skeletal-related event (SRE), and time to prostate-specific antigen (PSA) progression.

The study was unblinded on the recommendation of the Independent Data Monitoring Committee after a planned interim analysis at 520 death events showed a significant 4.8-month OS benefit for enzalutamide, vs. placebo (18.4 vs. 13.6 months; hazard ratio, 0.631; P < .0001), indicating a 37% reduction in the risk for death. A survival benefit was observed across all subgroups. Men in the enzalutamide group received therapy for longer than those in the placebo group, and more men in the enzalutamide group remained on study (28.9% vs. 4.8%) Dr. Shore pointed out.

Overall, enzalutamide was well tolerated. There were no differences between the enzalutamide and placebo groups with respect to lab abnormalities or cardiovascular events. In terms of serious adverse events, the only difference was that in the enzalutamide group, 5 of more than 800 men had seizures (0.6%).

"This is the first once-a-day agent that doesn't require concomitant steroids, and you can take it with or without meals," said Dr. Shore. Trials in earlier-stage disease with this agent are ongoing. One large multicenter trial will evaluate this agent in men who have not received docetaxel. There are also plans to evaluate it in M0 castrate-resistant prostate cancer and in the androgen-sensitive disease state, Dr. Shore said.

"This is a game-changing agent because of its tolerability and, more important, its efficacy and ease of administration," he said. "I think this is an exceptionally optimistic and exciting time for both clinicians and patients."

According to Medivation and Astellas, the US FDA has received a New Drug Application for enzalutamide. "I anticipate that FDA will review the data favorably, given the combination of efficacy and safety from the AFFIRM clinical trial," stated Oliver A. Sartor, MD, from the Departments of Medicine and Urology at Tulane University School of Medicine in New Orleans, Louisiana, who was not involved in the trial.

2012 AUA Annual Scientific Meeting, Abstract LBA1, presented 22 May 2012

Medscape Medical News, 25 May 2012

PROSTATE CANCER SCREENING CAN BE DIFFERENCE BETWEEN LIFE AND DEATH FOR SOME

Men of lower socioeconomic status and those from third world countries are a subset of patients who do need prostate-specific antigen screening, researchers said last week at the 107th Annual Scientific Meeting of the American Urological Association (AUA) in Atlanta, GA.

That's because these men often present with advanced, metastatic prostate cancer, Dr. Brian K. McNeil, from SUNY Downstate Medical Center, Brooklyn, NY, told Reuters Health in an interview.

"Considering the recent controversies regarding PSA screening, including the recent US Preventive Task Force recommendation against screening, we decided to study those patients in our population who presented to Downstate with metastatic prostate cancer to identify those who would suffer if PSA screening was eliminated," Dr. McNeil said.

He and his team searched a prospectively maintained androgen deprivation therapy database from their inner city hospital and identified 148 men who presented with metastatic prostate cancer. At presentation, the median age was 69, and the median Gleason sum was 8 on prostate biopsy.

(Continued on page 8)

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IADT VS. ADT

(Continued from page 1)

profile, that would be a clinically important endpoint," Hussain said. But the results of this controlled study is likely to persuade both doctors and patients that sporadic therapy has a dangerous downside, Roth said. "There is a price to pay and that price is nearly 2 years of survival," he said.

The international randomized trial was designed to show that IADT was not inferior in efficacy to continuous ADT, with an upper bound hazard ratio (HR) of 1.20. To test the issue, they enrolled 3,040 men with newly diagnosed metastatic disease and PSA levels of at least 5 ng/mL of blood. They were given ADT for 7 months, using goserelin (Zoladex®) and bicalutamide (Casodex®). Those who showed a response, defined as a PSA ≤4.0 ng/mL in months six and seven were assigned randomly to continuous ADT or to have it interrupted.

With a median follow-up of 9.2 years, Hussain reported, median overall survival of those in the continuous arm was 5.8 years, compared with 5.1 for those getting IADT. The difference yielded an HR for death of 1.09 in favor of continuous ADT, but the upper bound of the 95% confidence interval was 1.24, so that the investigators could not conclude that the two were equivalent.

When the researchers analyzed subgroups of patients, they found that IADT offered equivalent survival for extensive metastases. But surprisingly, continuous ADT was significantly better for minimal metastases, offering a median survival of 7.1 years versus 5.2 for IADT (HR 1.23, 95% CI 1.02 to 1.49). This was statistically significant at P=0.034, Hussain said.

"We found this rather striking and surprising, as it goes against conventional belief," Hussain said. This may indicate that there are other important biological differences between widespread and more limited metastatic prostate cancer, she added.

Reference:

Hussain M, Tangen CM, Higano CS, et al. Presented at the 2012 Annual ASCO meeting; Abstract 4.

MedPage Today, 3 June 2012

UNTREATED PROSTATE CANCER RESPONDS TO ZYTIGA

(Continued from page 1)

therapy (N Engl J Med 2011; 364: 1995-2005). Abiraterone subsequently received FDA approval for treatment of metastatic CRPC after progression on docetaxel (Taxotere®).

Investigators in 12 countries sought to address some of the limitations in a multicenter phase III clinical trial of abiraterone in men with metastatic CRPC not yet treated with docetaxel. They randomized men to daily abiraterone plus prednisone or to placebo plus prednisone. Recognizing that death and delay in disease progression can be significantly separated in time, investigators specified co-primary endpoints of OS and rPFS, Ryan said.

Secondary endpoints reflected the time frame of deterioration from asymptomatic status to clinical hallmarks of the disease process:

- Need for opiate pain relievers
- Initiation of chemotherapy
- Deterioration of performance status
- Time to PSA progression

Investigators defined rPFS by appearance of new lesions on bone scans, development of soft-tissue lesions on CT or MRI, and death from any cause. The protocol specified three interim analyses: one after occurrence of about 15% of OS events, a second after occurrence of 40% of events, and a third after occurrence of 55% of events.

The data and safety monitoring committee recommended stopping the trial after the second interim analysis, which came after 43% of OS events had occurred (P=0.008). Had the trial stopped after 40% of events, statistical significance would have been defined as P=0.0005. The primary analysis included 1,088 men, who had a median age of about 70 and PSA of about 40 ng/mL. More than 80% had bone metastases (>10 lesions in half of the men), half of the men had soft-tissue or nodal lesions.

After a median follow up of 22.3 months, 69% of abiraterone group had discontinued the drug, as had 84% of the placebo group. The most common reasons for discontinuation were radiographic progression (20% to 30%), clinical progression (20% to 25%), and both radiographic and clinical progression (10% to 11%).

When the trial stopped, the placebo arm had a median rPFS of 8.3 months and a median OS of 27.2 months, whereas the median for both endpoints had yet to be reached in the abiraterone group. The difference in favor of abiraterone in pPFS and OS translated into a 57% and 25% reduction in the hazard ratios, (P<0.0001 and P=0.0097, respectively).

The study revealed no new safety concerns, as adverse events were consistent with those observed in the phase III trial of post-chemotherapy patients, Ryan said. The most common adverse events (all grades) were fatigue (39%), fluid retention (28%), hypertension (22%), cardiac disorders (19%), hypokalemia (17%), and elevated liver enzymes (11% to 12%). Grade 3-4 adverse events were uncommon.

Invited discussant Susan Halabi, PhD, of Duke University in Durham, N.C., said that stopping the trial after an interim analysis introduced confounding factors that will bias follow-up data analysis. She acknowledged the overall trend favoring abiraterone but emphasized that the OS outcome remains only a trend. The secondary outcomes were more solid.

Source reference:

2012 ASCO Annual Meeting, Abstract LBA4518 presented 3 June 2012.

MedPage Today, 3 June 2012

PELVIC LYMPH NODE DISSECTION FOR PROSTATE CANCER: FREQUENCY AND DISTRIBUTION OF NODAL METASTASES IN A CONTEMPORARY RADICAL PROSTATECTOMY SERIES

Godoy G, von Bodman C, Chade DC, et al

J Urol 187: 2082-6, 2012

Purpose: We determined the frequency and distribution of metastases to pelvic lymph nodes in a contemporary American radical prostatectomy series.

Materials and methods: In 642 consecutive patients with clinically localized prostate cancer treated by a single surgeon between 2002 and 2009 pelvic lymph nodes were removed and submitted to the pathologist in separate packets (external iliac, obturator and hypogastric). We assessed the total number of nodes and the number with metastases in each packet.

Results: Complete pathological information was available for 427 patients, who had a median of 16 lymph nodes removed. Of the patients 35 (8.2%) had lymph node metastases, including 1.7% with low, 8.6% with intermediate and 23.9% with high risk cancer. Of those with nodal metastases 24 (69%) had positive lymph nodes in only 1 of the 3 areas, including the external iliac in 4 (11%), the obturator in 9 (26%) and the hypogastric in 11 (31%). Only 37% of the patients had positive nodes only in the external iliac area above the obturator nerve while 60% and 49% had at least 1 positive node in the obturator and the hypogastric area, respectively. Of the patients 80% had only 1 (49%) or 2 (31%) positive nodes.

Conclusions: In contemporary American patients with clinically localized prostate cancer, lymph node metastases were found more often and frequently exclusively in the obturator and hypogastric areas than in the external iliac area. Pelvic lymph node dissection limited to the external iliac area above the obturator nerve would identify and remove lymph node metastases in only a third of the patients with positive nodes found at full pelvic lymph node dissection.

GINSENG CAPSULES SEEM TO EASE CANCER-RELATED FATIGUE

Study found herb worked better than sham treatment, but only after about 2 months

The herb ginseng appeared to significantly reduce cancer-related fatigue compared to an inactive placebo, although it took several weeks for the herb's effects to take effect in the patients, a new study reports.

In the study, the researchers gave either a placebo or 2,000-milligram capsules of ground ginseng root to 340 patients who were being treated for cancer or had completed cancer treatment. Fatigue is extremely common among cancer patients; most of those in the study suffered from breast cancer.

The patients took capsules of pure American ginseng instead of some over-the-counter ginseng products that can include ethanol. Ethanol may be potentially dangerous to breast cancer patients, study researcher Debra Barton of the Mayo Clinic Cancer Center said in a news release from the clinic.

"After eight weeks, we saw a 20-point improvement in fatigue in cancer patients, measured on a 100-point, standardized fatigue scale," Barton said.

Those who took the ginseng capsules didn't report much improvement at four weeks, but at eight weeks they reported they felt less "worn out," "fatigued," "sluggish" or "tired," compared to those who took the placebo, the investigators found.

The study authors noted that ginseng didn't seem to have any side effects. They didn't specify how much the ginseng treatments would cost.

A previous Mayo Clinic study found that about one-quarter of patients who'd had cancer and suffered from fatigue said they felt "moderately better" or "much better" after taking 1,000-milligram or 2,000-milligram ginseng tablets. By comparison, only 10 percent of those who took the placebo reported those results.

Laura Murphy, a professor of physiology at Southern Illinois University Carbondale who's familiar with the research, said it's a helpful addition to existing knowledge. The cost of ginseng will be inexpensive compared to prescription drugs that could be used to treat fatigue, she said.

Why might ginseng help fatigue? It's not clear, said Murphy, who has studied the herb. "Essentially, when healthy people ingest ginseng, there are no notable effects," she said. "However, when an ill person takes ginseng, they tend to feel more normal."

The study, funded by the U.S. National Cancer Institute and the Breast Cancer Research Foundation, was scheduled to be released June 4 at the annual meeting of the American Society of Clinical Oncology in Chicago.

The data and conclusions of research presented at medical meetings should be viewed as preliminary until published in a peer-reviewed journal.

HealthDay News, 4 June 2012

US TOO WANTS TO ANSWER YOUR QUESTIONS!

Dr. Myers would love to provide direct answers to questions posed by Us TOO members. Instead of printing questions answered in the *Prostate Forum*, we'd rather provide readers who subscribe to both publications with fresh content. Questions about imaging, active surveillance, and biochemical relapse would be particularly appreciated right now.

If you have questions, please send them to <Jackie@ustoo.org> or call the Helpline at 800-808-7866.

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"You want a real cheap ANTI-AGING secret...well I have one for you!"

Mark A. Moyad, MD, MPH
University of Michigan Medical Center, Department of Urology

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

Bottom Line: One of the cheapest anti-aging secrets is _____ (did you really think I was going to give away the secret right at the beginning like I always do?)

Some things never change such as toilet paper, coat hangers, elevator call buttons, crying babies in the airplane seats in front and in back of you, and the fact that fiber may be the healthiest internal anti-aging ingredient that you can get your hands on folks. Another large prospective study on fiber has been published, this time from 10 European countries that included 452,717 men and women that were followed for an average of almost 13 years![1] This is a long time to be followed, I mean heck my wife and I have a private investigator follow my teenage kids when we are out of town just for a few days, so 13 years is a long time. Anyway I digress, but the researchers found a relationship between increased fiber intake from cereals and vegetables and a lower risk of dying from any cause, and the benefits were similar for men as well as women.

Isn't it interesting that these benefits were found from very cheap sources of fiber?! I mean we are not talking about fiber pills or powders here, but more "natural" sources of fiber. Researchers are also learning that fiber has multiple mechanisms of action from changing intestinal contents to help lower cholesterol, reduce markers of inflammation, promotes the feeling of fullness to reduce weight, allows more healthy bacteria to occupy the colon to lower the risk of infections, and brings water into the stool so that a healthy bowel movement can occur and you are not plugged up more than your local barber/salon shop drain after a full day of cutting hair. Some folks want clear cut data that fiber reduces the risk of prostate cancer or the progression of this disease, but that research is lacking. However, what is known is that cheap sources of fiber and getting just 20-30 grams a day from these sources may help you live longer and better because it has so many internal anti-aging properties (even reduces the risk of acid reflux, diverticulitis and hemorrhoids). Oh, and if you want to spend pennies then just buy Fiber One (look for the new 80 calorie option) cereal, All-Bran Buds cereal, or even a high fiber oatmeal brand such as Quaker Oats. You will not be disappointed…in other words…"Gentleman start your engines, and where the heck is that Sunday newspaper I need to read from cover to cover"…

Reference

1. Chuang SC, Norat T, Murphy N et al. Am J Clin Nutr, 2012 30 May [Epub ahead of print]

US TOO SEEKS BOARD MEMBER APPLICATIONS

Us TOO International, is seeking qualified individuals to serve on its Board of Directors. Members have been diagnosed with prostate cancer, are a member of such a man's family or significant other, or any person involved in or interested in support or treatment of such patients. Other qualifications include familiarity with an Us TOO chapter, ability to think globally, skills or experience deemed beneficial to the work of Us TOO and commitment to Us TOO's purpose and mission. See details at www.ustoo.org/SeekBoardMembers.asp. Send letters of nomination with a vita or resume to Thomas Kirk, President and CEO, Us TOO International, 5003 Fairview Avenue, Downers Grove, IL 60515 or e-mail tom@ustoo.org.

NADIA PROSVUE TEST

(Continued from page 2)

In an interview with Medscape Medical News, Dr. McDermed said that "by being able to measure more than 10 times below the detection limits of other assays, if there is a change in the PSA from month to month, we can measure it and it is a real change," not variability inherent in the assay itself. Geoff Metcalf, Vice President of Sales and Business Development at Iris Personalized Medicine, explained that this test is similar in its approach to a prognostic test for breast cancer. "It gives clinicians an idea about how well the patient will do."

"This is a major advance in the management of prostate cancer," Metcalf said. After RP, "most men are placed into risk categories using nomograms; with that, there are still many questions about whether a man will develop clinical recurrence," he said. "With this test, we are able, with 92.7% accuracy, to identify men who will not clinically recur within 8 years of RP," he said. "This is not PSA recurrence, but clinical recurrence detected by biopsies or imaging."

Independent commentator David I. Lee, MD, assistant professor of surgery/urology at the Perelman School of Medicine, University of Pennsylvania, in Philadelphia, said he thinks the test is "very clinical relevant." According to Dr. Lee, the gold-standard method of following men after RP for prostate cancer is monitoring PSA, which should be undetectable; if it becomes detectable, it is a sign of cancer recurrence.

"The ProsVue test, because of its very sensitive profile, may be able to detect recurrences earlier, enabling men to decide on other treatment options sooner," he stated. "There is no other assay that is of any use; therefore, the ProsVue test may become very useful because of its sensitivity," he added. According to Dr. Lee, this test might be especially useful for men with higher-risk pathology, in whom a slow ProsVue result might lead a man not to undergo adjuvant radiation. "Likewise, a concerning score may lead some men to start radiation or hormonal therapy earlier than otherwise contemplated," he said.

Medscape Medical News, 25 May 2012

DOCTOR CHODAK'S BOTTOM LINE *(Ref Key: article #, page #, column #)*

Author: *Winning The Battle Against Prostate Cancer, 2011*

Editors' note: Us TOO has invited certain physicians and others to provide information and commentary for the *HotSheet* to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and is not necessarily those of Us TOO International.

In this month's *HotSheet*, there are three very important reports with clinical implications for men with advanced prostate cancer. The first (**a1p1c1**) involves new information about the effect of intermittent hormone therapy (IHT) for men with metastatic prostate cancer. For many years, men have been using IHT rather than continuous HT, believing that survival is just as good but quality of life is improved during the drug holidays. Recently, a randomized study from Europe showed that the overall survival was not different, but men on IHT had a higher death rate from prostate cancer and a lower death rate from other causes. Now a larger, and longer randomized study has shown that IHT in men with metastatic disease actually has a lower survival rate compared continuous HT by about eight months. Going forward this means men will have to decide if a better quality of life is worth a reduced survival rate. Whether this is also true for non-metastatic disease requires another study.

THE BOTTOM LINE: IHT is inferior to continuous therapy in men with metastatic prostate cancer.

The other two important articles contain information from the 2012 ASCO meeting. One study (**a2p1c2**) tested enzalutamide (MDV3100), a new antiandrogen in men with metastatic prostate cancer who progressed after receiving docetaxel. The other study (**a3p1c3**) tested abiraterone in men with progressive metastatic disease who were naïve to chemotherapy. In both drug studies, the safety committees recommended stopping the studies early because the drugs showed significant benefit. For the enzalutamide, it improved survival while the abiraterone delayed the time to radiographic progression but had not yet reached a survival benefit. There were no major safety issues with abiraterone but enzalutamide caused seizures in 6 out of 1,000 men. FDA will review these results and then decide whether they should be approved. If they do, new questions will emerge. For men who have progressed on chemotherapy, the question becomes which drug should be given first or should both be given together. Enzalutamide is also being tested prior to chemotherapy and is highly likely to show a benefit too. If that occurs, the same questions will need to be answered in men naïve to chemotherapy.

THE BOTTOM LINE: Men with advanced castration resistant prostate cancer are likely to have two additional options, enzalutamide for those failing chemotherapy and abiraterone for those who have not yet been treated with it.

a4p2c2 Some men who have undergone a radical prostatectomy (RP) are still destined to develop a recurrence. The most useful predictors are the pathology report and the Gleason score. Now a new test is being used to help identify men who are unlikely to recur. The ProsVue slope separates men into a low chance and high chance for recurrence with the idea that it may help some men avoid unnecessary treatment. This test could benefit many men except for one major problem. At this time there is little evidence that men benefit from getting delayed radiation so even if they are in the high risk group, it is unclear what to do about it. One could easily make a case that both risk groups should not receive additional local therapy, and at this time there is no proof that hormone or chemotherapy will improve survival in either group. So for now, the test may not be so useful until we have proof that treating men based on the ProsVue test will improve survival.

THE BOTTOM LINE: The ProsVue test may one day be useful for all high-risk men but at this time, it is unlikely to be very useful for selecting treatment.

a5p2c3 Almost everyone is aware that Gleason score interpretation is highly subjective. Methods that could lower the variability would be very advantageous and could reduce the number of second opinions obtained. The idea of using image analysis is not new. This preliminary study is encouraging but at this time more data are needed to know its overall accuracy. It will be interesting to see how the method compares with pathologists with a expertise in interpreting prostate biopsies.

THE BOTTOM LINE: More data are needed to know if using standardized image analysis could substitute for the interpretation given by pathologists.

a6p3c3 The article by McNeil argues in support of screening claiming that without screening many men will not be diagnosed until their cancer has spread. Clearly, this is one of the discussion points that men should hear when presented the pros and cons of screening. However, much more discussion is needed for men to make an informed decision than just telling them about the risk of developing metastatic disease.

THE BOTTOM LINE: Telling men about the potential to develop metastatic disease if they don't get screened is an important but very incomplete part of what men need to know about screening.

a7p5c3 Another continuing controversy involves what to do about the pelvic lymph nodes at the time of RP. Should they be removed, should the surgeon wait for the frozen section results before removing the prostate, and which lymph nodes should be obtained? So far, no randomized study has shown a therapeutic benefit from removing the lymph nodes regardless of whether they do or do not contain cancer. Often, doctors remove some lymph nodes but do not wait for results. This is good for the doctor but clearly not good for the patient. When a more extensive dissection is done, more abnormal lymph nodes are detected, but complications can occur and surgery is longer. This report provides additional evidence that removing the external lymph nodes alone will often miss cancer and so this article supports doing a more extensive dissection.

THE BOTTOM LINE: If performed, a limited lymph node dissection is not going to be adequate.

SCREENING CAN BE DIFFERENCE BETWEEN LIFE AND DEATH

(Continued from page 3)

Of the men who underwent radiographic imaging, 50 (45%) had lymphadenopathy suspicious for metastasis, 14 (19%) had masses suspicious for visceral metastases and three (4%) had evidence of local progression. All patients had bone scans. Virtually all (97%) had positive findings, with 11 (7%) showing signs of cord compression.

The median time for rise of PSA levels after they reached a nadir was 228.5 days. The median survival duration was slightly more than four years. Two- and five-year cancer specific survival rates were 68% and 39%, respectively.

"The scary thing for me is that the US Preventive Services Task Force recommendations could discourage some men from getting screened who would benefit from screening. With the patients in our study, who knows what would have happened if they were screened and the cancer was detected much earlier," Dr. McNeil said.

Reuters Health, 29 May 2012

OGX-427 IMPROVES PROGRESSION-FREE SURVIVAL IN PROSTATE CANCER

OncoGenex Pharmaceuticals Inc. announced data from a Phase 2 study of its investigational compound OGX-427 in chemotherapy-naive metastatic castration resistant prostate cancer (mCRPC). Preliminary results show a higher progression-free survival (PFS) in patients taking OGX-427 plus prednisone at 12 weeks and with PSA declines, compared with those taking prednisone alone.

Sixty-four of 72 planned subjects have been randomized to the study and data on 42 men [22 who received OGX-427 plus prednisone and 20 who received prednisone alone] are now available at or beyond the 12 week assessment time point. Highlights are as follows:

In the OGX-427 plus prednisone arm, 71% of patients were progression-free at 12 weeks, vs. to 40% in the prednisone arm. The primary efficacy endpoint of this study is defined as PFS at 12 weeks where disease progression is based on any of the following parameters: rising PSA levels, measurable disease, bone lesions, global deterioration or requirement of palliative radiation therapy.

Fifty percent of men who received OGX-427 plus prednisone experienced a >50% decline in PSA, versus 20% of men who received prednisone alone. Among the 21 patients with baseline measurable disease, 4/9 (44%) vs. 0/12 (0%) responded in the OGX-427 plus prednisone arm and prednisone alone arms. There was 1 complete response in the OGX-427 plus prednisone arm.

The authors concluded that OGX-427 appears well-tolerated. Adverse events (AEs) have been predominately grade 1-2 and related to infusion reactions. Three grade 4 AEs have been reported and include dizziness, pulmonary embolus and hemolytic uremic syndrome.

OGX-427 is believed to work by inhibiting the production of Hsp27, a cell-survival protein expressed in many types of cancers including prostate, bladder, pancreas, breast and non-small cell lung cancer. Overexpression of Hsp27 is thought to be an important factor leading to the development of treatment resistance and is associated with negative clinical outcomes in patients with various tumor types.

www.dddmag.com,7 June 2012

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