LATITUDE: A Phase III, Double-Blind, Randomized Trial of Androgen Deprivation Therapy with Abiraterone Acetate Plus Prednisone or Placebos in Newly Diagnosed High-Risk Metastatic Hormone-Naive Prostate Cancer

Dr. Fizazi and colleagues presented their much anticipated results from the LATITUDE trial at the 2017 American Society of Clinical Oncology (ASCO) annual meeting. LATITUDE is a phase III, double-blind, randomized study that tested androgen deprivation therapy (ADT) with abiraterone acetate (AA) plus prednisone (P) vs. ADT + placebo in men newly diagnosed with high-risk metastatic hormone-naive prostate cancer.

Historically, ADT has been the standard of care (SOC), however most men with metastases progress to castrate-resistant prostate cancer (CRPC) driven by the reactivation of androgen receptor (AR) signaling. Dr. Fizazi noted that ADT + docetaxel is the new SOC for men with metastatic hormone-naive disease (with high disease burden) based on results from three randomized controlled trials – GETUG-15, CHAARTED and STAMPEDE.

Dr. Fizazi said the rationale for combining AA+P to ADT is three-fold: (i) the mechanism of resistance to ADT may develop early, (ii) ADT alone does not inhibit androgen synthesis by the adrenal glands or prostate cancer cells, and (iii) AA+P improves overall survival (OS) in metastatic CRPC patients and reduces tumor burden in high-risk, localized prostate cancer. This suggests a role for treatment with drugs inhibiting extragonadal androgen synthesis prior to the development of CRPC.

(Continued on page 4)

Adding Abiraterone to Standard Treatment Improves Survival in Advanced Prostate Cancer

The STAMPEDE clinical trial of nearly 2,000 men shows that adding abiraterone acetate (AA) to a standard initial treatment regimen for high-risk, advanced prostate cancer lowers the relative risk of death by 37%. The three-year survival rate was 76% with standard therapy alone vs. 83% with standard therapy plus AA. This is the largest study of AA as first-line therapy for advanced prostate cancer. The study was presented at the 2017 Annual Meeting of the American Society of Clinical Oncology (ASCO®).

“Abiraterone not only prolonged life, but also lowered the chance of relapse by 70% and reduced the chance of serious bone complications by 50%,” said lead study author Nicholas James, BSc, MBBS, PhD, Professor of Clinical Oncology at Queen Elizabeth Hospital in Birmingham, United Kingdom (UK). “Based on the magnitude of clinical benefit, we believe that the upfront care for men newly diagnosed with advanced prostate cancer should change.”

STAMPEDE is an ongoing multiarm, multistage randomized clinical trial conducted in the UK and Switzerland. The current analysis compared standard therapy with standard therapy plus AA in men with high-risk prostate cancer who were starting androgen-deprivation therapy (ADT).

Men had locally advanced or metastatic cancer and all were commencing long-term ADT for the first time. The standard protocol consisted of ADT for at least two years; men with locally-advanced cancer (48% of all men) could

(Continued on page 5)
Association Between Combined TMPRSS2:ERG and PCA3 RNA Urinary Testing and Detection of Aggressive Prostate Cancer

Sandra MG, Feng, Z, Howard DH, et al.
JAMA Oncol. 18 May 2017; published online ahead of print

Importance: Potential survival benefits from treating aggressive (Gleason score, ≥7) early-stage prostate cancer are undermined by harms from unnecessary prostate biopsy and overdiagnosis of indolent disease.

Objective: To evaluate the a priori primary hypothesis that combined measurement of PCA3 and TMPRSS2:ERG (T2:ERG) RNA in the urine after digital rectal examination would improve specificity over measurement of PSA alone for detecting cancer with Gleason score of 7 or higher. As a secondary objective, to evaluate the potential effect of such urine RNA testing on health care costs.

Design, Setting, and Participants: Prospective, multicenter diagnostic evaluation and validation in academic and community-based ambulatory urology clinics. Participants were a referred sample of men presenting for first-time prostate biopsy without pre-existing prostate cancer: 516 eligible participants from 748 prospective cohort and 561 eligible participants from 928 in the validation cohort. Study presented at the American Urological Association’s 2017 annual meeting.

Interventions/Exposures: Urinary PCA3 and T2:ERG RNA measurement before prostate biopsy.

Main Outcomes and Measures: Presence of prostate cancer having Gleason score of 7 or higher on prostate biopsy. Pathology testing was blinded to urine assay results. In the developmental cohort, a multiplex decision algorithm was constructed using urine RNA assays to optimize specificity while maintaining 95% sensitivity for predicting aggressive prostate cancer at initial biopsy. Findings were validated in a separate multicenter cohort via prespecified analysis, blinded per prospective-specimen-collection, retrospective-blinded-evaluation (PROBE) criteria. Cost effects of the urinary testing strategy were evaluated by modeling observed biopsy results and previously reported treatment outcomes.

Results: Among the 516 men in the developmental cohort (mean age, 62 years; range, 33–85 years) combining testing of urinary T2:ERG and PCA3 at thresholds that preserved 95% sensitivity for detecting aggressive prostate cancer improved specificity from 18% to 39%. Among the 561 men in the validation cohort (mean age, 62 years; range, 27–86 years), analysis confirmed improvement in potential cost-benefit in younger men.

Conclusions and Relevance: Combined urinary testing for T2:ERG and PCA3 can avert unnecessary biopsy while retaining robust sensitivity for detecting aggressive prostate cancer with subsequent potential health care cost savings.

MRI Accuracy for Prostate Cancer Challenged

Multiparametric magnetic resonance imaging (mpMRI) often misses clinically significant prostate tumors outside index lesions, according to a study presented at the American Urological Association’s 2017 annual meeting.

In a study including 244 prostate cancer (PCa) patients who underwent mpMRI with subsequent biopsy, Armando Stabile, MD, of Vita-Salute San Raffaele University in Milan, Italy, and colleagues found that mpMRI missed clinically significant PCa (Gleason sum of 7 or higher) outside of index lesions in 34% of cases.

When investigators stratified men according to targeted biopsy results, the detection rate of clinically significant PCa outside the index lesion was 10% and 30% of men with negative and positive targeted biopsy findings, respectively. On multivariate analysis, PSA level, prostate volume, positive digital rectal exam, and previous negative biopsy independently predicted the overall presence of clinically significant PCa outside the index lesion. PI-RADS, index lesion volume, and number of index lesions detected on mpMRI were not associated with overall detection of clinically significant PCa outside the index lesion. Despite the presence of clinical predictors, neither patient characteristics nor (Continued on page 6)
Doc Moyad’s What Works & What is Worthless Column, Also Known As “No Bogus Science” Column

“Testosterone Blood Test & Weight Loss for Prognosis? What?”

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

Editor’s Note: Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

A low total testosterone blood level at, or around, the time of prostate cancer diagnosis could be one characteristic of a more aggressive tumor. Another reason to lose weight/waist whenever you have the chance and perhaps get a testosterone level with your next and some subsequent PSA tests.¹

MD Anderson Cancer Center researchers published a really interesting paper recently that did not get enough attention, so let’s give it the attention it deserves!¹ A total of 762 men with prostate cancer were categorized as having low (below 230), intermediate (250-350), or normal (above 350 ng/dL) testosterone levels around the time of diagnosis. And, what they found when they looked at the men’s testosterone levels when first diagnosed with prostate cancer, they were significantly lower in the men with aggressive prostate cancers. And, there was even a significant increased risk of mortality from prostate cancer with a lower total testosterone at the time of diagnosis.²

Now, hey wait a second! Moyad is supposed to spend more time on diet and supplements than this stuff – right? Not really (I like to have conversations with myself). I remember being at a conference in the year 2001 (yes, I am getting old – I know this because I now get incredibly upset when I can’t find my reading glasses and/or have a bad bowel movement... these two things are related, by the way) and someone got up in the audience and asked if I thought a low testosterone at the time of diagnosis could be associated with a more aggressive prostate cancer. And, I said “I think so” based on all the men I had followed throughout the years. But what I also said to this man – I will never forget – is if higher weight and waist size is one of the main causes of a low testosterone, then you would think that one of the smartest things men can do after being treated for prostate cancer (especially localized disease) is to maintain a healthy weight or lose weight.

It is interesting in this MD Anderson study that men with a higher BMI (body mass index) did, in fact, have significantly lower levels of total testosterone at diagnosis. It also appears, from another study, that men carrying a low testosterone while on active surveillance could have a higher risk for prostate cancer progression and the need for treatment.³ Additional studies also suggest that these men have a lower likelihood of responding to different types of hormone therapy and even have a higher chance of becoming hormone resistant to drug treatment if they have a lower testosterone level.³,⁴ Other studies have suggested that testosterone is not a predictor of tumor aggressiveness but many of these studies looked at testosterone levels a long time before the diagnosis of prostate cancer. Regardless, if increasing body weight increases the risk of low testosterone and low testosterone and/or higher body weight/waist increases the risk of a more aggressive prostate cancer,⁵ then why not make lowering weight/waist before or after prostate cancer treatment about as important as anything else you can do for your health?

Are you following me on this? Does this make sense? Whatever it takes, or whatever the diet, or even a medical weight loss program... losing weight could make the difference between a nasty tumor and a nicer one for some men. “Hey, has anyone in this house seen my reading glasses!? I had All-Bran for dinner last night!!!” (Moyad circa 2017).

References:

Overall Survival Analysis of African American and Caucasian Patients Receiving Sipuleucel-T: Preliminary Data from the Proceed Registry

J Urol. 197: Suppl. e456-e457

Sipuleucel-T (sip-T) is an FDA-approved autologous cellular immunotherapy targeting prostatic acid phosphatase in select men with metastatic castration-resistant prostate cancer (mCRPC). Previous retrospective analyses of three sip-T phase 3 trials showed a 30.7-month overall survival (OS) advantage for African American (AA) patients vs. control while in the IMPACT trial, sip-T extended median OS by 4.1 months vs. control (McLeod AUA 2012 #P953). The PROCEED registry provides a prospective opportunity to confirm these observations in a larger group of AA men.

(Continued on page 8)

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-Value</th>
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<tr>
<td>Age, years (&gt; median vs. ≤ median)</td>
<td>1.437 (1.149–1.797)</td>
<td>&lt;0.001</td>
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<td>Prior chemotherapy (yes vs. no)</td>
<td>1.510 (1.155–1.973)</td>
<td>&lt;0.001</td>
</tr>
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<td>Alkaline phosphatase level, U/L (&gt; median vs. ≤ median)</td>
<td>1.680 (1.336–2.111)</td>
<td>&lt;0.001</td>
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<tr>
<td>Race (Caucasian vs. African American)</td>
<td>1.564 (1.200–2.037)</td>
<td>&lt;0.001</td>
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<td>Hemoglobin level, g/dL (&gt; median vs. ≤ median)</td>
<td>0.621 (0.491–0.785)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSA, ng/mL (&gt; median vs. ≤ median)</td>
<td>1.719 (1.354–2.182)</td>
<td>&lt;0.001</td>
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High-risk was defined as meeting at least two of three criteria: (i) Gleason score ≥8, (ii) ≥3 lesions present on bone scan, and (iii) presence of measurable visceral lesions. Men were stratified by the presence of visceral disease (yes/no) and Eastern Cooperative Oncology Group (ECOG) performance status (0, 1 vs. 2).

Men were randomized 1:1 to ADT+AA (1000 mg/day) + P (5 mg/day) [n=597] or ADT + placebo [n=602]. There were two primary endpoints: OS and radiographic progression-free survival (rPFS). Secondary endpoints included time to: (i) pain progression, (ii) PSA progression, (iii) next symptomatic skeletal event, (iv) chemotherapy, and (v) subsequent prostate cancer therapy. The study was conducted at 235 sites in 34 countries. Dr. Fizazi notes that the study was designed and fully enrolled prior to publication of the CHAARTED and STAMPEDE results.

Results from the first interim analysis presented at ASCO showed treatment arms to be well balanced, with >95% of men in both arms presenting with ≥3 bone metastases at screening. Over a median follow-up of 30.4 months, men treated with ADT+AA+P had a 38% risk reduction of death [hazard ratio [HR] 0.62, 95% confidence interval [CI] 0.51-0.76] compared to ADT + placebo. Median OS was not yet reached in the ADT+AA+P arm compared to 34.7 months in the ADT + placebo arm. OS rates at three years for the ADT+AA+P arm were 66%, compared to 49% in the ADT + placebo arm. OS benefit was favorable across all subgroups including ECOG 0 and 1-2, visceral metastases, Gleason ≥8 disease, and bone lesions >10. Second, there was also 53% risk of reduction of radiographic progression or death for men treated with ADT+AA+P (median 33.0 months; HR 0.47, 95%CI 0.39-0.55) compared to ADT + placebo (14.8 months). Third, there was statistically significant improvement across all secondary endpoints for ADT+AA+P.

The excellent results prompted the study to be discontinued after the first interim analysis. Adverse events were comparable in the two groups. High blood pressure (hypertension) only rarely required treatment discontinuation, and only two patients discontinued treatment due to non-fatal low blood potassium (hypokalemia). Two men in each arm died of cerebrovascular events, and 10 men treated with ADT+AA+P died of cardiac disorders compared to six men treated with ADT + placebo.

In conclusion, the phase III LATITUDE study demonstrated that ADT+AA+P led to a significantly improved OS with a 38% reduction in risk of death, significantly prolonged rPFS (53% reduction), and improvement across all secondary endpoints. The overall safety profile was consistent with the AA+P regimen reported in metastatic CRPC trials.

Based on these findings, Dr. Fizazi states, “The addition of AA+P to ADT can potentially be considered a new SOC for patients with high-risk, newly diagnosed hormone-naïve prostate cancer.”

Presented at the plenary session of the 2017 Annual ASCO Meeting

**Signature for Aggressive Variant CRPC Predicts Platinum Sensitivity**

A molecular signature for aggressive-variant prostate carcinoma (AVPC-MS) can predict which men with castration-resistant prostate cancer (CRPC) will benefit from cabazitaxel with or without carboplatin, and does so better than clinically defined AVPC, according to findings from a randomized phase II study (abstract 5013) presented at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting, held June 2-6 in Chicago.

“The AVPC-MS identifies a subset of men platinum-sensitive CRPC tumors,” reported lead study author Ana M. Aparicio, MD, of The University of Texas MD Anderson Cancer Center, Houston. “These findings should serve as the foundation for a therapeutically relevant classification of prostate cancer.”

AVPC represents a subset of prostate cancers that “shares the clinical, therapy response and molecular profiles of the small cell prostate carcinomas, a histological variant of the disease that responds poorly to androgen receptor directed therapies,” Dr. Aparicio explained.

AVPC have a molecular signature (AVPC-MS) defined as ≥2 tumor suppressor mutations in Tp53, RB1 and/or PTEN as determined using immunohistochemistry or genomic sequencing analyses. The researchers sought to evaluate whether or not this AVPC-MS predicted outcomes for patients treated with platinum-based chemotherapy.

They randomly assigned 160 men with metastatic castration-resistant prostate cancer to receive intravenous cabazitaxel (25 mg/m²) with or without carboplatin (AUC 4) every 21 days with growth factor, until patients reached 10 cycles or experienced unacceptable toxicity or disease progression. Patients underwent imaging examinations every other cycle. Tumor samples were obtained from 65 of the study participants and these were tested for Tp53, RB1, PTEN, AR-N terminus, AR-C terminus, and Ki67. Tumor DNA was also retrieved for sequencing from 27 tumor biopsies and 70 patient plasma samples.

Adding carboplatin to cabazitaxel therapy was safe and improved progression-free survival (PFS) and response rates among study participants overall, the researchers confirmed. At a median follow-up of 21.6 months, median PFS in the overall population (n = 160) was 4.6 months (95% CI, 3.5-5.8) with cabazitaxel vs. 7.4 months (95% CI, 5.6-8.3) with cabazitaxel/carboplatin (P = 0.004).

The AVPC-MS was predictive of treatment outcome. Men with AVPC-MS tumors saw a median PFS of 4.5 months on cabazitaxel and eight months with cabazitaxel and carboplatin (P = 0.0036), compared with 6.8 months and 5.4 months, respectively, among men with AVPC-MS-negative tumors.

**Web-Based Stress Management for Newly Diagnosed Cancer Patients (STREAM): A Randomized, Wait-List Controlled Intervention Study**


**Background:** Being diagnosed with cancer causes major distress, yet the majority of newly diagnosed cancer patients lack psychological support. Internet interventions overcome many barriers for seeking support. We assess efficacy and feasibility of a web-based minimal-contact stress management intervention (STREAM) for newly diagnosed cancer patients.

**Methods:** In a prospective, wait list controlled trial, newly diagnosed cancer patients were randomized within 12 weeks of...
Adding Abiraterone to Standard Treatment
(Continued from page 1)
also receive radiation therapy in addition to ADT. A novel approach to the clinical trial design meant this comparison recruited men much more quickly than most academic-led trials, and STAMPEDE will report randomized data from at least 10 comparisons over two decades.
At a median follow-up of 40 months, 262 and 184 deaths had occurred in the standard therapy and the ADT plus AA groups, respectively. Three-year overall survival (OS) rate was 83% in the ADT plus AA group vs. 76% in the standard therapy group. The addition of AA lowered the relative chance of treatment failure by 71% (measured by worsening scans or symptoms, or elevated PSA levels) compared with standard ADT therapy. Effects were consistent across the different subgroups of men enrolled in the trial.
Overall, side effects were similar between the two groups. Severe side effects were more common in the ADT plus AA group, occurring in 41% of men compared with 29% of men in the standard therapy group.
Main side effects that occurred more frequently with AA were cardiovascular problems such as high blood pressure; there were also more liver problems with AA.
There were two treatment-related deaths in the ADT plus AA group and one in the standard therapy group.
“This study provides strong evidence to support adding AA to standard hormone therapy, primarily for men with metastatic prostate cancer. It adds to a growing body of evidence that establishes AA as a standard of care in this setting,” said ASCO expert Sumanta Kumar Pal, MD.
This study was funded by grants from Cancer Research UK, the Medical Research Council, and Janssen, with additional contributions to the STAMPEDE protocol from Astellas, Clovis Oncology, Janssen, Novartis, Pfizer, and Sanofi-Aventis.
The content in this post has not been reviewed by ASCO and does not necessarily reflect the ideas and opinions of ASCO.
Presented at the 2017 ASCO Meeting, abstract LBA5003

Reducing ADT to 18 Months May Be Sufficient in High-Risk Prostate Cancer
Androgen deprivation therapy (ADT) can be safely reduced from 36 months to 18 months in high-risk prostate cancer patients, according to final results of a randomized phase III trial. However, the statistical design of the study may prevent definitive conclusions on the best duration of treatment.
Abdenour Nabid, MD, of Centre Hospitalier Régional Universitaire in Sherbrooke, Quebec, presented results (abstract 5008) of the “Duration of Androgen Blockade Combined With Pelvic Irradiation in Prostate Cancers” (PCS IV) trial at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting, held in Chicago. The trial included 630 men randomized to 36 months (310 men) or 18 months (320 men) of ADT (bicalutamide plus goserelin); all men received radiation therapy (RT) and were followed a median of 9.4 years.
All men had high-risk disease, and were well matched between the groups, with a median age of 71 years. The median PSA level in the 36-month group was 16.4 ng/mL, and in the 18-month group it was 15.4 ng/mL; the median Gleason score was 8 in both groups. In the full cohort, 24.1% of men had locally advanced (clinical stage T3-T4 disease), 44.3% had a PSA level above 20 ng/mL, and 59.7% had a Gleason score above 7.
Overall survival (OS) was similar between the two groups. At five years, the 36-month group had an OS rate of 90.9%, and the 18-month group had an OS rate of 86.1%. At 10 years, these rates were 62.4% and 62.0%, respectively. The hazard ratio (HR) for OS was 1.024 (95% CI, 0.813-1.289; non-significant P = 0.8411); a multivariate analysis confirmed this, with an HR of 1.01 (95% CI, 0.80-1.27; P = 0.9431).
A quality of life analysis favored the 18-month ADT duration. This was clinically significant and covered multiple aspects.
Disease-specific survival was also similar. At 10 years, the HR was 0.948 (95% CI, 0.582-1.546; P = 0.830). Biochemical failure at 10 years was more likely in the 18-month group, at 31.0% compared with 24.8%, for an HR in favor of the longer duration of 0.714 (95% CI, 0.532-0.952; significant P = 0.024).
Disease-free survival was similar, with an HR of 0.835 (95% CI, 0.683-1.020; P = 0.0768).
“In localized high-risk prostate cancer treated with RT and ADT, ADT duration can be safely reduced from 36 to 18 months,” Nabid concluded, adding that 18 months could represent a threshold effect of ADT beyond which little extra benefit is derived.
“Eighteen months of ADT represents a new standard of care.”
That conclusion, though, may be somewhat premature. Susan Halabi, PhD, of Duke University Medical Center in Durham, NC, was the discussant for the session, and she pointed out that a non-significant test result from a superiority comparison cannot be used to establish similarity between the two treatments.
“The optimal duration of ADT for high-risk localized prostate cancer is not known, and remains a clinically important question.”
The Cancer Network
7 June 2017

One RT Dose Enough for Metastatic Spinal Cord Compression
For patients with advanced, metastatic cancer who develop spinal cord compression, one dose of radiotherapy (RT) is as effective as several doses delivered over multiple hospital visits, according to British researchers at the annual meeting of the American Society of Clinical Oncology (ASCO).
The results come from a phase three trial (SCORAD III) conducted in 688 patients, which compared a single 8 Gy dose with 20 Gy delivered in five fractions over five days, and showed that the primary endpoint of ambulatory status at eight weeks was similar in both groups. The patients taking part in this study had metastatic cancer of the prostate (44%), lung (18%), breast (11%), and gastrointestinal tract (11%). The majority (73%) was male, and the median age was 70 years.
“For patients with a shortened life expectancy, such as the participants in this trial (who had a median overall survival of 13 months), the addition of radiation therapy may prevent definitive conclusions on the best duration of treatment. Disease-specific survival was also similar. At 10 years, the HR was 0.948 (95% CI, 0.582-1.546; P = 0.830). Biochemical failure at 10 years was more likely in the 18-month group, at 31.0% compared with 24.8%, for an HR in favor of the longer duration of 0.714 (95% CI, 0.532-0.952; significant P = 0.024).
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“The optimal duration of ADT for high-risk localized prostate cancer is not known, and remains a clinically important question.”
The Cancer Network
7 June 2017

PROSTATE CANCER HELPLINE: 1-800-808-7866 WWW.USTOO.ORG
Surveillance for Prostate Cancer Works for Younger Men

(Continued from page 1)

Younger men with low-risk prostate cancer had outcomes with AS similar to those of the general population of men who choose AS, according to another study reported at AUA. Three-fourths of men younger than 60 remained alive without definitive treatment after five years of follow-up, and more than half remained free of definitive treatment at 10 years. After a median follow-up of 5.1 years, five men developed metastatic disease and none died of prostate cancer during follow-up for as long as 22 years.

“Little information exists about the characteristics and outcomes of younger men who choose AS,” said Salari. To inform the issue, investigators at MGH and Sunnybrook Health Sciences Center in Toronto retrospectively reviewed the records for all men who began AS from 1995 to 2016. Of almost 2,200 men, 432 were younger than 60 at the start of AS, and these men formed the basis for data analysis.

The men had a median age of 55 and a median PSA level of 4.6 ng/dL at diagnosis; 97.7% of the cancers had a Gleason score ≤6, 91.9% had clinical T1 disease, 92.8% had ≤33% positive cores in prostate biopsies, and 77.2% had ≤20% involvement of any single core.

After five years of follow-up, 131/432 men (26%) had undergone definitive treatment, the principal reason being disease progression on biopsy (N=88, 67%). An additional 24 men (18%) opted for definitive treatment because of a rising PSA, and other patient-driven factors accounted for intervention in 15 cases (12%). “This corresponds very closely to the reported numbers for AS patients at large – specifically, older men who are on AS,” said Salari.

Among men who had definitive treatment, 82 (63%) had radical prostatectomy, 16 (12%) had external-beam radiation therapy, 14 (11%) had brachytherapy, and 17 (13%) had high-intensity focused ultrasound. Analysis of 68 pathologic specimens after definitive treatment showed that 60 of the men still have organ-confined disease (pathologic T2).

Statistical analysis of factors that influenced the decision to have definitive treatment identified two independent predictors: >20% involvement of any single biopsy core (HR 1.87, 95% CI 1.27-2.76, P=0.0016) and PSA density ≥0.15 (HR 1.98, 95% CI 1.17-3.35, P=0.011). Age, PSA level, Gleason score, clinical stage, and percent positive cores were not predictive.

“I find these data very compelling for young men who at least want to delay radical treatment for a period of years, with the acknowledgement that many of them do end up needing treatment at some point,” said Stacy Loeb, MD, of NYU-Langone Medical Center in New York City, the moderator of a news conference that included the study.

“This nationwide, rates of AS vary widely, from up to 60% to below 20%,” Loeb added. The proportion of younger men who choose AS is unclear. A study of men in Sweden, where AS is standard practice for early stage prostate cancer, showed that 88% of men ages 50 to 59 with very low-risk disease selected AS, as did 68% of men with low-risk disease.

“Most of the data and assumptions pertaining to AS come from academic medical centers that have resources and technology not available in many parts of the United States,” said Eric Sackoff, MD, who interned at MGH 40 years ago. He left Boston 10 years ago to practice urology in Appalachia, where patients have a very different mindset about interactions with physicians.

One RT Dose is Enough

(continued from page 5)

weeks), a single dose of RT should now become the standard of care,” commented lead investigator Peter Hoskin, MD, from the Mount Vernon Cancer Centre in Middlesex, United Kingdom. “For patients, this means fewer hospital visits and more time with family,” he added.

“This is a case where less is more,” agreed Joshua Jones, MD, from the University of Pennsylvania in Philadelphia, who was speaking as an ASCO expert.

“These are results from a large phase three study, and are practice-changing,” he said. “But there is one caveat: the patients in this study had a short life expectancy,” he emphasized. “For patients who are expected to live longer such as metastatic prostate cancer patients, it may still be better to use several doses of RT,” he opined.

Dr. Hoskin agreed. “Longer RT may be more effective for preventing regrowth of metastases in the spine,” he noted, and therefore “may still be better for patients with a longer life expectancy, but we need more research to confirm this.”

Once cancer spreads to the bones, it commonly affects the spine, the experts explained. Metastatic spinal cord compression develops in about 10% of patients with advanced cancer, and tumors pressing on the spine can cause back pain, numbness, and difficulties with walking. In more severe cases, spinal cord compression can lead to incontinence and paralysis, which obviously have “a devastating impact on quality of life,” Dr. Jones commented.

At enrollment, 66% of patients had ambulatory status 1 or 2 (able to walk normally) or 2 (able to walk with an aid such as a cane or a walker). Results at eight weeks following RT showed that 114/164 (69.5%) patients treated with a single dose and 129/176 (73.3%) treated with several doses had ambulatory status 1 or 2.

(Continued on page 8)
Doctor Chodak’s Bottom Line
Editor’s Note: Us TOO has invited certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO international.

P1, “LATITUDE: and Adding Abiraterone...”
The management of metastatic prostate cancer continues to evolve and offers patients further improvements in survival. The study by Fizazi et al. compared ADT plus placebo to ADT + abiraterone acetate + prednisone and found the combination significantly improved survival in men with newly diagnosed metastases. A recent report on the STAMPEDE study had similar findings with significantly higher survival in men receiving the combination. These findings are important but they do present some challenges. Previous data show a significant improvement in survival when docetaxel was started with ADT for metastatic disease rather than waiting until disease progression. Similarly, we now see that a benefit also occurs when abiraterone is started early. So, how does a patient now proceed and which of these two options is preferable? One might expect worse side effects using the chemotherapy and it is more complicated to deliver. Patients prefer the abiraterone option due to this drug’s lesser toxicity; however, there is the cost issue. Finally, patients may now wonder whether an additional study will be done comparing the two options to determine if one does offer a better survival.

The Bottom Line: Adding abiraterone acetate and prednisone to ADT in men with newly diagnosed metastatic disease improves survival over ADT alone and should be discussed with each patient faced with this decision.

P1, “Surveillance for...”
Can younger men with newly diagnosed, low-risk prostate cancer be managed safely with active surveillance or will their longer survival put them at too much risk? That is the focus of a report by Salari, et al. who analyzed 432 men under age 60 followed for a median duration of 5.1 years. Nearly all men had a Gleason score less than 7. By five years, 26% had undergone definitive therapy, mostly because of changes in pathology, and by 10 years it was about 50%. Importantly, only five men developed metastatic disease by five years; however, 40% of the men who did undergo definitive therapy had non-localized disease. Longer follow-up will be needed to determine their long-term risk.

The Bottom Line: AS for men under age 60 does not appear to pose a higher risk than for older men but longer follow-up is still needed before men can be given mature data.

P2, “MRI Accuracy for...”
There is a growing interest in using targeted mpMRI instead of random biopsies to diagnose prostate cancer. Part of the argument is that it reduces the diagnosis of low-risk disease while primarily finding higher-risk disease. However, the study by Stabile and coworkers questions whether that approach is good enough. They reported that higher-risk cancers were missed when only targeted biopsies were done, and whether or not biopsies were positive or negative. For the latter group, 10% had high-risk disease outside the targeted area. One can argue that missing a high-risk cancer in other areas does not matter for those men whose targeted lesion is positive. But missing 10% of high-risk cancers in men with a negative targeted biopsy is a concern. Based on this study, targeted MRI may not be the right approach at this time.

The Bottom Line: mpMRI may miss too many high-risk cancers to be able to replace random biopsies. However, scans should have been read by an independent group to determine if the missed cancers were due to incorrect interpretation. More studies are needed to establish the accuracy of this approach.

P4, “Signature for Aggressive...”
Tailoring chemotherapy in men with prostate cancer is improving as evidenced by the report from Aparacio, et al. They used a molecular test for the presence of aggressive variant prostate cancer in a study comparing cabazitaxel alone or in combination with carboplatin. For those men with the aggressive variant, the combination improved progression-free survival, although no data were reported on the impact for overall survival, which is definitely needed to confirm these observations. Increasingly, tailoring cancer therapy offers a great opportunity for sparing men from treatments that are unlikely to help their condition.

The Bottom Line: Genetic testing to identify an aggressive variant of prostate cancer may help identify men that will benefit from a combination of cabazitaxel and carboplatin.

P5, “Reducing ADT...”
A very important paper on the duration of ADT with external radiotherapy (RT) for high-risk prostate cancer was recently presented at ASCO. Nabid, et al. reported on a randomized study comparing 18 to the standard 36 months of ADT and found no significant difference in survival, but a significant improvement in quality of life. Based on this study, doctors should no longer use the longer duration of therapy and the challenge will be how to ensure that doctors are fully aware of these findings when counseling patients about to receive RT.

The Bottom Line: Eighteen months of ADT is now sufficient in combination with external radiation for men with high-risk prostate cancer and should replace the previously recommended 36 months duration.

Stress Management (Continued from page 4)
starting anti-cancer treatment to an immediate or delayed (control group) eight-week, web-based intervention. The intervention consisted of eight modules with weekly written feedback by a psychologist (“minimal-contact”) based on well-established stress management manuals. The aim of this study was to evaluate efficacy in terms of improvement in quality of life (QoL) using the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scale, decrease in distress using the Distress Thermometer (DT), and anxiety/depression using the Hospital Anxiety and Depression Scale (HADS), as compared to patients in the wait-list group. 120 patients were needed to show (80% power, two-sided α (false-positive rate) of 0.05) a clinically meaningful difference of ≥ 9 in the Functional Assessment of Cancer Therapy (FACT) score after the immediate intervention at eight weeks (T2).

Results: Of 225 patients who applied online, 128 (57%) were randomized. Median age was 52 (range 22-77) years. Most of the patients (108/128, 84%) were female. The majority of patients were treated in the curative setting (117/128, 91%) with chemotherapy for breast cancer (91/128, 71%). Self-reported DT, which served as a stratification factor, was

(Continued on page 8)
Sipuleucel-T and Race (continued from page 3)

Methods: PROCEED (NCT01306890) enrolled men with mCRPC. In this analysis, two Caucasian (CAU) men were matched to each AA man by baseline PSA, since PSA correlates with OS in patients receiving sip-T (Schellhammer 2013). OS and time to first anticaner intervention (tACI) after sip-T were examined; univariate and multivariate analyses evaluated independent factors associated with OS.

Results: 420 CAU patients were matched to 210 AA patients; all received a single sip-T infusion. CAU men had significantly higher median hemoglobin levels at baseline (P <0.001; 13.0 g/dL vs. 12.1 g/dL for AA men) and were more likely to receive prior local therapy (P = 0.02) or prior chemotherapy (P <0.001). CAU men had a longer tACI of 9.3 months vs. 7.6 months for AA men. However, AA patients had a significantly longer median OS of 39.5 months vs. 28.1 months for CAU patients (P <0.001; hazard ratio (HR) 0.665, 95% confidence interval (CI) 0.530-0.835). After univariate and multivariate analyses, six baseline characteristics were significantly associated with OS. Younger age, lower PSA or alkaline phosphatase, and higher hemoglobin levels were independently associated with longer OS. No prior chemotherapy and the AA race were also independent predictors of extended OS (see the table on page 6).

Conclusions: Post-sip-T, the median OS for AA men was significantly extended by nearly one year compared with matched CAU men. In this large prospective analysis, AA race emerged as an independent predictor of longer OS in multivariate analyses, confirming observations of prior retrospective analysis of phase 3 trial data. These results should stimulate additional studies on the biologic basis for AA men’s enhanced response to sip-T and potentially other immunotherapies.

Presented at the 2017 AUA Annual Meeting, Abstract PD24-12

One RT Dose (Continued from page 6)

(risk difference -3.78%).

“The overall survival was very similar between the two groups,” Dr. Hoskins noted. “The median was 12.4 weeks after single dose and 13.7 after several doses (hazard ratio 1.02; P = 0.81 [not significantly different]).”

“The proportion of patients experiencing grade 3 or 4 adverse events was similar in the two groups (20.6% with single dose vs. 20.4% with several doses), but there were fewer patients with grade 1 or 2 adverse events in the single-dose group (51.0% vs. 56.9%),” he noted.

“We now recommend using a single dose of RT in this setting, with the major benefit of requiring only a single instead of multiple hospital visits, important when considering the short survival of these patients,” Dr. Hoskins concluded.

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Stress Management (Continued from page 7)

greater than 4 on a 10-point scale in 96/128 patients (75%). At T2, FACT-F was significantly increased (p = 0.044; analysis of covariance [ANCOVA] adjusted for baseline-distress) and distress was significantly lowered (p = 0.032) in the intervention group as compared to the wait-list control. Median score (lower/upper quartile) for FACIT-F at baseline/T2 was 101.0/119.0 and 108.3/109.5. Median score (lower/upper quartile) of DT at baseline/T2 was 6/4 and 6/6 for the intervention and control group, respectively. The decrease in HADS was not significantly different between the groups (p = 0.273).

Conclusions: With STREAM, we open the field of minimal-contact online interventions to newly diagnosed cancer patients and show that an eight-week web-based stress management program is feasible and effective in improving QoL and distress. Clinical trial information: NCT02289014.

Presented at the 2017 annual ASCO meeting, abstract LBA10002

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