



“Fighting Prostate Cancer in California!”

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NEWS

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PRESIDENT'S MESSAGE

In February the American Society of Clinical Oncology (ASCO) held its Genitourinary Cancers Symposium in Orlando, Florida. As always, prostate cancer played an important role in the meeting. Some of the findings that were presented or announced appear elsewhere in this Newsletter written up by our Editor, Jonathan McDermed. Some highlights included interesting findings presented on the use of finasteride. A survival analysis using the Social Security Death Index with a followup of 18 years found little difference in mortality for those men randomized to finasteride for seven years. It did, however, reduce the risk of a prostate cancer diagnosis.

On another note, Phase III results of the PCS IV multicenter, randomized study on the suggested duration of androgen blockade for men with high risk prostate cancer found that such blockade combined with pelvic radiation can safely be reduced from 36 months to 18 months without changing outcomes. However, Dr. Anthony D'Amico stated that it is too soon to say. He did say that “36 months is not superior to 18 months; however, 18 months may still be inferior to 36.” So treatments and the timing (sequencing) of treatments is still undecided.

Later in March I will be attending the European Association of Urology (EAU) Meeting in Milan, Italy and I look forward to hearing about any new ideas on diagnosis and treatment of prostate cancer, all stages, which I will include in my next President's Message.

The Annual Board Meeting for CPCC was held in San Francisco at the end of January. Several important projects to be undertaken were discussed and Board Members are already designing and looking at ways to implement these new programs. Our other work continues, and we are still examining ways in which we can exert pressure on the U.S. Preventive Services Task Force to change their “D” recommendation which asserts that men without symptoms should not be tested. We may also be assisting efforts to create a much-needed Office of Men's Health in California.

Respectfully submitted,

MEREL GREY NISSENBERG

CLUES FOUND TO PROSTATE CANCER UPGRADING

Almost a third of men on active surveillance (AS) for prostate cancer had an upgrade in Gleason pathology grade during follow-up, biopsy results for almost 600 men showed. During median follow-up of 6.4 years, 31.3% of the localized cancers were upgraded.

D. Andrew Loblaw, MD, who practices at Sunnybrook Health Sciences Center in Toronto, reported at the Genitourinary Cancers Symposium that the proportion of men with upgraded tumors increased over time. “Gleason upgrading increases with time from diagnostic biopsies and might be higher in patients with initial Gleason 7 disease as opposed to Gleason 6,” Loblaw said.

Men with localized prostate cancer have a 10-year disease-specific survival exceeding 97%, making AS a reasonable option for many men. Considerable research has focused on factors that can identify men who have an increased risk of progression, but pathologic upgrading has received little attention, said Loblaw.

In an effort to gain some insight into those factors, he and his colleagues analyzed a prospective database of men entered into AS at Sunnybrook Health Sciences Center. Eligibility for AS required a biopsy Gleason score (GS) ≤ 6 and a PSA level ≤ 10 ng/mL. For men older than

70, the criteria consisted of a GS $\leq 3+4$ and a PSA level ≤ 15 ng/mL. Men had a repeat PSA every 3 months for 2 years and then every 6 months thereafter. Scheduled follow-up biopsies occurred after 1 year and then every 3 years until age 80.

The men and their physicians considered active treatment in the event of a PSA doubling time < 3 years, histologic upgrading, and clinical progression, as well as patient preference. As of August 2012, the database included 862 patients, including 592 who had at least one repeat biopsy. The subgroup of re-biopsied patients had a median age of 68 and a median baseline PSA of 5.5 ng/mL. Loblaw reported that 20.2, 0.3 and 79.4% of men had intermediate, high and low risk cancer, respectively.

Multivariate analysis of baseline and dynamic factors associated with upgrading identified clinical stage at diagnosis (OR 2.301, $P=0.0028$), percentage of involved prostate biopsy cores at diagnosis (OR 1.768, $P=0.0007$), PSA velocity > 2 (3.274, $P<0.0001$), and interval to re-biopsy (OR 1.437, $P=0.0102$).

Subsequently, 114 (62%) of men whose tumors were upgraded chose to undergo treatment. The investigators

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SHORTENED HORMONE THERAPY COURSE FEASIBLE FOR HIGH-RISK PROSTATE CANCER

Shortening the course of androgen blockade (AB) therapy from 36 months to 18 months when combined with radiation therapy (RT) does not appear to compromise outcomes in patients with high-risk prostate cancer, according to results of a randomized, multicenter, Phase III study reported at the 4th Annual Genitourinary Symposium held February 14-16, 2013 in Orlando, FL.

The study found that both overall survival (OS) and disease-specific survival (DSS) were similar in men who received 36 or 18 months of treatment.

AB is associated with uncomfortable and disturbing side effects that negatively impact quality of life (QOL). These include hot flashes, decreased libido, impotence, and fatigue. If a shorter course of AB effectively treated high-risk disease it could improve QOL for these men.

"A long list of side effects makes the lives of most of our patients quite miserable," commented lead author Abdenour Nabid, MD, associate professor at Centre Hospitalier de Universitaire de Sherbrooke in Sherbrooke, Canada. He hopes these results will convince doctors that they can stop AB after 1.5 years instead of 2 to 3 years.

The study enrolled 630 men with node-negative, high-risk prostate cancer treated with RT to the pelvic area and prostate bed. They were randomized to either 36 months (n = 310) or 18 months (n = 320) of AB therapy

(bicalutamide 50 mg for 1 month plus goserelin 10.8 mg every 3 months) given before, during, and after RT.

Patient characteristics were well balanced between the two arms. The majority of patients had stage T3-4 disease. At a median follow-up of 77 months, the 2 groups had no significant difference in biochemical failure, metastasis, bone-only metastasis, and cause of death. Mortality rates were 22.9% (71 men) in the longer-duration AB arm versus 23.8% (76 men) in the shorter-duration arm.

Of 147 deaths, 116 were deemed unrelated to prostate cancer. Five-year OS was 92.1% in the longer-duration arm vs 86.8% in the shorter-duration arm, and 10-year OS was 63.6% vs 63.2%, respectively. Five-year DSS was 97.6% and 96.4%, respectively, and 10-year DSS rates were 87.2% in both arms. Prostate cancer was reported as the main cause of death in 4.9% of the men.

"This study could change the standard of care from 36 months to at least 24 months and perhaps 18 months, if the full, peer-reviewed publication bears these findings out," said moderator Bruce Roth, MD, Professor, Department of Medicine, Washington University, St Louis, MO.

Presented at the 4th Annual Genitourinary Cancer Symposium, Orlando, FL, abstract 3.

OncLive, 14 February 2013

CHANGES IN SERUM PROSTATE-SPECIFIC ANTIGEN LEVELS AND THE IDENTIFICATION OF PROSTATE CANCER IN A LARGE MANAGED CARE POPULATION

Wallner LP, Frencher SK, Hsu JW, Chao CR, Nichol MB, Loo RK, Jacobsen SJ

BJU Int, 15 January 2013; Epub ahead of print

The use of a single, elevated PSA level to screen for prostate cancer is controversial given its reported low specificity and the questionable benefits of PSA screening on prostate cancer mortality. Current guidelines in the USA recommend against screening using a single PSA measurement. Previous studies suggest that using changes in PSA level over time, or PSA velocity, may improve the detection of prostate cancer and/or aggressive disease; however, this is also controversial as other studies suggest PSA velocity does not improve detection and may further contribute to the over-detection of indolent prostate cancer. Given the questions that remain regarding the use of the rate of change in PSA as a screening tool for prostate cancer because of previous conflicting studies, which to date have included small, highly selected populations, this study adds to the existing knowledge by assessing this question in general practice settings among a large, diverse population.

OBJECTIVE: To determine whether the rate of change in total serum prostate-specific antigen (PSA) levels accurately detects prostate cancer and to evaluate whether it adds any predictive value to a single measurement of serum PSA alone, in general practice settings.

MATERIALS AND METHODS: A retrospective cohort of 219,388 community-dwelling men, aged ≥ 45 years, en-

rolled in the Kaiser Permanente Southern California health plan, with no history of prostate cancer and at least three PSA measurements, were followed from 1 January 1998 to 31 December 2007, for the development of biopsy-confirmed prostate cancer. Annual percent changes in total serum PSA levels were estimated using linear mixed models. The accuracy of prostate cancer prediction was assessed for prostate cancer overall and for aggressive disease (Gleason score ≥ 7) and compared with that of a single measure of PSA level using area under the receiver-operating characteristic curves (AUCs).

RESULTS: The men in this cohort experienced a mean change of 2.9% in PSA levels per year and the rate of change in PSA increased modestly with age ($P \leq 0.001$). Annual percent changes in PSA accurately predicted the presence of prostate cancer (AUC = 0.963) and aggressive disease (AUC = 0.955) and had more predictive accuracy for aggressive disease than did a single measurement of PSA alone (AUC = 0.727).

CONCLUSIONS: Longitudinal measures of PSA improve the accuracy of aggressive prostate cancer detection when compared with a single measurement of PSA alone. Findings from this study provide insight into the usefulness of PSA velocity as a detection marker for aggressive prostate cancer.

ABIRATERONE CONTINUES TO SHOW SURVIVAL BENEFIT IN UPDATED INTERIM ANALYSIS

An updated interim analysis of the COU-AA-302 trial upholds the benefits of abiraterone acetate (Zytiga) in mildly symptomatic or asymptomatic patients with progressive metastatic castration resistant prostate cancer (mCRPC) untreated with prior chemotherapy. At a median follow-up of 27.1 months, radiographic progression-free survival (rPFS) and all secondary endpoints favored the abiraterone acetate arm.

The first interim analysis of COU-AA-302 was presented at the 2012 Annual Meeting of ASCO, and at that time, with a median follow-up of 22 months, results were so favorable for abiraterone acetate that an Independent Data Monitoring Committee recommended unblinding the study and offering all patients abiraterone acetate. COU-AA-302 was the first randomized controlled trial to show benefits for both overall survival (OS) and rPFS in mCRPC.

"The updated analysis resulted in expanded approval of abiraterone in untreated patients with metastatic CRPC and has expanded the way we treat this disease," said lead author Dana E. Rathkopf, MD, an assistant attending physician in the Genitourinary Oncology Service at Memorial Sloan Kettering Cancer Center in New York. "Abiraterone can be given pre-chemotherapy and is now approved across the spectrum of metastatic CRPC."

Abiraterone acetate is a specific inhibitor of CYP17 that blocks androgen biosynthesis and improves OS in mCRPC after treatment with docetaxel. The updated interim analysis presented at the 2013 Genitourinary Cancers Symposium, was prespecified, after 55% of the total OS events occurred. The present analysis confirms the benefits of abiraterone acetate in men with mCRPC who had not received prior chemotherapy.

The international COU-AA-302 trial was conducted at 150 sites around the world. Patients were randomized to receive oral abiraterone acetate 1000 mg plus oral prednisone 5 mg twice daily versus a placebo and prednisone. The co-primary endpoints were rPFS and OS.

At a median follow-up of 27.1 months, OS remained significantly superior with abiraterone acetate, with a median OS of 35.3 months in the experimental arm compared with 30.1 months in the control arm (hazard ratio [HR] = 0.79; 95% CI, 0.66 – 0.96; $P < .0151$). Abiraterone acetate (AA) was significantly superior to prednisone alone for the following endpoints: rPFS (median of 16.5 months for AA versus 8.3 months for prednisone [HR = 0.53; 95% CI, 0.45 – 0.62; $P < .0001$]); time to opiate use for cancer pain (not reached for AA versus median of 23.7 months [HR = 0.71; 95% CI, 0.59 – 0.85; $P = .0002$]); time to initiation of chemotherapy (median of 26.5 months for AA versus 16.8 months for prednisone [HR = 0.61; 95% CI, 0.51 – 0.72; $P < .0001$]); time to deterioration in ECOG performance status (12.3 months versus 10.9 months, respectively [HR = 0.83; 95% CI, 0.72 – 0.94; $P = .0052$]); and median time to PSA progression (11.1 months for AA versus 5.6 months for prednisone [HR = 0.50; 95% CI, 0.43 – 0.58; $P < .0001$]).

"Treatment with abiraterone reduced the risk of disease progression by 47%, and decreased the risk of death by 21%," Rathkopf said. "The updated analysis showed that the drug is safe and well tolerated with long-term exposure."

Presented at the 4th Annual Genitourinary Cancers Symposium, Orlando, FL, abstract 5.

OncLive, 15 February 2013

ANDROGENETIC ALOPECIA AND RISK OF PROSTATE CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

Amoretti A, Laydner H, Bergfeld W

J Am Acad Dermatol, 7 February 2013; Epub ahead of print

Background: Androgenetic alopecia (AGA) is a genetically determined skin condition strongly age dependent and androgens are assumed to play an important role in its development. A link between AGA and prostate cancer has been hypothesized because of their similar risk factors.

Objective: We sought to systematically review the evidence available on the association between AGA and risk of prostate cancer.

Methods: We searched the electronic databases MEDLINE and Cochrane for studies examining the association between AGA and risk of prostate cancer. We estimated pooled odds ratios (OR) and 95% confidence intervals. We also analyzed the OR for individual hair loss patterns, as defined by the Hamilton scale.

Results: A total of 7 case-control studies including 8994 patients – 4078 cases and 4916 controls – were reviewed. One cohort study was identified but did not meet our inclusion criteria. There was statistically significant association between vertex baldness and prostate cancer (OR 1.25; 95% confidence interval [CI] 1.09–1.44; $Z=3.13$; $P=0.002$). No statistically significant association between AGA (any pattern) and prostate cancer was identified (OR 1.03; 95% CI 0.93–1.13; $Z=0.55$; $P=0.58$).

Limitations: Only case-control studies, which may be subject to bias, met the inclusion criteria for this meta-analysis.

Conclusions: Vertex pattern AGA was associated with a significant increased risk of prostate cancer. Any pattern AGA did not show a significant increase in the risk of prostate cancer.

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CLUES TO PROSTATE CANCER UPGRADING

(Continued from page 1)

found that a higher proportion of the men that were treated had a GS of 8 (22% vs. 2.9% of untreated men), and treated patients had a significantly higher PSA velocity (1.2 vs. 0.42 ng/mL/y, $P=0.01$). The likelihood of upgrading increased over time, including 18.4% of men followed for up to a year to 36% of men followed for 7 to 8 years, 36% of men followed for 8 to 9 years, and 26% of men followed for more than 9 years.

Loblaw noted that intermediate-risk tumors had an upgrade probability more than double that of low-risk tumors – 1.9% per year compared with 0.75%, although the difference did not achieve statistical significance.

In the discussion, Eric Klein, MD, of the Cleveland Clinic, suggested the time has come to reconsider the focus of AS. "Should we say the goal of therapy or AS ought to be to avoid metastatic disease, rather than simply avoid death?"

Presented at the 4th Annual Genitourinary Cancer Symposium, Orlando, FL, abstract 1.

MedPage Today, 14 February 2013

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