US TOO PROSTATE CANCER EDUCATION & SUPPORT
HOTSHEET

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HIGHLIGHTS FROM ASCO'S 2008 GENITOURINARY CANCERS SYMPOSIUM—SAN FRANCISCO, CA, FEBRUARY 14-16, 2008

DENDREON PRESENTS DATA CORRELATING THE CUMULATIVE POTENCY OF PROVENGE® TO OVERALL SURVIVAL

Researchers from Dendreon Corporation presented data demonstrating the correlation of a measure of the cumulative potency of PROVENGE (sipuleucel-T), an investigational active cellular immunotherapy for hormone-refractory prostate cancer, with overall survival. This is the first time that an association between higher potency of an active immune therapy and increased patient survival has been reported. The correlation appeared to be independent of other important baseline prognostic factors.

In two Phase 3 trials, D9901 and D9902A, researchers evaluated cumulative product release parameters of PROVENGE, including CD54 upregulation (a measure of product potency defined as the increase of CD54 molecules expressed on Antigen Presenting Cells [APC] after incubation with the PROVENGE Antigen Delivery Cassette™ and the number of total nucleated cells (TNCs) among patients treated with sipuleucel-T (n=146).

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CELL GENESYS REPORTS ASSOCIATION BETWEEN IMMUNE RESPONSE AND PATIENT SURVIVAL IN PHASE 2 TRIAL OF GVAX IMMUNOTHERAPY FOR PROSTATE CANCER

Cell Genesys, Inc. (Nasdaq: CEGE) reported the results of an analysis examining the potential association between immune responses to GVAX immunotherapy for prostate cancer and increased patient survival in a Phase 2 trial in patients with metastatic, hormone refractory prostate cancer (HRPC). More than 400 patient-specific GVAX-induced antibody responses were identified in the sera of the treated patients by three different biochemical techniques confirming, as previously reported, that GVAX treatment results in a broad, multi-antigen immune response.

An ongoing analysis of these GVAX-induced antibody responses has shown that at least two of the antibody responses are associated with patient survival, an association that is independent of the dose and number of treatments administered. These data was presented by Dr. Thomas Harding

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LOW RISK SEEN IN MONITORING, NOT TREATING, SOME PROSTATE CANCERS

The vast majority of older men diagnosed with localized prostate cancer who initially forego treatment will die of something other than prostate cancer, researchers said last week. The finding supports the view that actively monitoring the cancer's progression until such time as treatment is needed - a strategy called watchful waiting - is a reasonable response to a diagnosis of early-stage disease for some men.

Using data from NCI's Surveillance, Epidemiology, and End Results (SEER) program, Dr. Grace Lu-Yao of The Cancer Institute of New Jersey and her colleagues asked what happened to 9,000 men who chose active surveillance rather than treatment in an era when screening with the prostate-specific antigen test increased.

After 10 years, 3 to 7 percent of those with low- or moderate-grade disease had died of prostate cancer, compared with 23 percent of men with high-grade cancers. The men were diagnosed between 1992 and 2002 and did not have treatment in the first 6 months after diagnosis. Half were over age 75.

Of the approximately 2,600 men who eventually underwent treatment for the disease, about half delayed therapy for more than a decade. Prostate cancers detected by screening tend to progress slowly, and many older men die with the disease, not of it.

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Co-Sponsors of the 2008 Genitourinary Symposium

ASCO American Society of Clinical Oncology · ASTRO American Society for Therapeutic Radiology and Oncology · SUO Society of Urologic Oncology

PATIENT SURVIVAL WITH GVAX *(Continued from page 1)*

and colleagues from Cell Genesys at the American Society of Clinical Oncology's Genitourinary Cancer Symposium held in San Francisco, CA.

Cell Genesys previously reported the results of two multicenter Phase 2 trials of GVAX immunotherapy for metastatic HRPC. The second of these two trials enrolled 80 patients. The serum of 65 patients (the total number for whom adequate sera were available) were examined to determine each patient's immune response to two specific antigens, HLA-A24 and FLJ14668, after GVAX treatment.

Thirty-four of 65 patients demonstrated an FLJ14668-specific antibody immune response. These 34 patients had a median survival of 43 months, compared to a median survival of 21 months achieved by the patients who did not generate anti-FLJ14668 antibodies (p=0.002). Twenty-two of these 65 patients received a dose of GVAX immunotherapy for prostate cancer comparable to that being evaluated in ongoing Phase 3 clinical trials. Of these 22 patients, 16 patients (73 percent) mounted an immune response to FLJ14668. These 16 patients achieved a median survival of 44.9 months. As previously reported, the median survival for all 22 patients in this treatment group was 35.0 months. Finally, of the 58 patients who were HLA-A24 genotype negative and therefore potentially able to mount anti-HLA-A24 specific antibody responses, 30 patients were found to be anti-HLA-A24 antibody positive. These 30 patients had a median survival of 43 months, compared to a median survival of 18 months in the patients who did not generate anti-HLA-A24 antibodies (p=0.05). Importantly, the apparent associations between the presence of these two specific antibody responses and survival were shown by multivariate analysis to be independent of both dose and duration of treatment.

"The findings reported today indicate a potential association between two specific GVAX-induced antibody responses and patient survival, an association consistent with the proposed mechanism of action for this product. We look forward to expanding these findings in a prospective analysis of the sera of patients treated in our two randomized controlled Phase 3 trials," stated Peter K. Working, Ph.D., senior vice president of research and development at Cell Genesys. "Since GVAX immunotherapy for prostate cancer is a multi-antigen product that can induce a broad immune response, we believe we have a unique opportunity to identify the widest possible array of specific antibody responses that may be associated with clinical benefit."

Cell Genesys is currently evaluating GVAX immunotherapy for prostate cancer in two Phase 3 multicenter, randomized, controlled clinical trials.

VITAL-1, which is fully enrolled with 626 patients, is designed to compare survival duration with GVAX cancer immunotherapy against Taxotere® (docetaxel) chemotherapy plus prednisone in asymptomatic patients with metastatic HRPC.

VITAL-2, which the company expects to fully enroll with approximately 600 patients in the first half of 2009, is designed to evaluate the safety and efficacy of GVAX immunotherapy for prostate cancer used in combination with Taxotere chemotherapy compared to the use of Taxotere chemotherapy and prednisone in symptomatic patients with metastatic HRPC. The primary endpoint again is an improvement in survival.

Abstract #261 "Identification of antibody responses induced in patients with metastatic hormone-refractory prostate cancer (mHRPC) treated with GVAX immunotherapy for prostate cancer." T. Harding.

ASCO 2008 Genitourinary Symposium
PRNewswire-FirstCall, 15 February 2008

WATCHFUL WAITING

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This study provides additional support for the use of active surveillance of localized prostate cancer in older men, particularly among those with lower grade tumors, commented Dr. Howard Sandler of the University of Michigan at the meeting.

Abstract #10 "Disease trajectory of untreated localized prostate cancer in elderly men: A population-based study." G. Lu-Yao, M.J. Barry, A. Zietman, et al.

ASCO 2008 Genitourinary Symposium
NCI Cancer Bulletin, 19 February 2008

PROVENGE®

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CD54 is a costimulatory molecule which serves as a marker for APCs. Its expression is increased when APCs become activated and this upregulation of CD54 serves as a potency release assay for PROVENGE.

Results showed that PROVENGE patients experienced improved survival if they received more cells across the three doses of PROVENGE (higher cumulative TNC count (p=0.019)) or higher cumulative CD54 upregulation values (p=0.009). The effect on survival for TNCs appeared to reflect in part the patients' baseline prognostic factors. However, the CD54 upregulation ratio appeared to be an independent predictor of survival in patients who received PROVENGE, as the correlation remained strong even after adjusting for baseline prognostic factors (p=0.022).

"We have been able to show a correlation between patient survival and a measure of the cumulative potency of PROVENGE; such a correlation between product potency and clinical outcome has not been previously demonstrated with an active immunotherapy," said Mark Frohlich, MD, chief medical officer of Dendreon. "These data provide further evidence that sipuleucel-T is actively engaging the immune system in a clinically meaningful way that prolongs patient survival."

PROVENGE may represent the first product in a new class of active cellular immunotherapies (ACIs) that are uniquely designed to use live human cells to engage the patient's own immune system with the goal of eliciting a specific long-lasting response against cancer. In clinical studies, patients typically received three doses of PROVENGE over a one-month period as a complete course of therapy.

For more information about Dendreon and its programs, visit their website <http://www.dendreon.com>.

Abstract #21"Cell Number and CD54 Expression in Sipuleucel-T Correlate with Survival in Metastatic Androgen Independent Prostate Cancer." R.B. Sims, N.M. Provost, D.L. Urdal, Y. Xu, M.W. Frohlich.

ASCO 2008 Genitourinary Symposium
PRNewswire-FirstCall, 14 February 2008

Radiation Reduces Mortality Risk of Recurrent Prostate Cancer

Ten-year prostate cancer survival was substantially higher for men given salvage radiotherapy alone or with hormonal therapy than for those who received no salvage therapy (86%, 82%, and 62%, respectively, P0.0001), reported Bruce Trock, M.D., of Johns Hopkins University, and colleagues.

The advantage extended even to those who waited for up to two years after biochemical recurrence to start radiotherapy, Dr. Trock told attendees at the American Society of Clinical Oncology Genitourinary Cancers Symposium. Early salvage treatment was critical; salvage radiotherapy improved prostate cancer-specific survival only if given 2 years after biochemical recurrence.

Currently only about a quarter of men with biochemical recurrence receive radiation and about half are not treated, commented Howard M. Sandler, M.D., of the University of Michigan Health System in Ann Arbor, who moderated a press conference where the results were presented. "By showing that there's a survival advantage to salvage radiotherapy, this study might increase the utilization of that particular androgen strategy after surgery," he said.

When adjuvant radiation therapy is given, Dr. Trock said, it is often done immediately after their surgery for men with high-risk features because trials have shown that doing so can prolong survival. If the findings of the retrospective study are validated, it may be safe to hold off on adjuvant radiation until recurrence, Dr. Trock said. "It could eventually support a way to determine who should get immediate adjuvant radiation and who could wait until the time of recurrence to have salvage therapy," he said.

Previous studies had been too small with not enough follow-up to answer the question of survival, and none looked at the benefit of waiting until overt metastasis developed, he said. So his group analyzed survival among 635 men treated at Johns Hopkins who developed prostate cancer recurrence after radical prostatectomy. Most (397) received neither salvage radiotherapy nor hormonal therapy, 160 underwent salvage radiotherapy alone, and 78 got both. Over the median follow-up of six years after recurrence, 18% of the men died from prostate cancer.

The effect of salvage radiotherapy appeared to differ by PSA doubling time (P<0.0001). Nearly all the men with a PSA doubling time of six months or more survived to five years regardless of radiotherapy after recurrence (98% for both). Men at higher risk with a doubling time of less than six months had just as good five-year survival if they had salvage radiotherapy (95%) (HR 0.14, 95% CI 0.05-0.39), but survival fell substantially -- to 60% -- among those who did not get radiation.

Ten-year survival showed a similar benefit for radiation: it was more pronounced among those with faster doubling times (86% versus 75% for doubling time of six months or longer and 82% versus 30% with doubling time of less than six months). Although it would be expected that prognostic factors would be different for men who received treatment compared with those who did not, the results were not changed after adjustment for Gleason score, year of surgery, and time from surgery to recurrence.

Survival also differed by PSA response to salvage radiotherapy with the highest survival rates among those with a stable drop in PSA compared with those whose PSA did not fall after treatment or who did not receive treatment. Surprisingly, though, there was still a survival benefit for men whose PSA fell initially and then rose again, Dr. Trock said.

However, he emphasized repeatedly, the findings were preliminary because of the retrospective nature of the study. He said a clinical trial is needed to validate the results.

Abstract #85 "Prostate cancer-specific survival in men with biochemical recurrence after radical prostatectomy: impact of salvage radiotherapy vs. observation." B. Trock, M. Han, S.J. Freedland, E.B. Humphreys, T.L. DeWeese, A.W. Partin, P.C. Walsh.

ASCO 2008 Genitourinary Symposium
MedPage Today, 14 February 2008

Bisphosphonate Effective Long Term in Prostate Cancer Hormone Therapy

Zoledronic acid (Zometa®, ZA) significantly increased T scores in both hips and the lumbar spine (P0.05) over more than a year of use in older high-risk men, according to a small randomized trial presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium. This was true even when the drug was started later in the course of therapy, reported William R. Broderick, MD, of Loyola University Medical Center in Maywood, IL, and colleagues.

Starting ZA later may allow men to avoid the drug's side effects of bone pain and renal impairment until bone mineral density (BMD) changes appear, Dr. Broderick said. Men who are at lower risk based on comorbidities and annual screening of BMD may be able to first pursue lifestyle modification, including exercise and smoking cessation, said co-author Nirmala Bhoopalam, MD, of Loyola and the VA Hospital in Hines, IL.

Longer-term use among men on androgen deprivation therapy (ADT) has not been studied; nor was there proof it would prevent bone loss if not started at the same time as ADT, the researchers noted. So, they randomized 93 men with nonmetastatic prostate cancer treated at VA medical centers to receive a double blind intravenous infusion every three months of 4 mg ZA or placebo. Men in both groups were also started on calcium, vitamin D, and weight-bearing exercise. Mean age was 70.5 years; 55% were Caucasian, 41% were African-American, and 4% were Hispanic, and mean BMI was 29.4. None of the men had osteoporosis at baseline, defined as a BMD T score of -2.0 or less as measured by dual energy X-ray absorptiometry. Follow-up scans were done at six and 12 months.

Overall, T-score percent change was significantly better with active treatment than placebo for the left and right hip (both P<0.05) and most dramatically so for the lumbar spine (6% increase versus more than 1% de-

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WHICH MEN ARE LIKELY TO HAVE PERSISTENT PROSTATE CANCER?

"Radiotherapy offers the chance of a cure for most patients," explained Mark K. Buyyounouski, MD, MS, attending physician in the radiation oncology department at Fox Chase Cancer Center. "For some, however, an elevated PSA level after treatment indicates the cancer is still around or has come back. Our new study shows how we can use biopsy information prior to treatment to help us predict which patients are most likely to still have disease after treatment. With this knowledge, we can better tailor treatment."

In the study presented by Buyyounouski, researchers compared prostate biopsies taken before treatment with those taken again two years after treatment. All the study volunteers had cancers that were intermediate or high risk. "Larger tumors are believed to be more likely to persist after treatment, but what defines a larger tumor has been controversial," said Buyyounouski. "What we found was that a high percentage of cancer observed in the biopsy before treatment correlated with a higher probability of a positive biopsy afterwards. This information is important because locally persistent cancer may result in later spread of the disease and possibly death."

Buyyounouski explained that other researchers have explored the use of biopsy information to identify higher risk of recurrence for men with prostate cancer. Using a percentage of positive biopsy cores has been advocated by some, but these types of studies compared the cores to PSA level after treatment and not post-treatment biopsies. "This study is important because the percentage of cancer seen in the biopsy before treatment is directly correlated with cancer seen in the biopsy in the same location two years after treatment," he explained.

Buyyounouski said current sophisticated radiation technologies such as IMRT could allow physicians to tailor treatment for these patients.

Abstract #88 "Predicting local persistence of prostate cancer using percentage of adenocarcinoma in pretreatment biopsy tissue." M.K. Buyyounouski, T. Li, T. Al-Saleem, E. Horwitz, A. Pollack.

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IMMEDIATE ANDROGEN SUPPRESSION QUESTIONED FOR NODE-POSITIVE PROSTATE CANCER

Neither overall nor disease-specific survival were significantly higher for men who held off than for those who started androgen suppression (AS) immediately, said Fritz H. Schröder, MD, PhD, of Erasmus Medical Center in Rotterdam, The Netherlands and colleagues. The issue of timing remains unresolved, though, because the large randomized trial was underpowered, he added. The power of the study to show a 50% difference between treatment groups was only 80%.

Nevertheless, the findings may challenge early endocrine therapy as the standard, commented Bruce J. Roth, MD, of Vanderbilt-Ingram Cancer Center in Nashville, TN, who chaired the conference program committee. "Now it's really a toss-up," he said. "It needs to be driven by patient decision after a lengthy discussion of what the implications of a longer duration of hormonal therapy are." The benefits in biochemical recurrence and potentially survival from early AS come at the price of increased cardiovascular mortality from additional years of hormonal therapy, Dr. Roth noted.

Early hormone therapy became the gold standard in the US primarily based on an Eastern Cooperative Oncology Group (ECOG) trial published in the New England Journal of Medicine in 1999 that showed a survival benefit with 7 years of follow-up. "Unfortunately, what most people don't realize was the study was heavily underpowered and unable to make those conclusions definitively," Dr. Roth said. The trial was designed to be a 230-patient trial but was stopped at 97 patients for lack of accrual.

Dr. Schröder's group undertook the European Organization for Research and Treatment of Cancer study 30846 to answer the same question of timing. Like the ECOG trial, it faced slow accrual and was closed in 1998 with 234 patients who had non-metastatic T2 to T3 prostate cancer and one to three positive nodes. Participants received no treatment for their primary prostate cancers. They were randomized to immediately start endocrine therapy with monthly injections of goserelin (Zoladex®) plus cyproterone acetate during the first four weeks or to the same regimen only upon disease progression. Nearly all patients in the delayed-treatment group started AS within four years. Delayed therapy offered a quality-of-life window of 18 months, Dr. Schröder said.

After a median 13 years of follow-up, there were no significant differences between the immediate and delayed treatment groups in overall survival (median 7.6 vs. 6.1 years, P=0.166). Causes of death were similar between groups, although prostate cancer-specific mortality was slightly higher with delayed than immediate endocrine therapy (60.9% vs. 58%).

"Without a larger study, which may be impossible to conduct at this point, one has to just take that data for what it is — not definitive," he added.

Abstract #5 Early versus delayed endocrine treatment of pN1-3 M0 prostate cancer without local treatment of the primary tumor: results of European Organization for the Research and Treatment of Cancer protocol 30846 after 13 years of follow-up -- a phase III study." F.H. Schröder.

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ZOMETA®

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crease, P<0.05). Among the 50 patients who had been on ADT for less than a year at baseline, BMD increased 5.95% with ZA but decreased 3.2% with placebo (P=0.0044). Among the 43 patients entering the study more than a year after initiating ADT, BMD increases were greater with ZA (6.1% vs. 1.6%, P=0.0005).

BMD in left and right hips also increased in both groups with active treatment (P<0.05), which is important, Dr. Bhoopalam said, because hip fractures are the type most worrisome to patients. However, the study was not of long enough duration to see an impact on fracture incidence.

Abstract # 177 "A phase III trial of zoledronic acid (Z) to prevent osteoporosis in men on early and prolonged androgen deprivation therapy (ADT) in a high risk VA population." W.R. Broderick.

ASCO 2008 Genitourinary Symposium
MedPage Today, 18 February 2008