Prostate Cancer Vaccine Provenge®: Is it really worth it?
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Objectives:

1. Overview on prostate cancer epidemiology, risk factors, and current treatment
2. Literature Review of Evidence that lead to FDA’s recent approval of Provenge®
3. Conclusion – Weighing the risks vs benefits of receiving Provenge®
I. Overview
   A. Prevalence
      1. Prostate cancer is the most common cancer, other than non-melanoma skin cancer, and the second leading cause of cancer-related death in men in the United States
      2. On January 1, 2008, in the United States there were approximately 2,355,464 men alive who had a history of cancer of the prostate
      3. In the U.S. in 2011: 240,890 New cases and 33,720 Deaths
      4. Approximately $9.9 billion spent each year in the U.S. on Prostate Cancer treatment

II. Risk Factors
   A. Age
      1. Most men with prostate cancer are over 65. This disease is rare in men under 45
      2. Risk increases with age
   B. Family History – 15% chance if Brother or Father are diagnosed
   C. Race
      1. African-American men have a higher incidence and at least double the mortality rate compared with men of other racial and ethnic groups
      2. Asians, Native Americans, and vegetarians have the lowest rates
   D. Epidemiologic studies have suggested that nutritional factors such as reduced fat intake and increased soy protein may have a protective effect against the development of prostate cancer
      1. High saturated fat intake – increases testosterone levels
      2. Soybean (isoflavones) - Prophylactic effect on Prostate Cancer

III. Screening & Diagnosis
   A. DRE (Digital Rectal Exam)
      1. The prostate is checked for hard or lumpy areas
   B. PSA (Prostate-Specific Antigen)
      1. Elevated PSA levels possibly indicate Prostate, Benign Prostatic Hyperplasia (BPH)
      2. Gives the Physician a reason to check for further signs of Prostate Cancer
      3. Benefits - Ability to detect early stages
      4. Harms – Screening detects some Prostate Cancers that would never have caused important clinical problems leading to over-treatment (Incontinence/Impotence)
      5. Guidelines recommend screening of high risk (African American men, Father, Brother, or son diagnosed before age 65) start at age 45
      6. Multiple family members affected before age 65 ; age 40
      7. ACS recommends that men with no symptoms of prostate cancer who are in relatively good health and can expect to live at least 10 more years have the opportunity to make an informed decision with their doctor about screening after learning about the uncertainties, risks, and potential benefits associated with prostate cancer screening – consider talk at age 50
C. Tumor Ultrasound & Biopsy
1. Determines Gleason score
2. Scores range from 0 to 10 (high grade)
3. Looks at tumor pattern
4. High-grade tumors tend to grow quickly and spread more

IV. Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>PSA Level</th>
<th>Gleason Score</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>T1a, T1b, or T1c</td>
<td>N0</td>
<td>M0</td>
<td>Lower than 10</td>
<td>6 or lower</td>
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<tr>
<td>IIA</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
<td>Lower than 10</td>
<td>6 or lower</td>
</tr>
<tr>
<td></td>
<td>Any T1a or T2a</td>
<td>N0</td>
<td>M0</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

A. Stage I
1. Low Gleason scores (2-4); PSA < 10
2. Generally, these tumors grow slowly and may never cause health problems
3. Watchful waiting is a common way of managing these cancers

B. Stage II
1. Gleason score (6-7); PSA < 20
2. Surgery and/or radiation therapy
3. But for older men whose cancer is not causing any symptoms, watchful waiting may be enough

C. Stage III
1. Spreading to seminal vesicles only; Any Gleason score; Any PSA level
2. Radiation and hormone therapy in combination, hormone therapy alone, and surgery (prostatectomy) and nearby lymph nodes

D. Stage IV
1. Spreading to tissues next to the prostate - lymph nodes, bones
2. These cancers are not considered curable
3. Hormone therapy, radiation, and surgery to relieve symptoms, Chemotherapy and vaccine trial to increase survival
V. Clinical Presentation/Complications³ (Appendix A)

A. Local Spreading - Cancer extends beyond the organ in which it started
   1. Early Stage - Asymptomatic
   2. Locally Invasive - Obstructive voiding symptoms (hesitancy, frequency, decreased force of stream, impotence)

B. Metastatic - cancer has moved to an entirely new part of the body, often through the lymph system or blood
   1. Lower extremity edema, anemia, weight loss, back pain
   2. Severe pain from pathologic fractures, spinal cord compression

VI. Current Treatments¹⁷

Fig. 3

A. Watchful waiting or active surveillance
   1. Advantages - Avoid possible side effects, QOL less affected, Risk of unnecessary treatment of small, indolent cancers are reduced
   2. Disadvantages - Risk of progression, Increased anxiety, Frequent exams and biopsies

B. Surgery
   1. Prostectomy

C. Hormone therapy
   1. Anti – Androgens
      a. Mechanism of Action - Androgen receptor inhibitor; prevents testosterone stimulation of cell growth in prostate cancer
      b. Bicalutamide (Casodex®)
         1. Oral: 50 mg once daily
         2. Tolerable at high doses
      c. Flutamide (Eulexin®)
         1. Oral: 250 mg 3 times/day
         2. ADV: Diarrhea, breast tenderness, nipple tenderness, hepatotoxicity
      d. Nilutamide (Nilandron®)
         1. Oral: 300 mg daily for 30 days starting the same day or day after surgical castration, then 150 mg/day
2. ADV: Mild nausea, alcohol intolerance, diminished ocular adaptation to darkness, rarely, interstitial pneumonitis occurs

e. Mechanism of Action
   1. Anti-androgens bind to ARs and competitively inhibit the binding of testosterone and dihydrotestosterone

f. Efficacy
   1. All have been proven equally effective but vary in toxicity and cost

2. Others
   a. Ketoconazole (Nizoral®)
      1. Oral: 400 mg 3 times/day
      2. Mechanism of action – androgen synthesis inhibitor: effectively reduces the testosterone production in both adrenals and testes
      3. Off-label indication

3. Medical castration
   a. Luteinizing hormone-releasing hormone agonists (LH-RH)
      1. Leuprolide (Lupron®, Eligard®)
         i. Eligard®: SQ
            1. 7.5 mg monthly or 22.5 mg every 3 months or 30 mg every 4 months or 45 mg every 6 months
         ii. Lupron®: 1 mg/day SQ
             Lupron Depot®: 7.5 mg/dose given monthly (every 28-33 days)
             Lupron Depot®-3: 22.5 mg every 3 months
             Lupron Depot®-4: 30 mg every 4 months
   
   2. Goserelin (Zoladex®)
      i. Prostate cancer, palliative: SubQ:
         o Monthly implant: 3.6 mg every 28 days
         o 3-month implant: 10.8 mg every 12 weeks
      ii. Prostate cancer, treatment (in combination with flutamide and radiotherapy; begin 8 weeks prior to radiotherapy):
          o Combination monthly/3-month implant:
             3.6 mg implant, followed in 28 days by 10.8 mg implant
          o Monthly implant (alternate dosing):
             3.6 mg; repeated every 28 days for a total of 4 doses
   
   3. Mechanism of Action
      i. Binds to GnRH receptors on pituitary gonadotropin-producing cells, causing an initial release of both LH and FSH and a subsequent increase in testosterone production from testicular cells. After ~1 week of therapy, GnRH receptors are down-regulated on the gonadotropin-producing cells, causing a decline in the pituitary response

4. Surgical castration
   a. Orchiectomy – removal of testicles
   b. Side Effects - Hot flashes, impaired sexual function, loss of desire for sex, and weakened bones

D. Chemotherapy
   1. Docetaxel (Taxotere®) I.V.: 75 mg/m² every 3 weeks
   2. Cabazitaxel (Jevtana®) I.V.: 25 mg/m²/dose once every 3 weeks
   3. Abiraterone (Zytiga®) Oral: 1000 mg once daily
   4. The only anticancer treatments that have demonstrated a prolongation of survival in RCTs for patients with castration-resistant prostate cancer

E. Emerging Therapy
   1. Cryosurgery
2. High-intensity focused ultrasound
3. Proton beam radiation therapy

F. Cancer vaccine therapy
   a. Sipuleucel-T (Provenge®) – The First FDA-approved autologous cellular immunotherapy

VII. Sipuleucel-T
A. Indication
   1. Asymptomatic or minimally symptomatic metastatic castrate resistant (hormone refractory) prostate cancer
   2. Usually given after surgery or when other medications have been tried without success

B. Mechanism of Action
   1. Autologous cellular immunotherapy (8,10,11)
      a. Trains the immune system to fight tumors. Referred to as a “vaccine” even though it treats disease instead of preventing it.
      b. Three days before each dose a sample of the patients’ white blood cells are taken at a cell collection center using a procedure called leukapheresis. This procedure takes about 3-4 hours. The sample will be sent to the manufacturer and combined with a protein to prepare a dose of sipuleucel-T injection
      c. (Fig 4.) Each dose of sipuleucel-T contains autologous mononuclear cells, including antigen presenting cells, that were activated ex vivo via culture with a recombinant fusion protein consisting of prostatic acid phosphatase (PAP) linked to granulocyte-macrophage colony stimulating factor (GM-CSF), an immune cell activator
      d. The goal of immunotherapy is to stimulate the body's natural defenses
      e. These cells attack and destroy, or at least prevent the proliferation of, cancer cells
      f. Specificity is attained by intentionally exposing the WBCs to a particular antigen associated with the prostate cancer. This exposure “trains” the white blood cells to target and attack the prostate cancer cells
      g. Clinically, this is expected to result in a decrease in the size and/or number of cancer sites, an increase in the time to cancer progression, and/or an increase in survival of the patient

Fig. 4
VIII. Sipuleucel-T vs Docetaxel

A. Sipuleucel – T

1. Treatment consists of three infusions at approximately two week intervals for one month
2. The cost for a complete course of treatment of three infusions is $93,000, which includes the cost of administration
3. For the extended survival period of 4.1 months with sipuleucel-T, the average monthly expenditure is $22,683 per month of added median survival
4. The average life expectancy for patients with advanced metastatic prostate cancer is 18 – 24 months
5. Sipuleucel-T prolongs survival beyond 4 months, compared to 2.4 months with the current standard therapy, docetaxel (Taxotere)

B. Docetaxel

1. Drug of choice for metastatic, hormone-refractory prostate cancer
2. Administered every three weeks for a total of 10 cycles. The cost of one cycle of docetaxel is $4,000, or a total of $40,000 for all 10 cycles
3. The median extended survival period for prostate cancer patients receiving docetaxel is 2.4 months, and an average cost of $16,667 per month of added survival
   a. This cost does not take into consideration the serious AEs associated with docetaxel (neutropenia, infections, anemia, N/V). These AEs can lead to extended
treatments and, therefore, increase the total cost of care, whereas common AEs with sipuleucel-T are infusion-related and short-lived

4. Quality of life has been reported to be superior with sipuleucel-T

IX. Reimbursement

1. The high cost of sipuleucel-T ($93,000) has attracted the scrutiny of federal agencies involved with health care spending. The Centers for Medicare and Medicaid Services (CMS) initiated a 12-month process, called the National Coverage Assessment (NCA), to decide under which circumstances it would cover the expensive treatment

X. Kantoff et al.6


<table>
<thead>
<tr>
<th>Objective</th>
<th>To show a significant effect on the time to disease progression and overall survival in CRPC patients with sipuleucel-T</th>
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<tbody>
<tr>
<td>Design</td>
<td>Randomized, placebo controlled, multi-center (75)</td>
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<tr>
<td>Patient Population</td>
<td>512 men with metastatic-castration prostate cancer with a mean age of 71 years old</td>
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<tr>
<td>Inclusion Criteria:</td>
<td>500 patients enrolled to analyze 304 deaths</td>
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<td>Power of 88% to detect a relative reduction risk of death of 31%</td>
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<td>Metastatic castration – resistant prostate cancer</td>
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<td>An expected survival of at least 6 months</td>
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<td>Men with any Gleason score</td>
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<td>Asymptomatic and minimally symptomatic</td>
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<td></td>
<td>Serum PSA ≥ 5 ng/mL</td>
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<td>Serum Testosterone &lt; 50 ng/dL</td>
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<td>Progressive disease</td>
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<td>Exclusion Criteria:</td>
<td>(ECOG) Eastern Cooperative Oncology Group performance status of 2 or more</td>
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<td>Visceral metastasis</td>
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<td>Pathological long bone fractures</td>
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<td>Spinal cord compression</td>
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<td>Tx &lt; 28 days</td>
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<td>Systemic glucocorticoids</td>
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<td>External beam radiation</td>
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<td>Surgery</td>
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<td>Systemic therapy for PC (except medical or surgical castration)</td>
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<td></td>
<td>Initiation/Discontinuation Bisphosphonate therapy</td>
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<td>Previous Tx with more than two chemotherapy regimens</td>
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<td>Undergone Chemotherapy within the previous 3 months</td>
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<td>Endpoints</td>
<td>Prognostic factors known to be adversely correlated with overall survival</td>
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<tr>
<td></td>
<td>Increased PSA levels</td>
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<td></td>
<td>Lactate dehydrogenase</td>
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<td>Alkaline phosphatase</td>
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<td>Bone metastasis</td>
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<td></td>
<td>Increased Gleason score</td>
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<td>Decreased performance status</td>
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<td></td>
<td>Presence of pain</td>
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<tr>
<td>Intervention and Methods</td>
<td>Patients were randomly assigned in a 2:1 ratio to receive either sipuleucel-T or placebo every 2 weeks, for a total of 3 infusions.</td>
</tr>
</tbody>
</table>
|            | Overall disease progressions were monitored at weeks 6, 14, 26 and 34 and every 12
weeks thereafter.
  o An increase of at least 50% in the sum of the products of diameters for index lesions
  o New appearance or unequivocal progression of nonindex lesions
  o At least two new lesions on bone scanning
  o New pathologic fracture or spinal cord compression
  • Median follow up of 34 months

Results

Primary Endpoint – Overall survival
• (61.6%) 210 of the 341 patients died in the sipuleucel-T group;
• (70.8%) 121 of the 171 patients died in the placebo group
• Hazard Ratio for death – 0.78
• 22% relative reduction in the risk of death (P=0.03)
• **4.1 month improvement in the median survival**
  Improvement in the rate of 3-year survival
  o 31.7% Sipuleucel – T vs 23% Placebo

Fig 6.

Secondary Endpoints
• Effect on the time to objective disease progression
  o The median time to objective disease progression was 14.6 weeks (3.7 months) in the sipuleucel-T group and 14.4 weeks (3.6 months) in the placebo group (hazard ratio, 0.95; 95% CI, 0.77 to 1.17; P=0.63)
• Safety
  o The treatment was associated with infusional adverse effects, including fever and chills, which were merely grade 1 or 2 in severity

Author’s Conclusion
“…sipuleucel-T prolonged survival among men with asymptomatic or minimally symptomatic metastatic castration-resistant prostate cancer. However, no significant effect on the time to objective disease progression was observed.”

Strengths & Weaknesses

Strengths
• Large Sample Size
• Increased External Validity – various centers

Weakness
• No explanation of how exactly Sipuleucel-T prolongs survival
Small, EJ; Schellhammer, PF, Higano, CS; et al. Placebo-Controlled Phase III Trial of Immunologic Therapy with Sipuleucel-T (APC8015) in Patients with Metastatic, Asymptomatic Hormone Refractory Prostate Cancer JCO July 1, 2006:3089-3094

**Objective**
To evaluate the safety and efficacy of sipuleucel-T in a placebo-controlled study

| Design | 19 U.S. Centers  
127 patients with asymptomatic metastatic hormone refractory prostate cancer (HRPC) were randomly assigned in a 2:1 ratio to receive three infusions of sipuleucel-T (n = 82) or placebo (n = 45) every 2 weeks  
- Median age-73 years of age  
- Median Gleason score – 7; |

| Patient Population | Inclusion Criteria  
- Confirmed adenocarcinoma of the prostate with radiologic evidence of metastases  
- Serum testosterone < 50 ng/dL  
- An expected survival of at least 3 months  
- Prior chemotherapy if 6 months had elapsed or 3 months with a CD4+ T-cell count > 400  
- Concurrent Bisphosphonate therapy if initiated 30 days before index date and not continued throughout study |

| Exclusion Criteria |  
- HIV, Leukemia, Hep B & C,  
- Patients who required concurrent systemic corticosteroids or prior immunotherapy  
- Cancer-related bone pain  
- Visceral Metastasis |

| Endpoints | Time to Disease Progression  
- Progressive disease on serial radiographic imaging tests  
- New cancer-related pain  
- Spinal cord compression  
- Nerve root compression  
- Pathologic fracture |

| Intervention & Methods | A centrally administered, block random assignment method encompassing all study centers was employed to assign patients to treatment in a 2:1 ratio  
Three sipuleucel–T infusions were given on weeks 0, 2, and 4.  
Every 8 to 12 weeks  
- Safety (physical examinations, adverse event assessments, laboratory tests)  
- Disease progression (radiographic imaging studies and pain assessment) |
### Results

- **Primary Endpoint** – Time to disease progression (TTP) (Fig. 7)
  - A total of 115 patients (90.5%) contributed a progression event to the primary analysis of TTP
  - Median TTP
    - Kaplan-Meier method
    - 11.7 vs. 10.0 weeks in sipuleucel-T group and placebo, respectively (P=0.052)

- **Secondary Endpoints**
  - Median overall survival (Fig. 8)
    - 25.9 vs 21.4 months in Sipuleucel-T group and placebo, (P= .01)
  - Safety/Toxicity
    - 95% received all three doses
    - 24.4% experienced a grade 3 or 4 toxicity in both groups
    - No single grade 3 or 4 toxicity occurred in more than 6% of patients
    - Rigors and pyrexia - infusion related

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#### Author's Conclusions

“...While sipuleucel-T fell short (P = .052) of demonstrating a statistically significant difference in TTP, it may provide a survival advantage to asymptomatic HRPC patients. Supportive studies are underway to confirm this effect. An immunotherapeutic approach such as sipuleucel-T may have more gradual antitumor effects that will be more apparent in patients with less aggressive disease.”

### Strengths & Weaknesses

- **Strengths**
  - Various centers in U.S.
  - Post study analysis of prognostic outcomes to assess the robustness of the survival benefit
  - Post study analysis of chemotherapy use

- **Weaknesses**
  - Small sample size
  - Funded by Dendreon Corporation
XII. Beer, et al

Beer, TM; Bernstein, GT; Corman, JM, et al. Randomized trial of autologous cellular immunotherapy with sipuleucel-T in androgen-dependent prostate cancer. Clin Cancer Res July 1, 2011 17; 4558

<table>
<thead>
<tr>
<th>Objective</th>
<th>To determine the biologic activity of sipuleucel-T in androgen-dependent prostate cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>• Double-blind, randomized, controlled trial</td>
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<tr>
<td></td>
<td>• Power</td>
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<tr>
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<td>o Based on a sample size of 159 patients</td>
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<td>o Accrual period of 3 years and a 2-year follow-up period</td>
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<td>o This sample size was expected to obtain 108 events, providing 80% power to detect an increase from 1 year to 1.75 years in median time to BF at the 0.05 level of significance using a 2-sided log-rank test</td>
</tr>
</tbody>
</table>

| Patient Population | • Patients with prostate cancer detectable by serum prostate-specific antigen (PSA) following radical prostatectomy |
|                   | • Inclusion Criteria:                                           |
|                   |   o An increase in serum PSA as the only sign of disease recurrence following a radical prostatectomy carried out at least 3 months and not more than 10 years prior to registration for histologically confirmed prostate cancer |
|                   |   o Patients who experienced their first PSA recurrence within 2 years of initial therapy were eligible regardless of the Gleason score; those who experienced their first PSA relapse between 2 and 10 years following initial therapy were eligible only if the Gleason score was ≥7 |
|                   |   o Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1 |
|                   |   o Life expectancy of at least one year                        |
|                   |   o Age between 18 and 80 years                                  |
|                   |   o Negative serology for HIV, human T-lymphotropic virus type 1 or 2, and Hep B and C were required, as were adequate hematologic, renal, and hepatic function. |
|                   |   o The tumor specimen had to be positive for PAP by immunohistochemistry. |
|                   |   o Therapeutic PSA response to primary therapy was required to have been < 0.4 ng/mL. |
|                   |   o Prior chemotherapy was permitted provided at least 4 months had elapsed |
|                   | • Exclusion Criteria                                             |
|                   |   o Prior orchiectomy, immunotherapy, or therapy with experimental agents |
|                   |   o History of other prior malignancies within 5 years of study entry |
|                   |   o Patients whose post-prostatectomy PSA reached 20 ng/mL       |
|                   |   o Concurrent participation in other clinical trials involving investigational agents was prohibited |

| Endpoints | • Primary Endpoint                                               |
|           | o Time to biochemical failure                                     |
|           |   ▪ Two PSA measurements ≥ 3.0 ng/ml                              |
|           |   ▪ Samples taken at baseline, weeks 0,2,13,25 and every 3 months until distant failure |
|           | • Secondary Endpoints                                            |
|           | o PSA doubling time (PSADT)                                      |
|           |   ▪ Has been shown to be the single strongest predictor of PC related mortality in this patient population |
|           | o Time to distant failure (Observation of metastasis on bone scan or CT scan) |
|           |   ▪ Scans performed every 12 months after BF, PSA ≥10ng/mL, or disease pain |
|           | o Immune Response                                                |
• Measured by APC activation via CD54 upregulation at weeks 0, 2, 4
• Correlations between immune parameters and overall survival have been proven in previous smaller studies
• Overall Survival
• Safety

**Intervention and Methods**
- Interventions and Methods
  - Patients received 3 to 4 months of androgen suppression therapy
  - Proven Link between prognostic importance of PSADT and steady state testosterone levels
  - Randomized 2:1 Sipuleucel-T (n=117) : control (n=59)
  - After BF an optional booster treatment with a single infusion of Sipuleucel –T or control was available (n=49)

**Results**
- Median time to BF
  - 18.0 months for sipuleucel-T and 15.4 months for control (HR = 0.936, P = 0.737)

Fig. 9

- Distant Failure
  - With only 16% of patients having developed distant failure, the treatment effect favored sipuleucel-T (HR = 0.728, P = 0.421)

- PSADT
  - 34.4% greater in the treatment arm vs control at PSA values obtained ≥ 90 days (P=0.046)
  - Sipuleucel-T patients had a 47.6% increase in PSADT following testosterone recovery (155 vs. 105 days, P = 0.038)

Fig. 10
• Immune Response
  o Seen as long as 67.4 months into study
  o Increase in T-cell proliferation vs control (pre and post booster)

Fig. 11

• Safety
  o Adverse Events - Sipuleucel-T: Fatigue, pyrexia, chills
  o Mild to moderate
  o Only 1 patient stopped therapy due to clinical toxicity

Author's Conclusions

• Treatment group had a longer time until PSADT
• Although PSADT not statistically linked to treatment effect
• Delayed BF may be a result of delayed treatment effect suggested by the immune response to sipuleucel-T
• Overall survival is still being observed
• Sipuleucel-T treatment was well tolerated and had a robust and sustained immune response
• Treatment effect on PSADT suggests the biological activity in this population
• Long-term follow-up will be necessary to determine if clinically important events, such as distant failure, are affected by therapy
Strengths & Weaknesses

Strengths
- Immune Response and effect of a booster dose was analyzed
- Biochemical activity was analyzed
- Various US centers
- Large trial

Weaknesses
- 90% patients were Caucasian
- Androgen Suppression Therapy specifics were not included
- Funded by Dendreon Corporation

XI. Conclusion

a. Sipuleucel –T is the first cancer vaccine to be approved by the FDA.

b. The role of this vaccine, as well as that of other promising immune approaches, should be further defined in additional studies that evaluate other prostate cancer patient populations, when is best to use immunotherapy, and its use in combination therapy

References:

3. Prostate Cancer: Goldman, Goldman’s Cecil Medicine, 24th (2011) Pgs. 1322-1324
5. Enock Anassi; Uche Anadu Ndef. Sipuleucel-T (Provenge) Injection The First Immunotherapy Agent (Vaccine) For Hormone-Refractory Prostate Cancer P&T®; April 2011; Vol. 36 No.4, 198-202
14. Food and Drug Administration;Division of Biostatistics Office of Biostatistics and Epidemiology Center for Biologics Evaluation and Research Cellular, Tissue and Gene Therapies Advisory Committee Meeting; Statistical Briefing Document; March 2007
15. Beer, TM; Bernstein, GT; Corman, JM, et al. Randomized trial of autologous cellular immunotherapy with sipuleucelT in androgen-dependent prostate cancer.

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