Disclosure

- Employment Dendreon Corporation
  - Chief Medical Officer
  - Salary & equity interest
Sipuleucel-T: Designed to Stimulate a Patient’s Immune System

The precise mechanism of action of PROVENGE is not known.
Randomized Phase 3 IMPACT Trial (IMmunotherapy Prostate Adenocarcinoma Treatment)

Asymptomatic or Minimally Symptomatic Metastatic Castrate Resistant Prostate Cancer (N=512)

2:1

Sipuleucel-T Q 2 weeks x 3

Control Q 2 weeks x 3

Treated at Physician Discretion

Treated at Physician Discretion and/or Salvage Protocol

Primary Endpoint: Overall Survival
Secondary Endpoint: Objective Disease Progression

Primary Endpoint: Overall Survival
Secondary Endpoint: Objective Disease Progression
IMPACT Overall Survival
Intent-to-Treat Population (331 Events)

34.1 Mo. Median Follow-Up
HR = 0.775 (95% CI: 0.614, 0.979)
P = 0.032 (Cox Model)
Median Survival Benefit = 4.1 Months

- Sipuleucel-T (n = 341)
  - Median Survival: 25.8 Mo.
  - 36 Mo. Survival: 31.7%

- Placebo (n = 171)
  - Median Survival: 21.7 Mo.
  - 36 Mo. Survival: 23.0%

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Sipuleucel-T</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>341</td>
<td>171</td>
</tr>
<tr>
<td></td>
<td>274</td>
<td>123</td>
</tr>
<tr>
<td></td>
<td>129</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>49</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>1</td>
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</tr>
</tbody>
</table>
**Adverse Events More Commonly\(^1\) Reported in Sipuleucel-T Group**

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>Sipuleucel-T (N = 338)</th>
<th>Control (N = 168)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chills</td>
<td>54.1%</td>
<td>12.5%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>29.3%</td>
<td>13.7%</td>
</tr>
<tr>
<td>Headache</td>
<td>16.0%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Influenza-Like Illness</td>
<td>9.8%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>9.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>7.4%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Hyperhidrosis</td>
<td>5.3%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Groin Pain</td>
<td>5.0%</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

\(^1\) Reported by \(\geq 5\%) of sipuleucel-T patients and having a \(\geq 2\)-fold difference from control. The majority of the most common AEs were mild or moderate in severity.

Safety results obtained from primary analysis did not substantively change with additional data obtained after study closure.
Sipuleucel-T Product Parameters

Key product attributes:

- Total nucleated cell count
- CD54 count
- CD54 ‘upregulation’

The precise mechanism of sipuleucel-T in prostate cancer has not been established.
CD54 Upregulation Potency Assay for APCs

APCs Cultured with Recombinant Antigen

Mean Fluorescence Intensity

Pre-culture

Post-culture
APC Activation Increases after Initial Sipuleucel-T Treatment

IMPACT study. Data presented: mean, SEM
Cytokine Secretion in Culture Indicates Progressively Increased T Cell Activation

IMPACT study. Data presented: mean, SEM
## Correlation Between Overall Survival and Cell Product Parameters

<table>
<thead>
<tr>
<th>Cell Product Parameters</th>
<th>P-Values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted(^1)</td>
</tr>
<tr>
<td>Cumulative TNC Counts ((x \times 10^9))</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Cumulative CD54(^+) Cell Counts ((x \times 10^9))</td>
<td>0.016</td>
</tr>
<tr>
<td>Cumulative CD54 Upregulation</td>
<td>0.002</td>
</tr>
</tbody>
</table>

\(^1\) From 3 Cox regression models. Each cell product parameter (cumulative CD54\(^+\) cell counts [ln], cumulative TNC counts [ln], and cumulative CD54 upregulation [ln]) incorporated as an independent variable in a Cox regression model stratified by study.

\(^2\) From 3 Cox regression models. Each cell product parameter (cumulative CD54\(^+\) cell counts [ln], cumulative TNC counts [ln], and cumulative CD54 upregulation [ln]) incorporated as an additional independent variable in the primary model with PSA (ln) and LDH (ln) as the common independent variables, all stratified by study.

Integrated data from three Phase 3 mCRPC studies (IMPACT, D9901, D9902A).
Overall Survival by Cumulative Product Parameter

TNC Count  CD54+ Cell Count  CD54 Upregulation

Sipuleucel-T patients with ≥ 1 infusion.

Integrated data from three Phase 3 mCRPC studies (IMPACT, D9901, D9902A).
Evaluation of T Cell Activation and Immune Response During Treatment Phase

**Day 0**
- Apheresis
- Buoyant Density Separations
  - Preculture
  - Determine IFNγ ELISPOT and Proliferative Responses

**Day 2**
- Ex-vivo Culture
  - PA2024
  - 37°C
- Wash
- Resuspend Cells in Lactated Ringers
- Final Product
- Determine Cytokine Production
Pre-Culture Proliferative Responses are Increased During the Treatment Cycle

IMPACT study. Data presented: mean, SEM
Pre-Culture ELISPOT Responses are Increased During the Treatment Cycle

IMPACT study. Data presented: mean, SEM
IMPACT Trial Time Points for Sipuleucel-T Treatment and Immune Monitoring

- **Treatment**
  - Wk 0
  - Wk 2
  - Wk 4
  - Infusion 1
  - Infusion 2
  - Infusion 3

- **Immune Monitoring**
  - Baseline
  - Wk 6
  - Wk 14
  - Wk 26
  - ELISA
  - Proliferation
  - ELISPOT
Sipuleucel-T Generates Persistent Antigen-Specific Humoral Responses

* P < 0.001 compared with control.
Anti-PA2024 Humoral Response Undergoes Class Switching

IMPACT study. Data presented: median and quartiles
Sipuleucel-T Induces Long-Lasting Proliferative Responses to PA2024 and PAP

* P < 0.001 compared with control.
• P = 0.009 compared with control.

IMPACT study. Data presented: mean, SEM
Sipuleucel-T Induces Long-Lasting ELISPOT Responses to PA2024 and PAP

* $P < 0.001$ compared with control.
• $P = 0.020$ compared with control.
### Immune Response to PA2024 and Overall Survival

<table>
<thead>
<tr>
<th>Response</th>
<th>Time Point</th>
<th>Week 6</th>
<th>Week 14</th>
<th>Week 26</th>
</tr>
</thead>
<tbody>
<tr>
<td>ELISA</td>
<td>N</td>
<td>134</td>
<td>89</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.079</td>
<td>0.744</td>
<td>0.610</td>
</tr>
<tr>
<td>Proliferation</td>
<td>N</td>
<td>63</td>
<td>42</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.712</td>
<td>0.057</td>
<td>0.874</td>
</tr>
<tr>
<td>ELISPOT</td>
<td>N</td>
<td>63</td>
<td>42</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>p-value</td>
<td>0.824</td>
<td>0.885</td>
<td>0.049</td>
</tr>
</tbody>
</table>

21 IMPACT study.
Overall Survival by Magnitude of Immune Response Above vs Below Median

**ELISA**
- Week 6

**Proliferation**
- Week 14

**ELISPOT**
- Week 26

IMPACT study.
Conclusions

- APC activation and cytokine profile of product suggests immunologic prime-boost
- Sipuleucel-T generates robust cellular and humoral immune responses *in vivo*
- IgM to IgG humoral responses consistent with class switching
- Response durations suggest immunological memory
- Correlations between immunologic parameters and overall survival
- Immunologic parameters in product and peripheral blood are candidate biomarkers for clinical activity of sipuleucel-T
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