“INNOVATIVE THERAPEUTIC CANCER VACCINES IN CUBA: AN UPDATE”

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Vaccine Division
CIM
## Estimated and Projected World Cancer Incidence by Selected Types of Cancer

<table>
<thead>
<tr>
<th>Year</th>
<th>Lung</th>
<th>Breast</th>
<th>Colon</th>
<th>Stomach</th>
<th>Liver</th>
<th>Prostate</th>
<th>Cervical</th>
<th>Esophageal</th>
<th>Lymphoma</th>
<th>Pancreatic</th>
<th>Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>1 352</td>
<td>1 200</td>
<td>1 025</td>
<td>935</td>
<td>627</td>
<td>680</td>
<td>492</td>
<td>463</td>
<td>364</td>
<td>233</td>
<td>160</td>
</tr>
<tr>
<td>2020</td>
<td>1 700</td>
<td>1 400</td>
<td>1 300</td>
<td>1 150</td>
<td>680</td>
<td>1 280</td>
<td>530</td>
<td>480</td>
<td>380</td>
<td>264</td>
<td>177</td>
</tr>
</tbody>
</table>

Percent Change (2005-2020)

- Lung: 1.5%
- Breast: 1.0%
- Colon: 1.6%
- Stomach: 1.4%
- Liver: -0.5%
- Prostate: 4.3%
- Cervical: 0.5%
- Esophageal: 0.2%
- Lymphoma: 0.3%
- Pancreatic: 0.8%
- Melanoma: 0.7%

## Estimated and Projected World Cancer Mortality by Selected Types of Cancer

<table>
<thead>
<tr>
<th>Year</th>
<th>Lung</th>
<th>Breast</th>
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<th>Lymphoma</th>
<th>Pancreatic</th>
<th>Melanoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>1 180</td>
<td>410</td>
<td>529</td>
<td>700</td>
<td>598</td>
<td>222</td>
<td>274</td>
<td>386</td>
<td>195</td>
<td>227</td>
<td>41</td>
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<tr>
<td>2020</td>
<td>1 100</td>
<td>400</td>
<td>620</td>
<td>730</td>
<td>632</td>
<td>245</td>
<td>190</td>
<td>395</td>
<td>200</td>
<td>243</td>
<td>43</td>
</tr>
</tbody>
</table>

Percent Change (2005-2020)

- Lung: -0.5%
- Breast: -0.2%
- Colon: 1.1%
- Stomach: 0.3%
- Liver: 0.4%
- Prostate: 0.7%
- Cervical: -2.4%
- Esophageal: 0.2%
- Lymphoma: 0.2%
- Pancreatic: 0.5%
- Melanoma: 0.3%

Source: US Census Bureau, NCI, WHO

## New Cases of Cancer (2006) and Mortality (2008) in Cuba (greatest frequency types)

<table>
<thead>
<tr>
<th>Localization</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>4 378</td>
<td>5 051</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>2 527</td>
<td>2 509</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>2 496</td>
<td>1 357</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>1 683</td>
<td>1 869</td>
</tr>
<tr>
<td>Cervical cancer</td>
<td>1 271</td>
<td>457</td>
</tr>
</tbody>
</table>

Source: National Cancer Registry and Department of Statistics. Cuban Health Ministry
The first cancer vaccine is now available for patients

FDA Approves Prostate Cancer Treatment

NBC Nightly News (4/29, story 3, 2:00, Williams) reported that "the FDA has approved" Provenge (sipuleucel-T), "a vaccine for prostate cancer.

Dendreon
Targeting Cancer, Transforming Lives™

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**MATURE ANTIGEN PRESENTING CELL**

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**DAY 1**
LEUKAPHERESIS

Apheresis Center

**DAY 2 - 3**
SIPULEUCEL-T IS MANUFACTURED

Dendreon

**DAY 3 - 4**
PATIENT IS INFUSED

Doctor’s Office

COMPLETE COURSE OF THERAPY: 3 CYCLES In 4 weeks

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![Survival Curve Graph](image)

- Sipuleucel-T (n=82)
- Placebo (n=45)

\[ P = 0.010 \text{ (log rank)} \]
\[ HR = 1.71 \text{ [95% CI: 1.13, 2.58]} \]

(Each circle represents a censored value)
NSCLC: The EGF-P64 Vaccine

Anti-EGF Ab blocks the EGF/EGFR binding

Inhibition of proliferation
NSCLC: The EGF-P64 Vaccine

Randomized POC Phase II CT in 80 NSCLC patients

Currently ongoing a Phase III pivotal trial in 579 NSCLC patients
An Unique Target: N-Glycolylated Mono Sialyl Lactosyl Ceramide

- Initially reported by us in human breast tumours in the early nineties
- Also expressed in other types of cancers: NSCLC, Colon, Stomach, Ovarian, Melanomas etc
- Almost absent in human normal tissues
- A potent immunosuppressor, mainly for CD4⁺ T cells
- Available from horse erythrocytes and fully synthetic

Vaccine formulation: 1E10 mAb in Al(OH)₃
NSCLC: Racotumomab (1E10) Idiotypic Vaccine

Randomized POC Phase II CT in 174 NSCLC patients

Interim analysis at 81 events

Starting a Multinational Phase III pivotal trial in 1 084 NSCLC patients
Very Small Sized Proteoliposomes: the Common Fact

GM3

OMVs Neisseria meningitidis

VSSP

Size: 24.7 ± 1.1 nm
Zeta potential: -25.5 ± 2.54 mV

Estévez F. et al., Vaccine 1999; 18:190-7
Very Small Sized Proteoliposomes: the Common Fact

# IFN-γ+/10⁵ CD8⁺ T cells

- Tumor-free
- EG.7 Tumor

- IFA
- VSSP
- DC
Breast Cancer: The GlycovaxGM3 Vaccine

NGcGM3 + Montanide ISA 51

Randomized POC Phase II CT in 79 MBC patients

Survival Analysis for Non Visceral Patients (ITT, n = 50/79)

<table>
<thead>
<tr>
<th></th>
<th>GlycoVaxGM3</th>
<th>Control</th>
<th>Log Rank (p)</th>
<th>Breslow (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>OS</td>
<td>N = 23</td>
<td>N = 27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>26.17</td>
<td>12.17</td>
<td>0.269</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Currently ongoing two Phase III pivotal trials, one in 776 MBC patients, other in 512 stage IIa, III patients
HeberProvac might be an innovative solution for prostate cancer

HeberProvac

- Synthetic peptide GnRHm1-TT (3mg)
- VSSP (245 µg)
- Montanide ISA-51 (350 µL)

Phase I Study: 8 hormone-sensitive metastatic prostate cancer patients

Biochemical and Immunological Findings

Clinical Update

- 5 patients with normalized prostate gland
- 1 patient with grade I prostate gland

POC Phase II study starting in 2010
CIGB 228: HPV E7 peptide for HLA-A*02 restricción in VSSP, SC injection

Phase I Clinical trial

- 7 patients with High Grade Cervical Dysplasia / HPV 16/ HLA-A*02, 4 doses of the vaccine
- End points: safety, colposcopy and histopathologic analysis, immunogenicity

- The vaccine was safe and well tolerated
- High-grade cervical dysplasias were resolved in 57% of patients
- Partial responses were obtained in 29% of patients
- Complete and partial responses observed in 86% of cases

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Colposcopy</th>
<th>Histology</th>
<th>Immunogenicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>01</td>
<td>CR</td>
<td>CR</td>
<td>+++</td>
</tr>
<tr>
<td>02</td>
<td>SD</td>
<td>SD</td>
<td>++</td>
</tr>
<tr>
<td>03</td>
<td>PR</td>
<td>PR</td>
<td>++</td>
</tr>
<tr>
<td>04</td>
<td>CR</td>
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</tr>
<tr>
<td>05</td>
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<td>++</td>
</tr>
<tr>
<td>06</td>
<td>CR</td>
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<tr>
<td>07</td>
<td>SD</td>
<td>SD</td>
<td>+</td>
</tr>
</tbody>
</table>

POC Phase II study starting in 2010

CIGB 228 might be an innovative solution for cervical cancer
Concluding Remarks

• Eight innovative therapeutic cancer vaccines are in development in Cuba as a consequence of the existence of the Cuban Biotech System

• Vaccine candidates are focused in the more frequent types of cancer affecting people in Cuba

• VSSP vaccine technology is the common fact present in the majority of these projects
Thanks for your attention!