Effect of Modified Citrus Pectin Treatment

On PSA Dynamics
In Non-Metastatic Biochemically Relapsed Prostate Cancer Patients

Interim Results
Ongoing Multi-Center Prospective Open Label Phase IIb Study
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**Background**

Galectin-3: Key Protein Driving Inflammation, Fibrosis, Cancer Progression

**N-terminal domain multimerization**

**Chimera-type**

**Pentamers & Lattices**

C-terminal domain carbohydrate recognition & binding (CRD)

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**Gal-3 and Mortality From All Causes**

- **Quintile-1**: 7.7
- **Quintile-2**: 9.4
- **Quintile-3**: 10.9
- **Quintile-4**: 12.6
- **Quintile-5**: 15.6

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**Cumulative Survival Rate (%)**

- **0%**
- **10%**
- **20%**
- **30%**
- **40%**
- **50%**
- **60%**
- **70%**
- **80%**
- **90%**
- **100%**

**Year**

- **0**
- **1**
- **2**
- **3**
- **4**
- **5**
- **6**
- **7**
- **8**
- **9**
- **10**
- **11**
- **12**
- **13**
Gal-3 Initiates Signaling Cascades
Via Binding Partners

- Carcinoembryonic antigen
- Mucin-1
- Lysosommal-membrane-associated glycoproteins
- Mac-1 and -3
- CD-98
- CD-45
- CD-71
- Fibronectin
- Collagen IV
- Elastin

- Laminin
- Hensin
- N-cadherin
- Desmoglein
- αβ3 Integrin
- VEGFR-2
- NG2 (neuron-glial antigen 2) chondroitin sulfate proteoglycan
- A3β1 Integrin
- Glycosaminoglycans (GAG’s)
- Prostate Specific Antigen (PSA)*
Gal-3
Master Conductor of the Tumor Microenvironment

- Intracellular effects:
  - Stimulates proliferation
  - Inhibits apoptosis

- Cell-Cell interaction:
  - Stimulates migration
  - Promotes invasion (metastasis formation)

- Environment regulation:
  - Stimulates angiogenesis
  - Inhibits immune surveillance

Increases cancer cell survival
Gal-3 Promotes Immune Suppression
Blocks T-Cell Surface Receptor Activity

Gal-3 crosslinks T-cell receptors & CD45 by binding glycans

• Suppresses immune surveillance
• Blocks T-cell receptor
• Downregulates T-cell signaling
• Inhibits dendritic, T cell & NK cell function

Wolfert & Boons. Nature Chemical Biology 2013
Gal-3 effects in cancer are mediated by 3 pathways

**Intracellular pathway**
- Loss of p53 repression of gal-3
- Induction of BCL2, RAS, MYC
- Prevention of apoptosis

**Extracellular pathway**
- Excretion of gal-3
- Formation of gal-3 lattices with matrix proteins
- Cell migration & Angiogenesis signaling

**Immune evasion pathway**
- Gal-3 blocks signaling molecules on the cell
- Gal-3 blocks CD45 on lymphocytes
- Prevention of NK recognition and killing
- T cell anergy / death

AML = Acute myeloid leukemia
MSC = Mesenchymal stromal cells

Ruvolo. Biochim Biophys Acta. 2015
Modified Citrus Pectin – Natural Inhibitor of Gal-3 Derived From Citrus Peel

Research demonstrates multiple benefits
- anti-inflammatory
- immunomodulatory
- antiproliferative
- anti-metastatic
- synergistic effects in combination with chemotherapy and radiotherapy
- reduction in multidrug resistance
Modified Citrus Pectin
Research Pathway in Cancer

In-vitro
Increased sensitivity to cytotoxic drugs & irradiation

Animal
Decreased metastases in different models

Human
- Phase II in Prostate cancer (PSADT effect)
- Interim results phase IIB: Marked improvement in PSADT (Ongoing study)


MCP Increased PSADT in Men with Biochemical Prostate Ca Relapse

Method
• 10 men with biochemical prostate cancer relapse used MCP 15 g/day for 1 year

Results
• PSADT increased (P<0.01) in 7 (70%) of 10 men after taking MCP for 12 months compared to before MCP Tx

Log-transformed PSA measurements $y$ for patient number 9 before and after taking MCP plotted against time $t$ in months and the fit of a linear spline with a break point at the time of treatment initiation ($t_0=13.67$ months) with MCP

MCP Phase II Study
PSADT Results at 1 Year

13 patients enrolled for tolerability, 10 Pts evaluated for efficacy.

* p<0.01

Interim Results – Multi Center Prospective Open Label Phase II Study

Effect of PectaSol-C Modified Citrus Pectin Treatment on PSA Dynamics in Non-Metastatic Biochemically Relapsed Prostate Cancer Patients

• 49 patients recruited so far
• Ongoing recruitment until 60 patients
• Expected disease progression rate of 80% at 6 months
MCP Effect on PSA Dynamics in Non-Metastatic Biochemically Relapsed Prostate Cancer (BRPC)

**Study Design: Single Arm Phase II**

<table>
<thead>
<tr>
<th>BRPC after primary tumor treatment (surgery/radiation)</th>
<th>6 months of oral MCP therapy (4.8 grams x 3/day)</th>
<th>Disease status (PSA, scans) @ 6mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months of oral MCP therapy (4.8 grams x 3/day)</td>
<td>Disease status (PSA, scans) @ 6mo</td>
<td>No Progression</td>
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<td>6 months of oral MCP therapy (4.8 grams x 3/day)</td>
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</tr>
</tbody>
</table>

- Rising PSA confirmed x 3 times
- Serum testosterone > 150, no ADT or > 3 months without ADT
- Negative PET-PSMA of bone scan + CT scan
- Monthly evaluation (toxicity, H&P, PSA)
- Scan @ 6mos
- Scans progression
- Limiting toxicity

*This material is being provided to health care professionals and it is not intended to be used in marketing to customers.*
Interim Results (n=44)

Progression is defined as negative change in PSDAT and 25% increase in PSA or positive Scans.

- No Progression: 77% (31 Pts)
- Progression: 23% (10 Pts)
Interim Results
(n=44)

- No improvement of PSADT (PSA Increase < 25%)
  - 7% (3 Pts)
- PSADT decrease
  - 18% (8 Pts)
- PSADT decrease & positive scans
  - 5% (2 Pts)
- PSADT improved
  - 70% (31 Pts)
Results (n=44) & Conclusions

- **77% No progression (34/44)**
- 31/44 (70%) PSADT Improvement vs. baseline (p<0.01)
- 3/44 (7%) PSA Increase < 25%, PSADT decrease
- **23% Disease Progression (10/44)**
- 8/44 (18%) Biochemical Progression (PSADT decrease)
- 2/44 (5%) PSADT decrease + Pos. Scans

- All patients had consecutive rise in 3 PSA tests before starting the study
- 57% (25/44) had stable or decreasing PSA levels after 6 months
- Strongly suggesting a benefit for MCP supplementation
- No safety issues. Most common SE – bloating

Expected disease progression rate of 80% at 6 months
Patient Testimonials

“In the last 2 years I consume (Modified Citrus Pectin) 3 times a day, I feel energetic with good mood and appetite and the overall feeling is much better than in the previous period. My PSA level is stable in the last 18 months opposed to a rising level previously, which is something I’m so thankful. I definitely recommend men with PC to give it a try. I am so thankful that I was recruited to this study.”
~ S. Sela

“I take (Modified Citrus Pectin) on a constant basis since I was recruited to the study (2 yrs ago), and after 3 month my blood test was better and no scan evidence of having tumours till today. I literally feel it improves my health and keep me feel good. I stopped for 2 months and then the PSA started to raise again, thus I’m sure it works.”
~ A. Anuar
Thank You
Clinical Trial Co-Investigators

- Dr. Mosh Frenkel
  Meir Medical Center, Kfar-Saba, Israel
- Dr. Avivit Peer
  Rambam Medical Center, Haifa, Israel
- Dr. Eli Rosenbaum
  Rabin Medical Center, Tel-Aviv Israel
- Dr. David Sarid
  Tel-Aviv Medical Center, Tel Aviv, Israel

- Dr. Daniel Keizman,
  Principal Investigator
  Meir Medical Center, Kfar-Saba, Israel
Current Status /Next Analysis:
• 49 patients recruited so far
• Ongoing recruitment until 60 patients
• Pre-planned analysis of 51 patients (ASCO 2019)

Thank You!

Isaac Eliaz, MD, MS LAc
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## Modified Citrus Pectin – Clinical Application

### Dosage Guidelines

<table>
<thead>
<tr>
<th>Condition</th>
<th>Categories</th>
<th>Dose (cap/power)</th>
<th>Frequency (x/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active Cancer</strong></td>
<td>Chemotherapy</td>
<td>5 grams</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Radiation</td>
<td>5 grams</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Hormonal Therapy</td>
<td>5 grams</td>
<td>3</td>
</tr>
<tr>
<td><strong>Post Therapy</strong></td>
<td>Full dose up to 5 years/time of greatest risk</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Post Therapy</strong></td>
<td>(&gt;5 yrs)</td>
<td>Continue at dose based on your condition &amp; Gal-3 level</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td>Take up to surgery &amp; resume right after surgery</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Special Instructions

- Up to 25 grams per day based on Gal-3 level
- 1 scoop = 5 grams
- 1 scoop = 6 capsules
- Empty stomach at least 15 min. before or 1 hour after food
- Powder can be mixed with any liquid, hot or cold

1 scoop = 5 grams

1 scoop = 6 capsules