Malignant Peritoneal and Pleural Fluid Samples are adequate for Molecular Profiling

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Disclosure:

• Caris Life Sciences
Introduction

• The diagnosis of a malignant effusion in the serosal cavities is a frequent event in the clinical setting of cancer

• Metastatic cancer cells may have unique characteristics that give them the ability to migrate from the primary tumor

• Since cancer patients often experience critical conditions, the analysis of the malignant fluid might be the only tissue sample available for these patients

• With the focus on targeted therapies, evaluation of different sample types for molecular studies is even more important
Introduction

• The Caris Target Now™ is proprietary evidence based molecular profiling system for solid tumors which provides specific and individualized molecular profiles for guidance of therapy in advanced stages and metastatic malignancies

• Associates therapeutic agents with potential benefit or potential lack of benefit, and may reveal treatments not previously considered
Caris Target Now Technologies

**IHC**
- Typically 18 predictive biomarkers
- Total of 30 IHCs – use depends on tumor type and progression

**Microarray**
- Looking at the over or under expression of the full genome of 24K gene targets, with reporting of 80 genes predicting response to therapies.

**FISH**
- Identifying gene copy number alterations in tumor tissue (HER2, EGFR, c-MYC, TOP2A, ALK, PIK3CA, cMET)

**Mutational Analysis**
- Identifying gene copy number mutations in tumor tissue (KRAS, BRAF, EGFR, c-KIT, PIK3CA)
Agents Associated with Clinical Benefit

**ON NCCN Compendium™**
- erlotinib
- cisplatin, carboplatin
- pemetrexed

**OFF NCCN Compendium™**
- fluorouracil
- gefitinib
- temozolomide
- caltridol, cholecalciferol
- sunitinib, sorafenib

Agents Associated with Lack of Clinical Benefit

- gemcitabine
- irinotecan
- doxorubicin, liposomal-doxorubicin, epirubicin
- lapatinib
- trastuzumab

Caris Target Now Final Report

Clinical History
For the submitted surgical pathology report, the patient is a 51-year-old female with a history of metastatic carcinoma of the lung.

Pathologic Diagnosis
Lung, left, soft tissue, invasive moderately differentiated adenocarcinoma of lung.

Agents Associated with Clinical Benefit

**ON NCCN Compendium™**
- erlotinib
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**OFF NCCN Compendium™**
- fluorouracil
- gefitinib
- temozolomide
- caltridol, cholecalciferol
- sunitinib, sorafenib

Caris Target Now is an evidenced-based molecular profiling service that associates biomarker status to agents with potential clinical benefit or potential lack of clinical benefit. Agents associated with clinical benefit are presented based on NCCN Compendium™ inclusion, relevance of tumor type, clinical trial evidence, and strength of biomarker expression. The agents are not ranked in order of potential or practical benefit. This information is the result of the research and not in any way a representation of the clinical benefit of a given agent. The selection of an agent is the responsibility of the treating physician. The report does not guarantee that any particular agent will be effective in the treatment of a particular condition. The selection of any of the agents associated with the selection of the treating physician. Caris Life Sciences does not represent that any patient will be reimbursed or paid for by any third-party insurer or other payers.

Caris Life Sciences offers all reasonable skill and care in the preparation of this report and believes that its findings will assist in the selection of appropriate treatments. Caris Life Sciences expressly excludes, all other representations, warranties, conditions and terms.

**Final Report**

An export oncology consultation can be arranged at a request made through our Clinical Services Department at 1-800-905-0377.

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Primary Objective

- Compare progression free survival (PFS) for therapy selected by molecular profiling with PFS for the last line of therapy on which the patient progressed.

\[ \frac{\text{PFS}_b}{\text{PFS}_a} > 1.3 \]

MP-selected therapy was defined as having benefit for patient.

PFS: length of time during and after treatment in which a patient is living with a disease that does not get worse.

Results: Primary Endpoints

- 27% of patients had PFS ratio > 1.3
- 95% confidence interval (CI): 17% - 38%
- P = 0.007

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Total Treated</th>
<th>Number with PFS Ratio &gt; 1.3</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>18</td>
<td>8</td>
<td>44</td>
</tr>
<tr>
<td>Colorectal</td>
<td>11</td>
<td>4</td>
<td>36</td>
</tr>
<tr>
<td>Ovarian</td>
<td>5</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>32</td>
<td>5</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>66</td>
<td>18</td>
<td>27</td>
</tr>
</tbody>
</table>

*Miscellaneous tumor types with PFS ratio > 1.3 included lung, cholangiocarcinoma, mesothelioma, eccrine sweat glands, and GIST (gastric).
### Results: Overall Survival

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median OS (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with PFS $\geq 1.3$ (responders)</td>
<td>18</td>
<td>9.7</td>
</tr>
<tr>
<td>Patients who did not respond to molecular-profiling-selected treatments (non responders)</td>
<td>48</td>
<td>3.2</td>
</tr>
<tr>
<td>All patients who received molecular profiling (responders + non responders)</td>
<td>66</td>
<td>5.0</td>
</tr>
<tr>
<td>Patients whose treatment was not selected by molecular profiling</td>
<td>40</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Patients with PFS $\geq 1.3$ had longer OS by 6.5 months compared to non responders and patients whose treatment was not selected by molecular profiling.
Study Conclusions

- Molecular profiling identified agents that would not have been the oncologist’s first choice (0% correlation)
- Results support use of molecular profiling as means to successfully identify new treatment targets for patients with metastatic tumors
- Molecular profiling suggested regimens resulted in longer PFS in 27% of patients
- Longer PFS was demonstrated in patients with different histological types of tumors
Objective

• The purpose of this study is to evaluate the feasibility of molecular profiling in pleural and peritoneal fluids
Material and Methods

• A computer search was conducted to retrospectively identify malignant fluid samples or cell blocks from January 2009 to April 2011
Results

172 Samples of peritoneal and pleural fluids

- 26% Others
- 28% Lung
- 27% Ovary
- 16% Breast
- 3% Pancreas
- 44 Samples
- 49 Samples
- 28 Samples
- 46 Samples
- 5 Samples
Based on 172 Samples of peritoneal and pleural fluids
Microarray

Based on 172 Samples of peritoneal and pleural fluids
FISH

Based on 172 Samples of peritoneal and pleural fluids
Sequencing

Based on 172 Samples of peritoneal and pleural fluids
Results

- Combined results of predictive markers from these various platforms were able to provide information on therapeutic guidance for associated clinical benefit or lack of clinical benefit for various therapies in 129 of the 172 cases (75%)

*Based on 172 Samples of peritoneal and pleural fluids*
Case #1

1994
70 y/o male diagnosed w/ Renal Cell Carcinoma

2009
Lung Metastasis

Radiation & Sorafenib, Sunitinib Everlimus

Caris Target Now Performed
Case #1

HE

EGFR IHC

TOPO1

SPARC IHC
Case#1

1994
Diagnosed w/ Renal Cell Carcinoma

2009
Radiation & Sorafenib, Sunitinib Everlimus
Lung Metastasis

2011
Based on CTN Results: Erlotinib Pazopanib (to target EGFR)
Caris Target Now Performed
Patient Doing Well No New Mets
Case #2: 59 year old female with history of metastatic lung cancer
Case #3: 48 year old female with history of metastatic breast cancer

- HE
- HER2/NEU IHC
- HER2/NEU FISH
- TOPO2 FISH
Case #4: 61 year old female with history of metastatic breast cancer
Conclusion:

- Molecular profiling of malignant effusions offers additional opportunities for testing when other tissue samples, such as needle core biopsy or tumor resection, are not available.

- Molecular profiling of effusion samples can provide insight into the molecular characteristics of malignant cells.

- Molecular profiling of malignant effusion can provide information to create targeted therapies for cancer.
Thanks