In-vivo isolation of circulating tumor cells in non-small cell lung cancer (NSCLC) patients by a medical device


1 Department of Thoracic Surgery, and 2 Clinical Immunology Medical University, ul. Szamarzewskiego 62, 80-569 Poznan, Poland
3 Prometheus Thearapeutics & Diagnostics, San Diego, USA
5 Bayer HealthCare, Müllerstraße 178, 13353 Berlin, Germany

Abstract

Currently, circulating tumor cells (CTCs) are isolated in vitro from small limited volumes of blood samples. Furthermore, CTC results for NSCLC as a prognostic and stratification biomarker are scarce. The aim of the study was to assess a functionalized and structured medical wire (FSMW) for in vivo isolation of CTCs directly from the blood of NSCLC patients, and to compare it to the Cell Search® method. The device was inserted in a cubital vein through a standard cannula for thirty minutes. The interaction of target CTCs with the FSMW was mediated by an antibody directed against the epithelial cell adhesion molecule (EpCAM). To confirm the CTCs binding to the wire, the immunohistochemical staining against EpCAM as well as CD45 for negative cell selection was performed. There were 72 applications of the wire in 48 stage I-IIIA NSCLC patients (12 double applications) and 12 non cancer patients. Enumeration data was available for 34 NSCLC patients and 8 non cancer patients. For 34 patients, samples were also tested in the Cell Search® system. The device was well tolerated in all 72 applications without side effects. We obtained in vivo isolation of CTC in 32 of 34 NSCLC patients (94.1 %) with a median (range) of 13 (0-300) CTCs. The sensitivity was similar for early and late stage NSCLC patients. In the non-cancer patients, no CTCs were detected (100 % specificity). In 2 of 34 samples (5.8 %), CTCs were detected by the Cell Search® method. In all matched pairs, the FSMW detected the same number or more CTCs compared to the Cell Search® method.

Functional Structured Medical Wire

- Insertion into patient’s vein at the doctor’s office
- 30 minutes exposure time in a vein
- Clinical sample
- Nanodetector
- Diagnostics
- PCR, etc.

Patient population

60 subjects
- 59 patients + 1 controls
- 49 subjects
- Functionality test
- 34 patients + 7 controls
- 23 NSCLC patients (comparison with reference)

Immunocytochemical analysis

- Positive against EpCAM
- Negative against CD45

Results in vivo captured CTCs

- Comparison of the methods, the FSMW in vivo and the CellSearch® method in vitro.
  - In 100% of paired samples: FSMW >> Cell Search

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Positive CTCs (%)</th>
<th>Detection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>IB</td>
<td>T2a</td>
<td>N0</td>
<td>M0</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>T2a</td>
<td>N1</td>
<td>M0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>IV</td>
<td>T2a</td>
<td>N1</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>V</td>
<td>T3</td>
<td>N1</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VI</td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VII</td>
<td>T3</td>
<td>N3</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>VIII</td>
<td>T3</td>
<td>N3</td>
<td>M0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>IX</td>
<td>T4</td>
<td>N2</td>
<td>M0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>X</td>
<td>T4</td>
<td>N3</td>
<td>M0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>XI</td>
<td>T4</td>
<td>N3</td>
<td>M0</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

SUMMARY

- There were no AEs. All patients showed very good biocompatibility and no side effects.
- FSMW sensitivity for in vivo isolation of CTCs in NSCLC patients was 94.1 % (32/34)
- In paired samples, only 1 patient with CTCs was detected by the CellSearch® system.
- Detection of CTC’s could be shown in all occurred tumor stages (especially early stages)
- The implementation of FSMW into clinical practice may improve early detection, prognosis and therapy monitoring of NSCLC patients as well as the molecular analysis of the CTCs, resulting in personalized treatment strategies

Source: www.nature.com, A. Marusyk, V. Almendro, K. Polyak “Intra-tumour heterogeneity: a looking glass for cancer (May 2012)”