A new medical device for in-vivo isolation of circulating tumor cells in prostate cancer patients

Gerit Theil¹, Kersten Fischer¹, Katrin Boehm¹, Kathrin Haubold², Thomas Krahn³, Nils G. Morgenthaler², Klaus Lücke², Raschid Hoda¹, Paolo Fornara¹

¹ Clinic for Urology and Kidney Transplantation Center, Martin Luther University Medical School Halle, Germany
² GILUPI GmbH, Am Mühlenberg 11, 14476 Potsdam, Germany
³ Bayer HealthCare, Müllerstraße 178, 13353 Berlin, Germany

Abstract

Currently, circulating tumor cells (CTC) are isolated in vitro from small limited volumes of blood samples. Furthermore, CTC results for prostate cancer as a prognostic and valid 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 prostate cancer patients, and to compare it with the Cell Search method or AdnaTestProstateCancerSelect/Detect.

The device was inserted in a cubital vein through a standard cannula for thirty minutes (Fig. 1). 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 different cytokeratin’s as well as CD45 for negative cell selection was performed (Fig. 3). There were 80 applications of the wire in 16 metastasized-prostate cancer patients (PCa-m), 24 local prostate cancer patients (PCa-l), 19 men with benign prostate hypertrophy (BPH) and 21 women as second control group. Enumeration data was available for 28 prostate cancer patients and 30 non cancer patients (Fig. 4). For 12 cancer and 14 non cancer patients, samples were also tested in the CellSearch® system (Fig. 5). Additional were blood samples of 14 non cancer patients and 4 cancer patients analyzed with AdnaTest (Fig. 8). The device was well tolerated in all 80 applications without side effects. We obtained in vivo isolation of CTCs in 20 of 28 samples from non cancer patients, and in 2 of 4 (50%), blood samples from cancer patients. The test is considered positive if a PCR fragment of at least 1 of 14 (7%) samples from non cancer patients was the CellSearch® CTC positive (Fig. 5). CTC were detectable by AdnaTest in 1 of 4 (7%) blood patients (68%). In the non cancer patients, on 6 of 30 wires CTCs were detected (80 % specificity). In 3 of 12 (25 %) samples of prostate cancer patients prostate cancer patients (71.4 %) with a median (range) of 2 (0-247) CTCs. The sensitivity of 82% in PCa-m patients was slightly higher than in PCa-l patients (mean of 3.9 ng/ml)

Results

in vivo captured CTCs

Figure 4: Results of CTCs captured in vivo with the FSMW in the blood of prostate cancer patients (mean of 18.91 CTCs) and control groups (BPH and women with a mean of 0.35 and 0.18 CTCs, respectively).

Analysis of PSA levels

Figure 6: Results of the PSA analysis from prostate cancer patients (with a mean of 9.9 ng/ml) PSA in PCa-m and PCa-l, respectively) and BPH patients (mean of 3.9 ng/ml).

Painless US study

Figure 7: Distribution of the Gleason-Grading.

Summary

- There were no AEs. All patients and showed very good biocompatibility and no side effects.
- FSMW sensitivity for in vivo isolation of CTCs in prostate cancer patients was 71.4% (20/28).
- In paired samples, only in 3 cases CTCs were detected by the CellSearch® and in 2 (2/4) cases AdnaTest® (Fig. 5/8).
- Detection of CTCs could be shown in all tumor stages (Fig. 7).
- The implementation of FSMW into clinical practice could improve prognostic and therapy monitoring of prostate cancer patients considerable and can also use for the molecular analysis of the CTCs, resulting in personalized treatment regiments.

Clinical trial design

Biocompatibility/ Functionality test

FSMW vs. AdnaTest

FSMW vs. CellSearch

Functional Structured Medical Wire (FSMW)

Decision

Diagnostic

Results

CTCs on device

In vivo captured CTCs

Figure 1: The biological functionalization of the wire is achieved using an antibody against the epithelial tumor marker EpCAM. EpCAM antibodies bound to a hydrogel coating of the wire mediate specific binding of EpCAM expressing target cells.

Immunocytochemical analysis

Figure 3: Immunocytochemistry analysis of CTCs captured in vivo with the FSMW in the blood of prostate cancer patients. The CTCs were identified and enumerated via positive Cytokeratin and Hoechst staining (respectively green and blue staining in top panels), size and morphological characteristics.

AdnaTest: ProstateCancer Select/Detect

Figure 8: Multiplex RT-PCR

- RT- : Reverse Transcription Control (water)
- C- : Negative Control (multiplex PCR)
- Pca+: Positive Control (multiplex PCR)
- PCa-m: PSA, PSMA, EGFR positive
- PCa-l: PSA, PSMA, EGFR negative

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