Isolation of circulating tumor cells in vivo by the CellCollector™ technology

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Abstract

Background: Circulating tumor cells (CTCs) are discussed as a prognostic biomarker. Whereas current methods isolate CTCs in vitro, the novel GILUPI CellCollector™ is an in vivo technology. The aim was to assess the GILUPI CellCollector™ system with non-small cell lung cancer (NSCLC), breast cancer (BC), colorectal cancer (CRC) and prostate cancer (PC) patients, and to compare it to the CELLSEARCH® method. Methods: The device was inserted in a cubital vein via a standard cannula for thirty minutes. CTCs were captured by an antibody directed against the epithelial cell adhesion molecule (EpCAM) on the GILUPI CellCollector™ surface. To confirm the CTC binding, immunohistochemical staining against EpCAM/Cytokeratins and CD45 was performed. More than 450 applications of the GILUPI CellCollector™ in cancer patients and over 50 controls were performed. Samples of 157 cancer patients and 22 control subjects were also tested in the CELLSEARCH® system. Results: The device was well tolerated in more than 500 applications without side effects. A direct comparison of the GILUPI CellCollector™ and CELLSEARCH® resulted in detection rates of 71.5% and 96%, respectively. Specificity rates were 91% and 93%, respectively. Regardless of the disease stage, in nearly all compared samples the number of CTCs detected with the GILUPI CellCollector™ was higher or equal to CELLSEARCH®. Conclusions: With a detection rate of around 70% this new device overcomes present limitations in CTC enrichment. Future implementation into clinical practice may improve early detection, prognosis and therapy monitoring of cancer patients. Captured CTCs are ready for molecular characterization and will help to establish personalized treatment regiments.

GILUPI CellCollector™ - an in vivo CTC isolating method

Figure 1: CTCs and cancer progression, Schematic model of metastatic model. Modified from Paris et al., 2013.

Patient recruitment in several clinical trials

Lung cancer
- 1st study - started in January 2010 and was finished in 2012
- 48 NSCLC patients and 12 non-cancer subjects

Prostate cancer
- Study started in January 2011
- 65 prostate cancer patients, 25 patients with diagnosed benign hyperplasia and 25 healthy
- Up to 8-time follow up visits to monitor cancer therapy over 3 years
- Study started in March 2013
- 20 lung cancer patients all stages with monthly follow up visits over 3-4 months after systemic therapy initiation

Breast cancer
- Study started in May 2010
- 78 breast cancer patients

Colorectal cancer
- Study started in February 2013
- 100 patients

NET cancer
- Case series started June 2013
- 30 Patients with neuroendocrine Tumors (e.g. pancreatic cancer)

Further diagnostic approaches

HER2 staining

Summary

- There were no product related AEs or SAEs. All patients showed very good biocompatibility and no side effects
- Summarized detection rate of 71.5% (196/274) for in vivo captured CTCs with the CellCollector™ in patients with lung-, breast-, prostate and colorectal cancer
- In patient-to-patient comparison, in 96% CTC enumeration results a higher or equal CTC number with the CellCollector™ compared to the CELLSEARCH® method
- Detection of CTCs could be shown in all occurred tumor stages (especially early stages)
- The implementation of the CellCollector™ into clinical practice may improve early detection and therapy monitoring of cancer patients via CTC enumeration
- Besides enumeration, the method may allow the molecular analysis of the CTCs, resulting in personalized treatment regiments.

Results

Immunocytochemical analysis

Figure 3: Immunocytochemistry analysis of CTCs captured in vivo with the GILUPI CellCollectors™ in the blood of NSCLC patients. The CTCs were identified and enumerated via positive EpCAM and/or Cytokeratin and DAPI staining and negative CD45 staining (respectively green, blue and red staining in top panels, incl. overlay), size and morphological characteristics. CTC examples represent 3 different NSCLC patients.

CTC enumerations

Figure 4: Results of CTC enumerations with the in vivo Detector CANCER01 compared to the CELLSEARCH® method of all samples received of the described studies.

Figure 2: Insertion of the GILUPI CellCollector™ through an 20 gauge indwelling cannula in a peripheral arm vein.

Figure 7: Breast cancer cells were captured by the GILUPI CellCollector™ (in vivo). Cells were identified by immunocytochemistry staining for epithelial markers (CKs), possible therapeutic target (HER2), and nuclear counterstaining using Hoechst33342. CD45 staining was done for negative cell selection.

Figure 6: Detection of CTCs in the blood of breast cancer patients using the in vivo Detector CANCER01.