Cytology-based Circulating Tumour Cell (CTC) Screening Test improves detection of Prostate Cancer

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Background
Circulating Tumour Cells (CTC) are biomarkers for
• early carcinogenesis / malignant potential 1
• cancer prognosis and treatment effectiveness 2,3
• CTC increase is associated with cancer progression and shorter survival.
• CTC decrease is associated with cancer containment or remission.
• Early detection CTC screening is suggested for patients with higher risk of malignancy, e.g. smoking, family history, HRT, >50 years.
• Several technologies have been developed to identify CTC, including the Isolation by Size of Epithelial Tumour (ISET) using filtration and analysis by microscopy using standard cytological criteria, validated in 80+ peer-reviewed articles over the last 20 years. www.rarecells.com/oncology
• The cytology-based ISET-CTC test provides high sensitivity (0.1 CTC/ml), and high specificity (0 0 CTC/ml in 600 healthy donors), and is superior to other marker-based CTC tests.

Methods

Isolation of CTC & analysis
10 ml of blood in EDTA → Mix with buffer
CTC cells are counted & analysed

Some FACTS: The ISET-CTC test can...
• Detect CTC in ALL cancer types, solid and blood type cancers
• Detect CTC of ALL sizes, including SMALL cell cancers
• Detect CTC independent of EpCAM markers used in other CTC tests, e.g. CellSearch. Some tumours don’t have or lose those markers over time. 6
• Distinguish between malignant CTC and benign atypical cells, single CTC and CTC clusters, viable and degenerated cells.
• CTC clusters have greater metastasising potential than single CTC 4
• Degeneration of cells suggests response to treatment.

Number of CTC/ml and cancer risk

0-3 low
3-20 moderate
>20 high
0 CTC = no evidence of malignancy

Results
• Between Sept-2014 and Mar-2019 we undertook 1800 CTC tests. 7
• 50% (n=900) of tests were CTC screening requests.
• CTC were detected in all cancer patients and in 50% of those screened.

o Group 1: Early detection: Follow-up imaging scans & biopsies within 1-10 months revealed cancerous lesions in 20% of asymptomatic patients with positive CTC counts, including early prostate cancer (50% males), breast, ovarian, lung or renal cancer (Table 1).

<table>
<thead>
<tr>
<th>Group 1: no tumour before CTC test</th>
<th>Early detection CTC screening &amp; follow-up scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>Age (yr)</td>
</tr>
<tr>
<td>Males</td>
<td>n=32, mean=66 yrs</td>
</tr>
<tr>
<td>Females</td>
<td>n=4, 37 yrs</td>
</tr>
<tr>
<td>Males</td>
<td>n=4, 47 yrs</td>
</tr>
<tr>
<td>Female</td>
<td>57 yrs</td>
</tr>
<tr>
<td>Male</td>
<td>54 yrs</td>
</tr>
<tr>
<td>Female</td>
<td>n=2, 44 yrs</td>
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</tbody>
</table>

CTC cytological criteria

<table>
<thead>
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<th>CTC &amp; clusters</th>
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<tbody>
<tr>
<td>Breast</td>
</tr>
<tr>
<td>Prostate</td>
</tr>
<tr>
<td>Colorectal</td>
</tr>
<tr>
<td>Gynaecological</td>
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<tr>
<td>CTC-4 criteria</td>
</tr>
<tr>
<td>1) atypical nuclei</td>
</tr>
<tr>
<td>2) morphed nucleus</td>
</tr>
<tr>
<td>3) high N/C ratio</td>
</tr>
<tr>
<td>4) irregular borders</td>
</tr>
<tr>
<td>5) clusters</td>
</tr>
</tbody>
</table>

IHC* for prostate cancer

Positive IHC results using PSA antibody on ISET-CTC were found in males with confirmed (scan/biopsy) prostate cancer (group 1a, group 2a), and subgroups of males screened positive for CTC (group 1b, 1d).

Conclusions
• CTC screening provides a sensitive tool for the early detection of patients at risk of developing cancer.
• CTC count is a better predictor for prostate cancer than standard PSA blood testing.
• Evidence-based integrative nutritional therapies, including vitamin D, curcumin, Kyolic garlic, green tea, and mushroom extract, can reduce CTC count and cancer risk.

Table 2: Positive IHC results using PSA antibody on ISET-CTC were found in males with confirmed (scan/biopsy) prostate cancer (group 1a, group 2a), and subgroups of males screened positive for CTC (group 1b, 1d).

Table 2: Results: IHC on ISET-CTC with PSA-antibody

References

Acknowledgements
Research assistants: Nikolaj Travica and Ranjini Dorairaj

May 2019