Optimal follow-up of cancer patients

Excellent precision as essential factor in the serial determination of tumor markers • Establishing individual patient’s baselines • Nobel Prize®-winning TRACE technology
Exceptionally precise, fast, and easy
Tumor markers on KRYPTOR Systems

• Extremely precise\textsuperscript{2–7}

• Minimal interference
due to TRACE technology\textsuperscript{8,9}

• Broad measurement range
due to “intelligent dilution”:
automated within-run dilution
in the first minutes of incubation

• Use of the well described
Fujirebio antibodies
(formerly Centocor)

Thermo Scientific
B·R·A·H·M·S KRYPTOR compact PLUS
Article number: 106172

Discover the Nobel Prize\textsuperscript{®}-winning KRYPTOR technology at
thermoscientific.com/kryptor
Precision is essential in the measurement of tumor markers, especially at low levels

Tumor markers are a powerful tool in therapy control and follow-up of cancer patients, and precision is a critical parameter when choosing an assay method. The course of a cancer disease is usually reflected by the individual course of tumor markers, and the individual course is derived from serial determinations of the leading tumor marker. The dynamics of these serial measurements are more important than the concentration of a single determination, therefore it is important to have reliable and precise measurement of the analyte. 1

Establishing the individual patient’s baseline is an important prerequisite for therapy control and follow-up; with baseline being the lowest measured marker level after primary therapy. In approximately 85% of cases, tumor marker levels decrease to those closer to the median concentration of healthy individuals after RO resection.

It should be noted that the median of the healthy population is usually much lower than the upper reference range limit (95th percentile), known as ‘cut-off’!

<table>
<thead>
<tr>
<th>Marker</th>
<th>95th percentile</th>
<th>Median of healthy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA 19-9</td>
<td>30.6 U/mL</td>
<td>9.8 U/mL</td>
</tr>
</tbody>
</table>

Table 1: Example for the difference of cut-off and median of the healthy population
For therapy control and follow-up, the leading tumor marker has to be chosen. A combination of at least two markers (marker of 1st and 2nd choice) is often useful (table 2).

Among therapy control and follow-up, several tumor markers can be helpful in screening, diagnosis and prognosis of selected tumor diseases (table 3).

### Table 2: Examples for the use of marker combinations (by courtesy of Dr. P. Stieber)

<table>
<thead>
<tr>
<th>Marker</th>
<th>Screening</th>
<th>Diagnosis</th>
<th>Follow-up</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEA</td>
<td>c-cell carcinoma</td>
<td>c-cell carcinoma</td>
<td>colon, breast, lung (NSCLC), c-cell</td>
<td>colon, stomach, breast</td>
</tr>
<tr>
<td>AFP</td>
<td>risk group</td>
<td>germ cell, HCC</td>
<td>germ cell</td>
<td>germ cell</td>
</tr>
<tr>
<td>CA 19-9</td>
<td>pancreas</td>
<td>pancreas, biliary ducts</td>
<td>stomach, colon</td>
<td></td>
</tr>
<tr>
<td>CA 125 II</td>
<td></td>
<td>ovary serous</td>
<td>ovary serous</td>
<td></td>
</tr>
<tr>
<td>CA 15-3</td>
<td></td>
<td>breast</td>
<td>breast</td>
<td></td>
</tr>
<tr>
<td>Chromogranin A</td>
<td>confirmation of carcinoid syndrome</td>
<td>neuroendocrine tumors (NET)</td>
<td>(neuroendocrine tumors (NET))</td>
<td></td>
</tr>
<tr>
<td>NSE</td>
<td>lung (SCLC)</td>
<td>lung (SCLC)</td>
<td>lung (SCLC)</td>
<td></td>
</tr>
<tr>
<td>CYFRA 21-1</td>
<td>lung (NSCLC)</td>
<td>lung (NSCLC), bladder</td>
<td>lung (NSCLC)</td>
<td></td>
</tr>
<tr>
<td>SCC</td>
<td>cervix, lung (NSCLC), ENT</td>
<td></td>
<td>cervix</td>
<td></td>
</tr>
<tr>
<td>hCG+β</td>
<td>risk group</td>
<td>germ cell, trophoblast tumors</td>
<td>germ cell, trophoblast tumors</td>
<td>germ cell, trophoblast tumors</td>
</tr>
<tr>
<td>PSA</td>
<td>prostate</td>
<td>prostate</td>
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<td></td>
</tr>
<tr>
<td>Calcitonin</td>
<td>c-cell carcinoma</td>
<td>c-cell carcinoma</td>
<td>c-cell carcinoma</td>
<td>c-cell carcinoma</td>
</tr>
<tr>
<td>hTG</td>
<td></td>
<td></td>
<td></td>
<td>diff thyroid carcinoma</td>
</tr>
</tbody>
</table>

### Table 3: Indications for Thermo Scientific™ B·R·A·H·M·S™ tumor markers examples for the use of marker combinations (by courtesy of Dr. P. Stieber)
Tumor markers on KRYPTOR Systems

Excellent precision and reproducibility

The unique TRACE™ technology utilised by KRYPTOR™ Systems eliminates the need for washing and separation steps, which significantly reduces the imprecision and variability inherent in many other systems.¹

It is this precise and consistent measurement of analyte concentration which makes tumor markers on KRYPTOR Systems an invaluable tool in the monitoring of cancer disease and in control of therapy.

### Table 4
Data on tumor marker precision: Examples for Thermo Scientific B·R·A·H·M·S Total PSA KRYPTOR

<table>
<thead>
<tr>
<th>Intra-assay precision</th>
<th>Serum pool</th>
<th>N</th>
<th>Mean [ng/mL]</th>
<th>CV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intra-assay precision</strong></td>
<td>3 calibrations, 2 kit lots, 2 calibrators, 20 days</td>
<td>Serum pool</td>
<td>N</td>
<td>Mean [ng/mL]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>40</td>
<td>3.5</td>
<td>2.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>8.1</td>
<td>2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>15</td>
<td>2.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>36.3</td>
<td>2.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>40</td>
<td>54.6</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

References

1. Thomas L. Clinical Laboratory Diagnostics. TM-Books Verlagsgesellschaft Frankfurt/Main, 938
7. Results of the survey "Oncocheck", distributed by the University of Lyon
Thermo Scientific Tumor Markers
A broad range of markers available

**Brain**
- NSE, CEA

**Pituitary Gland**
- Prolactin

**Liver**
- AFP, CEA, CA 19-9, Chromogranin A

**Gallbladder**
- CA 19-9, CEA

**Adrenal Gland**
- Chromogranin A

**Kidney**
- CEA, NSE

**Colon**
- CEA, CA 19-9, Chromogranin A

**Bladder**
- CYFRA 21-1, CEA, NSE

**Prostate**
- Total PSA, Free PSA

**Testicle**
- AFP, hCG+β

**Bone Metastases**
- Osteocalcin

**ENT (Ear, Nose, and Throat)**
- SCC, CYFRA 21-1, CEA

**Thyroid**
- **MTC:** Calcitonin, Chromogranin A, CEA
- **DTC:** Thyroglobulin, CEA

**Esophagus**
- SCC, CYFRA 21-1, CEA

**Breast**
- CA 15-3, CEA

**Stomach**
- CEA, CA 19-9, Chromogranin A

**Pancreas**
- CA 19-9, CEA, Chromogranin A

**Neuroendocrine Tumors**
- Chromogranin A, NSE

**Ovary**
- CA 125 II, CEA, AFP, hCG+β

**Uterus**
- SCC, hCG+β, CYFRA 21-1

**Cervix**
- SCC, CYFRA 21-1, CEA

**Vagina, vulva**
- SCC