Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

CNS Metastases in Breast Cancer
CNS Metastases in Breast Cancer

- **Versions 2003–2017:**
  Bischoff / Diel / Friedrich / Gerber / Huober /
  Loibl / Lück / Maass / Müller / Nitz / Jackisch /
  Jonat / Junkermann / Rody / Schütz / Fehm / Witzel

- **Version 2018:**
  Müller / Stickeler

unter Mitarbeit von:
Petra Feyer und Dirk Rades (DEGRO)


CNS Metastases in Breast Cancer (BC) Risk Factors

- **Primary Tumor:**
  - Negative estrogen receptor status (basal-like cell type / triple-negative)
  - High grading, high Ki-67 index
  - HER2 and/or EGFR (HER1) overexpression
  - Molecular subtype (Luminal B, HER2 positive, triple-negative)

  **Brain metastases are more likely to be estrogen receptor negative and overexpress HER2 and/or EGFR**

  **There is no evidence for BM-screening in asymptomatic BC-patients**

**Risk factors (see also references slide CNS incidence):**


Brain metastases (BM) are more likely to be estrogen receptor negative, and overexpress HER2 or EGFR.


There is no evidence for BM-screening in asymptomatic BC-patients

Breast-GPA:


Prognostic Factors for Survival:


116:3084-3092.


20. Tsao M, Xu W, Sahgal A: A meta-analysis evaluating stereotactic radiosurgery, whole-brain radiotherapy, or both for patients presenting with a limited number of brain metastases. Cancer 2012, 118:2486-2493


NCCTG N0574 (Alliance): A Phase III Randomized Trial of Whole Brain Radiation Therapy (WBRT) in Addition to Radiosurgery (SRS) in Patients with 1 to 3 Brain Metastases

Study design:
Patients with 1-3 brain metastases, each < 3 cm by contrast MRI, were randomized to SRS alone or SRS + WBRT and underwent cognitive testing before and after treatment. The primary endpoint was cognitive progression (CP) defined as decline > 1 SD from baseline in any of the 6 cognitive tests at 3 months. Time to CP was estimated using cumulative incidence adjusting for survival as a competing risk.*

Conclusion:
Decline in cognitive function, specifically immediate recall, memory and verbal fluency, was more frequent with the addition of WBRT to SRS. Adjuvant WBRT did not improve OS despite better brain control. Initial treatment with SRS and close monitoring is recommended to better preserve cognitive function in patients with newly diagnosed brain metastases that are amenable to SRS.

* Remark: No hippocampus-sparing was applied


Possible Factors for Decision Making Neurosurgery versus Stereotactic Radiosurgery

Factors in favor of neurosurgery:
- Histological verification e.g. after a long recurrence-free interval
- Need for immediate decompression, life-threatening symptoms
- Tumor size not allowing stereotactic radiotherapy

Factors in favor of primary radiotherapy:
- Tumor location poorly amenable to surgery
- More than four lesions

**Multiple Brain Metastases if Stereotactic Radiotherapy is not Indicated**

<table>
<thead>
<tr>
<th>Oxford</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBRT (supportive steroids*)</td>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Hippocampal-sparing radiotherapy</td>
<td>2b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Corticosteroids alone*</td>
<td>3a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Radiochemotherapy for control intracerebral</td>
<td>3b</td>
<td>C</td>
<td>-</td>
</tr>
<tr>
<td>WBRT in case of recurrence**</td>
<td>4</td>
<td>C</td>
<td>+/-</td>
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</table>

SRS = stereotactic radiosurgery  
FSRT = fractionated stereotactic radiotherapy  
WBRT = whole brain radiotherapy

* adapted to symptoms  
** can be discussed depending on the time-interval from first radiation, prior dose and localization if local therapy (surgery, SRS, FSRT) is not indicated and / or od possible


7. Krop IE, Lin NU, Blackwell K et al.: Trastuzumab emtansine (T-DM1) versus lapatinib plus capecitabine in patients with HER2-positive metastatic breast


Radiochemotherapy


Re-Bestrahlung bei Rezidiv


Chemotherapy


Anticonvulsants


Steroid


Leptomeningeal Carcinomatosis
Local Therapy

### Intrathecal or ventricular therapy

- **MTX 10–15 mg 2–3x/ week (+/- folinic acid rescue)**
  - LoE 2b
  - Grade B
  - AGO +

- **Liposomal cytarabine 50 mg, q 2w**
  - LoE 3b
  - Grade C
  - AGO +

- **Thiothepa**
  - LoE 3b
  - Grade C
  - AGO +/-

- **Steroids**
  - LoE 4
  - Grade D
  - AGO +/-

- **Trastuzumab (HER2 pos. disease)**
  - LoE 4
  - Grade C
  - AGO +/-

### Systemic Therapy

**Radiotherapy**

- **Focal (bulky disease)**
  - LoE 4
  - Grade D
  - AGO +

- **WBRT**
  - LoE 4
  - Grade D
  - AGO +

- **Neuroaxis (disseminated spinal lesions)**
  - LoE 4
  - Grade D
  - AGO +/-

*Due to poor prognosis consider best supportive care, especially in patients with poor performance status*

* Currently not available

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8. Chamberlain MC: Neoplastic meningitis and metastatic epidural spinal cord


oncology 2012, 10:45-53.

Trastuzumab intrathecal


MTX high dose