Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Osteonkologie und Knochengesundheit
Osteoonkologie und Knochegesundheit

- **Versionen 2002–2018:**
  Bischoff / Böhme / Brunnert / Dall / Diel / Fehm / Fersis / Friedrich/ Friedrichs / Hanf / Huober / Jackisch / Janni / Kolberg-Liedtke / Lux / Maas / Nitz / Oberhoff / Schaller / Scharl / Schütz / Seegenschmiedt / Solomayer / Souchon

- **Version 2019:**
  Diel / Kolberg-Liedtke
Metaanalysen and Reviews (metastatic breast cancer)


Results of Phase III trials (metastatic breast cancer)


6. Rosen LS, Gordon DH, Dugan W et al. Zoledronic acid is superior to pamidronate for the treatment of bone metastases in breast carcinoma patients with at least one osteolytic lesion. Cancer 100:36-43, 2004

Clinical relevance of bone resorption marker


Bisphosphonates for bone pain control

**Denosumab beim metastasierten Mammakarzinom**

<table>
<thead>
<tr>
<th>Evidenz</th>
<th>Grading</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduktion der Hyperkalzämie</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Reduktion skeletter Hallokomplikationen</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Reduktion von Knochenschmerzen</td>
<td>1a</td>
<td>A</td>
</tr>
<tr>
<td>Verlängerung der Zeit bis zum Auftreten von Knochenschmerzen</td>
<td>1b</td>
<td>A</td>
</tr>
<tr>
<td>Therapie nach ossärer Progression</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>Progression unter Bisphosphonaten</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>Bestimmung von Knochenresorptionsmarken zur Therapiekontrolle</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>Alleinige Therapie zur Analgesie bei Knochenschmerzen</td>
<td>5</td>
<td>D</td>
</tr>
</tbody>
</table>

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**Denosumab - Therapy of bone metastases and skeletal related complications**


**Statement: Progression under bisphosphonates**

Clinical relevance of bone resorption marker


Bisphosphonates for bone pain control

### Longer-Interval vs Standard Dosing of Zoledronic Acid

1. **CALGB 70604 trial**: n = 1822 patients with metastatic breast cancer, metastatic prostate cancer, or multiple myeloma, 795 completed the study
   - SRE after 2 yrs: 29.5% zoledronic acid every 4 weeks
   - 28.6% zoledronic acid every 12 weeks

2. **Optimize-2-trial**: n = 460 with metastatic breast cancer
   - SRE after 1 year: 22.0% zoledronic acid every 4 weeks
   - 23.2% zoledronic acid every 12 weeks

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3. Patients eligible for this trial had prior exposure to zoledronic or pamidronate for approx. 1 year or more

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1. Templeton AJ et al. Prevention of symptomatic skeletal events with denosumab administered every 4 weeks versus every 12 weeks: A noninferiority phase III trial (SAKK 96/12, REDUSE). J Clin Oncol 32:5s, 2014 (suppl; abstr TPS5095)


7. Hortobagyi GN, Van Poznak C, Harker WG et al. Continued Treatment Effect of Zoledronic Acid Dosing Every 12 vs 4 Weeks in
Women With Breast Cancer Metastatic to Bone: The OPTIMIZE-2 Randomized Clinical Trial. JAMA Oncol 3(7):906-912, 2017
### Reviews / Overview


### Rhenium (\(^{186}\text{Re}\)-HEDP)


**153Samarium (153Sm-EDTMP)**


**89Strontium (89Sr-Chlorid)**


**223Ra-dichloride:**


177Lu (Lutetium)-EDTMP


Recurrent bone pain in pre-irradiated parts of the skeleton


Magnetic resonance-guided focused ultrasound

Cryoablation / Radiofrequency ablation
Bisphosphonates


Denosumab


Bisphosphonates


**Denosumab**


### Adjuvante osteoprotektive Therapie zur Verbesserung der Prognose

<table>
<thead>
<tr>
<th>Therapie</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clodronate (oral)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausale Patientinnen</td>
<td>1a</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>Prämenopausale Patientinnen</td>
<td>1a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td><strong>Aminobisphosphonate (iv oder oral)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausale Patientinnen</td>
<td>1a</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>Prämenopausale Patientinnen</td>
<td>1a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td><strong>Denosumab (6 x 120 mg/3–4w + 14 x 120 mg/3m)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausale Patientinnen Stadium II und III</td>
<td>1b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td><strong>Denosumab (60 mg s.c. q6m)</strong></td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
</tbody>
</table>


Adjuvant Aminobisphosphonates


Denosumab

Guidelines


Bisphosphonates


Denosumab


Bisphosphonates


Denosumab


Raloxifen


Strontium renalate

1. German guidelines for the treatment of osteoporosis by the DVO: