Occurrence of skeletal-related events (SRE) in patients with solid tumors (ST): early versus late initiation of SRE preventative agents (SPA)

Intorcia M¹, Hohmann D², Giannopoulou C¹, Ansorge S³, Diel I⁴

¹Amgen (Europe) GmbH, Zug, Switzerland, ²Amgen GmbH, Munich, Germany, ³Arvato Health Analytics, Munich, Germany; ⁴Schwerpunktpraxis für Gynäkologische Onkologie (SPGO), Mannheim, Germany
Disclosures

- M Intorcia and D Hohmann are employees of Amgen and hold stock
- C Giannopoulou is an employee of Amgen
- I Diel has received consulting fees for participation in advisory boards and has given several presentations at speakers’ bureaus for Amgen
- S Ansorge was an employee of Arvato Health Analytics GmbH at the time of this research. This research was sponsored by Amgen (Europe) GmbH and Arvato Health Analytics conducted it under contract with Amgen.
Introduction: bone metastases (BM) and SREs

Bone is a frequent site of metastases in solid tumors\(^1\)

- Around 70% of patients with metastatic breast or prostate cancer and 36% with metastatic lung cancer develop BM\(^1\)

- Patients with BM often develop SREs, which include:\(^2,3\)
  - Spinal cord compression
  - Pathological fractures
  - Surgery (surrogate marker)
  - Radiation therapy (surrogate marker)

- In the absence of SPAs (osteoprotective substances), the proportion of patients with an SRE at 2-year follow-up is 64%, 49% and 46% in advanced breast, prostate and lung cancer, respectively\(^4-6\)

---


SPA, SRE preventative agent; SRE, skeletal-related event
Introduction: impact of SREs

- SREs affect morbidity and quality of life, and have been associated with reduced overall survival as well as increased healthcare costs\(^1\)–\(^5\)

![Survival probability for breast cancer patients with BM +/- SRE](image)

<table>
<thead>
<tr>
<th>SRE</th>
<th>Germany</th>
<th>Italy</th>
<th>Spain</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-vertebral fracture</td>
<td>1720</td>
<td>2087</td>
<td>3209</td>
<td>2254</td>
</tr>
<tr>
<td>Vertebral fracture</td>
<td>2124</td>
<td>2142</td>
<td>6968</td>
<td>1015</td>
</tr>
<tr>
<td>Radiation to bone</td>
<td>1694</td>
<td>2461</td>
<td>2378</td>
<td>704</td>
</tr>
<tr>
<td>Spinal cord compressions</td>
<td>5847</td>
<td>4884</td>
<td>7903</td>
<td>12,082</td>
</tr>
<tr>
<td>Surgery to bone</td>
<td>9407</td>
<td>3348</td>
<td>4263</td>
<td>7447</td>
</tr>
</tbody>
</table>

- Administration of antiresorptive drugs, including bisphosphonates and denosumab, is necessary to prevent SREs in patients with solid tumors and BM
  - Osteoprotectivs should be provided at diagnosis of metastatic bone disease
- Real-world data on SRE-preventative agents use are needed to guide clinical decisions

Objectives and methods

Objectives: This exploratory analysis estimated the time from diagnosis to occurrence of first and subsequent SREs in patients with early versus late treatment initiation with SPA

Study design

- Retrospective analysis of a German healthcare insurance company database including data from approximately 3 million patients (approximately 4–5% of the total sickness fund population in Germany)
- At the time of the analysis the database contained data from 2007 to 2015

Key eligibility criteria

- Age ≥18 years
- Patients with solid tumors coded with ≥2 outpatient or 1 inpatient diagnoses and newly diagnosed with BM after July 2011
- Received SPA within 9 months of inclusion in the study

Outcomes

- Time from BM to occurrence of first and subsequent SREs in patients with early (≤3 months) versus late (>3–9 months) treatment initiation with SPA

BM, bone metastasis; SPA, SRE preventative agent; SRE, skeletal-related event
Methods

Patients included in the study were grouped according to whether they received early (≤3 months) or late (>3–9 months) treatment initiation with SPA.

The two cohorts were adjusted for imbalances in baseline demographics with matched pairs, randomly selecting three patients from the early group for every patient in the late group (without replacement).

After adjustment, all relevant covariates were balanced.
# Results: patient selection flow chart

<table>
<thead>
<tr>
<th>Patients with solid tumors and newly diagnosed BM (N=3,914)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No hypercalcemia diagnosis (N=3,706)</td>
</tr>
<tr>
<td>All information available (N=2,400)</td>
</tr>
<tr>
<td>Received SPA within 9 months (N=971)</td>
</tr>
<tr>
<td>Received SPA early* (N=823) or late† (N=148)</td>
</tr>
<tr>
<td>Adjusted with matched pairs: early* (N=444) or late† (N=148)</td>
</tr>
</tbody>
</table>

*≤3 months; †>3–9 months

BM, bone metastasis; SPA, skeletal-related event preventative agent
## Results: baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unmatched population</th>
<th>Matched population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early (&lt;3 months) N=823</td>
<td>Late (&gt;3–9 months) N=148</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>452 (54.9)</td>
<td>70 (47.3)</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>69.7 (11.4)</td>
<td>70.1 (10.9)</td>
</tr>
<tr>
<td>Mean CCI (SD)</td>
<td>10.1 (2.1)</td>
<td>10.2 (2.1)</td>
</tr>
<tr>
<td>Cancer type, n (%)</td>
<td>Breast cancer + BM</td>
<td>370 (45.0)</td>
</tr>
<tr>
<td></td>
<td>Prostate cancer + BM</td>
<td>262 (31.8)</td>
</tr>
<tr>
<td></td>
<td>Lung cancer + BM</td>
<td>134 (16.2)</td>
</tr>
<tr>
<td></td>
<td>Other + BM</td>
<td>57 (6.9)</td>
</tr>
<tr>
<td>SRE, n (%)</td>
<td>173 (21.0)</td>
<td>34 (23.0)</td>
</tr>
<tr>
<td>Osteoporosis, n (%)</td>
<td>138 (16.8)</td>
<td>17 (11.5)</td>
</tr>
<tr>
<td>Renal disease, n (%)</td>
<td>147 (17.9)</td>
<td>32 (21.6)</td>
</tr>
<tr>
<td>Cardiovascular disease, n (%)</td>
<td>101 (12.3)</td>
<td>20 (13.5)</td>
</tr>
</tbody>
</table>

- Mean age and number of baseline SREs was similar for both early and late initiators of SPA
- Other baseline characteristics (cancer type and incidence of osteoporosis) varied between cohorts, which were adjusted for in the stratified population
Results

**Time to first SRE**

Median (95% CI) time to first SRE was 19 months (12, 33) for early initiators and 7 months (4, 20) for late initiators.

**Time to second SRE**

Median (95% CI) time to second SRE was 39 months (33, NR) for early initiators and 21 months (13, NR) for late initiators.

Pathological fractures and the need for radiotherapy were the most common SREs, in line with previous reports.¹

---

¹ Coleman R et al. Ann Oncol 2014;25(Suppl. 3):iii12437

CI, confidence interval; NR, not reached; SPA, SRE preventative agent; SRE, skeletal-related event
Conclusions

• In this analysis of data from patients with solid tumors and BM, the median time to occurrence of first and second SREs was longer for early versus late initiators of SPA (SRE-preventative agents).

• These results indicate that patients with solid tumors should receive SPA (osteoprotective drugs) without delay (≤3 months) following diagnosis of BM.

• This analysis was limited by its exploratory design, small sample size and short follow-up.

• The association between time to treatment and SRE incidence warrants further investigation.

BM, bone metastasis; SPA, SRE preventative agent; SRE, skeletal-related event