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

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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.

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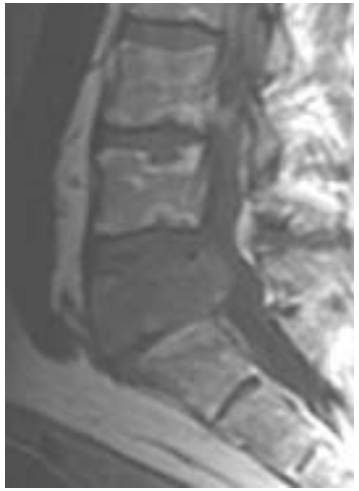
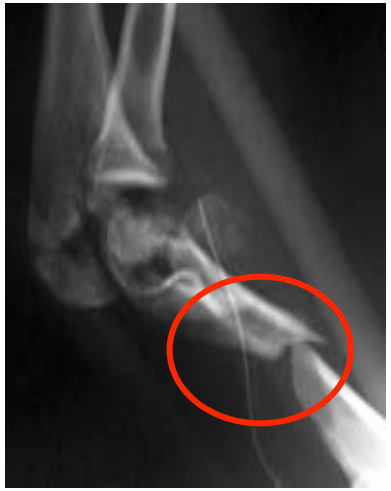
Introduction: bone metastases (BM) and SREs

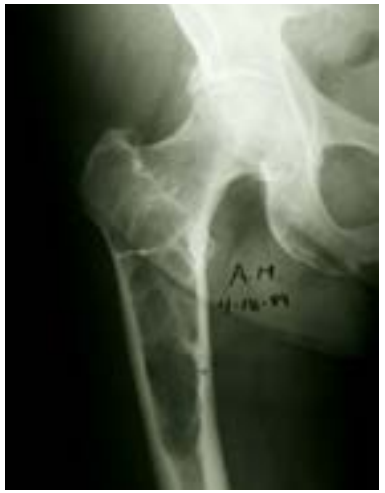
- Bone is a frequent site of metastases in solid tumors[1]
  - Around 70% of patients with metastatic breast or prostate cancer and 36% with metastatic lung cancer develop BM[1]
- Patients with BM often develop SREs, which include:[2,3]



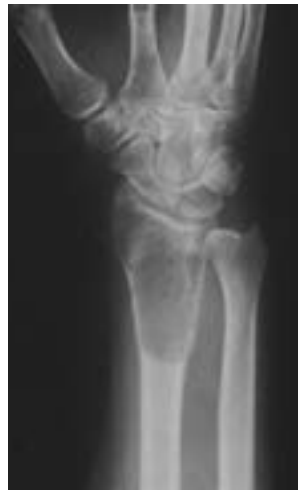
Spinal cord compression



Pathological fractures



Surgery (surrogate marker)



Radiation therapy (surrogate marker)

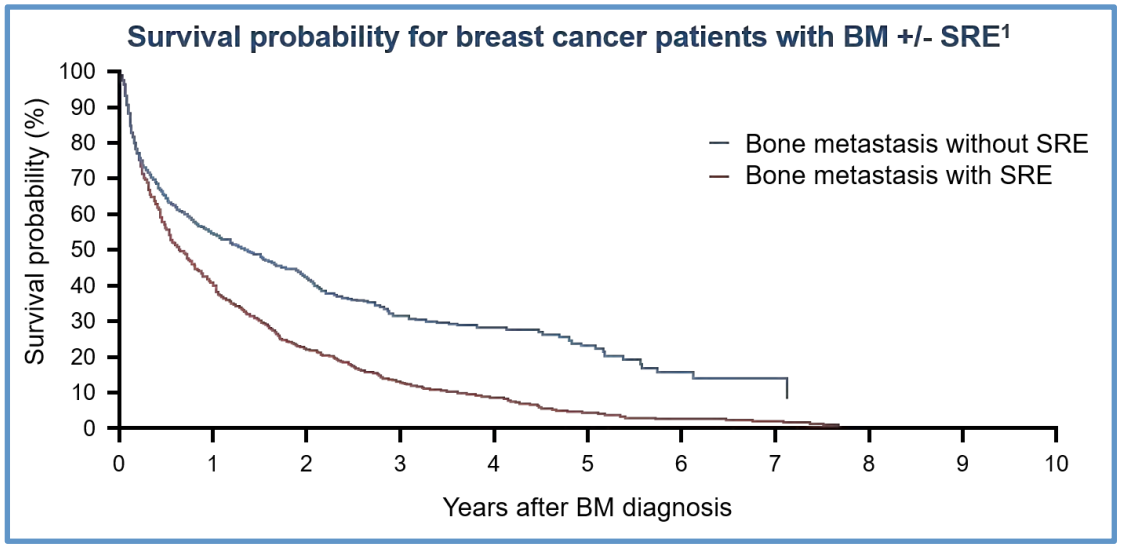
- In the absence of SPAs (osteoprotective substances), the proportion of patients with an SRE at 2-year follow-up is 64%, 49% and 46% in advanced breast, prostate and lung cancer, respectively[4–6]

1. Coleman R et al. Clin Cancer Res 2006;12:6243s–49s
2. Raje N and Roodman GD. Clin Cancer Res 2011;17:1278–86
3. Coleman R et al. Ann Oncol 2014;25(Suppl. 3):iii12437
4. Lipton A et al. Cancer 2000;88:1082–90
5. Saad F et al. J Natl Cancer Inst 2004;96:879–82
6. Rosen LS et al. Cancer 2004;100:2613–21

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]



SRE	Mean cost per SRE (€)[5]			
	Germany	Italy	Spain	UK
Non-vertebral fracture	1720	2087	3209	2254
Vertebral fracture	2124	2142	6968	1015
Radiation to bone	1694	2461	2378	704
Spinal cord compressions	5847	4884	7903	12,082
Surgery to bone	9407	3348	4263	7447

- Administration of antiresorptive drugs, including biphosphonates 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

1. Yong M et al. Breast Cancer Res Treat. 2011;129:495–503
2. Coleman R et al. Ann Oncol 2014;25(Suppl. 3):iii12437
3. Howard LE et al. Prostate Cancer Prostatic Dis 2016;19:380–4
4. Sathiakumar N et al. Breast Cancer Res Treat 2012;131: 231–8
5. Hechmati G et al. J Med Econ 2013;16:691–700

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

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

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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

SPA, SRE preventative agent; SRE, skeletal-related event

Results: patient selection flow chart

Patients with solid tumors and newly diagnosed BM (N=3,914)

↓

No hypercalcemia diagnosis (N=3,706)

↓

All information available (N=2,400)

↓

Received SPA within 9 months (N=971)

↓

Received SPA early* (N=823) or late† (N=148)

↓

Adjusted with matched pairs: early* (N=444) or late† (N=148)

*≤3 months; †>3–9 months

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

Results: baseline characteristics

Characteristic	Unmatched population		Matched population	
	Early (≤3 months) N=823	Late (>3–9 months) N=148	Early (≤3 months) N=444	Late (>3–9 months) N=148
Female, n (%)	452 (54.9)	70 (47.3)	211 (47.5)	70 (47.3)
Mean age, years (SD)	69.7 (11.4)	70.1 (10.9)	70.4 (11.1)	70.1 (10.9)
Mean CCI (SD)	10.1 (2.1)	10.2 (2.1)	10.2 (2.2)	10.2 (2.1)
Cancer type, n (%)				
Breast cancer + BM	370 (45.0)	52 (35.1)	156 (35.1)	52 (35.1)
Prostate cancer + BM	262 (31.8)	52 (35.1)	156 (35.1)	52 (35.1)
Lung cancer + BM	134 (16.2)	27 (18.2)	81 (18.2)	27 (18.2)
Other + BM	57 (6.9)	17 (11.5)	51 (11.5)	17 (11.5)
SRE, n (%)	173 (21.0)	34 (23.0)	97 (21.8)	34 (23.0)
Osteoporosis, n (%)	138 (16.8)	17 (11.5)	51 (11.5)	17 (11.5)
Renal disease, n (%)	147 (17.9)	32 (21.6)	94 (21.2)	32 (21.6)
Cardiovascular disease, n (%)	101 (12.3)	20 (13.5)	59 (13.3)	20 (13.5)

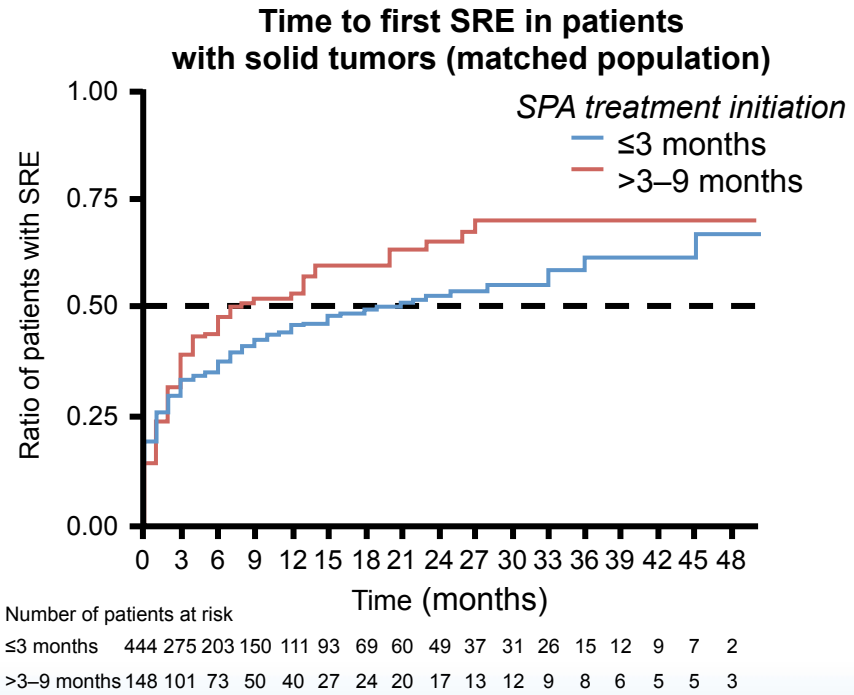
- Mean age and number of baseline SREs was similar for both early and late initiators of SPA
- Other baseline characteristics (cancer type and incidence of osteoporosis) varied between cohorts, which were adjusted for in the stratified population

BM, bone metastasis; CCI, Charlson Comorbidity Index; SD, standard deviation; SPA, SRE preventative agent; SRE, skeletal-related event

Results

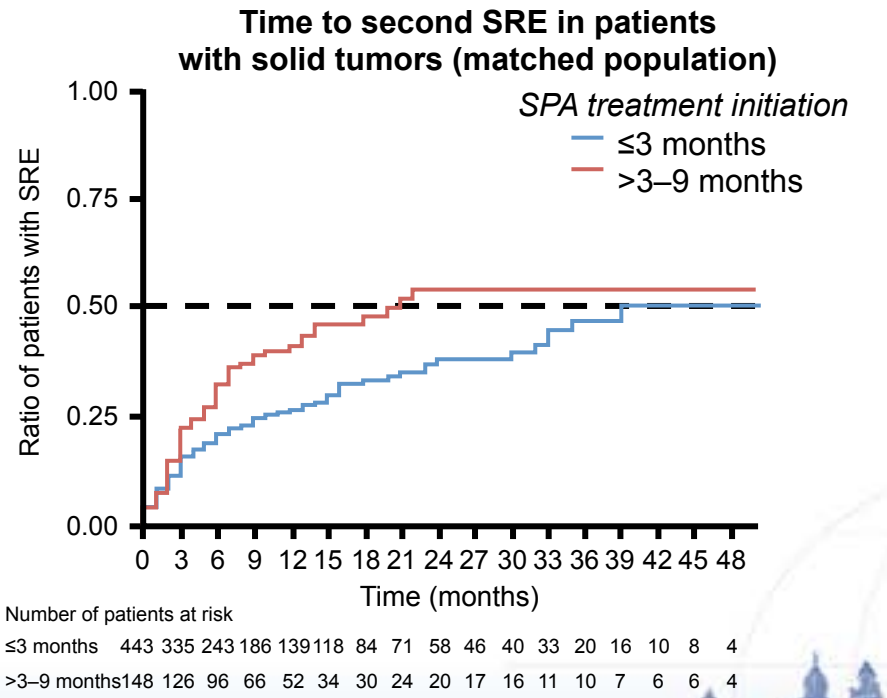
Time to first SRE

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]

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

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

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

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