Patterns of care for patients with metastatic bone disease in solid tumors – a cross-sectional study (SAKK 95/16)

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BACKGROUND

- Bone metastases are common in solid tumors and can lead to pain and symptomatic skeletal events (SSEs), such as pathological fractures, radiotherapy or surgery to bone, spinal cord compression and hypercalcemia (1).
- Randomized clinical trials have demonstrated that bone-targeted agents (BTAs) such as bisphosphonates, or receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitors (e.g. denosumab) reduce the incidence and delay the onset of SSEs (2).
- Questions of timing of treatment start, duration of treatment, and optimal dosing intervals of BTAs remain unanswered (3).
- The current treatment practice of 3–4 weekly therapy with BTAs could expose patients (pts) to an increased risk of adverse effects.
- Trials (e.g. SAKK 96/12) investigating the effect of different dosing intervals of denosumab on bone metastases are in progress (4).

METHODS

- **Primary objective:** Cross-sectional study to assess current real-world clinical practice for all pts with bone metastases in Switzerland, irrespective of BTA treatment.
- **Inclusion criteria:** Pts with solid tumors and at least one bone metastases.
- **Exclusion criteria:** Pts enrolled or planned to be enrolled in the SAKK 96/12 trial.
- **Primary outcomes:** Physicians were asked to report the criteria for the indication and administration of BTAs in pts with bone metastases of solid tumors in Switzerland (physician-related outcomes) during a period of 3 months. Patterns of care was assessed by questions about reasons for BTA administration, treatment pattern, patient characteristics, and actual treatment. Pts completed a pain and bone-pain related quality of life questionnaire.
- **Statistics:** Patient characteristics and outcome variables were analyzed using descriptive statistics. Frequencies (%) were calculated for categorical or ordinal variables, and medians (ranges) for continuous variables.

Conflict of interest:
Michael Mark, Karin Ribi, Corinne Schär, Daniel Dietrich, and Ursina Zürrer declare no conflict of interest.
Beat Thürlimann holds stock of Novartis and Roche, received consultation fee from Amgen and Roche.
Roger von Moos participated in advisory boards from Amgen, Bayer, Novartis and Roche.

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RESULTS

- Datasets of a total of 417 pts were collected in the defined interval.
- 86 oncologists from 18 sites in Switzerland participated between November 2017 and May 2018 in the study.
- The most frequently underlying tumor entity was breast cancer (40.5%, 169/417), followed by prostate cancer (25.4%, 106/417), and lung cancer (14.9%, 62/417).
- *Physician-related outcomes:* Most of the physicians reported to start treatment with BTAs according to current guidelines (70.9%, 61/86). A minority would first assess the risk (high vs low) for developing symptomatic skeletal events (SSEs) in order to decide about the optimal timepoint of treatment initiation (24.4%, 21/86). Factors contributing to define high risk are depicted in Table 1.
- *Patterns of care:* The majority of the pts has been treated with BTAs immediately after the diagnosis of bone metastases (73.6%, 307/417). Denosumab was the most frequently used BTA (78.5%; 241/307), and a 3-4 week interval was most common (88.9%; 273/307). The main reasons for treatment with BTAs were high risk of bone complications (43%, 132/307), bone pain (21.8%, 67/307), and location of bone metastases (10.1%, 31/307), respectively. No association between bone pain and BTA treatment or risk categorization was found (see Table 2). SSEs were reported in 7.8% of treated vs 7.6% of non-treated pts, and were similar in pts rated as low or as high risk (see Table 3).

Table 1. Factors contributing to define a high risk situation (N=86 investigators)

Factors (multiple choice)	Number of investigators	Percent
Former skeletal related events (SREs)	77	89.5
Lytic bone metastases	75	87.2
High burden of metastatic disease	58	67.4
Pain score	53	61.6
Elevated alkaline phosphatase	38	44.2
Age	31	36.0
Elevated markers for bone turnover	17	19.8
Osteoplastic bone metastases	16	18.6
Elevated lactate dehydrogenase (LDH)	15	17.4
There are no reliable factors to estimate the risk of SREs	3	3.5

RESULTS - continued

Table 2. Frequencies and percentage of pts with current bone pain by BTA treatment (no, yes) and by risk status (high, low) (N=400 pts with known risk status)

BTA treatment	Risk status	Group size	Current bone pain	
			Number of patients	Percent
No	All	106	15	14.2
Yes		294	47	16.0
All	High	235	42	17.9
	Low	165	20	12.1
No	High	40	9	22.5
No	Low	66	6	9.1
Yes	High	195	33	16.9
Yes	Low	99	14	14.1

Table 3. Frequencies and percentage of pts with SSE's by BTA treatment (no, yes) and by risk status (high, low) (N=399 pts with known risk status)

BTA treatment	Risk status	Group size	Current complications	
			Number of patients	Percent
No	All	105	8	7.6
Yes		294	23	7.8
All	High	234	18	7.7
	Low	165	13	7.9
No	High	39	5	12.8
No	Low	66	3	4.5
Yes	High	195	13	6.7
Yes	Low	99	10	10.1

CONCLUSIONS

- The majority of the pts was treated according to current guideline recommendations with regard to start and interval of BTA treatment.
- The number of SSEs was low irrespective of BTA treatment and risk classification for SSEs.
- This may reflect a high impact of the systemic cancer treatment on SSE reduction, or a selection of pts according to risk factors not identified as the ones reported in the literature.

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