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Original Research

Treatment and pattern of bone metastases in 1094 patients with advanced breast cancer – Results from the prospective German Tumour Registry Breast Cancer cohort study

Jan Schröder [a,1], Thomas Fietz [b,2], Andreas Köhler [c,3], Volker Petersen [d,4], Hans Tesch [e,5], Lisa Spring [f,6], Annette Fleitz [f,6], Martina Jänicke [f,6], Norbert Marschner [g,*], the TMK-Group (Tumour Registry Breast Cancer)

[a] *Centre for Haematology and Oncology, Kettwiger Str. 62, 45468 Mülheim, Germany*
[b] *Centre for Internal Medicine, Haematology and Oncology, Virchowstr. 10c, 78224 Singen, Germany*
[c] *Centre for Haematology and Oncology, Röntgenstr. 6-8, 63225 Langen, Germany*
[d] *Centre for Oncology, Kurze Str. 5, 89522 Heidenheim, Germany*
[e] *Centre for Haematology and Medical Oncology at Bethanien, Im Prüfling 17-19, 60389 Frankfurt/Main, Germany*
[f] *Clinical Epidemiology and Health Economics, iOMEDICO, Hanferstr. 28, 79108 Freiburg, Germany*
[g] *Centre for Interdisciplinary Oncology and Haematology, Wirthstrasse 11c, 79110 Freiburg, Germany*

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Abstract A high proportion of patients with breast cancer develop bone metastases, yet data on routine treatment with bone-targeted agents (BTA) are rare. We report real-life outcome data of patients with breast cancer metastasised to the bone treated by office-based oncologists in Germany.

The ongoing, prospective, multicentre, population-based cohort study Tumour Registry Breast Cancer (TMK) was started in 2007 in 140 centres across Germany.

* *Corresponding author*. Fax: +49 761 386 8710.
E-mail addresses: jan.schroeder@onkologie-mh.de (J. Schröder), fietz@onkologie-bodensee.de (T. Fietz), dr.koehler@onkologie-langen.de (A. Köhler), vp@tumorpraxis-heidenheim.de (V. Petersen), hans.tesch@telemed.de (H. Tesch), lisa.spring@iomedico.com (L. Spring), annette.fleitz@iomedico.com (A. Fleitz), martina.jaenicke@iomedico.com (M. Jänicke), norbert.marschner@onkologie-freiburg.de (N. Marschner).
[1] Fax: +49 208764404.
[2] Fax: +49 77317976699.
[3] Fax: +49 61033018273.
[4] Fax: +49 7321342810.
[5] Fax: +49 6956005625.
[6] Fax: +49 7611524250.

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Bone metastasis;
Diphosphonates;
Denosumab

This interim analysis of 1094 patients with bone metastases revealed differences among the tumour subtypes: at start of first-line therapy, 36% of the patients with hormone receptor (HR)-positive and only 20% of the patients with HR-negative tumours presented with bone-only metastasis. The majority of patients with bone metastases (89%, n = 976) received BTA therapy. In 2014–2015, 37% of the patients received the bisphosphonate zoledronic acid and 36% the antibody denosumab. Median duration of BTA therapy was 20 months (interquartile range 31.5 months), starting a median of 3 weeks after diagnosis of bone metastases, and ending a median of 7 weeks before death. The median overall survival (OS) also varied among the types of metastasis at start of first-line therapy ranging from 54 months (95% confidence interval [CI] 37.6–70.8), 38 months (95% CI 29.4–44.2) to 28 months (95% CI 24.2–31.0) for patients with bone-only metastases, non-visceral with or without bone metastases and visceral with or without bone metastases respectively.

We show that choice and duration of BTA therapies are in conformity with guidelines applicable in Germany. To our knowledge, this is the first presentation of data on incidence, metastatic pattern, treatment and survival of patients with bone metastases in routine practice.

1. Introduction

Breast cancer is the leading cause of cancer deaths in women, with half a million deaths worldwide every year [1]. More than 90% of these deaths are caused by metastasis [2]. Despite recent advances, treatment of advanced breast cancer remains palliative, and the survival times for the patients vary greatly. Breast cancer displays a distinct metastatic pattern with the skeleton as predominant metastatic site [2,3]. About 65–75% of the patients with metastatic breast cancer develop bone metastases [4,5]. However, these numbers stem from data arising out of autopsies in the 1970s, and current data on the pattern and incidence of bone metastases in advanced breast cancer on population level are limited [6–8]. Prognosis for patients with distant metastasis to the bone is more favourable than for those with visceral or multiple metastases [9–11]. Treatment of bone metastases is generally palliative, aiming at reducing the symptoms, improving quality of life and possibly prolonging survival. Several bone-targeted agents (BTAs) are approved and are currently considered the standard of care [12–14]. The main types of bone-targeted agents are bisphosphonates and the RANK-ligand (RANKL) inhibitor denosumab. Bisphosphonates induce apoptosis of osteoclasts and thus inhibit bone resorption [15] and reduce the skeletal morbidity rate [16]. The synthetic antibody denosumab specifically inhibits the maturation of osteoclasts and was shown to be superior to zoledronic acid in reducing skeletal-related events (SREs) such as surgery or radiotherapy to the bone, pathological fracture, spinal cord compression or hypercalcaemia [17]. Efficacy of these BTAs in treatment of bone metastases has been established in randomised controlled trials (RCTs) [16,18]. However, the demographic and medical characteristics of the general population often differ from patients enrolled in clinical trials. There are only few data on the use of BTAs in routine care, and existing data are often limited by retrospective collection [6,19,20].

In this article, we present data on patients with breast cancer metastasised to the bone. Data are derived from a prospective clinical cohort study covering patients treated by office-based medical oncologists in Germany. We show the metastatic pattern of 1094 patients at start of their first-line therapy as well as during the course of the disease. Furthermore, we present details on the BTA therapy and show that the overall survival (OS) varies among patients with differing metastatic pattern.

2. Patients and methods

2.1. Data source

The Tumour Registry Breast Cancer (TMK) is an ongoing, open, longitudinal, multicentre, observational, prospective cohort study which started in 2007. The study was approved by the responsible ethics committee and is registered at ClinicalTrials.gov (TMK registry, NCT01351584). The TMK methodology has previously been described in detail [21].

Eligible patients for the present analysis were women aged ≥18 years with advanced breast cancer at the start of their first palliative systemic antineoplastic treatment. Administration of each BTA is documented with the date of first and last dose, dosage and route of administration. Data on the location of metastases are documented at inclusion and then updated upon any change, but at least every 6 months. In order to collect representative data for routine treatment in Germany, a large number of outpatient-centres for medical oncology located all over Germany take part in the TMK. At the time of this analysis, 140 such study sites were actively participating.