



ELSEVIER

Contents lists available at ScienceDirect

## Journal of Bone Oncology

journal homepage: [www.elsevier.com/locate/jbo](http://www.elsevier.com/locate/jbo)

## Review article

## Future directions for bone metastasis research – highlights from the 2015 bone and the Oncologist new updates conference (BONUS)



Ricardo Fernandes<sup>a</sup>, Peter Siegel<sup>b</sup>, Svetlana Komarova<sup>b,c</sup>, John Hilton<sup>a,d</sup>, Christina Addison<sup>d</sup>, Mohammed F K Ibrahim<sup>a</sup>, Joel Werier<sup>d,e</sup>, Kristopher Dennis<sup>f</sup>, Gurmit Singh<sup>g</sup>, Eitan Amir<sup>h</sup>, Virginia Jarvis<sup>a</sup>, Urban Emmenegger<sup>i</sup>, Sasha Mazzarello<sup>d</sup>, Mark Clemons<sup>a,d,\*</sup>

<sup>a</sup> Department of Medicine, Division of Medical Oncology, The Ottawa Hospital and University of Ottawa, Ottawa, Canada

<sup>b</sup> Department of Medicine, Goodman Cancer Research Centre, McGill University, Montreal, Canada

<sup>c</sup> Faculty of Dentistry, McGill University, Montreal, Canada

<sup>d</sup> Ottawa Hospital Research Institute and University of Ottawa, Ottawa, Ontario, Canada

<sup>e</sup> Department of Surgery, Division of Orthopaedic Surgery, The Ottawa Hospital and University of Ottawa, Ottawa, Canada

<sup>f</sup> Ottawa Hospital Division of Radiation Oncology and University of Ottawa, Ottawa, Ontario, Canada

<sup>g</sup> McMaster University, Hamilton, Canada

<sup>h</sup> Division of Medical Oncology, Department of Medicine, University Health Network and Princess Margaret Hospital and University of Toronto, Toronto, Canada

<sup>i</sup> Division of Medical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada

## ARTICLE INFO

## Article history:

Received 30 November 2015

Received in revised form

10 February 2016

Accepted 10 February 2016

Available online 23 February 2016

## Keywords:

Bone metastases

Cancer

Animal models

Cancer-induced pain

## ABSTRACT

In an era of reduced peer-reviewed grant funding, performing academic bone oncology-related research has become increasingly challenging. Over the last 10 years we have held an annual meeting to bring together clinicians, clinician/scientists and basic biomedical researchers interested in the effects of cancer and its treatment on skeletal tissues. In the past these “Bone and the Oncologist New Updates Conference (BONUS)” meetings have served as critical catalyst for initiating productive research collaborations between attendees. The 2015 BONUS meeting format focused on potential key research themes that could form the basis of a coordinated national research strategy to tackle unmet clinical and research needs related to complications associated with cancer metastasis to bone. The three themes planned for discussion were: Is bone metastases-related pain the main issue facing patients? Are there new therapeutic targets for patients with bone metastases? How do we more firmly link basic science with clinical practice? We present a summary of lectures and commentaries from the attendees to serve as an example that other similarly motivated groups can model and share their experiences. It is our hope that these presentations will result in comments, feedback and suggestions from all those researchers interested in this important area.

© 2016 The Authors. Published by Elsevier GmbH. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

Over the last two decades, there has been a substantial increase in our understanding of the underlying biology of bone metastasis as well as the development and widespread incorporation of inhibitors of osteoclast function, namely bisphosphonates and denosumab, into clinical practice [1–3]. However, more recently there has been an international fall in peer-reviewed grant funding [4]. This trend is also clearly evident in the declining grant support provided by the

three Canadian federal funding agencies (Canadian Institutes of Health Research (CIHR), Natural Sciences and Engineering Research Council of Canada (NSERC) and Social Sciences and Humanities Research Council (SSHRC) [4]. This has led to increased challenges in performing academic bone metastasis research. The “Bone and the Oncologist New Updates” (BONUS) meeting is an annual Canadian multidisciplinary conference on the interaction of bone and cancer biology [5,6]. The focus of the 2015 BONUS Conference (16 and 17 April 2015) was to discuss potential key research themes that could form the basis for a coordinated national research strategy to tackle unmet clinical and research needs related to complications associated with cancer metastasis to bone.

This article captures a two-day programme of multidisciplinary presentations, panel discussions and interactive dialogue on planning

\* Corresponding author at: Division of Medical Oncology, The Ottawa Hospital Cancer Centre, 501 Smyth Road, Ottawa, Canada.

E-mail address: [mclemons@toh.on.ca](mailto:mclemons@toh.on.ca) (M. Clemons).

**Table 1**  
Some unmet clinical and basic science questions.

Basic Science	Clinical
Are osteoclasts the only stromal cell type that should be targeted therapeutically?	What are the major issues affecting cancer patients with bone metastasis?
Are there new cancer/bone-stromal targets that should be developed?	What do patients, nurses and clinicians feel are the most immediate concerns (bone pain, mobility issues, and survival)?
What is our understanding of the biological mechanisms of pain associated with bone metastasis?	Why do bisphosphonates and denosumab for metastatic bone cancers fail to prolong overall survival?

a national strategy for bone metastasis research. We aimed to review the data on bone pain management, expand our capacity to address current and future development challenges, place strategies in the context of the widespread use of bone-targeting agents and to act as a forum for feedback and comments from other researchers interested in this field.

### 1.1. Preliminary discussions leading to BONUS 2015

Prior to the BONUS 2015 meeting a preliminary meeting was held in Montreal in November of 2014. The “working group” felt that the development of specific research questions focused on “bone metastasis” should be formulated from the starting point of unmet clinical needs. In particular, the following issues were felt to be of key importance: Understanding the biology associated with the process of bone metastasis initiation and progression and developing potential treatment strategies to improve outcome of patients with bone metastases. Several questions were discussed that are outlined in Table 1. There was also a strong feeling that research initiatives should incorporate questions that cut across the cancer care continuum from basic biomedical research to clinical translation and patient outcomes. Based on the priorities discussed during the preliminary meeting, the following themes were selected for in-depth discussion at the 2015 BONUS meeting: Is bone metastases-related pain the main issue facing patients? Are there new therapeutic targets for patients with bone metastases? How do we more firmly link basic science with clinical practice? Each of these themes will be summarised below.

**Theme 1.** : Is bone metastases-related pain the main issue facing patients?

This session consisted of presentations about metastasis-related bone pain from the perspectives of patient experience and clinical care.

“What are the current limitations of bone-targeted agents in relation to bone pain in patients with bone metastases?” Eitan Amir, MD

While any malignancy may metastasise to bone, it is most prevalent in advanced breast (70–80%), prostate (70–80%), thyroid (60%), lung (10–50%) and renal cancers (30%) [7–11]. The consequences of bone metastases include reduced survival, morbidity and pain that negatively affect the patient's quality of life (QoL) as well as skeletal-related events (SREs) [11,12]. Despite the fact that randomized trials of bisphosphonates, and denosumab, have shown reduced incidence of SREs, prolonged time to occurrence of SREs and an improvement in pain control, clear improvements in overall Quality of Life (QoL) have not been realized with their use. Two trials comparing pamidronate to placebo showed that patients in the pamidronate arms experienced less pain; however, there was no difference in the overall QoL [13]. Similarly, in the randomized trial comparing denosumab to zoledronic acid, improvements in QoL were observed in both arms with denosumab not showing consistently greater magnitude of improvement over

the entire trial period. Whether QoL improvements resulted from the administration of bone targeted therapy or the concurrent administration of systemic anti-cancer therapy is unclear especially as the placebo-controlled randomized trials of bisphosphonates did not show differences in QoL between arms [13–14]. Given that bone-targeting agents have not been found to affect overall or progression-free survival and have known risks and adverse effects, including rare but severe toxicities such as hypocalcaemia and osteonecrosis of the jaw (ONJ) [15–17], this lack of improvement in QoL is disappointing. As we have likely reached the limits of therapeutic osteoclast inhibition with bisphosphonates and denosumab there is increasing interest in the effects of other anti-cancer agents on the bone. For example, the use of new treatments for prostate cancer such as abiraterone acetate, enzalutamide and radium 223 have all shown decreased rates of SREs as well as improvements in survival. As a result, there is a need to develop better agents not only to reduce bone pain but to also identify strategies to optimise the use of bone-targeted agents as SREs become less common. As more effective cancer treatments become available, it will be important to further explore optimal dosing of bone-targeting agents in these patients.

“What do patients with bone metastases need?” Virginia Jarvis, RN

Virginia Jarvis, a nurse specialist in pain and palliative care, followed up with a discussion of known as well as poorly understood needs of patients with bone metastases in ambulatory and palliative care. Pain assessment for patients with bone metastasis presents unique problems as pain is often incidental in nature with high pain scores with movement and minimal to zero pain scores at rest making the standard 0–10 verbal scoring system an ineffective tool. The Brief Pain Inventory was discussed as a pain assessment instrument that could best inform health care professionals to the actual pain state and help guide the clinician to the choice of appropriate treatments that may include interventional therapies that go beyond the World Health Organisation Analgesic Ladder. Indeed, in a large recently presented study, risk of SREs was correlated with worsening pain scores on the Brief Pain Inventory [19]. The unmet needs of patients include treatments such as physiotherapy, occupational therapy and social work as pain affects mobility, activities of daily living, the ability to drive and financial decline. Following this presentation there was extensive discussion around whether bone pain was the major issue facing patients or reduced mobility. This could be an important direction for future studies and requires further evaluation.

“What are orthopaedic surgeons doing in 2015 for patients with painful bone metastases?” Joel Werier, MD

Orthopaedic stabilisation of osseous metastatic lesions can provide rapid and effective pain relief in patients presenting with significant bone destruction and impending or pathologic fracture. It is essential to develop a collaborative relationship between engaged orthopaedic surgeons and medical as well as radiation oncologists in order to facilitate multidisciplinary care of an individual patient. A clear understanding of life expectancy, patient expectations, and tumour biology

Download English Version:

<https://daneshyari.com/en/article/2136073>

Download Persian Version:

<https://daneshyari.com/article/2136073>

[Daneshyari.com](https://daneshyari.com)