

Review of: "Personalized (tailored) treatment with antiresorptive drugs (bisphosphonates, denosumab) in patients with bone metastases from solid tumors – A “Pico” document by Rete Oncologica Piemonte-Valle D’Aosta Bone Metastatic Disease Study Group"

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Potential competing interests: No potential competing interests to declare.

The manuscript describes the state of the art on the bone metastatic treatment and deals with the treatment options in this condition based on the Italian Guidelines “Bone Metastases” released by AIOM as well as the European ESMO Clinical Practice Guidelines 2020 and ASCO-Cancer Care Ontario, that indicate several medical treatment options with antiresorptive agents for bone metastases from solid tumors, with an established preference for prolonged (indefinite) treatment with monthly zoledronic acid or monthly denosumab. In this work they instead proposed some criteria for TREATMENTS with ANTIRESORPTIVE DRUGS for BONE METASTASES FROM SOLID TUMORS that can be INDIVIDUALIZED based on different parameters:

1. Known activity data (SRE reduction/delay)
2. Duration of treatment reported in studies (annual vs biennial vs indefinite)
3. Commitment to the oncological structure (monthly vs quarterly; intravenous versus subcutaneous versus oral)
4. Economic cost of the drug (pamidronate vs zoledronic acid vs ibandronate vs denosumab)
5. Commitment to the patient (number of accesses to hospital facilities)
6. Risk of medium- and long-term side effects (mainly: nephrotoxicity, MRONJ) that would help to support the use of cost effective treatments. Their proposal is of interest but we should remain that the reasons of the extensive use of zoledronic acid in bone metastatic cancers is that this drug is the most potent bisphosphonates as antiproliferative drug inducing proliferation of osteoblasts in the nanomolar concentration ranges and cytotoxicity against osteoclasts at higher concentrations (Savino et al., Eur J Med Chem. 2018; Scala et al., Cancer 2019). Despite of this, it is true zoledronic acid causes a number of ADR including renal ADR that may limit in some patients its use, see Maqoud et al., Pharmaceutics. 2021; Scala et al. Front Pharmacol 2022) so that its extensive use must be monitored to avoid or reduce severe ADR in some high risk patients.