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Abstract Submission FORM

IMPACT OF ANTIANGIOGENIC AGENTS ON MEDICATION-RELATED OSTEONECROSIS OF THE JAW (MRONJ): A MONOINSTITUTIONAL EXPERIENCE

SECTION: *1A - Epidemiology*

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Background.
Medication-Related Osteonecrosis of the Jaw (MRONJ) is well known as a side effect of Bone Modifying Agents (BMAs), including bisphosphonates (BPs) and denosumab (DMB), both at "low dose" (administered mostly in patients with osteoporosis and non-malignant diseases) and at "high dose" (principally in patients with bone metastases of solid cancer and in myeloma patients) [1].
MRONJ was initially reported only in metastatic bone cancer and multiple myeloma patients receiving intravenous BPs, but reports quickly included osteoporosis patients treated with oral BPs and finally patients receiving DMB and several biological agents[2].
Since 2009, the use of antiangiogenic agents (AAs) alone or in combination with BMAs has been linked to MRONJ occurrence in different patient populations. AAs reported as involved in cases of MRONJ include: anti-vascular endothelial growth factors (VEGF drugs), tyrosine-kinase inhibitors (TKIs), mammalian target of rapamycin (m-TOR) inhibitors[2].
However, literature is scarce about number of MRONJ cases receiving AAs, as most of papers are case reports and case series with few patients. Impact of AAs on the total of MRONJ cases and risk estimates of MRONJ due to AAs cannot be drawn from isolated case reports and limited case series.

Patients and methods.
We investigated administration of agents with antiangiogenic activity among 89 MRONJ cases observed at Alessandria Hospital between 2005 and 2023 in patients with metastatic solid cancer (breast, colorectal, renal, thyroid, lung, ovary cancer); myeloma was excluded by this analysis. We looked for use of:

a) Anti VEGF agents (bevacizumab, aflibercept)
b) Tyrosine kinase inhibitors (sunitinib, sorafenib, pazopanib, lenvatinib, etc.)
c) mTOR inhibitors (everolimus).

Results. Out of 89 MRONJ cases, we found 16 patients (18%) that have received AAs:

- 8 renal cancer patients: 1 treated with sunitinib alone (without bone metastases); 1 treated with sunitinib for years and later also with denosumab; 6 with bone metastases, receiving BMAs (zoledronic acid or denosumab) due to bone metastases and several AA agents (mostly sunitinib, pazopanib, everolimus) as systemic cancer treatment (usually for more lines);
- 4 breast cancer patients with bone metastases, receiving BMAs (zoledronic acid/denosumab) and bevacizumab together with chemotherapy;
- 2 colorectal cancer patients: 1 without bone metastases and developing MRONJ due to bevacizumab, 1 with bone metastases receiving DNB and bevacizumab plus aflibercept;
- 1 patient with ovary cancer receiving bevacizumab together with chemotherapy (without BMAs);
- 1 patient with bone metastases from thyroid cancer, treated with zoledronic acid and lenvatinib;

Conclusions. The possible impact of AAs on the MRONJ global occurrence in metastatic cancer population is not irrelevant.
We observed both MRONJ cases due to AA alone (4) and MRONJ cases in which AAs could have increased the MRONJ risk due to BMAs (12).
Estimates of MRONJ risk due to AAs are to be drawn by analysis of large patient populations treated with BMAs and/or AAs.

REFERENCES:

1. *Bedogni et al Italian position paper (SIPMO-SICMF) on medication-related osteonecrosis of the jaw (MRONJ). Oral Disease 2024 at https://doi.org/10.1111/odi.14887*
2. *Fusco et al. Expert Opin Drug Saf. 2016 Jul;15(7):925-35. doi: 10.1080/14740338.2016.1177021.*

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