Bisphosphonate-associated osteonecrosis of the jaw: evidence coming from the Italian post-marketing surveillance

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Introduction: Bisphosphonate (BP) associated osteonecrosis of the jaw (BONJ) has emerged as an important safety issue [1-3]. Although several cases of BONJ had been described, data from regulatory pharmacovigilance databases have not been taken into account yet.

Aim: To analyze data from the Italian Pharmacovigilance Adverse Event (AE) Spontaneous Reporting System [*Rete Nazionale Farmacovigilanza*] (RNF) to further our knowledge on BONJ.

Methods: From 2004 to 2011, RNF received 723 reports of ONJ or possible ONJ after BP administration. These reports were analyzed for the BP type, the duration of treatment, the dose and how recently the BP was used before ONJ or possible ONJ onset.

Results: The two major patient groups reporting ONJ or possible ONJ after BP administration were those treated with zoledronate for skeletal-related events associated with cancer disease (mainly breast cancer and multiple myeloma) and those treated with alendronate for osteoporosis. ONJ or possible ONJ cases emerged after a long term drug exposure with median time ranged from 1.3 to 6.3 years, depending on BP type. Interestingly, few ONJ cases emerged early with very short BP time exposure never published until now. Moreover, we found that in 178 reports ONJ or possible ONJ occurred after BP therapy cessation. The analysis of these cases, based on how recently the last BP dose was used, showed a great variability in terms of time frame between the last dose and the event onset (from 2 to 80 months).

Conclusion: These new evidences highlight the notion that BONJ is a very complex safety issue whose several questions are still open. National spontaneous reporting databases, which represent one of the major sources of data during the post-marketing phase, can contribute to a better understand of this complex safety issue.

References

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