

Medication-Induced Osteonecrosis of the Jaw: A Review of Cases from the Food and Drug Administration Adverse Event Reporting System (FAERS)

48th Annual
**SCIENTIFIC
DAY 2022**

Hardeep S. Ahdi, DO; Thomas Adam Wichelmann, DO; Sasirekha Pandraveda, DO; Eli Ehrenpreis, MD, FACC

Department of Internal Medicine; Advocate Lutheran General Hospital, Park Ridge IL

PROBLEM

- Limited ongoing data regarding medications related to Osteonecrosis of the Jaw

BACKGROUND

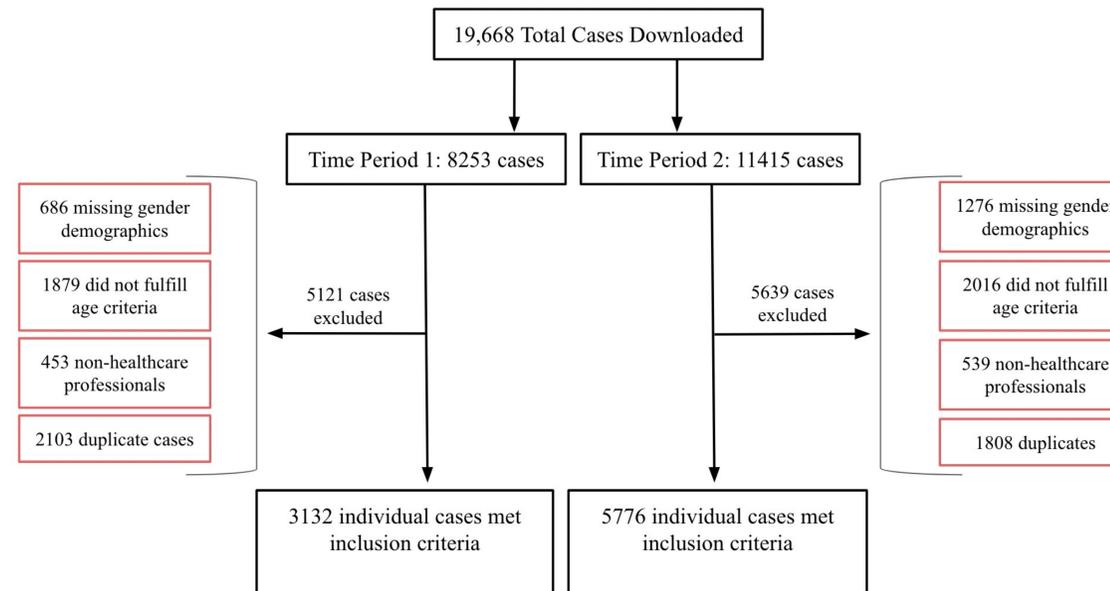
- Osteonecrosis of the jaw (ONJ) is defined as the presence of exposed bone in the mouth, which fails to heal after appropriate intervention over a period of 6-8 weeks
- ONJ is a rare but serious adverse drug reaction (ADR) commonly associated with bisphosphonate and denosumab therapy
- FAERS is a large database of voluntarily reported adverse drug reactions associated with post-marked FDA-approved medications as well as natural substances, vaccines, and medical devices
- Prior research utilized the FAERS Database to explore this ADR.
- Previously identified drug classes associated with ONJ included bisphosphonates, RANKL inhibitors, antiangiogenic agents, and m-TOR inhibitors
 - Proposed mechanism of action (MOA): antiresorptive properties and bone remodeling impairment via alterations in the formation of new blood vessels

OBJECTIVE

- Our study aims to build upon the prior findings, reporting trends of medication induced ONJ over time and identifying newly described medications

METHODS

- By May 2021, the FAERS database contained a total of 22,002,078 reported cases of ADRs
- We searched the FAERS database for all reported cases of medication related osteonecrosis of the jaw (MRONJ) from 2010-2021
- Cases lacking patient age or gender were excluded. Only adults (18+) and reports from Healthcare Professionals were included. Duplicate cases were removed
- The top 20 medications were identified and described for April 2010-December 2014 ("Time Period 1") and April 2015-January 2021 ("Time Period 2")



RESULTS

- Between 2010-2014: 64.7% female, 35.3% male; average age was 66.1 +/- 11.1 years
- Between 2015-2021, 64.3% female, 35.7% male; average age was 69.2 +/- 11.5 years
- Novel drugs and classes described between 2010-2014:
 - Lenalidomide,
 - Corticosteroids (prednisolone and dexamethasone)
 - Docetaxel and paclitaxel
 - Letrozole
 - Methotrexate,
 - Imatinib
 - Teriparatide
- Novel drugs and classes described between 2015-2021:
 - Palbociclib,
 - Pomalidomide
 - Radium-223
 - Nivolumab
 - Cabozantinib
- Zoledronic acid was the most frequently reported medication associated with ONJ during Time Period 1
- Denosumab was the most frequently reported medication associated with ONJ during Time Period 2

Top 10 Drugs: 2010-2014

- Zoledronic Acid: 1903 cases; 60.8%
- Alendronate: 576 cases; 18.4%
- Denosumab: 506 cases; 16.2%
- Pamidronate: 301 cases; 9.6%
- Ibandronate: 112 cases; 3.6%
- Lenalidomide: 82 cases; 2.6%
- Risedronate: 81 cases; 2.6%
- Sunitinib: 56 cases; 1.8%
- Bevacizumab: 50 cases; 1.6%
- Prednisolone: 42 cases; 1.3%

Top 10 Drugs 2015-2021

- Denosumab: 3148 cases; 54.5%
- Zoledronic Acid: 2027 cases; 35.1%
- Alendronate: 447 cases; 7.7%
- Ibandronate: 200 cases; 3.5%
- Lenalidomide: 150 cases; 2.6%
- Pamidronate: 115 cases; 2.0%
- Bevacizumab: 114 cases; 2.0%
- Prednisolone: 103 cases; 1.8%
- Risedronate: 101 cases; 1.7%
- Dexamethasone: 99 cases; 1.6%

CONCLUSIONS

- While stricter inclusion criteria and removal of duplicate cases led to fewer overall identified cases of MRONJ when compared to prior research, our data represents a more reliable analysis of MRONJ reports to the FAERS database with improved accuracy
- Our study identifies cases of several newly described drugs and drug classes that have not been previously described in literature and provides further description of the various medications associated with ONJ and elucidate patient demographics associated with the ADR
- Further evaluation of the MOA of these medications, including anti-angiogenesis, immunomodulation, cytotoxicity, and hormonal effects may shed light on their potential to contribute to this ADR
- A limitation of this study includes the use or exposure to multiple medications, making it difficult to determine the individual causes of MRONJ as well as the clinical indication for these drugs

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Any Questions?

Please contact: Hardeep.ahdi@aah.org