

ONJ (MRONJ) Update 2024: Osteonecrosis of the Jaw Related to Bisphosphonates and Other Drugs—Prevention, Diagnosis, Pharmacovigilance, Treatment—A National Italian Symposium

Vittorio Fusco^{1,2}, Martina Coppini^{3,*}, Gaetano La Mantia³, Paolo G. Arduino⁴, Fortunato Buttacavoli³, Alessio Gambino⁴, Francesco M. Erovigni⁴, Alberto Bedogni^{5,6} and Giuseppina Campisi^{3,7}

- ¹ Translational Medicine Unit, DAIRI Department of Integration, Research and Innovation, Azienda Ospedaliera-Universitaria “SS Antonio E Biagio e Cesare Arrigo”, 15121 Alessandria, Italy; fusco.dott.vittorio@gmail.com
 - ² Oncology Unit, Department of Medicine, Azienda Ospedaliera-Universitaria “SS Antonio E Biagio e Cesare Arrigo”, 15121 Alessandria, Italy
 - ³ Unit of Oral Medicine and Dentistry for Fragile Patients, Department of Rehabilitation, Fragility, and Continuity of Care, University Hospital Palermo, 90127 Palermo, Italy; gaetano.lamantia@unipa.it (G.L.M.); fortunato.buttacavoli@unipa.it (F.B.); giuseppina.campisi@unipa.it (G.C.)
 - ⁴ Unit of Oral Rehabilitation, Maxillo-Facial Prosthodontics and Dental Implantology, Department of Surgical Science, CIR Dental School, 10126 Turin, Italy; paologiacomo.arduino@unito.it (P.G.A.); alessio.gambino@unito.it (A.G.); francesco.ervogni@unito.it (F.M.E.)
 - ⁵ Regional Center for Prevention, Diagnosis and Treatment of Medication and Radiation-Related Bone Diseases of the Head and Neck, University of Padua, 35128 Padua, Italy; alberto.bedogni@unipd.it
 - ⁶ Department of Neurosciences (DNS), University of Padua, 35128 Padua, Italy
 - ⁷ Department of Biomedicine, Neuroscience and Advanced Diagnostics (BIND), University of Palermo, 90127 Palermo, Italy
- * Correspondence: martina.coppini@unipa.it



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Abstract: On 24 February 2024, Italian physicians, dentists and oral care specialists, students, nurses, psychologists, dental hygienists, and other professionals met (live or online) to discuss controversial issues about medication-related osteonecrosis of the jaw (MRONJ). One section hosted international experts who gave lectures about MRONJ experiences in North America, Europe, and Italy. A second section summarized the principal points of an Italian MRONJ position paper published in February 2024 by experts from the Italian Societies of Oral Pathology and Medicine (SIPMO) and Maxillofacial Surgery (SICMF). The following section collates expert opinions about open issues and required fields of research: different definitions of MRONJ and impact on staging; the assessment of individual MRONJ risk before the start of antiresorptive therapy; surgery and implantology in patients at risk for MRONJ; cancer patients without metastases and prevention of cancer-treatment-induced bone Loss (CTIBL); the role of dental hygiene professionals; combined (medical and surgical) and surgical therapy for MRONJ in-patients and out-patients; and legal aspects and claims related to MRONJ diagnosis and treatment. Scientific contributions from hospitals and universities all over Italy were presented in specific sessions (epidemiology; case series; special case reports; prevention experiences; MRONJ treatment). Conclusions: the conference confirmed the importance of the adequate imaging study of bone in the diagnosis and staging of MRONJ cases, the role of surgery in MRONJ treatment, and the value of oral hygiene in the MRONJ prevention.

Keywords: osteonecrosis; jaw; jaws; osteonecrosis of jaw; bisphosphonate; denosumab; ONJ; BRONJ; MRONJ; staging

1. Introduction

Osteonecrosis of the jaw (ONJ), or medication-related osteonecrosis of the jaw (MRONJ), is an adverse drug reaction that has been described as the progressive destruction and death of bone that affects the mandible and maxilla of patients exposed to treatment with medications known to increase the risk of disease in the absence of previous radiation treatment [1,2].

ONJ has been commonly referred to as medication-related ONJ (MRONJ) since 2014, after a position paper was published by a task force from the American Association of Oral Maxillofacial Surgeons (AAOMS) [3].

The first reports of ONJ were published in 2003–2004 [4–6] in patients treated with bisphosphonates, and thus the term bisphosphonate-related osteonecrosis of the jaw (BRONJ) became popular, but the term MRONJ is now more common due to the increase in drugs (in number and classes) potentially related to the disease [3,7,8]. MRONJ is more frequently observed in cancer patients with bone metastases and myeloma patients receiving “high doses” of antiresorptive treatments (bisphosphonates and denosumab) with/without biological agents, but it is also diagnosed in patients receiving “low doses” of bisphosphonates or denosumab for osteoporosis and other nonmalignant bone disorders, and in cancer patients receiving “low doses” of antiresorptive drugs to prevent or correct bone loss known as cancer-treatment-induced bone loss (CTIBL) [9–11].

Since 2003–2004, alerts about BRONJ started among clinicians and researchers in Italy; in following years, Italian professionals that were involved in ONJ study and research played a relevant part in papers contributing to increasing awareness and knowledge on this topic. In a previous paper [12], a short story about the role of Italian oral care specialists, oncologists, hematologists, and bone specialists was summarized, with emphasis on collaboration among members of Italian scientific societies of oral medicine and pathology (SIPMO, Società Italiana di Patologia e Medicina Orale) and maxillofacial surgery (SICMF, Società Italiana di Chirurgia Maxillo-Facciale), as well as the promoting role of the “Rete Oncologica di Piemonte e Valle d’Aosta”, a cancer network that includes professionals (physicians, nurses, technicians, supporting staff, data managers, etc.) of all the healthcare units that manage and treat patients with cancer and hematologic disorders in two regions in Northwest Italy.

Dedicated meetings and conferences were held in Alessandria in 2008, 2009, 2010, 2011, 2014, and 2018, with slides and reports of communications (mostly in Italian) made available on the website of the cancer network [13] and presented contributions relating to 2014 and 2018 meeting editions published in English in scientific journals [14,15].

In 2019 and 2020, important practice guidelines and documents about MRONJ diagnosis, treatment, and management were published, including a joint MASCC, ISOO, and ASCO clinical practice guideline [16], together with a European document written by experts that analyzed current challenges [17] and new Italian recommendations published online (in Italian) [18]. One following consensus document was then written by some Italian experts and published in English [19].

A new edition of the “ONJ (MRONJ) UPDATE” conference was planned to be held in Alessandria in 2020, but due to the COVID-19 pandemic, the conference was delayed to 2021 and changed into a web event, which was successful [12].

In 2022, a new position paper by the AAOMS [7], with an unmodified definition of MRONJ in comparison to a previous 2014 paper [3], raised further discussion [20].

In 2023, a position paper by the joint societies, SIPMO and SICMF, was submitted, and a definitive version was published in January 2024 [2].

Here, we report a summary of the 2024 edition of the “ONJ (MRONJ) UPDATE” meeting, held both in-person (at Turin University) and online (with hundreds of participants) on 24 February 2024.

2. Materials and Methods

As in the previous versions of the event, the Scientific Committee selected the speakers for discussion of controversial issues and for educational sessions. Foreign speakers were invited to speak in English, and Italian speakers were invited to speak in Italian with slides preferably in English (to permit the dissemination of congress reports abroad).

Furthermore a “call for abstract” was launched via email to Italian professionals and published on several websites, searching for researchers interested in presenting scientific communications essential to MRONJ, divided into five subgroups:

1. MRONJ case series (at least 10 cases) and epidemiological studies;
2. Case reports/recent issues;
3. MRONJ prevention and follow-up experiences;
4. MRONJ treatment experience reports (at least 10 cases);
5. Miscellanea.

Instructions for the included authors: English language; original works (or updates of previous papers) not yet presented to Italian or international congresses in this form; contribution to knowledge about recent MRONJ issues; limits for length of the abstract (600 words; 3 references) and number of authors (eight).

Some MRONJ experts (oral care specialists, maxillofacial surgeons, oncologists, etc.) were named by the Scientific Committee as reviewers, and were asked to vote (from 1 to 10) on all of the presented abstracts (except for contributions from their own institution).

The authors of all accepted abstracts were invited to send a short oral presentation (3 min), as pre-recorded talks with slides, to be uploaded to YouTube. On the basis of the median votes given by reviewers, the Scientific Committee selected some presentations to share on symposium day and other presentations for awards.

The day was recorded chronologically and made fully available on YouTube, as a whole event (<https://www.youtube.com/watch?v=iGZ8ka0Pozc> (accessed on 1 March 2025)) or separate talks or group of talks (Vittorio Fusco—YouTube, <https://www.youtube.com/@vittoriofusco9482> (accessed on 1 March 2025)).

All the presented abstracts that were published in the journal *Dental Cadmos* [20] and are available (<https://www.dentalcadmos.com/volume/abstract-onj-mronj-update-2024/> (accessed on 1 March 2025)) and citable.

3. Results

The meeting was held on 24 February 2024 in a hall of the Dental School at the University of Turin (with one hundred attending participants) and streamed online (250 registered online attendees).

Paolo G. Arduino (professor at the University of Turin, Italy) and Vittorio Fusco (oncologist at Alessandria, Italy) gave a warm welcome and introduced the program.

3.1. First Session

Professors Umberto Romeo (professor of oral diseases at the University of Rome, Italy) and Lorenzo Lo Muzio (rector of the University of Foggia, Italy) were chairmen of the session, including pre-recorded presentations (in English) and titled “Twenty years of Osteonecrosis of the Jaw”.

Cesar A. Migliorati (professor of Oral Medicine at University of Florida, USA) presented “BRONJ/MRONJ: an American tale?”, showing the first reports of MRONJ in the

USA and Brazil in 2002–2003 and the AAOMS position papers (in 2007, 2009, 2014 and 2022) and other articles (talks and slides are available on YouTube) [21].

Sven Otto (maxillofacial surgeon at the University of Munich, Germany) presented “The European Consensus”, talking about the evolution of MRONJ research in Europe and the ongoing attempt to create a European consensus document [22].

Giuseppina Campisi (Professor of Oral Diseases at the University of Palermo, Italy) summarized “MRONJ in Italy” with a unique contribution of Italian specialists and scholars to knowledge in this field [23].

3.2. Second Session

Professors Umberto Romeo (Professor of Oral Diseases at the University of Rome La Sapienza, Italy) and Paolo Garzino-Demo (Professor of Maxillofacial Surgery at the University of Turin, Italy) introduced the speakers of the session dedicated to the Italian Position Paper on MRONJ, published in February 2024 in the journal *Oral Diseases* by Alberto Bedogni et al. [2], on behalf of the Italian Societies of Oral Medicine and Pathology (SIPMO) and of Maxillofacial Surgery (SICMF).

Talks (in Italian) and slides (in English) are available on YouTube (at <https://www.youtube.com/watch?v=iGZ8ka0Pozc> (accessed on 1 March 2025)).

Vittorio Fusco (oncologist at Alessandria, Italy) illustrated epidemiology data and classes of MRONJ risk [2].

Alberto Bedogni (maxillofacial surgeon at the University of Padua, Italy) described the contents of an Italian position paper, covering the following aspects: MRONJ definition, MRONJ diagnosis pathway, imaging of possible and ascertained cases, the staging of MRONJ disease [2], and the underlying differences between the latest AAOMS criteria [7] and those that have already been used in previous years [24–26].

Paolo Vescovi (Professor of Oral Diseases at the University of Parma, Italy) reassumed the risk-reducing measures (also known as *prevention* measures) recommended in the Italian position paper [2].

3.3. Third Session

The third session, entitled “Towards the future (open issues)” was chaired by Mario Airoldi (oncologist at the City Hospital of Turin, Italy) and Claudio Marchetti (Professor of Maxillofacial Surgery at the University of Bologna, Italy), and was designed to collate talks by Italian experts on the discussed themes or controversial issues.

Ciro Emiliano Boschetti (maxillofacial surgeon at the University of Campania, Naples, Italy) described differences between the AAOMS’s definition of MRONJ [7] and that of the Italian group, SIPMO-SICMF [2]. The differences were previously debated in the *Journal of Oral Maxillofacial Surgery* both before and after the 2022 AAOMS position paper [25] was published [20,26].

Boschetti also underlined differences in the proposed staging systems: one mostly based on clinical signs as formulated by AAOMS [7] versus one based on radiological signs evaluated using computed tomography and formulated by SIPMO-SICMF [2].

Francesco Erovigni (oral surgeon at the University of Turin, Italy) examined problematic decisions about dental and oral prescriptions before the start of antiresorptive therapy.

Umberto Romeo analyzed the possible surgical options during antiresorptive therapy in patients at high or low risk of MRONJ.

Rodolfo Mauceri (oral surgeon at the University of Palermo, Italy) described the possible placement and risks of implants in patients at risk of MRONJ.

Francesco Bertoldo (rheumatologist at the University of Verona, Italy) talked about patients at low risk of MRONJ due to antiresorptive treatment of cancer-treatment-induced bone loss (CTIBL).

Antonella Abbinante (University of Foggia, Italy) discussed the role of hygienist specialists in the so-called prevention (actually, measures aiming to reduce the risk of MRONJ occurrence) and management of MRONJ.

Giacomo Oteri (Professor of Oral Surgery at the University of Messina, Italy) described the options of combined (medical and surgical) therapy in MRONJ out-patients, with specific details of piezoelectric tools.

Alberto Bedogni illustrated the results of extended surgery in in-patients with MRONJ.

Vilma Pinchi and Ilenia Bianchi (forensic specialists at the University of Florence, Italy) reported on possible legal disputes in this field.

The slides of all the talks are available on YouTube (<https://www.youtube.com/watch?v=iGZ8ka0Pozc> (accessed on 1 March 2025)).

3.4. Fourth Session

In the last session, some selected abstracts were shown and discussed (as “180 s” pre-recorded video presentations in Italian with slides), and several other contributions were awarded. The pre-recorded presentations of almost all the proffered abstracts are available on YouTube (Vittorio Fusco—YouTube, <https://www.youtube.com/@vittoriofusco9482> (accessed on 1 March 2025)). The review committee (experts and known authors of papers essential to MRONJ) included the following: Paolo G. Arduino, Monica Pentenero (Professor of Oral Diseases at the University of Turin, Italy); Vittorio Fusco, Mario Migliario (Professor of Oral Care at the University of Piemonte Orientale, Novara, Italy); Claudio Caldarelli (maxillofacial surgeon, Turin), and Maurizio Giordano (oral care specialist, Turin).

As specified above, the presented abstracts are available in a Special Issue of the journal *Dental Cadmos* [27].

A total of 66 communications from Italian hospitals, universities, or oral care private centers (in Alessandria, Ancona, Bari, Brescia, Cagliari, Chieti, Cuneo, Messina, Milan, Naples, Negrar, Novara, Padua, Palermo, Pescara, Pisa, Rome, Treviso, Trieste, Turin, Vercelli, Verona) and collaborative groups (e.g., the Rete Oncologica MRONJ study group) were accepted, divided in twelve subgroups:

1. Epidemiology case series: 6 abstracts
2. Clinical aspects/clinical experiences (at least 10 cases): 8 abstracts
3. Osteoporosis and non-malignant disease: 3 abstracts
4. Drug-related case reports: 6 abstracts
5. Clinical-related case reports: 10 abstracts
6. Other case reports: 4 abstracts
7. MRONJ prevention and follow-up experiences: 6 abstracts
8. Treatment—surgery: 5 abstracts
9. Treatment—others: 6 abstracts
10. Biology of MRONJ: 3 abstracts
11. Imaging of MRONJ: 6 abstracts
12. Miscellanea—other: 3 abstracts

(See Supplementary S1 for details and lists of communications).

4. Discussion

One of the main topics of the 2021 edition of the national MRONJ meeting [12] was the limited value of the AAOMS's definition of MRONJ, based on clinical aspects (bone exposure or bone can be probed, lasting at least 8 weeks), and of the AAOMS staging system,

principally based on signs and symptoms (pain, pus discharge) that can be modified by medical treatment (antibiotics and other drugs).

The debate about MRONJ definition was again put in the spotlight by a contribution to the section “Simply Put: JOMS Information for Patients” in the *Journal of Maxillofacial Surgery* (August 2021 issue) named “Medication-Related Osteonecrosis of the Jaw (MRONJ)” by Elie M. Ferneini [28]; the author describes MRONJ as “a progressive death of the jawbone in a person exposed to a medication known to increase the risk of disease, in the absence of a previous radiation treatment. Such medications are used to treat osteoporosis (brittle bones) or cancer such as multiple myeloma. The most common medications are bisphosphonates” [28]. Alberto Bedogni et al. [25] underlined the similarity of this definition with that proposed by Italian researchers [1], in contrast with that proposed by the AAOMS in 2014 [3].

A few months later, a new AAOMS position paper was published in the May 2022 issue of the same journal [7] that left the definition and the staging system substantially unchanged, increasing the discussion again [20,26].

In February 2024, the publication of the Italian position paper (SIPMO-SICMF) on MRONJ by the journal *Oral Diseases* [2] came some weeks before a new national MRONJ meeting, which confirmed the widespread interest of Italian oral care specialists, oncologists, bone specialists in this jawbone disease. Several invited speakers and many presented abstracts underlined the importance of both clinical and radiological aspects of the disease in early diagnosis and treatment, as well as a greater efficiency of and better attitude towards a combined (medical and surgical) treatment versus a pure medical “palliative” treatment or a “wait and see” strategy. Furthermore, the value of periodical oral hygiene procedures in the reduction in MRONJ risk was highlighted. Finally, the significant under-reporting of MRONJ cases to pharmacovigilance data authorities suggests the need to better train all the professionals involved [29].

5. Conclusions

We hope that the 2024 ONJ (MRONJ) UPDATE event might increase awareness of the debated issues on MRONJ among health professionals, aiming to implement the best practices for patients and caregivers.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/oral5020025/s1>. Supplement S1 (English translation of the event program and list of proffered communications).

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Abbreviations

The following abbreviations are used in this manuscript:

ONJ	Osteonecrosis of the Jaw
MRONJ	Medication-Related Osteonecrosis of the Jaw
AAOMS	American Association of Oral Maxillofacial Surgeons
SIPMO	Società Italiana di Patologia e Medicina Orale
SICMF	Società Italiana di Chirurgia Maxillo-facciale
MASCC	Multinational Association for Supportive Care in Cancer
ASCO	American Society of Clinical Oncology
ISOO	International Society of Oral Oncology
CT	Computed Tomography

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