### Abstract

ONJ is an uncommon condition mainly reported in oncological patients receiving BPs. We previously demonstrated that routinely application of preventive measures before, and during BP therapy, lead to a reduction of 70% in the incidence of ONJ (Ripamonti et al. 2009). However, a therapy is still needed in order to treat patients who develop ONJ. Recently, we investigated the effect of the localized application of a medical ozone oil suspension (O3 oil) on ONJ lesions. Ten cancer patients (seven with breast cancer, with prior breast cancer) treated with active ONJ lesions < 2.5 cm, in good clinical condition, were treated with antibiotic therapy 10 days prior to the initiation of the treatment consisting in the repeated application of O3 oil on ONJ lesions, at 3 days interval, for a maximum of 10 applications. Herein we report the results obtained in the first 10 patients enrolled with a follow up of at least 6 months, while the second stage of the trial, according to the Simon two-stage design, is currently ongoing to better estimate the response rate.

### Methods

#### Eligibility criteria

- Cancer patients who previously received N-BPs treatment in the absence of odontoiatric preventive measures.
- Osteonecrosis of the jaw (ONJ) is an uncommon (<1%), adverse event which has been reported in patients receiving complex cancer treatment regimens, including BPs.
- The exact etiology of ONJ is still unclear, however putative risk factors include concurrent disease, tooth extractions or invasive dental surgery during the course of BP therapy, duration of administration and type of BP, poor oral hygiene and use of concomitant cancer drugs such as chemotherapy, thalidomide, and corticosteroids.
- Prevention and treatment management of ONJ is essential in view of the considerable benefits of BPs, in the prevention of bone metastases-related SREs.
- The application of simple preventive measures such as proper dental hygiene, avoidance of dental procedures during BP treatment, and frequent dental examinations have been shown to effectively reduce ONJ incidence and rate.

#### Patient demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Patients (N=10)</th>
<th>Age range, years</th>
<th>Sex, n</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>46-74</td>
<td>8</td>
<td>2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Onj stage and treatment of osteonecrosis of the jaw (AAOMS 2009)*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical findings and symptoms</th>
<th>Treatment recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No clinical evidence of necrosis in bone, but non-specific clinical findings and symptoms</td>
<td>No treatment indicated, Patient education</td>
</tr>
<tr>
<td>1</td>
<td>Exposure/necrosis in bone that is asymptomatic and have no evidence of infection</td>
<td>Systemic management, including the use of pain medication and antibiotics</td>
</tr>
<tr>
<td>2</td>
<td>Exposure/necrosis in bone that is asymptomatic and have no evidence of infection</td>
<td>Antibacterial mouth rinse, Clinical follow-up on a quarterly basis, Patient education and review of indications for continued bisphosphonate therapy</td>
</tr>
<tr>
<td>3</td>
<td>Exposure/necrosis in bone that is asymptomatically and have no evidence of infection</td>
<td>Symptomatic treatment with systemic antibiotics, Oral antibacterial mouth rinse, Pain control, Superficial debridement, soft tissue initiation, Antibacterial mouth rinse, Antibiotic therapy, Surgical debridement/excision for longer-term palliation of infection and pain</td>
</tr>
</tbody>
</table>

#### Conclusions

- This current study demonstrates that O3 oil may have a useful clinical application and could be considered as a possible strategy for managing and treating ONJ. The results of this study demonstrated that the application of medical ozone oil suspension rapidly and completely resolved ONJ in all the patients treated. However, these results should be considered as preliminary due to the small sample size of this study and warrants further investigation in a larger patient population.
- Previous investigators have demonstrated that the incidence of ONJ can be drastically reduced with the introduction of dental preventive measures before and during BP therapy.1,2
- Emerging promising therapeutic options such as O3 oil indicate that ONJ can also be treated, enabling cancer patients to recover and heal from this debilitating condition.
- Cancer patients and clinicians should consider the substantial benefits of BPs towards management of skeletal health as opposed to the possible risks posed by ONJ, which is preventable and also manageable.

#### References


### Table 1. Staging and Treatment of Osteonecrosis of the Jaw (AAOMS 2009)*

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Findings and Symptoms</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No evidence of necrosis in bone, but non-specific clinical findings and symptoms</td>
<td>No treatment indicated, Patient education</td>
</tr>
<tr>
<td>1</td>
<td>Exposure/necrosis in bone that is asymptomatic and have no evidence of infection</td>
<td>Systemic management, including the use of pain medication and antibiotics</td>
</tr>
<tr>
<td>2</td>
<td>Exposure/necrosis in bone that is asymptomatic and have no evidence of infection</td>
<td>Antibacterial mouth rinse, Clinical follow-up on a quarterly basis, Patient education and review of indications for continued bisphosphonate therapy</td>
</tr>
<tr>
<td>3</td>
<td>Exposure/necrosis in bone that is asymptomatically and have no evidence of infection</td>
<td>Symptomatic treatment with systemic antibiotics, Oral antibacterial mouth rinse, Pain control, Superficial debridement, soft tissue initiation, Antibacterial mouth rinse, Antibiotic therapy, Surgical debridement/excision for longer-term palliation of infection and pain</td>
</tr>
</tbody>
</table>

#### Figure 2A. Response to O3 Oil Treatment

- Complete response to treatment
- No. of applications
- No. of patients
- No. of patients vs. No. of applications

#### Figure 2B. Number of Patients vs. Number of Applications

- Complete response to treatment
- No. of applications
- No. of patients
- No. of patients vs. No. of applications

---

**Poster # 194**

**Medical Ozone Oil Suspension Applications Heal Osteonecrosis of the Jaw (ONJ) in Patients Treated with Bisphosphonates (BPs): Preliminary Results of a Single Institution Protocol**

Ripamonti C, Maniezzo M, Giringhelli R, Fagnoni E, Campa T, Mariani L and Siriali G

Palliative Care Unit, IRCCS Foundation, National Cancer Institute of Milan, Milan, Italy; Dental Team, IRCCS Foundation, National Cancer Institute of Milan, Milan, Italy; Dental Team, Sanpaolo, Venice, Italy; and Medical Statistic and Biometry Unit, IRCCS Foundation, National Cancer Institute of Milan, Milan, Italy.