

## **"Evaluation study of EstrEmo (Extraction from emo-components): a medical-surgical protocol using PRP (Platelet-Rich Plasma) for dental extraction in patients in therapy with aminobisphosphonates"**

**Background:** The nitrogen-containing bisphosphonates (NBPs) are drugs efficiently used in the treatment of metabolic and malignant bone diseases for their ability in inhibiting bone. BRONJ (Bisphosphonate - Related Osteonecrosis of the Jaw) associated with NBPs therapy is a detrimental effect first reported in 2003 and "characterized by the progressive destruction and necrosis of the jaw bone and / or maxillary bone of subjects exposed to treatment with NBPs, in the absence of a previous radiation treatment ". The pathogenic mechanisms of BRONJ have not yet been defined, in contrast, have been recognized risk factors, which are divided into three broad categories: drug - relative, systemic and local. Among the local risk factors, "the oral surgical procedure" and/ or "the presence of inflammatory disease, dental-periodontal" are strongly associated with an increased risk of BRONJ in patients receiving therapy with NBP. Not performing an oral surgical procedure stops the healing of infection / inflammation in the jaw bones, increasing the risk of BRONJ: in such cases, surgery would be responsible for BRONJ risk reduction for elimination of infection / inflammation. Several medical and surgical protocols have been proposed in the literature (eg systemic antibiotics and topical antiseptics pre-and / or post- surgery, performing procedures extractive atraumatic and mobilization of mucoperiosteal flaps). It was recently proposed the application of PRGF (Plasma Rich in Growth Factors) or PRP (Platelet - Rich Plasma) in the post-extraction alveolar, for the regeneration of bone tissue.

**Purpose:** The aim of the present randomized clinical trial will be to evaluate a new medical and surgical protocol for tooth extraction in subjects under treatment with aminobisphosphonate (NBP) for cancer and/or osteo-metabolic diseases (secondary prevention). In detail, EstrEmo involves in addition to the traditional protocol the intra-alveolar application of growth factors (Platelet-Rich Plasma - PRP) and the mobilization of a surgical flap to promote healing by first intention. The objective is to estimate the safety and the efficacy of this experimental protocol in terms of reduction of BRONJ development risk compared with the traditional surgical protocol without PRP.

**Patients and Methods:** The present prospective case-control hospital-based randomized clinical trial will include cancer and non-cancer patients under treatment with bisphosphonates that need to dental extractions (secondary prevention of BRONJ). Patients will be consecutively enrolled at the Sector of Oral Medicine – Dept. Surgical, Oncological and Oral Disciplines of AOUP Policlinico of Palermo and they will include in a random manner in the Test (T) and Control (C) group. In T group, dental extractions will be performed with a split-thickness flap; healing will be stimulated by filling the extraction site with autologous PRP. Local and systemic infection control will be obtained with administration of pre-and post-operative systemic antibiotic drugs and local antiseptic. For the C group, the same protocol will be performed, except that the use of PRP (standard protocol). The clinical signs will be evaluated after the extraction, respectively at 1 week ( $T_1$ ), 1 months ( $T_2$ ), 6 months ( $T_3$ ), 1 years ( $T_4$ ) and 2 years ( $T_5$ ). Radiological follow up (OPT and CT) will be performed at  $T_3$ ,  $T_4$  and  $T_5$ .

**Result:** Validate the safety and effectiveness of EstrEmo protocol by univariate and multivariate statistical analysis of the clinical and radiologic variables in cancer and non cancer patients compared to standard extraction medical and surgical procedure.