1. ABSTRACT

- **Title**

Prospective Observational Study to Describe Characteristics and Management of Postmenopausal Women With Osteoporosis Treated With Prolia® in France and its use in Routine Clinical Practice

- **Keywords**

Denosumab; postmenopausal osteoporosis; prospective study.

- **Rationale and Background**

Denosumab is a fully human monoclonal antibody approved for reimbursement in France in September 2013 for the treatment of postmenopausal osteoporosis (PMO). Persistence with osteoporosis therapy is important for optimal reduction of fracture risk and is therefore a major issue in PMO management.

- **Research Question and Objectives**

This study aimed at describing persistence with denosumab in routine clinical practice in France.

- **Study Design**

This was a multicenter prospective observational study conducted in France in PMO patients who receive Prolia® (60 mg SC). Patients were followed for 30 months.

- **Setting**

The study was conducted in rheumatologists and general practitioners randomly selected from a list of rheumatologists (either in hospital or private practice nationwide) and from a list of general practitioners managing patients with osteoporosis. The study planned to involve approximately 110 active sites in France.

- **Subjects and Study Size, Including Dropouts**

A sample size of approximately 400 patients would provide a half-width of the 95% CI around the 12-month persistence estimate of 3.8%. Postmenopausal women with osteoporosis who received their first prescription of Prolia® in the last 4 weeks were eligible to participate in the study. Before any study-specific activity, appropriate written informed consent had to be obtained. Patients who were withdrawn prior to completion of the study were not replaced.

- **Variables and Data Sources**

Clinical information obtained through routine clinical practice were recorded where available, as per their routine clinical care. Study-related data were recorded in an electronic Case Report Form (eCRF) by the Investigator or delegate, in accordance with the data reported in the medical record.

- **Results**

The analysis was performed on 478 patients included by 86 physicians (59 rheumatologists and 27 general practitioners), between June 16, 2015 and February 1, 2016.

Overall, the 12-month persistence rate was 86.2% (95% CI 83.10 ; 89.28) and the 24-month persistence rate was 72.0%; (95% CI 67.96 ; 76.04). According to Kaplan-Meier analysis, the estimated proportion of patients persistent at 12 and 24 months was

respectively 86.0% and 76.1% and median time to non persistence was not reached by 24 months.

More than 85% of patients prescribed with Prolia® had received bisphosphonates (BPs) before Prolia® initiation, approximately 80% fulfilled the definition of increased risk of fracture and 70% had at least one contra-indication situation related to BP use.

Osteoporosis-related fracture during study follow-up occurred in 8.4% of patients (vertebral fracture in 3.8% and non-vertebral fracture in 4.6%). Overall, 78 (16.3%) patients discontinued denosumab, 44.9% as per patient request and 34.6% due to adverse events considerations. Out of these, 76.3% of patients did not switch to an alternative treatment. However, no multiple vertebral fractures occurred upon treatment cessation.

Concerning safety results, 11% of patients experienced at least one treatment-related AE and less than 1% of patients experienced a serious treatment-related AE. No patient experienced any atypical femoral fracture during the course of the study.Osteonecrosis of the jaw (resolved after surgical cleaning) occurred in only one patient.

- **Discussion**

The study highligths the importance of injectable treatments in the management of osteoporosis by improving persistence to treatment. 12-month and 24-month persistence confirm the high level of persistence of denosumab in PMO women. As such this study adds to the body of evidence supporting the good level of treatment adherence in PMO women initiating Prolia® treatment. Moreover, Prolia® was generally well tolerated with less than 1% of patients experiencing a serious treatment-related AE. No multiple vertebral fracture was observed after Prolia® discontinuation.

- **Marketing Authorization Holder(s)**

Amgen Europe B.V

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