Title: Prospective Observational Study to Describe Characteristics and Management of Patients With Osteoporosis Treated With Prolia® in Routine Clinical Practice in Poland.

Amgen Protocol Number 20160178

AMG 162 - Prolia® (denosumab)

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Confidentiality Notice

Investigator's Agreement

I have read the attached protocol entitled **Prospective Observational Study to Describe Characteristics and Management of Patients With Osteoporosis Treated With Prolia® in Routine Clinical Practice in Poland** dated **24.10.2016**, and agree to abide by all provisions set forth therein.

I agree to comply with the International Conference on Harmonisation Tripartite Guideline on Good Clinical Practice (as applicable by local law).

I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of Amgen Inc.

_____
Signature

_____ _____
Name of Principal Investigator Date (DD Month YYYY)

Protocol Synopsis

Title: Prospective Observational Study to Describe Characteristics and Management of Patients With Osteoporosis Treated With Prolia® in Routine Clinical Practice in Poland.

Study Phase: Observational

Indication: Treatment of osteoporosis (OP) in postmenopausal women and men at increased risk of fractures.

Study Objective: The objective of this prospective, observational study in Poland is to describe characteristics of patients treated with Prolia® in routine clinical practice in Poland during the 12 months of treatment.

Hypotheses: The study is descriptive in nature, and a formal hypothesis will not be tested in this observational, single-arm study.

Study Outcomes:

Description of osteoporosis patient population treated with Prolia®:

- socio-demographic landscape
- disease related data e.g. BMI, previous fracture, falls, BMD
- treatment patterns with Prolia® e.g number of Prolia® received, occurrence of patient having osteoporosis-related laboratory examinations pre-treatment with Prolia® and during the study, occurrence of patient having radiologic bone assessments pre-treatment with Prolia®
- Safety data – incidence of AE or SAE

Study Design:

This is a multi-center, one country, non-interventional, prospective, observational study in osteoporosis patients population who received at least one injection of Prolia® 60 mg Q6M, SC (subcutaneous) in Poland. This observational study will not alter the routine clinical management of patients and will comply with all applicable local regulations in Poland.

Prolia® naive patients will be eligible to enroll within 8 weeks after initiation of Prolia® treatment (ie 8 weeks after receiving the first injection). The decision to treat the patient with Prolia® must be made independent of and prior to their enrollment in the study. However, writing of the prescription for Prolia®, the first Prolia® injection and/or signing of informed consent may happen at the same visit. It is expected that patients will receive their scheduled Prolia® injection every 6 months as part of their routine clinical care.

Approximately 600 patients will be enrolled in Poland - into two separated subgroups 300 subjects each. (First group patients treated in big osteoporosis centers specialized only in osteoporosis treatment, second group patients treated in small/other type centers - orthopedic, rheumatologic, family doctor outpatients.

The estimated duration of enrollment is 12 months. No study drug will be administered as part of the study. The protocol will specify that investigators will offer participation in the study to all patients treated with Prolia® during the enrollment period until they reach their contracted number of patients. Detailed data obtained as part of routine clinical practice will be collected at the initial visit, either directly or from medical record, to characterize the patient population. It is anticipated that patients will return to the clinic every 6 months to receive their Prolia® prescription and/or injections. After the initial visit, information regarding Prolia® prescription and administration, procedures pertaining to osteoporosis and Prolia®, concomitant medication use, and non-serious and serious AEs will be collected during routine clinical visits and recorded for up to approximately 12 months after entering the study.

The study will describe the profile of patients treated with Prolia® and the clinical management of these patients during the first 12 months of treatment. Patient and site characteristics will be collected at baseline according to the following 3 dimensions:

- Socio-demographic related
- Condition-related (osteoporosis)
- Patient-related

Sample Size:

Approximately 600 patients in Poland - 300 patients in big osteoporosis centers and 300 patients in small/other type centers - orthopedic, rheumatologic, family doctor outpatients.

Summary of Patient Eligibility Criteria:

Patients will meet the following inclusion criteria at enrollment into the observational study:

- Women with a clinical diagnosis of PMO or men with diagnosis of osteoporosis, have received their first injection of Prolia® within 8 weeks prior to enrolling in this study
- Decision has been made to treat patient with Prolia® 60 mg once every 6 months
- Appropriate written informed consent has been obtained

Patients meeting the following exclusion criteria are not eligible to participate in the observational study:

- Patients who are participating in ongoing or have participated denosumab clinical trials in the past
- Participation in other clinical or device trials in the last 6 months
- Contra-indication for treatment with Prolia®
- Subject has any kind of disorder that, in the opinion of the investigator, may compromise the ability of the subject to give written informed consent.

Amgen Investigational Product Dosage and Administration: None

Non Amgen Investigational Product Dosage and Administration: None

Non Amgen Non-investigational Product Dosage and Administration: None

Control Group: None

Procedures:

There are no procedures or changes to routine clinical management of patients with osteoporosis. It is anticipated that patients will return to the site every 6 months to receive their Prolia® prescription and/or injections. Patients will be followed for approximately 12 months after their initial visit.

Clinical information obtained for routine clinical practice will be recorded where available, including Prolia® administration, previous and current therapies, medical history (including fracture), AEs and serious AEs and co-morbidities (Appendix A). For a full list of study procedures, including the timing of each procedure, please refer to Section 7 and Appendix A (Information Obtained during Routine Clinical Practice).

Statistical Considerations:

This is an observational study for which the analysis will be descriptive in nature; no formal hypothesis will be tested. Frequency distributions will be described for categorical variables. Continuous variables will be summarized by the number of non-missing values, mean, standard deviation, median, lower and upper quartiles and minimum and maximum values. All study outcomes and baseline characteristics will be summarized. For selected study outcome related to the clinical management of these patients, point estimate and 95% confidential interval will be provided. Summary of the study outcomes and selected baseline variables will be provided. Appropriate outcomes specific for an injection will be summarized by injection (1^{st}, 2^{nd}, 3^{rd}). Two separate subanalysis for osteoporosis centers and small/other type centers - orthopedic, rheumatologic, family doctor outpatients are planned.

All AEs and serious AEs to Prolia® will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). Patient incidence of AEs and serious AEs will be tabulated by system organ class and preferred term. Moreover, AEs and serious AEs leading to discontinuation of Prolia® or associated with a fatal outcome will be tabulated by system organ class and preferred term.

For a full description of statistical analysis methods, please refer to Section 10.

Sponsor*:* See Protocol Title Page