

TITRE DU PROJET : EXOSTIC - Évaluation de l'Exposition au long court aux traitements de l'OSTéoporose des françaises âgées de plus de 50 ans Inclues au sein des Cohortes SNIIRAM et CONSTANCES

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RÉSUMÉ

Rational

Osteoporosis (OP) is characterized by reduced bone mass and disruption of bone architecture, resulting in increased bone fragility and increased fracture risk. OP affects about 2.3 million patients in France. The most frequent fractures are those at the hip, spine and distal forearm, in women these account for the majority of fractures after the age of 50 years. Hip fracture is the most serious osteoporotic fracture. The absolute number of osteoporotic fractures that occurred in France in 2010 is estimated to be 380 000 and the frequency is rising due in part to the aging population. A variety of treatments options are currently available. Clinical trials of osteoporosis treatments have demonstrated efficacy, ranging from 30% to 70%, in reducing risk for osteoporotic fractures. The most prescribed anti-osteoporotic treatments are bisphosphonates and strontium that represent 88% of prescriptions in France and have the particularity to be stored in the bone tissue during a lifetime length.

This raises issues about possible side effects that would arise even after the patient is no longer taking the treatment. Potential consequences of this accumulation are long term adverse events including atypical femoral fractures, osteonecrosis of the jaw, hypersensitivity reaction, severe infection, cancer, venous thromboembolism and stroke that are more difficult to document according to their rarity.

In France, last institutional recommendations date from 2006 and don't deal with osteoporosis treatment renewal after a first four year sequence. These factors may result in large variability in osteoporosis treatment patterns among individual women over the long term. It is likely that a significant proportion of women end up with a very high cumulative dose of several different antiosteoporotic treatments when they reach the age of 70 or 80 years. Considering that for most available treatment, long term benefit risk ratio is still unknown, it is of crucial importance to obtain data on these long-term exposures and their effects on individuals.

Because the real-world is not a clinical trial, long term benefit-risk assessment of OP drugs remains unclear. There is a need for further observational research to explore the impact of treatment with osteoporosis drugs over 5 years, and first of all describe how the population is treated in the clinical practice.

The goal is to describe and analyze exposure to antiosteoporosis drugs in a large nationwide healthcare database, necessary to evaluate "real-world" benefit risk ratio for various anti-osteoporotic drug treatments.

The main objectives are:

-To measure individual overall length of exposure to antiosteoporosis drugs in a cohort of women aged 50 years and more in the SNIIRAM medico-administrative database, from 2007 to 2016.

-To describe individually the types, frequencies, dosages, treatment switches, treatment interruptions, discontinuations and adherence to anti-osteoporosis treatment prescriptions over time -In the sample of patients also included in the CONSTANCES cohort study from 2013 to 2016: a. analyze the exposure taking into account the observance; b. compare declared data with reimbursement data regarding individual long-term consumption of anti-osteoporosis drugs

-To create a large database for further use in long-term benefit-risk ratio assessment of antiosteoporosis drugs among this population

Design: An observational descriptive study will be conducted within the Système National d'Information Inter-Régime de l'Assurance Maladie (SNIIRAM) and the Programme Médicalisé des Systèmes d'Information (PMSI) databases, which offer the opportunity to follow in a long term a large and representative sample of patients treated or not with OP agents, with data on treatments, compliance. Drug exposure will be compared to declarative data in a sample of patients also included in the Constances cohort, where questionnaire can be directly administered to the patients.

Study population: All women aged over 50 years old in 2011 within the SNIIRAM, which represents more than 9,800,000 individuals. In this sample, approximately 36 000 women aged over 50 years will be also included in the Constances cohort and will complement SNIIRAM data. Retrospective data will be collected for all patients included in the SNIIRAM regarding their anti-osteoporosis treatment history (type of treatment, length of treatment).

Data collection in the CONSTANCES sample: Data will be collected for all participants recruited in the Constances cohort on the basis of an additional questionnaires, which will be sent and treated within the CONSTANCES Cohort framework.

Follow-up: The first extraction will contain data scheduling from 2007 to 2016, and extraction will be conducted each year afterwards from the SNIIRAM to build the cohort prospectively.

Significance

Our design based on an already funded cohort (Constances) and medico-administrative database (SNIIRAM) with a large sample of older individuals and long term follow-up provides an unparalleled opportunity to advance the understanding of the exposure of the French population to antiosteoporotic drugs and further document benefits and risks of anti-osteoporosis treatment in the population. By use the results of this project focused on exposure description based both on administrative and declarative data, we will enable the improvement of our knowledge of how the population is exposed to osteoporosis drugs in a real life setting. Answers to these questions are eagerly anticipated and of particular importance to scientists and policy-makers nationally and internationally, and also physicians and patients.