Reviewer's report

Title: Teriparatide use during an economic crisis: baseline data from the Greek cohort of the Extended Forsteo Observational Study (ExFOS)

Version: 3 Date: 28 October 2014

Reviewer: Imre Pavo

Reviewer's report:

The paper describes the baseline characteristics of the Greek subset of an ongoing non-interventional international prospective study (ExFOS) about the teriparatide (TPTD) use in clinical practice. In addition, the results are presented in parallel to the baseline characteristics of a similar study conducted years ago (EFOS). Moreover, the authors are discussing the potential impact of changed reimbursement conditions on the enrollment of the two studies. They conclude that some differences exist in patient characteristics between the two cohorts and that the economic crisis did not markedly impact the prescription habit of teriparatide. The paper provides new and important insight on patients treated with TPTD in Greece. The description of clinical characteristics is sound. It needs to address, however, several open questions.

Major compulsory revisions:

Major comments:

1. Statistical power of the analyses. In line 105: “sample size large enough (#300 patients) to allow [...to be described using summary statistics.” What was the consideration for this calculation? Was this a protocol pre-defined analysis or a post hoc? It is not clear how the fluctuation of the patient enrollment has been analyzed and how the results and conclusions between reimbursement and enrollment speed were elaborated. The separate presentation of the male population in some aspects could be challenging due to low number (n=34). These needs to be clarified and added to the limitations.

2. Comparison between the results and those from the EFOS study is sensitive as they are two separate studies and not designed for comparisons. It is appropriate to describe some of the major findings of the two studies parallel to each other while avoiding any direct comparison and conclusions from these comparisons. It is difficult to interpret the differences in baseline characteristics as clinical practice in Greece. Results (baseline characteristics, treatment adherence, etc) of prospective non-interventional studies are heavily influence by the investigator selection and usually not representing the overall clinical practice in a geography. It is also not clear whether or not the EFOS and ExFOS investigators were identical. Thus, the results and conclusions regarding the differences between the enrollment speed and other characteristics of the two studies as a function of changes in the reimbursement system can be interpreted only with limitations.
Other comments:
Line 31-33, 35: it is a direct comparison, needs to be avoided
Line 65-72: not directly relevant, should be deleted
Line 93: which reimbursement details were collected and with which methods? This needs clarification and additions
Line 105: need to include considerations for statistical power of the analyses performed
Line 136: would suggest to include the data of Figure 1 simply into the text instead of as a separate figure
Line 138-139 and Fig 2 and 3. The purpose of separate presentation of left and right total hip and femoral neck BMD values needs to be explained if there is a good reason. It is not clear from the Method of the paper or form the method of reference 19 how the investigational sites were instructed to perform BMD measurements in the hip area. The Method needs to be extended (was recent prior study measurement recorded?), and if there is no specific reason, the left and right values pooled. Figure 2 data could be better presented in a simple Table or in the text.
Line 178-179: how was this analyzed? There was a considerable fluctuation between monthly enrollments which admittedly could have various reasons. If this is stated however, needs to be substantiated.
Line 180-192: the title should be “Description” instead of “Comparison”. Any statement referring to direct comparisons need to be avoided
Line 194-204: general part, not closely relevant to the study, could be deleted
Line 211-215: these are part of the objective to the study, should be in the Intro as objectives. The corresponding methods needs to be described in the Methods
Line 216: the title suggest direct comparison – should be avoided
Line 240-244: with all comments above this direct comparison should be avoided
Line 252-286: The title is not relevant to the study, should be focus on changes in reimbursement criteria rather on general socio-economic considerations. It is not clear how much this description is relevant to the findings. Again, if the study wants to analyze the relationship between prescription practice reflected in enrollment rate as a function of reimbursement conditions, appropriate analyses needs to be performed and described. If not performed/described, this portion of the Discussion has limited relevance only.

Minor Essential Revisions
Line 24: body mass index instead of bone mineral density
Line 29 and 164: 4.2 (7.7) days spend in bed – per months?

Discretionary Revisions
Line 145: had occurred instead of “had been sustained”
Line 147: suffered instead of “had sustained”
Line 153-155: please check the relevance of the gender comparison due to low sample size of male patients

Line 229: the speculation about the treatment naïve patients could be answered from the database potentially as the fact that the mean duration of most recently occurred fracture (2.6 year, line 146) is reported, suggests to me that the authors could analyze the relationship between the time of fracture and pre-treatment/no pre-treatment. If possible to perform, this could add value to the paper

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I am full time employee and shareholder of Eli Lilly and Company similar to some of the authors. The paper is about a clinical study sponsored by Eli Lilly and Co.