Reviewer’s report

Title: Patterns and trends of utilization of incretin-based medicines between 2008 and 2014 in three Italian geographic areas

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Reviewer: György Jermendy

Reviewer's report:

This is a descriptive study on the real-world utilization of incretin-based medicines in the Italian clinical practice. Database from three geographic areas (Tuscany, Caserta, Umbria) was used and the period of 2008-2014 was retrospective analyzed. The overall study population was near to 5 million and new users of GLP-1-RA (n=7,357) and DPP-4-i (41,907) were identified. The authors found an increased incidence of use of both GLP-1-RA and DPP-4-i between 2008 and 2011 which slightly decreased thereafter. As for prevalence, a steady increase of use of GLP-1-RA and DPP-4-i was observed between 2008 and 2013, with a plateau in 2014. The percentage of new DPP-4-i users with age above 65 years increased significantly during the study period. The leading medication among GLP-1-RA was liraglutide while metformin/DPP-4-i fixed dose combinations were the most frequently prescribed drugs among DPP-4-i class in 2014. Although monotherapy with either GLP-1-RA or DPP-4-i is not reimbursed in Italy, around 12% of new users had not received any antidiabetic drug before starting incretin based therapy.

This is a confirmatory study from Italy indicating that antidiabetic treatment practice has changed over time in patients with type 2 diabetes due to availability of incretin based therapy. Although novelties could not be identified at international level, data from Italy may be useful.

The manuscript is well written. However, some points should be addressed for clarification.

1. Two regions (Tuscany, Caserta) was investigated from 2008 to 2014, however data from Umbria was available only from 2011 to 2014. What was the cause to involve Umbria with a different period of observation? Stating that the incidence increased between 2008 and 2011, which is slightly decreased thereafter in the total cohort is misleading as no data were available in Umbria before 2011.

2. Authors provide data about the persistence of both GLP-1-RA and DPP-4-i (60.6% and 62.4% during the first year of incretin-based therapy). Persistence for a longer period (2 or 3 years) would be of interest. How were the death cases handled? Only censored data can be used in persistence analysis.

3. While DPP-4-i may be used in monotherapy as a first drug, GLP-1-RA should be used only in combination for treating patients with type 2 diabetes (exenatide: with metformin, SU or TZD, lixisenatide or liraglutide: with oral drugs or basal insulin). No doubt, using GLP-1-RA as an initial therapy in type 2 diabetes is not approved according to the label. Although the authors discuss the potential causes of such clinical practice, it should be stated clearly, that GLP-1-RA
should not be used as initial monotherapy at present.

4. Undoubtedly, antidiabetic treatment in patients with type 2 diabetes should be performed individually. Nevertheless, reimbursement of a drug may influence the patient's preference. As reimbursement policy is obviously country-specific, some data about this policy from Italy would be useful.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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