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Executive Director

Letter of support for Leuven Postprandial Distress Scale (LPDS) as PRO in Postprandial Distress Syndrome (PDS)

On the basis of the qualification advice, the Agency issues this letter of support to the TARGID consortium, to encourage the further validation work and the use of the proposed PRO in clinical trials with patients suffering from Postprandial Distress Syndrome (PDS), a subgroup of patients with functional dyspepsia (FD) as defined by the Rome III criteria.

The applicant has developed and undertaken a large part of the necessary validation exercise for a patient reported outcome (PRO) tool for the assessment of the symptoms of postprandial distress syndrome.

The finally proposed form of the questionnaire contains 3 domains/questions which related to:
a) The inability to finish a meal due to early satiety
b) The feeling of food lying heavily in the stomach
c) Feeling bloated in the stomach.

The questionnaire is presented to the patients in the form of three questions which define five grades of severity (0-4), and which are supported by pictograms expressing the associated severity. The questionnaire is to be evaluated on a daily basis and the mean of the values of the three symptoms is proposed to represent the severity of that day. A weekly score can be calculated from the daily scores and is currently proposed for the primary use of the scale.

Functional dyspepsia – in its subdivision into “post-prandial distress syndrome” and “epigastric pain syndrome” as proposed by the Rome III diagnostic criteria – is one of the most frequent gastrointestinal diagnoses. However, the clear recognition and identification of FD and its subgroups as distinct disease entities has been a matter of controversy during recent years. Development and regulatory assessment (and approval) of new medicinal products for the treatment of functional dyspepsia has come to an almost complete standstill within the last decade.

This not only relates to the problems of full recognition of PDS as disease entity and the problems of symptomatic overlap with other functional and non-functional upper gastrointestinal syndromes and

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diseases, but also to the lack of validated tools for the identification and assessment of relevant symptoms in these patients.

Irrespective of the solution of the problems associated with the acceptance of FD and PDS as distinct disease entities, the applicant has undertaken the drafting and validation of a PRO in order to provide a reliable tool to be used as primary endpoint in clinical trials in the syndrome/disease entity.

The proposed tool has been developed in the early phases using standard methods, including focus group interviews and cognitive debriefing interviews. The results of this early validation work have been published in a peer reviewed journal (see: Carbone F et al: Functional dyspepsia: outcome of focus groups for the development of a questionnaire for symptom assessment in patients suffering from postprandial distress syndrome (PDS); Neurogastroenterol Motil 2014; 26: 1266-1274). Due to the nature of the documentation of the early validation exercise and the development steps undertaken, it remained partly unclear whether the overall development can be regarded to be optimal, e.g. with regard different subpopulations or a mixed PDS-EPS population included in different phases of the construction of the questionnaire.

The further validation of the score was undertaken with the means of an interventional study, evaluating the psychometric properties of the questionnaire with regard to construct validity, convergent validity, known groups (criterion validity), reproducibility (test re-test validity), and internal consistency. A minimally clinically important difference was also determined. The final results of this interventional study, as well as the final results of the “validation part”, are currently pending.

The drafting and validation work have been carried out with the French and Dutch versions of the questionnaire, and appropriate translation (linguistic validation) work has been carried out for a variety of other European languages.

The development of the LPDS scale as outcome measure to be used in future trials in PDS is considered to be a valuable contribution to improve the available armamentarium to assess patient well-being in the field of functional dyspepsia, where currently no specifically validated outcome measures are available. However, due to some open questions in the early validation and the currently still incomplete nature of the pivotal validation work, a final qualification of the PRO was not deemed possible at this point of time.

The Agency is encouraging further validation work of this PRO. Future sponsors of clinical trials in the field of PDS are invited to consider use of LPDS as an outcome measure in clinical trials and thereby provide additional data supporting a final qualification of this PRO in the future.

Sincerely,

Guido Rasi
Executive Director