Retmarker

Innovation in Diabetic Retinopathy

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Upon Retmarker application, EMA issues Letter of Support for Micro-Aneurysm Formation Rate biomarker

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Micro-Aneurysm Formation Rate as calculated by a validated automated method seems a very promising biomarker for enriching a patient population at higher risk for the development of Clinically Significant Macular Oedema.

Coimbra, Portugal, February 9th, 2015 – The Retmarker Company (formerly known as Critical Health) is in a process to qualify the Micro-Aneurysm Formation Rate (MAFR), measured with a validated automated method as an enrichment biomarker for studies of clinically significant macular oedema (CSMO), a sight-threatening complication of Diabetic Retinopathy (DR). Such biomarker could be used to enrich a clinical trial population to those at higher risk of developing CSMO.

The European Medicines Agency (EMA) recognizes the "*need to identify biomarkers that predict development of CSMO to facilitate the design of clinical trials of a aiming to intervene in early stages of DR"*, justified by the fact that "*event rates are sparse during the relatively short duration of an interventional trial*" and as "*the rate of progression is also highly variable between subjects*".

RetmarkerDR is the underlying software product that provides a validated (class IIa medical device) and automated calculation of the MAFR, i.e., the number of new micro-aneurysms per time period, a sign of DR activity.

Usage of validated technology has the advantages of "***allowing a rapid, objective and automated evaluation of the MAFR*** *which is an important advantage, especially in the conduct of large clinical trials*" says EMA.

EMA complements it by expressing that "***MAFR as calculated by a validated automated method seems as a very promising biomarker for enriching a patient population at higher risk for the development of CSMO****. It seems to be a complement to other markers (e.g. metabolic control) for the risk of progression of DR as an additive value is indicated.*"

The Letter of Support does not represent a formal qualification at this moment, rather an incentive and recognition of the potential of the work being carried. *"Upon EMA's manifestation of interest, further studies will be conducted with our current partners and others interested in this fundamental research topic with access to Diabetics' databases and/or national registries*" concludes João Diogo Ramos, Retmarker's CEO.

The Retmarker Company and its Partners continue to innovate, in a clear example of translational research, by combining state-of-the-art software development with leading medical research in DR, the leading cause of blindness in the working age population in the Western World.

Full copy of EMA's Letter of Support, signed by Mr. Andreas Pott, Deputy Executive Director, attached.

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About Retmarker technology

Retmarker is a patented and certified medical device family of software products addressing retinal diseases.

RetmarkerDR is an innovative clinical research product that allows to track the activity of micro-aneurysms, namely the Micro-Aneurysms Formation Rate (MAFR).

Similar mathematical algorithms are also applied in Retmarker Screening, a product used daily since 2011 in Diabetic Retinopathy screening programs, that allows the implementation of highly reliable and efficient screening programs at an extremely low cost.

7 January 2015
EMA/775397/2014
Executive Director

Letter of support for micro-aneurysm formation rate (MAFR) biomarker

On 07 June 2013 the applicant Critical Health S.A. requested qualification of micro-aneurysm formation rate (MAFR) measured with a validated automated method, as an enrichment biomarker for studies of clinically significant macular oedema (CSMO) pursuant to Article 57(1)(n) of Regulation (EC) 726/2004 of the European Parliament and of the Council.

During its meeting held on 01 – 04 September 2014, the SAWP agreed on the advice to be given to the applicant. During its meeting held on 22 - 25 September 2014, the CHMP adopted the advice to be given to the applicant.

The applicant proposes the micro-aneurysm formation rate (MAFR) measured with a validated automated method as a biomarker to enrich a clinical trial population to those at higher risk of developing clinically significant macular oedema (CSMO). MAFR as calculated by a validated automated method seems as a very promising biomarker for enriching a patient population at higher risk for the development of CSMO. It seems to be a complement to other markers (e.g. metabolic control) for the risk of progression of DR as an additive value is indicated. The restriction to a target population of subjects with type 2 diabetes and ETDRS DR severity grades 20 to 35, i.e. mild to moderate DR may also be reasonable. The MAFR as calculated by a validated method also has the advantages of allowing a rapid, objective and automated evaluation of the MAFR which is an important advantage, especially in the conduct of large clinical trials. However, to proceed to a qualification opinion, additional data are needed.

In a clinical trial of interventions aiming to prevent development of CSMO in subjects in earlier stages of diabetic retinopathy (DR), event rates are sparse during the relatively short duration of an interventional trial. The rate of progression is also highly variable between subjects. There is currently no comprehensive risk calculator to identify patients who are at an increased risk for the development of CSMO within a reasonable time frame. EMA agrees that there is a need to identify biomarkers that predict development of CSMO to facilitate the design of clinical trials of a aiming to intervene in early stages of DR. The biomarker letter of support is issued on the basis of this qualification advice.

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