4th Nuclear Technologies for Health Symposium
February 13-14, 2020
Nantes, France

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Title:

Effect of Neflamapimod on neuroinflammation using DPA-714 in PET scan in selected Alzheimer disease patients.

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Abstract:

Background and objectives

In Alzheimer disease pathophysiology, there are a large amount of evidence showing a deleterious impact of neuroinflammation on disease progression (Henstridge et al., 2019). Microglial activation seems to be one of the main actors responsible for the chronic immune response (Heppner et al., 2015). Furthermore, the p38 alpha MAPK has been recognized as a leading therapeutic target for a broad range of central nervous system disorders (Correa and Eales, 2012). A novel compound VX-745 or Neflamapimod seems to be the most selective inhibitor of the the p38 alpha MAPK (Alam 2015). We have therefore started a proof of concept study to assess the effect of Neflamapimod on neuroinflammation in a population of Alzheimer disease patients at an early stage.

Hypothesis

We expect to observe a decrease of neuroinflammation among treated patients in comparison to the placebo groups, after 12 weeks of treatment. We also expect to see an improvement in their cognitive abilities.

Methods

Our main objective will be to compare the level of microglial activation in PET scan. Inlfammation will be assessed using DPA-714 as one of the most specific radioligand of the translocator protein (Chauveau et al., 2009). TSPO polymorphisms will be considered in our analyses. In addition, we plan to investigate the effect on Neflamapimod on the neuropsychological status of our patients, on brain structure, and on biomarkers of inflammation.

Results

Preliminary results of the study will be stated. Our methods of analysis for DPA-714 images will be highlighted for further discussion.