Abstract Title: Results of a multicentre phase 3 trial on florbetaben for ß-amyloid brain PET in Alzheimer disease

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Abstract: The aim of this global phase 3 trial was to confirm that florbetaben PET can detect ß-amyloid in vivo in the brain and to validate the use of this ligand as biomarker by comparing identical brain regions in the scan with the respective post mortem specimens. 204 end-of-life patients recruited from 17 centers across 4 continents underwent MRI and florbetaben PET scanning. 10 healthy individuals were also included to support specificity. Co-registered regional MRI-PET data were analyzed by 3 independent blinded readers. Assessment of the images was done on a regional basis for 6 pre-specified regions and on a subject level taking into account a visual scoring method proposed for clinical practice. A total of 31 brains were included in the analysis (186 regions and additional 60 regions from the healthy volunteers negative per default). The autopsy was photodocumented in detail to allow for alignment with the MRI/PET images. ß-amyloid in the tissue was detected by silver-staining and immunohistochemistry. The presence or absence of ß-amyloid was determined by a consensus panel of 3 neuropathologists blinded to all clinical and imaging data. Based on the regional comparison, florbetaben detected ß-amyloid with a sensitivity of 77% and specificity of 94%. Comparison of the visual subject level analysis with the post mortem diagnosis revealed a sensitivity 100% and specificity of 92%. The inter-reader agreement was 0.66 for the regional comparison and 0.87 for the subject level comparison, respectively. The results of this global phase 3 trial confirm, that florbetaben is able to detect ß-amyloid in the brain during life with a high sensitivity and specificity and thus, is a suitable biomarker for this purpose.

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