images and requires additional careful PVC even for a simple semi-quantitative analysis, preventing the use of THK523 in research or clinical settings.

Conclusion

This study has shown that despite selective, non-invasive in vivo assessment of PHF-tau in humans being possible, a single aspect of the in vivo behaviour of a tracer can derail its further development. This highlights the need for careful in vivo proof of concept studies at the initial stages of the development before embarking on more complex quantification approaches involving invasive procedures such as arterial cannulation or engaging in costly phase II studies. Better tau tracers, some of them already being evaluated in humans [23, 25–27], will be required for applications such as monitoring disease progression and assessing efficacy of anti-tau therapy. The development of ^{18}F-THK523 has shown to be a significant step towards the integration of tau imaging with Aβ imaging, moving us towards meeting the desired goal of earlier diagnosis of AD to assist the development of preventative treatments as well as identifying subjects for early therapeutic interventions.

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Conflicts of interest None.

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Authors' contributions

Dr. Villemagne had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

Drs. Villemagne, Furumoto, Fodero-Tavoletti, Kudo, Rowe and Okamura participated in the design, acquisition, analysis and interpretation of the data and writing of this manuscript.

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