Florbetapir

[18F]-florbetapir [18F]-AV-45

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Radiopharmaceutical Name	(E)-4-(2-(6-(2-(2-(2-([18F]-fluoroethoxy)ethoxy)ethoxy)pyridin-3-yl)vinyl)-N-methyl benzenamine Abbreviations: [18F]-florbetapir [18F]-AV-45, **florbetapir**	
Radiopharmaceutical Image	**Normal by Distribution Sample**	**Radiopharmaceutical Structure**
Radionuclide	^{18}F Half-life 109.7 minutes Emission: positron Emax 1.656 MeV	
Emission: positron		
MICAD	http://www.ncbi.nlm.nih.gov/books/NBK32300/	
Molecular Formula and Weight	$C_{20}H_{27}FN_2O_3$ 361.44 g atom mole^{-1}	
General Tracer Class	Diagnostic PET Radiopharmaceutical	
Target	Amyloid-beta peptide	
Molecular Process Imaged	β-amyloid binding compound targeting the extracellular senile plaques found in the brain (especially hippocampus and associative regions of the cortex) and implicated as the main causes of neuronal degeneration and cell death in Alzheimer disease.	

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Mechanism for in vivo retention	Increased binding affinity for aggregated β-amyloid fibrils in Alzheimer diseased brains but not to control brain.
Metabolism	After an initial, rapid penetration into the brain, there is a quick washout to background level of brain white matter.
Radiosynthesis	From MICAD [http://www.ncbi.nlm.nih.gov/books/NBK32300/]: [^{18}F]AV-45 was readily synthesized by standard ^{18}F-fluorination of *N*-BOC-protected *O*-tosylated derivative with ([^{18}F]KF/Kryptofix 2.2.2, 120°C for 10 min), followed by hydrolysis (HCl, 120°C for 5 min) [1]. The radiochemical yield was 10-30% with the specific activity of 37-185 GBq/mmol (1-5 Ci/mmol) at the end of synthesis. Radiochemical purity was >99% as determined with high-performance liquid chromatography (HPLC). Total synthesis time was not reported. Yao et al. [20] reported that [^{18}F]AV-45 was prepared in 105 min using a tosylate precursor with Sumitomo modules for radiosynthesis under GMP-compliant conditions. The overall yield was 25.4 ± 7.7% with a HPLC purity of 95.3 ± 2.2% (*n* = 19). The specific activity of [^{18}F]AV-45 was 470 ± 135 GBq/μmol (12.7 ± 3.6 Ci/μmol, *n* = 19).
Availability	USA: FDA Approval February 10, 2012. Prescribing information: http://pi.lilly.com/us/amyvid-uspi.pdf
Status with USP / EuPh	USP and EuPh monographs are not available and at the best of our knowledge, no drafts are under development (as of May 2012).
Recommended Activity and Allowable mass	Recommended activity for Amyvid is 370 MBq (10 mCi), maximum 50 μg mass dose, administered as a single intravenous bolus in a total volume of 10 mL or less through a short catheter [max. 1.5 inches or less]. Follow the injection with an intravenous flush of 0.9% sterile sodium chloride.
Dosimetry	The effective dose equivalent is reported to be 0.019 mSv/MBq for the standard adult (7.0 mSv for a 370 MBq administration). The critical organ is the gallbladder wall (143 μGy/MBq), but liver, intestine and urinary bladder have also the greatest exposure.
Pharmacology and Toxicology	Most common adverse reactions reported in clinical trials (n=496) were: headache n=9 (1.8%), musculoskeletal pain n=4 (0.8%), fatigue n=3 (0.6%), nausea n=3 (0.6%), anxiety n=2 (0.4%), back pain n=2 (0.4%), blood pressure increased n=2 (0.4%), claustrophobia n=2 (0.4%), feeling cold n=2 (0.4%), insomnia n=2 (0.4%), neck pain n=2 (0.4%). Drug interactions (from PI): Pharmacodynamic drug-drug interaction studies have not been performed in patients to establish the extent, if any, to which concomitant medications may alter Amyvid image results. Within a clinical study of patients with a range of cognitive impairment, some patients with probable AD were receiving the following medications:

	donepezil, galantamine, memantine. Mean cortical Standardized Uptake Value (SUV) ratios did not differ between the patients taking or not taking these concomitant medications. In *in vitro* tests, none of the drugs tested, including the acetylcholinesterase inhibitors donepezil, galantamine, and tacrine, altered florbetapir F 18 binding to its target.
Current Clinical Trials	The NIH clinical trials registry (www.clinicaltrials.gov) should be consulted for a list of current trials using ^{18}F-florbetapir. As of May 13, 2012, it listed 28 clinical trials. Of these 28 clinical trials, 9 were recruiting or preparing to recruit subjects. All of the clinical trials are for using Florbetapir to image beta-amyloid pathology in patients with mild cognitive impairment or dementia due to Alzheimer disease.
Reference Site / Person	The best reference site for US-based physicians is the manufacturer (http://www.amyvid.com) or call the Lilly Answers Center at 1-800-LillyRX (1-800-545-5979), Monday through Friday, 9 am to 5 pm ET (toll-free number), which will connect you with a Health Care professional who can provide additional information.
Imaging Protocol	The imaging protocol recommended by the manufacturer is a 10-minute PET images acquired 30 to 50 minutes after single intravenous bolus injection in a total volume of 10 mL or less. The ACRIN website is a useful source of protocol information http://acrin.org/. A guide to image interpretation is included in the prescribing information and on the manufacturer website. ^{18}F-florbetapir has been quantified by the use of the standardized uptake value ratio (SUVR) with the cerebellum as the reference region. In 3 patients with Alzheimer disease, SUVR was higher than in healthy controls (1.51±0.30 vs. 1.17±0.011) at 50 min after injection with 382 MBq (2).
Human Imaging Experience	Listed below are selected early references but the use of Florbetapir PET/CT is growing rapidly (MICAD or PubMed will help to find the most recent reports of human imaging studies). Nordberg A. *PET imaging of amyloid in Alzheimer's disease.* Lancet Neurol. 2004;3(9):519–27. [PubMed] Yao C.H., Lin K.J., Weng C.C., Hsiao I.T., Ting Y.S., Yen T.C., Jan T.R., Skovronsky D., Kung M.P., Wey S.P. *GMP-compliant automated synthesis of [^{18}F]AV-45 (Florbetapir F 18) for imaging beta-amyloid plaques in human brain.* Appl Radiat Isot. 2010;68(12):2293–7. [PubMed] Lin KJ, Hsu WC, Hsiao IT, Wey SP, Jin LW, Skovronsky D, Wai YY, Chang HP, Lo CW, Yao CH, Yen TC, Kung MP. Whole-body biodistribution and brain PET imaging with [^{18}F]AV-45, a novel amyloid imaging agent--a pilot study. Nucl Med Biol. 2010;37(4):497-508. Wong DF, Rosenberg PB, Zhou Y, Kumar A, Raymont V, Ravert HT, Dannals RF, Nandi A, Brasić JR, Ye W, Hilton J, Lyketsos C, Kung HF, Joshi AD, Skovronsky DM, Pontecorvo MJ. In vivo imaging of amyloid deposition in Alzheimer disease using the radioligand ^{18}F-AV-45 (florbetapir [corrected] F 18). J Nucl Med. 2010;51(6):913-20. Erratum in: J Nucl Med. 2010 Aug;51(8):1327.

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