

Longitudinal CBF Changes Associated With ARIA Development In Alzheimer Disease Following Amyloid-targeted Therapies

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Early interval cerebral blood flow (CBF) changes after donanemab therapy, particularly at the cortical-CSF interface may predict subsequent development of ARIA before conventional MRI findings become apparent.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES																				
➤ Amyloid-targeting therapies improve outcomes in Alzheimer's disease (AD) but are associated with amyloid-related imaging abnormalities (ARIA), occurring in approximately 20% of treated patients. ➤ Conventional MRI is relatively insensitive to early physiological changes preceding ARIA. ➤ Arterial Spin Labeling (ASL) MRI enables non-invasive quantification of cerebral blood flow (CBF) and may detect treatment-related vascular changes earlier. ➤ We investigated whether early longitudinal regional CBF changes predict subsequent ARIA following donanemab therapy.	➤ Prospective observational study ➤ AD patients treated with donanemab ➤ Baseline and 2-month post-treatment MRI including multi-delay ASL Image Processing Brain extraction → Tissue segmentation → Image coregistration Quantification of CBF in: Whole brain (WB), Gray matter (GM), White matter (WM), Cortical-CSF interface Statistical Analysis ➤ Interval CBF change (baseline → 2 months) ➤ Comparison between patients with and without ARIA ➤ Multivariable logistic regression	➤ 35 patients included (median age 74 years, 60% female). ➤ 10 patients (28%) developed ARIA (median of 3 months after donanemab treatment) ➤ Interval ASL assessment from baseline to 2-month, showed overall increase in CBF values in whole brain (WB), white matter (WM), gray matter (GM) and CSF-cortical interface in patients without ARIA; while these values were decreased in patients who developed ARIA, although without reaching statistical significant (p>0.05) (see Table). ➤ Interval change of CSF-cortical interface after treatment (16% increase in patients without ARIA vs. 6.9% decrease in those with ARIA) remained as the only independent variable (p=0.0489) in a multivariate logistic regression analysis. ➤ A total of 8 out 10 (80%) of patients who developed ARIA did not have any improvement in CSF-cortical interface perfusion	➤ Results showed that early interval CBF changes following Donanemab treatment (baseline to 2-month posttreatment) might be promising in prediction of ARIA. ➤ While our study was underpowered, early improvement of CSF-cortical interface perfusion, which has been proposed as a measure of glymphatic function, showed promise as an independent predictor of ARIA with 80% sensitivity. ➤ Larger studies are needed to validate and establish statistical significance.	Sperling RA, et al. <i>Alzheimer's Dement.</i> 2011. Cummings J, et al. <i>Nat Rev Neurol.</i> 2023. Alsop DC, et al. <i>Magn Reson Med.</i> 2015. CONTACT Kambiz.Nael@ucsf.edu																				
<table><tr><th>Interval change from baseline to 2-month posttreatment</th><th>ARIA (+), N=10</th><th>ARIA (-), N=25</th><th>P value</th></tr><tr><td>CBF/percentage interval change in whole brain</td><td>-1.8/-3.5%</td><td>+4.8/+11%</td><td>0.49</td></tr><tr><td>CBF/percentage Interval change in gray matter</td><td>-2.0/-4%</td><td>+2.8/+8.2%</td><td>0.60</td></tr><tr><td>CBF/percentage interval change in white matter</td><td>-1.2/-3.6%</td><td>+1.9/+10%</td><td>0.49</td></tr><tr><td>CBF/percentage interval change in CSF-cortical interface</td><td>-0.25/-6.9%</td><td>+0.60/+16.4%</td><td>0.11</td></tr></table>					Interval change from baseline to 2-month posttreatment	ARIA (+), N=10	ARIA (-), N=25	P value	CBF/percentage interval change in whole brain	-1.8/-3.5%	+4.8/+11%	0.49	CBF/percentage Interval change in gray matter	-2.0/-4%	+2.8/+8.2%	0.60	CBF/percentage interval change in white matter	-1.2/-3.6%	+1.9/+10%	0.49	CBF/percentage interval change in CSF-cortical interface	-0.25/-6.9%	+0.60/+16.4%	0.11
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