

## Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

## **eMethod. PET Imaging Acquisition and Visual Interpretation**

Study 1 participants received an intravenous administration of 370 (+/- 10%) MBq of Flortaucipir F 18 and underwent 20 min of PET imaging (4 x 5 min acquisition frames) beginning approximately 80 min after injection. Study 2 participants received an intravenous administration of 240 (+/- 10%) MBq of Flortaucipir F 18 and underwent 30 min of PET imaging (6 x 5 min acquisition frames) beginning approximately 75 min after injection. Flortaucipir imaging was obtained a mean±SD of 24±10.7 days from baseline clinical assessments in Study 1, and 17±18.3 days from baseline measures in Study 2.

Scans that were considered unevaluable (e.g., head out of field of view; severe motion; low counts) by at least 3 of the 5 readers were not used in any efficacy analyses. Following the criteria as shown in Figure 1, readers examined specified brain regions and scored each as negative or positive depending on the presence of elevated flortaucipir signal more than 65% above the cerebellar reference region signal. Readers then gave an assessment of global tau uptake as either an advanced, moderate, or negative AD tau pattern.

**eTable 1. Inter-reader Consistency of Flortaucipir Scan Visual Interpretation**

	<b>Number of Scans</b>	<b>% agreement</b>	<b>Fleiss' Kappa 95% CI</b>
<b>Study 1</b>	159	94.5%	0.89 (0.84, 0.94)
<b>Study 2</b>	205	91.4%	0.75 (0.71, 0.80)

**Note:** % agreement was calculated as the sum of agreeable pairs of readers from each scan, divided by total number of possible combinations of reading pairs.

**eTable 2. Risk for Clinical Progression Based on Individual Reader's Visual Interpretation Results: Advanced AD Pattern vs. Non-Advanced AD Pattern**

		Study 1				Study 2				Pooled			
		% Event		HR 95% CI	P-value	% Event		RR 95% CI	P-value	% Event		RR 95% CI	P-value
	Reader	Advanced	Non-Advanced			Advanced	Non-Advanced			Advanced	Non-Advanced		
CDR-SB	Reader 1	36 (58.1%)	31 (44.9%)	1.64 (1.00, 2.67)	0.05	117 (75.5%)	26 (52.0%)	1.52 (1.15, 2.01)	0.003	145 (71.4%)	50 (44.6%)	1.49 (1.18, 1.87)	0.001
	Reader 2	37 (56.1%)	30 (46.2%)	1.59 (0.97, 2.60)	0.06	112 (74.2%)	31 (57.4%)	1.33 (1.04, 1.70)	0.02	141 (70.5%)	54 (47.0%)	1.39 (1.12, 1.72)	0.003
	Reader 3	33 (56.9%)	34 (46.6%)	1.48 (0.91, 2.42)	0.11	126 (73.3%)	17 (51.5%)	1.46 (1.05, 2.04)	0.03	152 (69.7%)	43 (44.3%)	1.40 (1.09, 1.79)	0.009
	Reader 4	39 (59.1%)	28 (43.1%)	1.68 (1.02, 2.74)	0.04	114 (75.0%)	29 (54.7%)	1.46 (1.13, 1.89)	0.004	145 (71.4%)	50 (44.6%)	1.49 (1.19, 1.87)	<0.001
	Reader 5	39 (59.1%)	28 (43.1%)	1.70 (1.04, 2.77)	0.04	119 (72.6%)	24 (58.5%)	1.25 (0.96, 1.64)	0.10				
	<b>Majority</b>	<b>36 (57.1%)</b>	<b>31 (45.6%)</b>	<b>1.58 (0.97, 2.85)</b>	<b>0.07</b>	<b>119 (73.5%)</b>	<b>24 (55.8%)</b>	<b>1.36 (1.03, 1.79)</b>	<b>0.03</b>	<b>147 (70.0%)</b>	<b>48 (45.7%)</b>	<b>1.40 (1.11, 1.76)</b>	<b>0.005</b>
MMSE	Reader 1	30 (48.4%)	13 (18.8%)	2.54 (1.30, 4.96)	0.006	109 (70.8%)	24 (49.0%)	1.40 (1.01, 1.94)	0.04	131 (65.2%)	34 (30.6%)	1.68 (1.24, 2.29)	<0.001
	Reader 2	30 (45.5%)	13 (20.0%)	2.26 (1.15, 4.41)	0.02	108 (72.0%)	25 (47.2%)	1.50 (1.09, 2.06)	0.01	131 (66.2%)	34 (29.8%)	1.81 (1.34, 2.45)	<0.001
	Reader 3	29 (50.0%)	14 (19.2%)	2.42 (1.25, 4.67)	0.009	116 (67.8%)	17 (53.1%)	1.19 (0.83, 1.71)	0.35	138 (63.9%)	27 (28.1%)	1.66 (1.16, 2.37)	0.006
	Reader 4	31 (47.0%)	12 (18.5%)	2.55 (1.29, 5.04)	0.007	105 (69.5%)	28 (53.8%)	1.24 (0.92, 1.67)	0.15	128 (63.7%)	37 (33.3%)	1.52 (1.14, 2.02)	0.004
	Reader 5	31 (47.0%)	12 (18.5%)	2.42 (1.22, 4.80)	0.01	112 (68.7%)	21 (52.5%)	1.23 (0.88, 1.72)	0.22				
	<b>Majority</b>	<b>30 (47.6%)</b>	<b>13 (19.1%)</b>	<b>2.51 (1.29, 4.89)</b>	<b>0.007</b>	<b>112 (69.6%)</b>	<b>21 (50.0%)</b>	<b>1.35 (0.96, 1.89)</b>	<b>0.08</b>	<b>134 (64.4%)</b>	<b>31 (29.8%)</b>	<b>1.68 (1.22, 2.32)</b>	<b>0.001</b>
ADAS	Reader 1	35 (56.5%)	23 (33.3%)	1.37 (0.77, 2.44)	0.28	95 (63.3%)	17 (34.7%)	1.75 (1.15, 2.65)	0.009	121 (61.1%)	34 (30.6%)	1.71 (1.23, 2.36)	0.001
	Reader 2	37 (56.1%)	21 (32.3%)	1.56 (0.87, 2.78)	0.13	93 (63.7%)	19 (35.8%)	1.70 (1.14, 2.53)	0.009	119 (61.0%)	36 (31.6%)	1.65 (1.21, 2.26)	0.001
	Reader 3	33 (56.9%)	25 (34.2%)	1.30 (0.74, 2.29)	0.37	101 (60.5%)	11 (34.4%)	1.61 (0.97, 2.67)	0.06	127 (59.6%)	28 (29.2%)	1.74 (1.21, 2.51)	0.003
	Reader 4	37 (56.1%)	21 (32.3%)	1.55 (0.88, 2.75)	0.13	95 (64.6%)	17 (32.7%)	1.91 (1.26, 2.91)	0.003	122 (61.6%)	33 (29.7%)	1.80 (1.30, 2.49)	<0.001
	Reader 5	37 (56.1%)	21 (32.3%)	1.49 (0.84, 2.67)	0.17	97 (61.0%)	15 (37.5%)	1.49 (0.97, 2.31)	0.07				
	<b>Majority</b>	<b>35 (55.6%)</b>	<b>23 (33.8%)</b>	<b>1.36 (0.77, 2.41)</b>	<b>0.29</b>	<b>98 (62.4%)</b>	<b>14 (33.3%)</b>	<b>1.77 (1.12, 2.80)</b>	<b>0.01</b>	<b>124 (60.5%)</b>	<b>31 (29.8%)</b>	<b>1.73 (1.35, 2.25)</b>	<b>&lt;0.001</b>

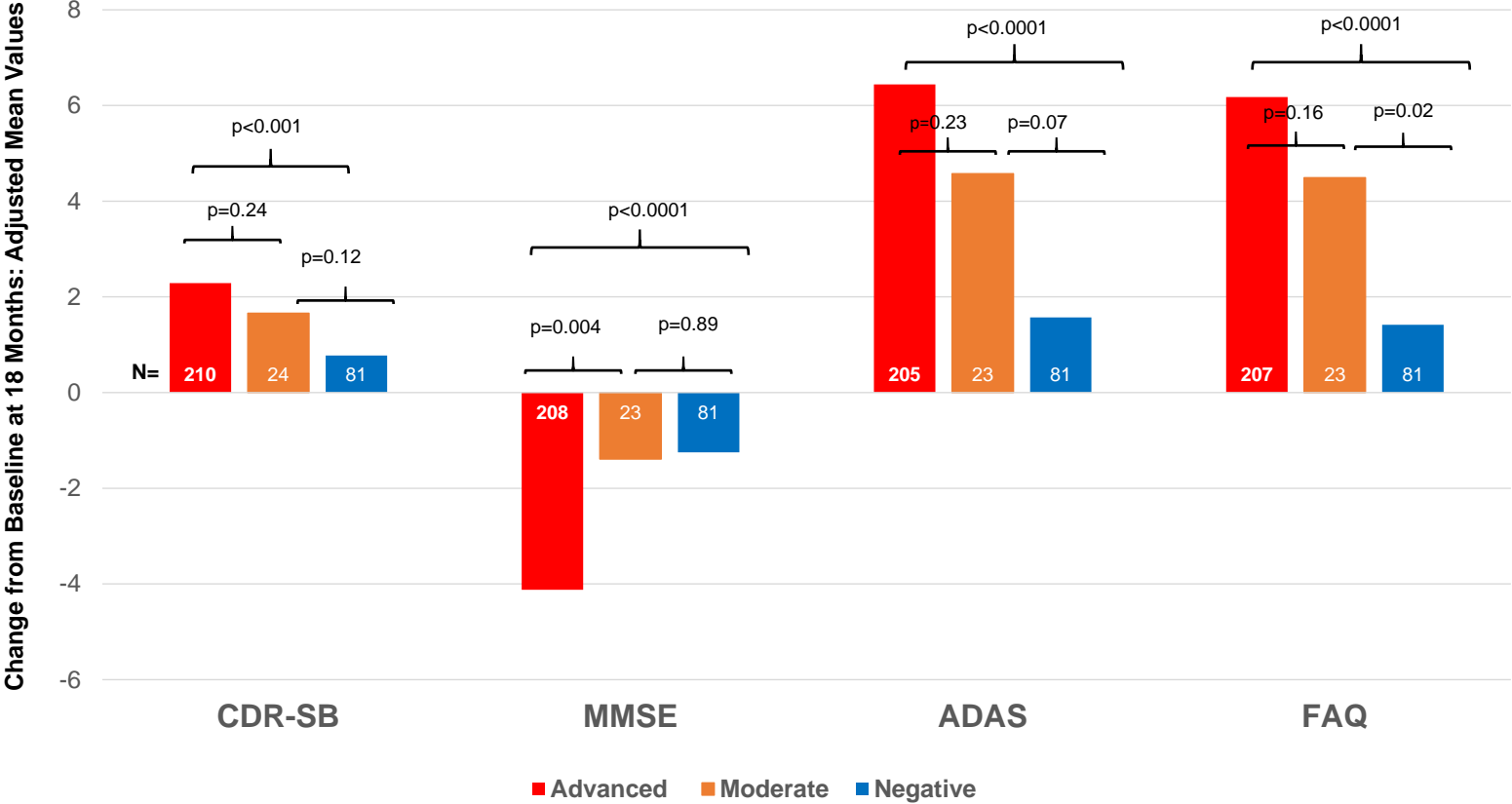
		Study 1				Study 2				Pooled			
		% Event		HR 95% CI	P-value	% Event		RR 95% CI	P-value	% Event		RR 95% CI	P-value
	Reader	Advanced	Non-Advanced			Advanced	Non-Advanced			Advanced	Non-Advanced		
FAQ	Reader 1	47 (75.8%)	24 (34.8%)	2.88 (1.73, 4.80)	<0.001	107 (70.9%)	27 (55.1%)	1.34 (1.02, 1.77)	0.04	142 (71.4%)	46 (41.4%)	1.72 (1.35, 2.19)	<0.001
	Reader 2	49 (74.2%)	22 (33.8%)	2.76 (1.65, 4.62)	<0.001	105 (70.9%)	29 (55.8%)	1.33 (1.01, 1.73)	0.04	141 (71.6%)	47 (41.6%)	1.71 (1.35, 2.17)	<0.001
	Reader 3	44 (75.9%)	27 (37.0%)	2.63 (1.60, 4.34)	<0.001	116 (69.5%)	18 (54.5%)	1.29 (0.92, 1.80)	0.14	150 (70.4%)	38 (39.2%)	1.78 (1.35, 2.34)	<0.001
	Reader 4	50 (75.8%)	21 (32.3%)	3.06 (1.81, 5.19)	<0.001	105 (70.9%)	29 (55.8%)	1.37 (1.05, 1.79)	0.02	143 (71.9%)	45 (40.5%)	1.76 (1.38, 2.24)	<0.001
	Reader 5	50 (75.8%)	21 (32.3%)	2.85 (1.69, 4.81)	<0.001	109 (68.6%)	25 (61.0%)	1.11 (0.85, 1.46)	0.44				
	<b>Majority</b>	<b>47 (74.6%)</b>	<b>24 (35.3%)</b>	<b>2.79 (1.67, 4.64)</b>	<b>&lt;0.001</b>	<b>111 (70.3%)</b>	<b>23 (54.8%)</b>	<b>1.32 (0.98, 1.78)</b>	<b>0.06</b>	<b>146 (70.5%)</b>	<b>42 (40.4%)</b>	<b>1.74 (1.35, 2.25)</b>	<b>&lt;0.001</b>
CDR Global	Reader 1	28 (45.2%)	20 (29.0%)	2.52 (1.40, 4.52)	0.002	71 (45.8%)	16 (32.0%)	1.59 (1.00, 2.50)	0.05	94 (46.5%)	31 (27.7%)	1.78 (1.26, 2.52)	0.001
	Reader 2	29 (43.9%)	19 (29.2%)	2.30 (1.28, 4.15)	0.006	68 (45.0%)	19 (35.2%)	1.37 (0.89, 2.11)	0.15	90 (45.2%)	35 (30.4%)	1.55 (1.12, 2.15)	0.009
	Reader 3	25 (43.1%)	23 (31.5%)	2.08 (1.17, 3.69)	0.013	75 (43.6%)	12 (36.4%)	1.32 (0.79, 2.19)	0.29	96 (44.2%)	29 (29.9%)	1.55 (1.07, 2.25)	0.02
	Reader 4	29 (43.9%)	19 (29.2%)	2.23 (1.23, 4.04)	0.008	68 (44.7%)	19 (35.8%)	1.43 (0.93, 2.19)	0.10	91 (45.0%)	34 (30.4%)	1.55 (1.12, 2.16)	0.009
	Reader 5	29 (43.9%)	19 (29.2%)	2.07 (1.15, 3.76)	0.02	72 (43.9%)	15 (36.6%)	1.29 (0.81, 2.05)	0.29				
	<b>Majority</b>	<b>28 (44.4%)</b>	<b>20 (29.4%)</b>	<b>2.37 (1.32, 4.26)</b>	<b>0.004</b>	<b>71 (43.8%)</b>	<b>16 (37.2%)</b>	<b>1.28 (0.82, 2.02)</b>	<b>0.28</b>	<b>94 (45.0%)</b>	<b>31 (29.5%)</b>	<b>1.60 (1.13, 2.27)</b>	<b>0.009</b>
Note: Study 1 and Study 2 used different reader for reader #5. Thus, pooled analyses were not conducted for Reader 5													

**eTable 3. Risk for Clinical Progression Based on Individual Reader’s Visual Interpretation Results: Advanced AD Pattern vs. Non-Advanced AD Pattern**

		Study 1			Study 2			Pooled		
		LS Means (SE)		P-value	LS Means (SE)		P-value	LS Means (SE)		P-value
	Reader	Advanced	Non-Advanced		Advanced	Non-Advanced		Advanced	Non-Advanced	
CDR-SB	Reader 1	2.16 (0.35)	0.61 (0.31)	0.001	2.33 (0.19)	1.35 (0.30)	0.003	2.18 (0.15)	0.99 (0.19)	<0.001
	Reader 2	2.06 (0.34)	0.65 (0.32)	0.003	2.29 (0.19)	1.51 (0.29)	0.02	2.16 (0.15)	1.04 (0.19)	<0.001
	Reader 3	2.13 (0.36)	0.71 (0.31)	0.003	2.23 (0.18)	1.39 (0.36)	0.03	2.12 (0.15)	0.97 (0.21)	<0.001
	Reader 4	2.01 (0.34)	0.66 (0.32)	0.005	2.29 (0.19)	1.42 (0.29)	0.007	2.13 (0.15)	1.05 (0.19)	<0.001
	Reader 5	2.10 (0.33)	0.58 (0.32)	0.002	2.22 (0.19)	1.55 (0.32)	0.05			
	<b>Majority</b>	<b>2.09 (0.35)</b>	<b>0.66 (0.32)</b>	<b>0.003</b>	<b>2.22 (0.22)</b>	<b>1.31 (0.38)</b>	<b>0.03</b>	<b>2.28 (0.17)</b>	<b>0.98 (0.24)</b>	<b>&lt;0.001</b>
MMSE	Reader 1	-3.35 (0.67)	-0.30 (0.59)	0.001	-4.87 (0.34)	-2.12 (0.53)	<0.001	-4.18 (0.27)	-1.32 (0.35)	<0.001
	Reader 2	-3.13 (0.67)	-0.39 (0.61)	0.003	-4.91 (0.34)	-2.24 (0.51)	<0.001	-4.15 (0.27)	-1.40 (0.35)	<0.001
	Reader 3	-3.50 (0.68)	-0.32 (0.58)	0.001	-4.52 (0.33)	-2.53 (0.66)	0.005	-4.00 (0.27)	-1.38 (0.39)	<0.001
	Reader 4	-3.15 (0.65)	-0.32 (0.61)	0.002	-4.70 (0.34)	-2.54 (0.53)	<0.001	-3.99 (0.27)	-1.59 (0.36)	<0.001
	Reader 5	-3.19 (0.65)	-0.29 (0.61)	0.002	-4.59 (0.34)	-2.71 (0.59)	0.004			
	<b>Majority</b>	<b>-3.29 (0.67)</b>	<b>-0.33 (0.59)</b>	<b>0.001</b>	<b>-4.89 (0.38)</b>	<b>-2.12 (0.65)</b>	<b>&lt;0.001</b>	<b>-4.13 (0.31)</b>	<b>-1.27 (0.42)</b>	<b>&lt;0.001</b>
ADAS	Reader 1	6.47 (1.01)	2.45 (0.91)	0.005	6.03 (0.58)	2.76 (0.91)	0.001	6.15 (0.44)	2.70 (0.58)	<0.001
	Reader 2	6.46 (0.98)	2.35 (0.92)	0.004	6.11 (0.58)	2.83 (0.87)	0.001	6.19 (0.44)	2.70 (0.57)	<0.001
	Reader 3	6.84 (1.02)	2.32 (0.87)	0.001	5.71 (0.56)	2.90 (1.09)	0.02	6.11 (0.43)	2.43 (0.62)	<0.001
	Reader 4	6.09 (0.97)	2.53 (0.93)	0.01	6.06 (0.57)	2.60 (0.89)	<0.001	6.15 (0.44)	2.68 (0.57)	<0.001
	Reader 5	5.94 (0.98)	2.71 (0.94)	0.02	5.83 (0.57)	3.06 (0.98)	0.01			
	<b>Majority</b>	<b>6.41 (1.00)</b>	<b>2.50 (0.91)</b>	<b>0.006</b>	<b>6.53 (0.66)</b>	<b>1.97 (1.18)</b>	<b>0.006</b>	<b>6.40 (0.51)</b>	<b>2.30 (0.71)</b>	<b>0.001</b>

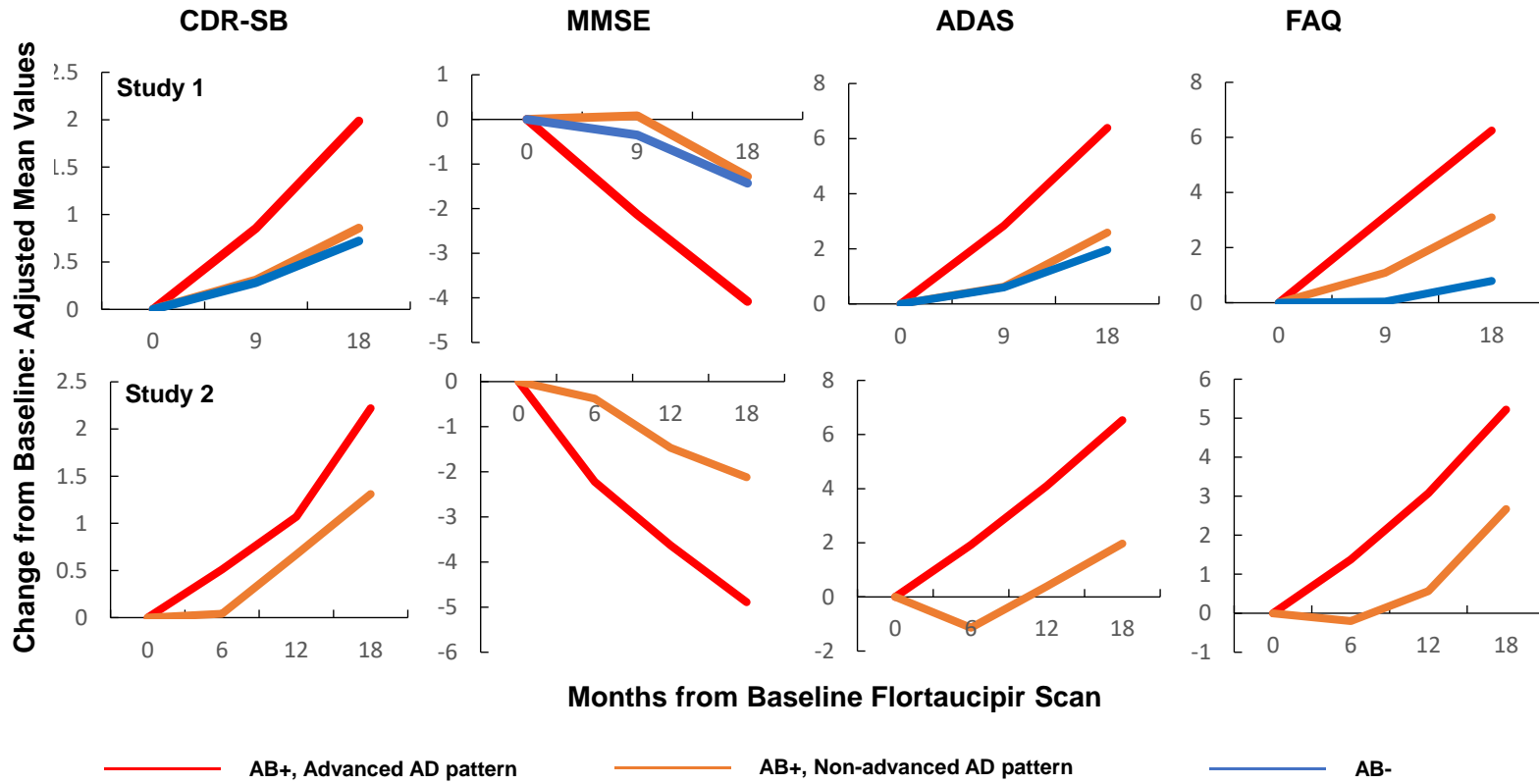
		Study 1			Study 2			Pooled		
		LS Means (SE)		P-value	LS Means (SE)		P-value	LS Means (SE)		P-value
	Reader	Advanced	Non-Advanced		Advanced	Non-Advanced		Advanced	Non-Advanced	
FAQ	Reader 1	7.02 (0.75)	1.74 (0.69)	<0.001	5.20 (0.47)	2.56 (0.75)	0.002	6.15 (0.37)	2.00 (0.47)	<0.001
	Reader 2	6.84 (0.74)	1.73 (0.70)	<0.001	5.14 (0.48)	2.87 (0.74)	0.006	6.02 (0.37)	2.22 (0.47)	<0.001
	Reader 3	6.81 (0.78)	2.14 (0.68)	<0.001	5.04 (0.46)	2.33 (0.89)	0.005	6.08 (0.36)	1.73 (0.51)	<0.001
	Reader 4	6.74 (0.73)	1.72 (0.71)	<0.001	5.15 (0.47)	2.66 (0.74)	0.002	6.04 (0.37)	2.14 (0.47)	<0.001
	Reader 5	6.86 (0.72)	1.60 (0.70)	<0.001	4.98 (0.47)	3.05 (0.80)	0.03			
	<b>Majority</b>	<b>6.93 (0.75)</b>	<b>1.78 (0.69)</b>	<b>&lt;0.001</b>	<b>5.22 (0.54)</b>	<b>2.67 (0.90)</b>	<b>0.01</b>	<b>6.15 (0.40)</b>	<b>2.10 (0.55)</b>	<b>&lt;0.001</b>
Note: Study 1 and Study 2 used different reader for reader #5. Thus, pooled analyses were not conducted for Reader 5										

**eFigure 1. Change from Baseline at 18 Months by Flortaucipir Scan Patterns, Pooled Data from Study 1 and Study 2**

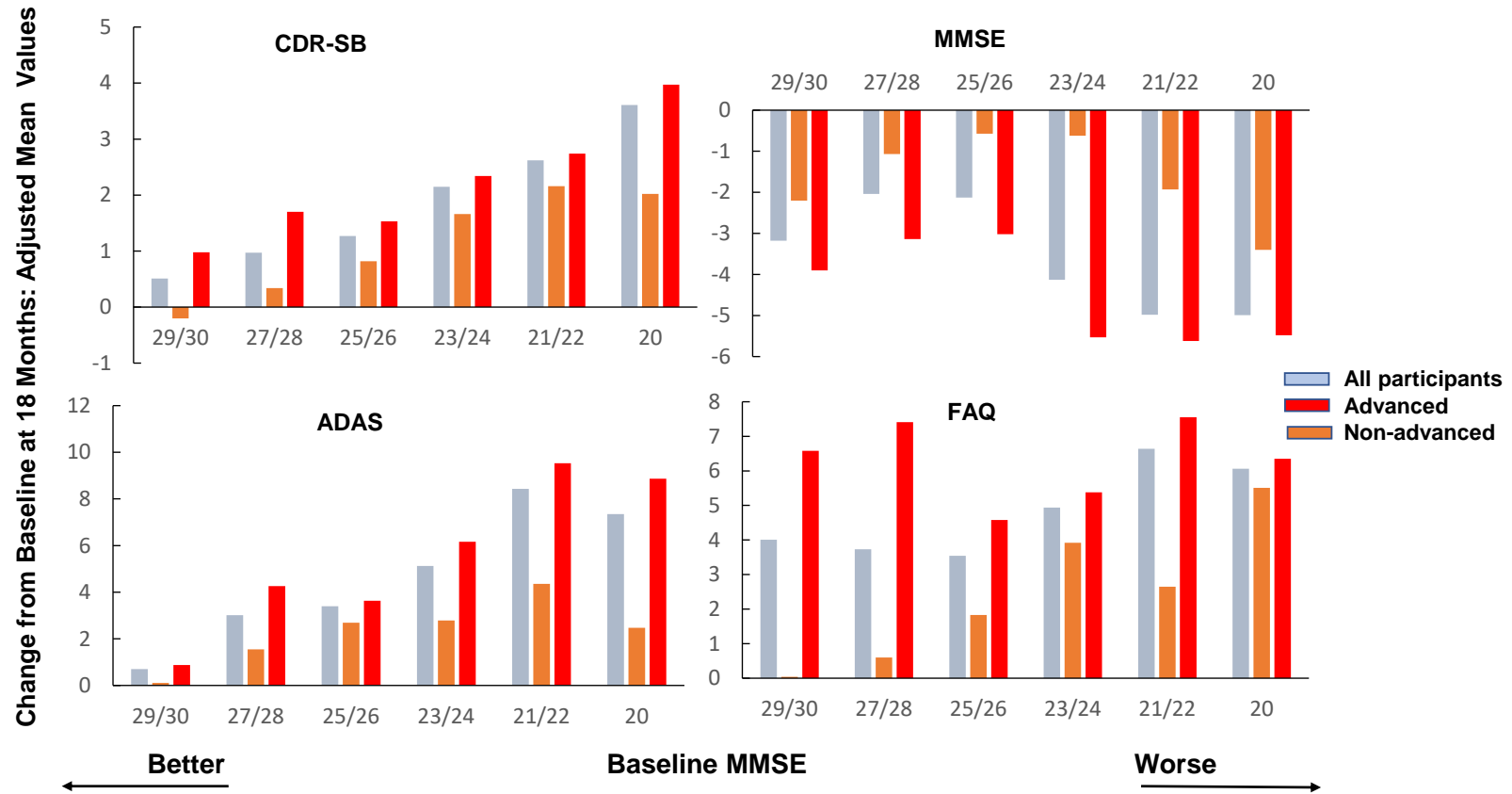




eFigure 2. Change from Baseline Values at Each Follow-up Visit by Amyloid-Tau Groups



eFigure 3. Change from Baseline: Adjusted Mean Values at 18 Months by Baseline MMSE, Pooled Data



**eFigure 4. Flow diagram for subject enrollment and disposition**

**Study 1**

**Study 2**

