# ADNI Florbetapir scan counts

<table>
<thead>
<tr>
<th>Number of Florbetapir scans</th>
<th>N</th>
<th>SMC</th>
<th>EMCI</th>
<th>LMCI</th>
<th>AD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>265</td>
<td>104</td>
<td>302</td>
<td>223</td>
<td>198</td>
<td>1093</td>
</tr>
<tr>
<td>2</td>
<td>215</td>
<td>77</td>
<td>219</td>
<td>153</td>
<td>51</td>
<td>715</td>
</tr>
<tr>
<td>3</td>
<td>127</td>
<td>1</td>
<td>115</td>
<td>72</td>
<td>7</td>
<td>322</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>0</td>
<td>3</td>
<td>7</td>
<td>1</td>
<td>18</td>
</tr>
</tbody>
</table>

# ADNI AV1451 scan counts

<table>
<thead>
<tr>
<th>Number of AV1451 scans</th>
<th>N</th>
<th>SMC</th>
<th>EMCI</th>
<th>LMCI</th>
<th>AD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>11</td>
<td>23</td>
<td>22</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>12</td>
</tr>
</tbody>
</table>

2148

112
### Amyloid Imaging

- **Followup**
  - N=700
- **New**
  - (N=300)

- Choose:
  - Florbetapir
  - Florbetaben

Every 2 Years

### Tau Imaging

- All
  - (N=1000)
  - [^{18}F]AV1451

- 3 additional scans over 4 years
- 20% of Amyloid Positive
- 80% of Amyloid Negative

### FDG Imaging

- MCI/AD
  - (N~650)
  - FDG

- 1 additional scan at 4 years
- 20% of Amyloid Positive
- 80% of Amyloid Negative
Baseline Florbetapir Distribution

31% are Florbetapir+

36% are Florbetapir+

48% are Florbetapir+

67% are Florbetapir+

86% are Florbetapir+

Normal
N= 264

SMC
N=104

EMCI
N=303

LMCI
N=224

AD
N=193

Baseline florbetapir cortical SUVR
Florbetapir rate of change

>2 florbetapir scans

3 florbetapir scans

Baseline florbetapir SUVR (composite ref region)

Baseline florbetapir SUVR (composite ref region)
Florbetapir trajectories by diagnosis

3 florbetapir scans (N=322)

4 florbetapir scans (N=18)
Florbetapir change in amyloid-negative normals

Accumulators (slope>0)

Non-accumulators

Early Accumulation Regions

Cortical Summary Regions

Florbetapir
Change in amyloid-negative normals
Negative normal accumulators are more likely to experience cognitive decline.
AV1451 PET SUVR quantification

Braak staging approach

Medial temporal

Braak I/II

Inferolateral temporal

Braak III/IV

Neocortical

Braak V/VI

ADNI AV1451 PET summary – Braak Staging

Medial temporal

Inferolateral temporal

Neocortical

Whole brain average

N=100

Amyloid -

Amyloid +

AV1451 Braak 1/2 (PVC)

AV1451 Braak 3/4 (PVC)

AV1451 Braak 5/6 (PVC)

AV1451 Braak All (PVC)
RID 4521
74 yo APOE4+ male
• Recently converted from MCI
• MMSE=14
• ADAS-cog=37
• Florbetapir SUVR = 1.61

RID 4765
80yo APOE4+ male
• Recently converted from EMCI
• MMSE=20
• ADAS-cog=19
• Florbetapir SUVR = 1.32
AV1451 tau and cognitive performance

Medial temporal

Inferolateral temporal

Neocortical

Interaction
p=0.005

ADAS-cog

AV1451 Braak 12

AV1451 Braak 34

AV1451 Braak 56

p=0.005

Medial temporal

Inferolateral temporal

Neocortical

Florbetapir+

Florbetapir-
AV1451 comparison in 2 samples

Maass et al. in revision
N=49 (22 N/SMC, 21 MCI, 6 AD) with AV1451-PET and CSF measurements within 1.5yrs

CSF tau

R²=0.20

CSF ptau

R²=0.23

CSF Aβ42

R²=0.28

CSF tau

R²=0.12

CSF ptau

R²=0.14

CSF Aβ42

R²=0.16
U Penn CSF AlzBio3 and AV1451

N=24 (11 N, 10 MCI, 3 AD) with AV1451-PET and CSF measurements within 3 yrs

- **CSF tau** $R^2=0.28$
- **CSF ptau** $R^2=0.19$
- **CSF Aβ** $R^2=0.49$
- **CSF Aβ** $R^2=0.29$

$R^2$ values indicate the proportion of variance explained by the model with AV1451 Braak staging. Higher $R^2$ values suggest a stronger association between the variables.
Recent AV1451-CSF tau studies

Harvard Aging Brain Study  N=31 Normals

Wash U N=41 Normal, 11 Impaired

Chhatwal et al. Neurology 2016

Upcoming PET Core work

Pipeline for florbetaben +/- categorization for ADNI3 tau scanning schedule

AV1451 quantification methods

Cross-sectional and longitudinal relationships between florbetapir, AV1451, CSF, cognition
Thank you
CSF Elecsys and AV1451

N=49 (22 N/SMC, 21 MCI, 6 AD) with AV1451-PET and CSF measurements within 1.5yrs

R²=0.45

R²=0.45

R²=0.28

R²=0.24

R²=0.24

R²=0.16
**Tau, neurodegeneration & cognitive change**

**Entorhinal/hippocampal Braak I/II**

**FDG**

**Hippocampal volume**

- **Florbetapir+**
- **Florbetapir-**

Interaction $p=0.01$

Interaction $p=0.02$

Interaction $p=0.01$

**AV1451 SUVR Braak12**

**FDG**

**Hippocampal Volume**

- Post Cingulate Gyrus
- L Angular Gyrus
- R Angular Gyrus
- L Inf Temporal Gyrus
- R Inf Temporal Gyrus

Diag_1

MCI

N

- Florbetapir+
- Florbeatpir-

Interaction $p=0.01$

Interaction $p=0.02$

- CP T S D
- TBI TBI+PTSD

Diagnosis 1

MCI

N

- Florbetapir+
- Florbeatpir-

Interaction $p=0.01$
Florbetapir+ only

Age
Sex
Education
ApoE4 +

AV1451 PET
p<0.001

FDG PET
p=0.003

Hippocampal Vol
p=0.002

p=0.009

ADAS-cog
Long ADAS-cog
Hipp/entorhinal AV1451

-0.55**

Hippocampal volume

-0.96 **

ADAS-cog

0.32* (0.75**)

Indirect effect: 0.29 [0.09, 0.60]
Florbetapir annual change distribution

Baseline florbetapir-

- 61% are APOE4+
- 40% are APOE4+
- 70% are APOE4+
- 38% are APOE4+
- 0% are APOE4+

Baseline florbetapir+

- 73% are APOE4+
- 92% are APOE4+
- 71% are APOE4+
- 66% are APOE4+
- 66% are APOE4+

Total N = 697

Normal
N = 208

SMC
N = 73

EMCI
N = 218

LMCI
N = 149

AD
N = 49
Nonaccumulators

Accumulators

1.0

1.5

2.0

1.0

1.5

2.0

1.0

1.5

2.0

1.0

1.5

2.0

1.0

1.5

2.0

1.0

1.5

2.0

1.0

1.5

2.0

>2 yr Florbetapir Trajectories

Baseline florbetapir -

Baseline florbetapir +

Florbetapir SUVR annual change

78% of Florbetapir+ are Accumulators

51% of Florbetapir- are Accumulators (15% convert to +)

76% of Florbetapir+ are Accumulators

59% of Florbetapir- are Accumulators (20% convert to +)

71% of Florbetapir+ are Accumulators

58% of Florbetapir- are Accumulators (15% convert to +)

67% of Florbetapir+ are Accumulators

58% of Florbetapir- are Accumulators (11% convert to +)

68% of Florbetapir+ are Accumulators

44% of Florbetapir- are Accumulators (0% convert to +)

Total N= 697
Nonaccumulators

Accumulators

1.0
1.5
2.0

1.0
1.5
2.0

Florbetapir SUVR annual change factor (AV45_NONTP_wcereb_BIN1.11)

91% of Florbetapir+ are Accumulators

56% of Florbetapir- are Accumulators (17% convert to +)

77% of Florbetapir+ are Accumulators

63% of Florbetapir- are Accumulators (23% convert to +)

76% of Florbetapir+ are Accumulators

58% of Florbetapir- are Accumulators (5% convert to +)

33% of Florbetapir+ are Accumulators

50% of Florbetapir- are Accumulators (0% convert to +)

Total N = 219

Baseline florbetapir -
Baseline florbetapir +
### ADNI FDG scan counts

<table>
<thead>
<tr>
<th>Number of FDG scans</th>
<th>N</th>
<th>SMC</th>
<th>EMCI</th>
<th>LMCI</th>
<th>AD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>343</td>
<td>106</td>
<td>306</td>
<td>409</td>
<td>241</td>
<td>1408</td>
</tr>
<tr>
<td>2</td>
<td>258</td>
<td>167</td>
<td>279</td>
<td>112</td>
<td>816</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>92</td>
<td>1</td>
<td>181</td>
<td>75</td>
<td>349</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td></td>
<td>162</td>
<td>58</td>
<td>305</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>72</td>
<td></td>
<td>146</td>
<td></td>
<td>218</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>39</td>
<td></td>
<td>105</td>
<td></td>
<td>144</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>25</td>
<td></td>
<td>56</td>
<td></td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td></td>
<td>28</td>
<td></td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>919</td>
<td>106</td>
<td>474</td>
<td>1371</td>
<td>486</td>
<td>3359</td>
</tr>
</tbody>
</table>
A second (or third?) tau tracer in ADNI?

Strong commitment to adding a second tau tracer to ADNI3 - As of today, no additional tracers available for summer 2017 startup

Requirements for a tau tracer

- Preclinical/clinical supportive data
- Regulatory pathway
- Manufacture at no cost to ADNI
- Distribution to a substantial proportion of sites