<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>
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<td>241</td>
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### 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>264</td>
<td>104</td>
<td>303</td>
<td>224</td>
<td>193</td>
<td>1089</td>
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<tr>
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<td>210</td>
<td>74</td>
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<td>150</td>
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<td>701</td>
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<tr>
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<td>93</td>
<td>0</td>
<td>94</td>
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<td>241</td>
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<td>Total</td>
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<td>178</td>
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<td>423</td>
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### ADNI AV1451 scan counts

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<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>7</td>
<td>8</td>
<td>8</td>
<td>11</td>
<td>1</td>
<td>35</td>
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</table>
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

Total
N=1089

Baseline florbetapir cortical SUVR

Frequency
Does Baseline Florbetapir Threshold Affect Rate of Cognitive Decline?

Rate of Decline Plateaus at ~ SUVR 1.25
Proportion of subjects positive at 1.25 = 50% (MCI), 35% (EMCI), 15% (N)

Subjects with >1.5 yr AVLT followup
Linear mixed effects models, adjusting for age, sex, education, and APOE4 status, with random intercept and slope
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+

Normal
N = 208

SMC
N = 73

EMCI
N = 218

LMCI
N = 149

AD
N = 49

Total N = 697

Frequency

Annual florbetapir change (WM ref region)
≥2 yr Florbetapir Trajectories

Nonaccumulators

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 +)

N= 208

N= 73

N= 218

N= 149

N= 49

Total N= 697
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
Negative normal subjects who accumulate florbetapir more likely to decline cognitively

Episodic memory change

Time (yrs)
relative to baseline florbetapir

Florbetapir - after 4 yrs
Florbetapir + after 4 yrs

Florbetapir Non-accumulators
Florbetapir Accumulators

p=0.035
p=0.025
Braak staging

- Braak I/II (blue)
- Braak III/IV (green)
- Braak V/VI (red)
AV-1451 mean images

<table>
<thead>
<tr>
<th>Young Adults</th>
<th>PIB- Older Adults</th>
<th>PIB+ Older Adults</th>
<th>Alzheimer’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=5</td>
<td>N=17</td>
<td>N=16</td>
<td>N=15</td>
</tr>
</tbody>
</table>

Example AV1451 scans

81yo EMCI Female
Braak1/2 = 1.18
Braak3/4 = 1.17
Braak 5/6 = 1.08

77yo EMCI Female
Braak1/2 = 1.32
Braak3/4 = 1.18
Braak 5/6 = 1.11

74yo AD Female
Braak1/2 = 2.00
Braak3/4 = 1.81
Braak 5/6 = 1.78

SUVR Threshold = 0.5 - 2.5
ADNI AV1451 summary

Baseline florbetapir -
Baseline florbetapir +
AV1451 tau and cognitive performance

Baseline florbetapir -
Baseline florbetapir +
**Amyloid Imaging**

Followup
N=700

New
(N=300)

Florbetapir or Florbetaben

Every 2 Years

Florbetapir or Florbetaben

**Tau Imaging**

All
(N=1000)

[18F]AV1451

80% of Amyloid Positive
20% of Amyloid Negative

3 additional scans over 4 years

[18F]AV1451

[18F]AV1451

[18F]AV1451

**FDG Imaging**

MCI/AD
(N~650)

FDG

20% of Amyloid Positive
80% of Amyloid Negative

1 additional scan at 4 years

[18F]AV1451
We want to retain as many “rollover” subjects as possible

Projections for ~300 new subjects with florbetaben

Many sites will be scanning new subjects with florbetaben, returning subjects with florbetapir

Amyloid PET will guide tau scan frequency
Subjects randomly selected based on the 80%/20% stratification
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 2016 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

1 or more additional tracers could be available late 2016/early 2017?