Disease Modifying Drugs for Alzheimer’s – The Current Landscape
AD: Current Therapy Algorithm

1. Diagnosis
2. Cholinesterase Inhibitor
3. Progression or Moderate-Severe Disease
4. Memantine
5. Psychotropics for Behavioral Changes (any stage of disease)
A disease-modifying agent must:

- Affect the underlying process leading to cell death
- Produce a meaningful impact on disease course
D-M: Increasing Drug-Placebo Difference Over Time
The Original Amyloid Cascade Hypothesis

Alzheimer’s is the cumulative product of a series of pathological events that may begin with the deposition of beta-amyloid in the brain.
Where are the new drugs?

- Not from lack of trying

112 drugs in testing in 2018
Welcome to the Evolution/ Revolution
Around the corner ..... 

Aducanumab

May be first disease modifying therapy

Removes amyloid from brain

Best effect when started early

FDA reviewing
Aducanumab

Before treatment

Placebo  Low dose  Medium dose  High dose

After one year of treatment

EMERGE: Longitudinal change from baseline in CDR-SB

Adjusted mean change from baseline (±SE)

Analysis visit (weeks)

0 26 50 78

Placebo n=547
Low dose aducanumab n=543
Medium dose aducanumab n=547
High dose aducanumab 513 431 299
Side Effects

- Aria E

- Aria H
Operational Issues

- Identification of candidates
- Mild sx, amyloid +
- Infusion center capacity
- Surveillance for ARIA
“Mr. Osborne, may I be excused? My brain is full.”