Kieger – Thoughts from the Street

Alzheimer's Disease
AD/PD Conference 2017: On the Verge of Something

Zurich, April 12, 2017

We attended the 13th International Conference on Alzheimer`s & Parkinson's Diseases in Vienna. Messages we received from the meeting are very encouraging, but patience for new therapies will be needed. Participants felt that we are on the verge of something.

Excitement in the Alzheimer's Disease (Alzheimer's) community for Biogen's aducanumab (anti-abeta antibody) data remains high, as for the first time a disease modifying agent yielded a clinically relevant signal in 2015. The community seems to agree, that the recent failures of Lilly's solanezumab (another anti-abeta antibody) and Merck's BACE inhibitor do not question the current understanding of the disease but will help to positively influence future initiatives. Recent research work recognises that Alzheimer's is a highly heterogenous disease - every patient is different – and that several disease mechanisms are at play.

Alzheimer's disease prevalence
Alzheimer's affects roughly 5.5 mn people in the U.S. and over 15 mn people worldwide. It is estimated that 10% of people aged 65 and older, and about 30% of people over 85, suffer from Alzheimer's. Due to the anticipated rapid growth of the over-65 segment of the U.S. population from currently 48 mn to 88 mn by 2050 (1), the Alzheimer's patient population is expected to increase rapidly to 14 mn by 2050 in the US alone (2). The risk to develop Alzheimer's for women is twice as high as for men.

Alzheimer's disease costs

The costs of health care and long-term care for individuals with Alzheimer's or other dementias are substantial. Total payments in 2017 for all individuals with Alzheimer's or other dementias are estimated at USD 259 bn (increasing to > 1 tn in 2050) (3).

Alzheimer's trials: Flying a plane and building it at the same time

Clinical trial design in Alzheimer`s is much more complex than in many other disease areas. The disease starts long before any clinical symptoms are manifested. Disease mechanisms remain difficult to assess; the right clinical trial design – e.g. when should the treatment start, at what dose, for what patients, what endpoints should be assessed – remains a big challenge. Furthermore, the human brain is difficult to access for analysis – e.g. no biopsies can be taken. Therefore, clinical trials, even if negative, help to build knowledge and understanding of disease mechanisms. Alzheimer's trials remain far from optimized yet. Participants do not expect to get a final disease modifying therapy with one of the ongoing clinical trials. What people hope for are positive signals which could form the base for further research. As one participant stated: "It is like flying a plane while building it at the same time."

Alzheimer's disease mechanisms and drug development

The exact cause of Alzheimer`s is unknown, but genetics and environmental factors appear to play a role. Study findings have shown changes in the brain starting 10 to 20 years before the onset of dementia symptoms in people genetically destined to get Alzheimer's (4). Alzheimer's related changes in the brain– amyloid plaques and tau tangles among others – contribute to the cognitive impairment observed in Alzheimer's (5).

Researchers continue to work on elucidating the biological mechanisms of Alzheimer's, paving the way for the development of novel therapies. Agents with potential disease-modifying characteristics have successfully navigated through Phase I/II studies and are advancing to Phase III programs using the latest PET imaging technology and biomarkers to select the appropriate patient population with mild forms of Alzheimer's disease.

Alzheimer's insights

Abeta plaques, which follow a cascade of aggregation, remain the most discussed disease mechanism. Research has shown that not every form of Abeta is toxic. Next to Abeta plaques, Tau tangles seem to play an important but poorly understood role already early in the disease. Microglia as part of the observed brain inflammation in Alzheimer's patients seems to negatively affect the neuron synapses. With several disease mechanisms interacting with each other, the end game for Alzheimer's will be combination therapy. However, as explained above, confirmed single agent activity is required to launch combination therapy trials.

Another important cornerstone in new Alzheimer's drug development is the work on imaging, which received a clear boost at the conference with demonstrated advancements for Tau-PET imaging.

Interestingly, one group even presented an effect of PD-1 therapy in Alzheimer's in animal models. If results are confirmed, the knowledge gained on PD-1 therapy in oncology could help to boost therapies for Alzheimer's.

Take aways

The road for Alzheimer's treatments remains bumpy. But the direction is the right one. Technology and clinical trials (even if failed) will help to shape the understanding of the disease. The unmet medical need is huge, the market potential immense. Stay tuned!

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