BioMarketing Insight

Creating markets & marketing strategies

Newsletter

June 15, 2016

Greetings!

Welcome to BioMarketing Insight's monthly newsletter.

We have a new mobile friendly newsletter. Love to receive your feedback.

Last month I covered "Paid to Go on Vacation and Get a Good Night's Rest?" If you missed last month's article, click here to read it. This month's newsletter will cover 2016 Translational Imaging Symposium Highlights.

Read on to learn more about this topic and other current news. The next newsletter will be published on July 15th.

We encourage you to share this newsletter with your colleagues by using the social media icons at the top, or by simply forwarding this newsletter or use the link at the bottom of this newsletter. Should you or your colleagues want to join my mailing list, click on the icon below or scan the QR code.

Please email me, Regina Au, if you have any questions, comments, or suggestions.

Table of Content

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Commercializing a Product?

If you are developing a product and have not conducted the business due diligence to determine commercial viability or success, contact me for an appointment. For successful commercial adoption of your product or looking to grow your business, contact me for an appointment.

For more information on our services, click on the links below:

Product Development
Market Development
Marketing Strategies

Top

The Ascent of Precision Medicine

I am pleased to announce that I was interviewed to identify the trailblazers in personalize medicine for an article entitled "The Ascent of Precision Medicine" in PharmIQ. To read the article, click here to log in (free).

Top

Genetic Modification: Science Fact

I am pleased to announce that my article "Genetic Modification: Science Fact" on recent advances in the CRISPR technology has been published in the European BioPharmaceutical Review (EBR). To read an electronic version, click here and scroll down the table of content to my article.

Top

Regenerative Medicine: Tomorrow's World

I am pleased to announce that my article "Regenerative Medicine: Tomorrows World" regarding remarkable advances in regenerative medicine has been published in the European Biopharmaceutical Review (EBR). To read an electronic version, click here and scroll down the table of content to the last article.

Top

Translational Imaging Symposium Highlights May 12, 2016

Scientists have been trying to understand Neurodegenerative diseases; Alzheimer's (AD), Parkinson's Disease (PD) and Huntington's Disease (HD) for decades and while they have made some progress, they are a long ways from finding a treatment for AD. What do we know so far?

Background: In the beginning, scientists believed beta-amyloid deposits were the key to predicting whether a person was going to develop AD.

This was done through various imaging techniques such as PET, CT and MRI. Many scientists have tried to develop a drug that would decrease the amount of amyloid plaque in the brain, but unfortunately, it did not stop the progression of the disease. They also found that with some patients who had amyloid plaque, they did not go on to develop AD.

Then, scientists starting looking at Tau deposits through imaging. However, Tau imaging posed several challenges, some related to the singularities of Tau aggregation and others related to radiotracer design. Several groups around the world are working on the development of imaging agents that will allow the *in vivo* assessment of Tau deposition in aging and in neurodegeneration. They found that Tau was more representative of how the disease progressed but don't fully understand the relationship between beta amyloid and Tau. In addition to beta-amyloid and Tau, scientists are also investigating other pathways, including alpha synuclein, TDP- 43 and SOD1.

This year, Dr. Richard Hargreaves, Vice President of Neuropharmacology and Biomarkers at Biogen, talked about conducting smarter drug discovery by using biomarkers in lieu of the old methods. He emphasized "The Biomarker Suite", which is based on three things: 1) Pathway - in demonstrating the proof of biological targets engaged in the diseases to determine Pharmacokinetics and Pharmacodynamics (PK/PD); 2) Disease - understanding the clinical aspects of the disease better; and 3) Safety - of the drug. He believes these three things will drive better decisions based on molecules and mechanism of action for drug development.

Tau is becoming more important as a target in AD and tauopathies. Studies indicated that Tau is spreading and accumulating. Scientists have shown that Tau PET patterns mirror clinical and neuroanatomical variability in AD.

One of the biggest obstacles in finding a treatment for neurodegenerative diseases is that it is very difficult to get drugs across the blood brain barrier (BBB). Dr. Ajay Verma, Vice President of the Neurology Drug Discovery and Development Center at Biogen, discussed intrathecal drug delivery to the brain to get around the BBB. When a fluorescent tracer was delivered intrathecal in animals, scientists discovered that the caudal to rostral gradient was slow and the tracer traveled very slowly to the brain with a lot of variability. But the tracers readily flowed into the brain along the outside of the penetrating blood vessels.

They also discovered that the once hypothesized amount of spinal fluid in the body was not 150 cc/ml, but actually approximately 413 cc of total spinal fluid. There is a lot of space in the spine and the turnover of spinal

fluid is 4-5 times/day. Further investigation confirmed that "small channels 'piggybacking' the blood vasculature allow the CSF to flow into the brain tissue along para-arterial spaces and exit via a para-venous route."

Scientists later found that astrocytes and their long projections or "end-feet" were involved in the water channel aquaporin-4 and played a role in intervening 'couplers' of a bulk interstitial fluid (ISF) flow or cleansing of the brain interstitial fluid. Transgenic animals that lack this aquaporin-4 exhibited a 70 percent reduction in the clearance of large solutes, such as Amyloid-β peptide which could explain why there is an accumulation of plaque. This 'peri-vascular' route for CSF-ISF exchange constitutes a complete anatomical pathway, which scientist dubbed the glymphatic system.

The more volume that was given as a bolus, the faster the tracer would travel up the nervous system to the brain. In addition, they found that the agent got to the grey matter faster than the white matter. All this information will help researchers find the most effective way to deliver drugs to the brain in understanding these diseases and track the efficacy of drugs in animals and hopefully in humans.

Dr. Mark Mintun, President of Avid Radiopharmaceuticals, summed things up in an "Update on Tau and Amyloid Imaging in Alzheimer's: How do They Relate?" The first question asked was, "Does the amount of amyloid matter?"

This is what he found:

1. In Alzheimer's patients with mild dementia, 27% were amyloid negative (we already know that some patients with amyloid plaque do not go on to develop neurodegenerative disease).
2. If one is amyloid negative, one is usually Tau negative.
3. If one is diagnosed cognitive impairment at an early age, AD is more progressive and the amount of Tau accumulation is greater.
4. If one is diagnosed at an older age, and is amyloid positive, the Tau is lower.
5. There is a correlation shown between cognitive testing and regional Tau signaling.
6. If Tau signal is increased over time, it is a reliable biomarker of neuro-degeneration.
7. How do you validate this?

Top

Closing Thoughts

What does this all mean? We know that Alzheimer's (AD) and other neurodegenerative diseases are very complex and that they are hard to study because we don't know the biology, nor do we have samples as we do in cancer, with tissue biopsies that help us to study the disease more efficiently . All we know is that it's a disease of the aging and that by the time symptoms appear, it may already be too late to prevent the progression of the disease. In past symposiums, it was predicted that the accumulation of beta amyloid and Tau, or perhaps something we have not discovered yet, occurs long before symptoms appear. Some say that in order to prevent or halt the progression of AD, we need to diagnose people 10 years before the onset of symptoms. But how do you accomplish this?

This is the reason why biomarkers are so important in trying to predict who is at increased risk to develop AD and then develop a drug treatment, according to Dr. Hargreaves. Right now, the only tool that can be used to study Alzheimer's is imaging.

Today, Tau seems to correlate with the progression of AD, but there is also a relationship with beta-amyloid. What is the relationship with Tau and beta-amyloid? Scientists are still trying to figure that out and from there, what is the trigger that leads to AD?. For now, is it feasible to image (CT, PET, MRI) everyone who is 65 years old and over without bankrupting the healthcare system? What about those who are younger than 65 years old?

The study by Dr. Mintun showed that if you are diagnosed with AD symptoms at a younger age (50 to 65 yo), you are more likely to have a more progressive onset of AD and accumulation of Tau. Dr. Mintun commented that a blood test for biomarkers is imperative, because it is noninvasive and less expensive than performing imaging tests.

Both Dr. Hargreaves from Biogen and Dr. Hostetler from Merck were advocating for open sourcing, that is, sharing of information that would benefit all researchers and move the field forward tremendously. Both were willing to share their information with others, dubbed the pre - competitive space.

In addition, it was reported at the end of May that Dr. Rudolph Tanzi, Director of Genetics and Aging Research at Massachusetts General Hospital, and Harvard University Professor of Neurology, came a little closer to answering the question, what triggers AD or "why does it take root?"

Dr. Tanzi and Dr. Robert Moir, Harvard Assistant Professor of Neurology and MGH neurology researcher, have discovered that infections are some of the root causes of Alzheimer's. Eight years ago, Dr. Moir noticed that there were similarities between beta-amyloid plaque build-up and antimicrobial peptides, small proteins that act as the first line of defense against microbial pathogens that triggers your innate immune system to kick in. Your brain only uses an innate system. It uses these peptides to kill everything in sight which leads to Alzheimer's inflammation, even when there isn't an infection, called "sterile infection", when the brain perceives a threat.

Beta-amyloid plays a role as an antimicrobial peptide. In mice that had no plaque, when salmonella was introduced to cause experimental meningitis, the bacteria precipitated the accumulation of amyloid plaque overnight, which you normally wouldn't see until the mice are 3-4 months old. They believe that ..." not only is amyloid playing this role to protect against infection, but in addition the infection itself can precipitate the formation of amyloid and its consistent with how these peptides work."

This is the start of some promising work and I'm sure that at next year's symposium, there will be new information bringing us a little bit closer in finding a treatment.

Should you want additional information regarding this symposium or the trends in this market, feel free to contact me at 781-935-1462 or email me.

Top