Global Biomarkers Standardization Consortium

December 18, 2019

9 a.m. Central/ 10 a.m. Eastern/ 3 p.m. GMT / 4 p.m. CET

Summary

Attendees: (Names taken from webinar attendee information if a name was submitted. This is not a complete list of attendees due to phone call ins. There were ~71 attendees): ADx Eugeen and Erik, Alexander Jethwa, Anne Fagan, Christopher Weber, Danielle Graham, Dannili, Doug, Esurace, Gopi Ganji, Hanno Steen, Helen Hu, Horton W., J. Dage, Johan Lindborg, Jose Luis Molinuevo, Kelley Faber, Kira Sheinerman, Kristina Malzbender, Kristina Malzbender, Kwasi Mawuenyega, Kyarasheski, Leslie Shaw, Maryline Simon, Maria Carrillo, Melissa Budelier, Rebecca Edelmayer, April Ross, Michelle Mielke, Mike Edler, Miskotp, Nathan, Nfandos, Nicolas Ashton, Nina Silverberg, P.W.van Zalm, Pedro Pesini, Randall Bateman, Rianne Esquivel, Richard Dennis, Rmartone, Robert Dean, Robert Umek, Rosa Canet-Aviles, Rutzs, Schaues, Silvia Fossati, Stefania Forner, Stephen Zicha, Sylvain Lehmann, Tforoud, Tobias Bittner, Tony Bannon, Vicki Clements, William Chen, Sebastien Boulo, Manu Vandijck, Henrik Zetterberg, Johan Gobom, Charlotte Teunissen, Bruce Lamb

- Welcome (Rebecca Edelmayer)
    - Dr. Christopher Weber is the new director, Global Science Initiatives at the Alzheimer's Association and will be the taking the lead for the GBSC and Dr. Emily Meyers, Associate Director, Research Projects, will provide project management support to the GBSC.

- Update on plasma p-tau as a biomarker for Alzheimer's disease (Henrik Zetterberg)
    - The measurements of total-tau were unconvincing but plasma p-tau worked. In the TRIAD discovery cohort, plasma p-tau181 increased in MCI and AD and in the TRIAD validation cohort p-tau181 in relation to clinical diagnoses was a correlation and there was a correlation with MK-6240 tau PET.

- Update(s) on plasma/serum NfL round robin(s) and plasma Abeta (Johan Gobom)
    - Developing a certified reference material for plasma Nfl, the objective is to link results of routine samples to the international system of units as a common reference. A commutability study was done with different candidate reference methods. Cerebrospinal fluid pooled, with spiked Nfl was only commutable at low levels.
    - The next steps are: begin a Round robin study checking correlation between methods; perform a commutability study to identify a suitable candidate reference material, this should yield results comparable to clinical samples; identify a suitable

master calibrator; reference measurement procedure; certified reference material and then integration of CRM.
    - Will continue without a mass spectrometry method it is an option but mass spectrometry might not be sensitive enough to measure. Other immunoassays might be better options.

- Update on the biorepository on mistreated samples for development on preanalytical protocol for blood (Charlotte Teunissen)

    - The group has created a draft protocol and 8 different preanalytical conditions will be elaborated further, will stop collecting feedback and will be further working on the protocol.
    - The gold standard is plasma that has been centrifuged immediately and frozen immediately at -80°C, but it also depends on experiments. Look at conditions relative to one another. The WG has been working with fresh plasma and at different periods when it is centrifuged but always frozen at least once.
    - P-tau will be included.

- MODEL-AD Program (Bruce Lamb)

    - The goal of MODEL-AD is to develop animal models for late onset AD.
    - MODEL-AD can collaborate with GBSC on the alignment of mouse and human phenotypes. They provide preclinical testing of the most promising models and therapeutics.
    - Developed humanized Aβ and tau models and conduct cross-species phenotype analysis
    - Preclinical testing core- emphasis on fluid biomarkers, pharmacokinetic and translational pharmacodynamics.
    - How to integrate human fluid biomarkers in the MODEL-AD phenotyping
    - NIH funded TREAT-AD Consortium

- Discussion

    - Randy Bateman discussed that p-tau217 and p-tau181 are specific for AD, p-tau217 to a greater degree. There are other phosphorylated tau isoforms that are specific and change at different stages.
    - Randy Bateman plans to develop mass spectrometry assays for p-Tau.
    - There will be a second plasma/serum NfL Round robin and Roche will participate, unsure if Siemens will participate.
    - Henrik will plan to follow up on plasma amyloid 40 and 42 Round robin.
    - The correlation of CSF p-Tau and t-Tau with PET is comparative to plasma pTau isoforms.
    - For the biorepository on mistreated samples, the first pilot study can accommodate around 10 different assays and it will contain 290 samples for simultaneous analysis for each marker. It would be good to include p-Tau and t-Tau in the pilot but the biorepository will be further expanded in the future.
    - Henrik is drafting a manuscript on the data presented at AAIC on plasma Aβ40-42.
    - Additional questions were: Is Aβ42/40 for 2 vendors going to FDA on this ratio. Is it better with mass spec vs. immunoassay that is going before the FDA?