Global Biomarkers Standardization Consortium of CSF biomarkers

Tuesday, March 27, 2018

9 a.m. Central/ 10 a.m. Eastern/ 3 p.m. BST

Meeting Summary

CSF Appropriate Use Criteria – Les Shaw

- A workgroup (WG) consisting of experts in the field, was convened February 2017 by the Alzheimer's Association to develop appropriate use criteria with the purpose to assist healthcare practitioners with guidance based on evidence and the experience of WG members, and ethical standards for patient care-on the appropriate and inappropriate use of LP and CSF AD biomarker testing.
- The WG builds on the published 2013 Johnson et al. Amyloid PET AUC and intended to support clinicians in identifying appropriate patients for LP and CSF

        - Diagnostic accuracy based on clinical criteria alone is not optimal, sensitive and specificity is ~80% & 70%, respectively, and at earlier disease stages accuracy is substantially lower.
        - From the systemic review the majority of the studies the reference standard was clinical diagnosis but the WG supplemented it by using amyloid PET detection of AD pathology as the reference standard.
        - Using amyloid PET as the reference standard increases sensitivity and specificity.
    - The WG rated 14 clinical indications as either appropriate or inappropriate.
    - Currently, expert reviewers are reviewing the manuscript and their feedback will be incorporated before the submission of the publication.

CSF Pre-analytics Protocol – Jim Hendrix

- The Alzheimer's Association convened a WG comprised of various companies and academic participants to develop a consensus around a CSF pre-analytical protocol.
- The consortium plans to present an oral presentation at AAIC and at the F2F GBSC meeting. Jim will provide an update at AAN.
- The objective of the pre-analytical protocol is for it to be utilized in clinical practice and simple to use.

Working in Parallel with the CRM Release – Ingrid Zegers & Henrik Zetterberg

- 3 Aβ42 certified reference materials were released in December 2017.
- The 3 CRMs are of different levels and assigned using mass spectrometry reference methods measured in 5 different labs. Values are:
    - Certified value 0.45 µg/L with an uncertainty $U_{crm,rel}$ of 0.07 µg/L
    - Certified value 0.72 µg/L with an uncertainty of 0.11 µg/L
    - Certified value 1.22 µg/L with an uncertainty of 0.18 µg/L
- The expandable uncertaintyT

to tubes and a lower value for the intermediate point.

- Sarstedt Low binding screw cap micro tube was advised for use.
- Euroimmun studies for implementation of CRM outlook: method development for proportional dilution will require further optimization: # of intermediary points, robustnes