Potential TBI Biomarkers and Therapeutics

TBI Endpoints Development Initiative Obtains Regulatory Support for Biomarkers of TBI

Well-defined endpoints and changes to clinical trial design are needed to support successful regulatory-driven development of diagnostics and therapeutics for TBI. This includes advancing the identification, validation, implementation, and dissemination of clinical outcome assessments (COA) and biomarkers for acceptable use in regulatory review of U.S. Food and Drug Administration (FDA)-qualified medical device and drug development tools for mild to moderate TBI. The TBI Endpoints Development (TED) Initiative, a network of public and private partnerships led by scientists at the University of California (San Francisco, CA) seeks to provide the foundational framework for improved clinical trials which can be used to support regulatory approvals for TBI diagnostics and therapeutics.

In January 2018, the FDA issued a second Letter of Support for the TED Initiative's work in advancing the biomarkers glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase-L1 (UCH-L1) for use in improved TBI clinical trial design. The TED research group has added to the evidence-base for these biomarkers in recent publications, including a meta-analysis of UCH-L1's diagnostic value and correlation with CT scan results following TBI (*Shahjouei et al., 2018*). From 13 reports across 10 original studies, findings were assessed for risk of bias according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) method. Serum UCH-L1 had high accuracy but high risk of bias in predicting CT scan findings. The risk of bias was low for plasma UCH-L1, but the accuracy was only considered moderate in predicting CT scan findings. The authors conclude that further research is necessary to determine whether and how UCH-L1 levels may be used as an alternative to CT scanning.

In addition to advancing work with GFAP and UCH-L1, the TED Initiative is looking at the use of other blood-based biomarkers such as spectrin breakdown products, neurofilament proteins (for axonal injury), tau (for neurodegeneration), myelin basic protein (for white matter injury), and other potential non-protein biomarkers as theranostic targets for TBI.

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REFERENCES:

Shahjouei, S., Sadeghi-Naini, M., Yang, Z., Kobeissy, F., Rathore, D., Shokraneh, F., . . . Wang, K. K. W. (2018). The diagnostic values of UCH-L1 in traumatic brain injury: A meta-analysis. Brain Inj, 32(1), 1-17. doi:10.1080 02699052.2017.1382717