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Clinical and Analytical Performance of Glial Fibrillary Acidic Protein and Ubiquitin C-Terminal Hydrolase L1 Biomarkers for Traumatic Brain Injury in the Alinity Traumatic Brain Injury Test

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Abstract : The Alinity i TBI test is Therapeutic Goods Administration (TGA) registered and is a panel of in vitro diagnostic chemiluminescent microparticle immunoassays for the measurement of glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase L1 (UCH-L1) in plasma and serum. The Alinity i TBI performance was evaluated in a multi-center pivotal study to demonstrate the capability to assist in determining the need for a CT scan of the head in adult subjects (age 18+) presenting with suspected mild TBI (traumatic brain injury) with a Glasgow Coma Scale score of 13 to 15. TBI has been recognized as an important cause of death and disability and is a growing public health problem. An estimated 69 million people globally experience a TBI annually1. Blood-based biomarkers such as glial fibrillary acidic protein (GFAP) and ubiquitin C-terminal hydrolase L1 (UCH-L1) have shown utility to predict acute traumatic intracranial injury on head CT scans after TBI. A pivotal study using prospectively collected archived (frozen) plasma specimens was conducted to establish the clinical performance of the TBI test on the Alinity i system. The specimens were originally collected in a prospective, multi-center clinical study. Testing of the specimens was performed at three clinical sites in the United States. Performance characteristics such as detection limits, imprecision, linearity, measuring interval, expected values, and interferences were established following Clinical and Laboratory Standards Institute (CLSI) guidance. Of the 1899 mild TBI subjects, 120 had positive head CT scan results; 116 of the 120 specimens had a positive TBI interpretation (Sensitivity 96.7%; 95% CI: 91.7%, 98.7%). Of the 1779 subjects with negative CT scan results, 713 had a negative TBI interpretation (Specificity 40.1%; 95% CI: 37.8, 42.4). The negative predictive value (NPV) of the test was 99.4% (713/717, 95% CI: 98.6%, 99.8%). The analytical measuring interval (AMI) extends from the limit of quantitation (LoQ) to the upper LoQ and is determined by the range that demonstrates acceptable performance for linearity, imprecision, and bias. The AMI is 6.1 to 42,000 pg/mL for GFAP and 26.3 to 25,000 pg/mL for UCH-L1. Overall, within-laboratory imprecision (20 day) ranged from 3.7 to 5.9% CV for GFAP and 3.0 to 6.0% CV for UCH-L1, when including lot and instrument variances. The Alinity i TBI clinical performance results demonstrated high sensitivity and high NPV, supporting the utility to assist in determining the need for a head CT scan in subjects presenting to the emergency department with suspected mild TBI. The GFAP and UCH-L1 assays show robust analytical performance across a broad concentration range of GFAP and UCH-L1 and may serve as a valuable tool to help evaluate TBI patients across the spectrum of mild to severe injury.

Keywords : biomarker, diagnostic, neurology, TBI
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