



US DEPARTMENT OF DEFENSE

BLAST INJURY RESEARCH PROGRAM COORDINATING OFFICE

Treatments for Neurotrauma Operation Brain Trauma Therapy Extended Studies

The Operation Brain Trauma Therapy (OBTT) represents a consortium of seven of the top experimental traumatic brain injury (TBI) centers in the world, combining their expertise to identify and bring forward new treatments for TBI. Member institutions span the military and civilian academic centers in partnership with industry, including:

- Safar Center for Resuscitation Research at the University of Pittsburgh School of Medicine (Pittsburgh, Pennsylvania)
- Miami Project to Cure Paralysis at the University of Miami School of Medicine (Miami, Florida)
- Neuroprotection Program at Walter Reed Army Institute of Research (Silver Spring, Maryland)
- Virginia Commonwealth University (Richmond, Virginia)
- Banyan Biomarkers, Inc. (San Diego, California)
- University of Florida (Gainesville, Florida)
- Messina University (Messina, Italy)

This group brings unprecedented expertise in experimental TBI research and all the necessary tools for preclinical drug screening and biomarker development and evaluation to bear for the benefit of the Service members suffering from TBI.

OBTT uses a two-tier screening process to rapidly evaluate the potential of new drugs. In Tier A, established models of TBI in rats are used to screen the potential new therapies, using a standard battery of tests. Those agents that perform well advance to Tier B, in which more advanced tests are performed in rats. In each tier, biomarkers of TBI are also evaluated. The most promising agent each year from Tier B advances to secondary screening in micropigs. To date, OBTT has tested 12 therapies across three rodent models, in approximately 2,000 rats, and conducted over 5,000 individual biomarker assessments. Thus far, of the eight drugs that have completed testing, two of these drugs, levetiracetam and glibenclamide, have shown promising effects in one or more of the TBI rat models. Levetiracetam was identified as the most promising therapy to date, and was advanced to testing in micropigs. Glibenclamide has shown promise specifically in contusions and might represent an excellent candidate for a precision medicine approach in patients specifically with cerebral contusions.

The findings from the OBTT and OBTT-Extended Studies have been presented and published at many locations in FY17 (Table 1).

In conclusion, the current lack of an effective therapy for TBI is a critical problem facing Service members, and the work of OBTT in developing new treatment options is of considerable importance for those who are injured.





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TABLE 1: Published Findings from OBTT and OBTT-Extended Studies (Table used with permission from the authors)

Event/Journal	Date	Title	Authors
American Spinal Cord Association (Albuquerque, New Mexico)	April 27-29, 2017	Preclinical and Clinical Strategies to Take TBI Therapy to the Finish Line	Kochanek PM
National Neurotrauma Society (Snowbird, Utah)	July 9-12th, 2017		
Abstract A06-08 and DBA-02. J Neurotrauma 34 (2017)		Circulating GFAP levels to monitor therapeutic response to glibenclamide in controlled cortical impact: Findings from OBTT	Mondello S, Shear D, Bramlett H, Dixon CE, Dietrich WD, Wang K, Hayes R, Lafrenaye A, Povlishock JT, Tortella F, Kochanek, PM
Abstract A18-01. J Neurotrauma 34 (2017)		Evaluation of minocycline in the Miami fluid percussion model of traumatic brain injury: An OBTT consortium study	Bramlett, H, Furones-Alonso O, Sanchez-Molano, J, Truettner J, Moreno W, Treu R, Dietrich, WD
Abstract A18-02. J Neurotrauma 34 (2017)		Evaluation of minocycline in the controlled cortical impact model of traumatic brain injury: An OBTT consortium study	Dixon CE, Yan H, Ma X, Empey P, Poloyac S, Feldman K, Kochanek P
Abstract A18-10 and DBA-07. J Neurotrauma 34 (2017)		Evaluation of minocycline in the WRAIR PBBI model: Studies from the operation brain trauma therapy (OBTT) consortium	Okada-Rising S, Pandya J, Caudle K, Browning J, Pedersen R, Sun J, Shear D





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Event/Journal	Date	Title	Authors
Abstract A22-07 and DBA-09. J Neurotrauma 34 (2017)		Overview of the first 12 therapies evaluated by Operation Brain Trauma Therapy, a pre-clinical multi-center drug and biomarker screening consortium for TBI	Kochanek PM, Bramlett HM, Dixon CE, Tortella FC, Dietrich WD, Mondello S, Hayes RL, Wang KKW, Povlishock JT, Lafrenaye AD, Poloyac SM, Empey PE, Gilsdorf J, Shear DA
Abstract B08-20. J Neurotrauma 34 (2017)		Operation Brain Trauma Therapy: Levetiracetam treatment for traumatic brain injury in the micro pig	Lafrenaye A, Wang, K, Hayes R, Gorse K, Walker S, Ogino Y, Kochanek P, Povlishock J
Abstract A22-05 J Neurotrauma 34 (2017)		Roadmap for successful translational preclinical traumatic brain injury therapy testing	Hawkins B, Mondello S, Dixon CE, Hayes RL, Smith DH, Dietrich WD, Bramlett HM, Amrstead WM, Hall ED, Saatman KE, LaPlaca MC, Noble-Haeusslein LJ, Ferguson AR, Dash P, Valadka AB, Meaney DF, Poloyac SM, Zhang L, Bass CR, VandeVord P, Shultz SR, Buki A, Shear DA, Long JB, Hinds SR, Robertson CS, Prough DS, Kochanek, PM, DeWitt DS
2017 MHSRS (Orlando Florida)	August 27-30, 2017	Overview of the first 12 therapies being evaluated by Operation Brain Trauma Therapy, a pre-clinical multi-center drug and biomarker screening consortium for traumatic brain injury	Kochanek PM, Bramlett HM, Dixon CE, Tortella FC, Dietrich WD, Mondello S, Hayes RL, Wang KKW, Povlishock JT, Lafrenaye AD, Poloyac SM, Empey PE, Gilsdorf J, Shear DA
J Neurotrauma 33:1729-1731, 2016 (editorial)		Hidden perils of the “wild blue yonder” after traumatic brain injury	Kochanek PM, Bayır H
Lancet Neurol 16:578-580, 2017 (commentary)		Adding insight to injury: A new era in neurotrauma	Jha RM, Kochanek PM

