Cethrin

Multiple lines of evidence have validated the Rho pathway as important in controlling the neuronal response to growth inhibitory proteins after central nervous system (CNS) injury. A drug called BA-210 (trademarked as Cethrin(®)) blocks activation of Rho and has shown promise in pre-clinical animal studies in being used to treat spinal cord injury (SCI). This is a report of a Phase I/IIa clinical study designed to test the safety and tolerability of the drug, and the neurological status of patients following the administration of a single dose of BA-210 applied during surgery following acute SCI. Patients with thoracic (T2-T12) or cervical (C4-T1) SCI were sequentially recruited for this dose-ranging (0.3 mg to 9 mg Cethrin), multi-center study of 48 patients with complete American Spinal Injury Association assessment (ASIA) A. Vital signs; clinical laboratory tests; computed tomography (CT) scans of the spine, head, and abdomen; magnetic resonance imaging (MRI) of the spine, and ASIA assessment were performed in the pre-study period and in follow-up periods out to 1 year after treatment. The treatment-emergent adverse events that were reported were typical for a population of acute SCI patients, and no serious adverse events were attributed to the drug. The pharmacokinetic analysis showed low levels of systemic exposure to the drug, and there was high inter-patient variability. Changes in ASIA motor scores from baseline were low across all dose groups in thoracic patients (1.8±5.1) and larger in cervical patients (18.6±19.3). The largest change in motor score was observed in the cervical patients treated with 3 mg of Cethrin in whom a 27.3±13.3 point improvement in ASIA motor score at 12 months was observed. Approximately 6% of thoracic patients converted from ASIA A to ASIA C or D compared to 31% of cervical patients and 66% for the 3-mg cervical cohort. Although the patient numbers are small, the observed motor recovery in this open-label trial suggests that BA-210 may increase neurological recovery after complete SCI. Further clinical trials with Cethrin in SCI patients are planned, to establish evidence of efficacy [1)].

Case series

To predict the feasibility of conducting clinical trials of acute SCI within Canada, Thibault-Halman et al., have applied the inclusion/exclusion criteria of six previously conducted SCI trials to the RHSCIR dataset and generated estimates of how many Canadian individuals would theoretically have been eligible for enrollment in these studies. Data for SCI cases were prospectively collected for RHSCIR at 18 acute and 13 rehabilitation sites across Canada. RHSCIR cases enrolled between 2009-2013 who met the following key criteria were included: non-penetrating traumatic SCI; received acute care at a RHSCIR site; age >18- <75 years, and had complete admission single neurological level of injury data. Inclusion and exclusion criteria for the Minocycline in Acute Spinal Cord injury (Minocycline), Riluzole, Surgical Timing in Acute Spinal Cord Injury Study (STASCIS), Cethrin, Nogo antibody study (NOGO) and Sygen studies were applied retrospectively to this dataset. The numbers of patients eligible for each clinical trial were determined. 2166 of the initial 2714 cases (79.8%) met the key criteria and were included in the dataset. Projected annual numbers of eligible patients for each trial was: Minocycline 117 cases; Riluzole 62 cases; STASCIS 109 cases; Cethrin 101 cases; NOGO 82 cases; and Sygen 70 cases. An additional 8.0% of the sample had a major head injury (GCS≤ 12) and would have been excluded from the trials. RHSCIR provides a comprehensive national dataset which may serve as a useful tool in the planning of multicentre clinical SCI trials [2)].

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Fehlings MG, Theodore N, Harrop J, Maurais G, Kuntz C, Shaffrey CI, Kwon BK, Chapman J, Yee A, Tighe A, McKerracher L. A phase I/IIa clinical trial of a recombinant Rho protein antagonist in acute spinal cord injury. J Neurotrauma. 2011 May;28(5):787-96. doi: 10.1089/neu.2011.1765. PubMed PMID: 21381984.

2)
Thibault-Halman G, Rivers CS, Bailey C, Tsai E, Drew B, Noonan V, Fehlings M, Dvorak MF, Kuerban D, Kwon BK, Christie S. Predicting recruitment feasibility for acute spinal cord injury clinical trials in Canada using national registry data. J Neurotrauma. 2016 Sep 14. [Epub ahead of print] PubMed PMID: 27627704.