Oral Presentations

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PAPER 600

CNS Transplantation of Purified Human Neural Stem Cells in Neuronal Ceroid Lipofuscinoses: Phase I Trial

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Introduction: An open-label dose-escalation Phase I trial of a highly purified, expandable population of human central nervous system stem cells (HuCNS-SC) was conducted in subjects with advanced stage infantile and late-infantile neuronal ceroid lipofuscinoses (INCL and LINCL). This investigation is the first US FDA authorized use of human neural stem cells for clinical testing.

Methods: Six pediatric subjects underwent bilateral intracerebral and intraventricular transplantation of HuCNS-SC. The low-dose cohort received a target dose of 500 million cells, and high-dose cohort received a target dose of 1 billion cells, followed by 12 months of immunosuppression. Subjects were assessed both pre- and post-transplant with a comprehensive battery of tests and brain magnetic resonance (MR) imaging.

Results: HuCNS-SC transplantation in combination with immunosuppression was well-tolerated by all six subjects. The subject's neurological and neuropsychological outcomes were consistent with the underlying disease. One subject with INCL expired due to natural progression of the disease 11 months post-transplant. A brain autopsy revealed no HuCNS-SC related toxicity. DNA PCR testing of post-mortem brain tissue provided evidence of donor cell engraftment and survival. The remaining five subjects completed the Phase I trial assessments and enrolled in a separate 4-year long-term follow-up study.

Conclusions: This Phase I study, representing the first clinical trial of purified and expanded neural stem cells, utilized a novel dosing and implantation paradigm. Based on the safety profile and post-mortem evidence of donor cell survival, further investigation of HuCNS-SC transplantation appears warranted.

PAPER 601

Comparison of Outcomes of Surgery and Observation in the International Study of Unruptured Intracranial Aneurysms

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Introduction: The International Study of Unruptured Intracranial Aneurysms was designed as a prospective cohort study with a longitudinal follow-up. The purpose of this analysis was to compare the surgical outcome in the surgical subgroup with those of the untreated subgroup.

Methods: Patients were subdivided into cohorts based upon observation or treatment practices in 61 centers from 1991-1998. 1691 patients were in the observational cohort, and 1917 patients were in the surgical cohort. The cohorts were followed for a median follow-up of 9.2 years. Outcomes were determined prospectively and with central review. Analysis of hemorrhage, mortality, and short-term and long-term morbidity and mortality were assessed. Risk-benefit ratios were also calculated.

Results: Significant differences in baseline variables between the surgical and observed patients were aneurysm size, symptoms, age, prior subarachnoid hemorrhage (SAH) or not group, geographical region, family history, hypertension, and myocardial infarction history. The results show comparability of groups using the 1680-patient propensity-based score subset. Using either analysis regression analysis adjusting for covariates or the propensity score method, the results showed a benefit in prevention of hemorrhage by surgery (p less than 0.01). However, when procedure-related outcomes are included, no significant difference at 1, 5, or 10 years in the combined aneurysm or procedure-related endpoint was evident between cohorts. Interestingly all-cause mortality was significantly lower in the surgery group.

Conclusions: Comparison of long-term results showed that surgical intervention demonstrated a benefit in reducing hemorrhage risk. However, procedural risk negates any short-term benefit for 10 years.

PAPER 602

Does Surgical Treatment for Cervical Spondylotic Myelopathy Result in Long Term Benefit? Two Year Outcomes of the AO Spine North America CSM Multi-Center Prospective Study in 280 Subjects

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Introduction: Cervical spondylotic myelopathy (CSM) is the commonest cause of spinal cord impairment. However, the long-term benefit of surgical treatment remains uncertain. To address this question, we undertook a multicenter prospective study to examine long-term outcomes in patients undergoing surgery for CSM.

Methods: A total of 280 subjects were enrolled at 12 North American sites and were stratified using the modified Japanese Orthopedic Association (mJOA) scores into mild (greater than 15), moderate (12-15), and severe (less than 12). To date, 160 patients have 2-year follow-up data available (40% females; mean age 56 ± 12 years). Outcomes assessments included the mJOA, Neck Disability Index (NDI), Nurick score, and SF-36.

Results: Postoperatively, all outcome parameters improved (p less than 0.001) in patients with mild, moderate, and severe CSM.

Improvements plateaued at 12 months after surgery and were maintained at 2 years. The mJOA improved by an average of 3.00 points (95% CI 2.54, 3.47); NDI improved from 37.75 to 27.10, average improvement 10.64 (95% CI 7.44, 13.84; the Nurick scores improved from 4.05 ± 0.99 to 2.43 ± 1.49, average improvement 1.62 (95% CI 1.38, 1.86); the SF-36 PCS scores improved from 38.30 ± 11.25 to 42.82 ± 10.08 and the SF-36 MCS scores improved from 41.70 ± 10.84 to 46.07 ± 11.37, average improvement 4.53 (95% CI 2.94, 6.12).

Conclusions: This large prospective clinical study showed that surgical treatment for mild, moderate, and severe CSM results in objective improvement in generic and disease-specific health outcomes that are maintained at 2-year follow-up.

PAPER 603

Natural History of Meningiomas

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Introduction: The aim of this study was to delineate the natural history of meningiomas with regard to their clinical and radiographic characteristics.

Methods: Follow-up of one or more years was available in 223 patients with 251 tumors who were managed conservatively by a single surgeon between 2003 and 2008. Data were stratified according to age, sex, tumor location, symptom, initial tumor diameter, calcification, magnetic resonance imaging (MRI) intensity, and edema. Tumor growth was defined as a minimum increase of 2 mm in maximal diameter. Volumetric study was also performed for 154 tumors.

Results: Growth was observed in 114 tumors (45.4%) with a mean follow-up of 3.8 years. Factors related to tumor growth were age 60 years or younger ($p = 0.0006$), absence of calcification ($p = 0.034$), high intensity on MRI T2WI ($p = 0.004$), and edema ($p = 0.018$). Kaplan-Meier plots and Cox proportional hazards regression analysis revealed the following factors associated with short time to progression: age 60 or younger (HR = 1.5, 95%CI = 1.0-2.3), diameter greater than 25 mm (HR = 1.9, 95%CI = 1.2-3.0), absence of calcification (HR = 4.1, 95% CI = 2.5-7.4), and high intensity on MRI T2WI (HR = 1.6, 95% CI = 1.0-2.5). Volumetric analysis showed that absence of calcification, high intensity on MRI T2WI, diameter greater than 25 mm, and edema were factors associated with a higher annual growth rate.

Conclusions: This study consists of the largest meningioma patient population for the delineation of natural history to date. A higher growth rate was observed in patients below the age of 60 and in tumors characterized by a high signal on MRI T2WI, edema, diameter greater than 25 mm, and no calcification.

PAPER 604

Surgical Treatment of Spontaneous Spinal Cerebrospinal Fluid Leaks

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Introduction: Spontaneous intracranial hypotension is an important cause of secondary headache. It is caused by spontaneous spinal cerebrospinal fluid (CSF) leaks. Treatment may require neurosurgical intervention. We report our experience with 81 patients undergoing surgery for spontaneous spinal CSF leaks.

Methods: We reviewed the medical records and imaging studies of 81 consecutive patients with spontaneous spinal CSF leaks who underwent surgical exploration at Cedars-Sinai Medical Center, Los Angeles, California, between January 1, 2001 and June 30, 2009. Follow-up ranged from 3 to 104 months (mean 25 months).

Results: There were 60 women and 21 men with a mean age of 42 years (range 18 to 85 years). Brain magnetic resonance imaging (MRI) was normal in 22 patients and abnormal (brain sagging, pachymeningeal enhancement, subdural fluid collections) in 59 patients. All patients had undergone epidural blood patching but remained symptomatic. Surgery was directed at the site of the CSF leak/spinal meningeal diverticulum. Sixty-one patients underwent one surgical procedure and 20 patients underwent two to four surgical procedures to repair multiple spinal CSF leaks/meningeal diverticula, for a total of 120 procedures. A good outcome was obtained in 67 patients (83%); in 90% (45 of 59) of those with an abnormal brain MRI and in 64% (14 of 22) with a normal MRI ($p = 0.27$). Complications consisted of postoperative pseudomeningocele/transcutaneous CSF leak in three patients (4%) and wound infection in one patient (1%). There were no neurologic complications.

Conclusions: Surgical treatment for intractable spontaneous intracranial hypotension is associated with low risk and good outcome. Multiple surgeries are required in about one-fourth of patients.

PAPER 605

Favorable Outcomes of Neurosurgical Patients in a Neurosurgeon Directed Multidisciplinary Neuro Critical Care Unit

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Introduction: A multidisciplinary team is imperative to the successful management of critically ill patients with neurological diseases. Physicians and staff of different disciplines must come together to favorably impact patient outcomes. We describe quality improvement projects and the consequent impact on mortality of a neurosurgeon directed, 16 bed, Neuro Critical Care Unit (NCCU) over a one-year period of time.

Methods: 1157 patients admitted to an NCCU care unit in a tertiary care, university setting, were analyzed over a one-year period. Results of 20 quality assurance benchmark goals from the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and our own University of Wisconsin health care initiatives were compared to data from the Centers for Disease Control (CDC) and the University Health Consortium (UHC). The data mined from the UHC database reflects outcomes of the University of Wisconsin NCCU as compared to university hospitals nationwide and is based on DRG data and ICD-9 diagnosis codes.

Results: Patients that have been ventilated greater than 96 hours in the NCCU have a mortality rating of 0.56 indicating a relative risk reduction of death as the outcome by 44%. For patients ventilated less than 96 hours, we have a relative risk of mortality of 0.88 indicating a 12% relative risk reduction. For those patients who are not intubated in the ICU, we have a mortality of 0.73 indicating a 27% relative risk reduction in mortality.

Conclusions: Quality patient outcomes stem from a strong neurosurgery department, a strong multidisciplinary team focused on a holistic approach to patients and their families, and constant assessment of outcome data to improve areas that are lacking.

PAPER 607

A Novel, Reproducible, and Objective Method for Volumetric MRI Assessment of Enhancing Brain Tumors

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