GP.04

Smart human neural stem cells to degrade scar and optimize regeneration after traumatic cervical spinal cord injury

CS Ahuja (Ajax) M Khazaei (Ajax) P Chan (Ajax) J Bhavsar (Ajax) Y Yao (Ajax) Z Lou (Ajax) J Wang (Ajax) M Fehlings (Ajax)*

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Background: Human induced pluripotent stem cell-derived neural stem cells (hiPS-NSCs) represent an exciting therapeutic approach for traumatically spinal cord injury (SCI). Unfortunately, most patients are the in chronic injury phase where a dense perilesional chondroitin sulfate proteoglycan (CSPG) scar significantly hinders regeneration. CSPG-degrading enzymes can enhance NSC-mediated recovery, however, nonspecific intrathecal administration causes off-target effects. We aimed to genetically engineer hiPS-NSCs to express a scar-degrading ENZYME into their local environment to enhance functional recovery. **Methods:** A bicistronic scar-degrading ENZYME and RFP reporter vector was non-virally integrated into hiPS-NSCs and monoclonalized. ENZYME activity was assessed by WST-1 and DMMB biochemical assays and an *in vitro* CSPG spot assay with hiPS-NSC-derived neurons. To assess *in vivo* efficacy, T-cell deficient rats (N=60) with chronic (8wk) C6-7 SCIs were randomized to receive (1)SMaRT cells, (2)hiPS-NSCs, (3)vehicle, or (4)sham surgery. **Results:** SMaRT cells retained key hiPS-NSC characteristics while stably expressing ENZYME. The expressed ENZYME could appropriately degrade *in vitro* and *ex vivo* CSPGs. While blinded neurobehavioural and immunohistochemical assessments are ongoing at 40wks post-injury, an interim analysis demonstrated human cells extending remarkably long (≥20,000µm) axons along host white matter tracts. **Conclusions:** This work provides exciting proof-of-concept data that genetically-engineered SMaRT cells can degrade CSPGs and human NSCs can extend long-distance processes in chronic SCI.

GP.05

The risk of malignancy after stereotactic radiosurgery

AM Wolf (London) K Naylor (London) D Kondziolka (New York)*

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Background: A major concern of patients undergoing Gamma Knife radiosurgery (GKS) for benign tumors and other conditions is the risk of a separate secondary malignancy or malignant transformation. The incidence of radiosurgery-associated malignancy based on long-term follow-up remains unknown. **Methods:** We conducted a population-based cohort study to estimate the incidence rate of both malignant transformation and a separate radiation-associated malignancy in patients undergoing GKS from 1987 to 2016 at 5 centers. **Results:** 11 527 patients underwent radiosurgery for meningioma (n=3261), arteriovenous malformation (n=2868), trigeminal neuralgia (n=1982), vestibular schwannoma (n=1957), pituitary adenoma (n=1193), other (n=266). The follow-up time ranged from 0.3 to 23.8 years. Four cases of malignant transformation and 3 new malignant brain tumors were reported, two of which were not within the irradiated field. The incidence of malignant transformation was 6.6 per 100 000 patient-years and of new malignancy, either locally or distant, was 5 in 100 000 patient-years. These risks are not higher than the Central Brain Tumor Registry of the United States derived annual incidence rate of all primary malignant CNS tumors of 7.15 per 100 000. **Conclusions:** Physicians can safely counsel patients that the risk of malignancy after stereotactic radiosurgery remains extremely low, even at long-term follow-up of greater than 10 years.

CNS Chair's Select Abstracts

A.01

Parkinson's disease prognosis by early motor subtypes

N Hey (Saskatoon) ML Rajput (Saskatoon) AH Rajput (Saskatoon) A Rajput (Saskatoon)*

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Background: Studies of autopsy-confirmed cases suggest that Parkinson's disease (PD) prognosis can be predicted using motor symptom severity at first visit. We evaluated the association between motor symptom subtype at first visit and severity at eight years disease duration among clinically-diagnosed cases at the Saskatchewan Movement Disorder Program. **Methods:** Retrospective data review identified 374 patients with first visit within three years of symptom onset, a clinical diagnosis of idiopathic PD, and a follow-up visit eight years after symptom onset. Subtypes were grouped as tremor-dominant (TD) if tremor was greater than rigidity and bradykinesia, akinetic-rigid (AR) if rigidity or bradykinesia was greater than tremor, and mixed (MX) if patient was neither TD nor AR based on assessment of all four limbs. Primary outcome was disease severity as measured by Hoehn & Yahr score at eight years after symptom onset. **Results:** The most common subtype was AR (n=164) followed by MX (n=156). TD was least common (n=54). There was no significant difference between subtypes in H&Y scores at eight years disease duration. **Conclusions:** These findings suggest that early PD prognosis cannot be predicted based on motor symptoms in all four limbs at first visit. Earlier studies had longer follow-up and future studies will examine progression at longer periods of disease duration.

A.02

Long-term outcomes in the management of central neuropathic pain syndromes

MD Staudt (London) AJ Clark (Halifax) AS Gordon (Toronto) ME Lynch (Halifax) PK Morley-Forster (London) H Nathan (Ottawa) C Smyth (Ottawa) LW Stitt (London) C Toth (Burnaby) MA Ware (Montreal) DE Moulin (London)*

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Background: Central neuropathic pain syndromes are a result of central nervous system injury, most commonly related to stroke, spinal cord injury, or multiple sclerosis. These syndromes are much less common than peripheral etiologies, with less known regarding optimal treatment. The objective of this study was to determine the long-term clinical effectiveness of the management of central relative to peripheral neuropathic pain at tertiary pain centers. **Methods:** Patients diagnosed with central (n=79) and peripheral (n=710) neuropathic pain were identified from a prospective observational cohort from seven Canadian tertiary centers. Data regarding patient

characteristics, analgesic use, and patient-reported outcomes were collected at baseline and 12-month follow-up. The primary outcome was the composite of reduced average pain intensity and pain interference. Secondary outcomes included assessments of function, mood, and quality-of-life. **Results:** At 12-month follow-up, 13.5% (95%CI,5.6-25.8) of patients achieved ≥30% reduction in pain, whereas 38.5% (95%CI,25.3-53.0) achieved a ≥1 point reduction in pain interference; 9.6% (95%CI,3.2-21.0) of patients achieving both these measures. Patients with peripheral neuropathic pain were more likely to achieve this primary outcome at 12-months (25.3% of patients; 95%CI,21.4-29.5) (p=.012). **Conclusions:** Patients with central neuropathic pain were less likely to achieve a meaningful improvement in pain and function compared to patients with peripheral neuropathic pain at 12-month follow-up.

A.03

Durable clinical and MRI efficacy of alemtuzumab over 6 years in CARE-MS II patients with RRMS who relapsed between Courses 1 and 2

MS Freedman (Ottawa) S Broadley (Gold Coast) A Chinea (San Juan) G Izquierdo (Seville) J Lycke (Gothenburg) BA Singer (St Louis) B Steingo (Fort Lauderdale) H Wiendl (Münster) S Wray (Knoxville) M Melanson (Cambridge) K Thangavelu (Cambridge) A Boster (Columbus) on behalf of the CARE-MS II and CAMMS03409 Investigators*

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Background: In RRMS patients with inadequate response to prior therapy, 2 alemtuzumab courses (12 mg/day; baseline: 5 days; 12 months later: 3 days) significantly improved outcomes over 2 years (y) versus SC IFNB-1a (CARE-MS II [NCT00548405]), with durable efficacy over a 4-y extension (NCT00930553). We present 6-y efficacy (2-y core study plus 4-y extension) in patients with relapse (relapsers) between Courses (C) 1 and 2. **Methods:** Annualized relapse rate (ARR); 6-month confirmed disability worsening (CDW); MRI disease activity (Gd-enhancing lesions; new/enlarging T2 hyperintense lesions); brain volume loss (BVL; derived by relative change in brain parenchymal fraction). **Results:** 105/435 (24%) patients relapsed between C1 and C2; 33% (relapsers) versus 55% without relapse (non-relapsers) received neither alemtuzumab retreatment nor another disease-modifying therapy through Y6. ARR (Y1: 1.2) declined post-C2 (0.5), remaining low through Y6 (0.2 [0.1, non-relapsers]; 10/105 [10%] relapsed). Through Y6, patients remained CDW-free (60% [relapsers]; 75% [non-relapsers]), Gd-enhancing lesion-free (94% [relapsers]; 90% [non-relapsers]), new/enlarging T2 hyperintense lesion-free (68% [relapsers]; 69% [non-relapsers]), and MRI disease activity-free (68% [relapsers]; 69% [non-relapsers]). Alemtuzumab slowed median percent yearly BVL (Y6: -0.13% [relapsers]; -0.10% [non-relapsers]). **Conclusions:** Patients relapsing between C1 and C2 improved post-C2 through Y6. These findings support administering 2 alemtuzumab courses to achieve optimal and durable benefit.

A.04

High times? Prevalence and perceptions of marijuana use among patients with epilepsy

*G Moores (Oakville) A Lockey (Calgary) A Attar (Hamilton)**

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Background: Despite medical advances, almost a third of people with epilepsy have medically refractory epilepsy (MRE). With failure of pharmaceutical options, patients are turning to alternative treatment options. Marijuana use in epilepsy has received extensive attention. Two recent studies evaluated the opinions of marijuana use in individuals with epilepsy, but had discrepant marijuana use rates. **Methods:** The first 200 adult patients with a known diagnosis of epilepsy seen at Hamilton General Hospital after June 1, 2017 were invited to participate. Standardized paper questionnaires gathered information about demographics, epilepsy history, and marijuana use. **Results:** One hundred forty participants returned questionnaires; 29.5% were active marijuana users; 24.5% had consumed marijuana in the past. Increased seizure frequency was significantly associated with marijuana use. There was a non-significant trend towards increased marijuana use with males and MRE. Almost half the active marijuana users noted improvement in seizure frequency. No participants experienced worsening of epilepsy with marijuana use. Side effects were common (30%), most frequent being mood. **Conclusions:** Prevalence of marijuana use among people with epilepsy is higher in our study population compared to an Australian cohort, but similar to Canadian studies. Marijuana use was significantly associated with increased seizure frequency. The majority of patients perceived benefit with regard to seizure control.

A.05

Association between timing of direct enteral tube placement and outcomes after acute stroke

RA Joundi (Toronto) G Saposnik (Toronto) R Martino (Toronto) J Fang (Toronto) MK Kapral (Toronto)*

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Background: The relationship between timing of direct enteral feeding tube (DET; gastrostomy/jejunostomy) placement and outcomes after stroke is unknown. **Methods:** We used the Ontario Stroke Registry and linked administrative databases to identify patients with acute stroke between 2003-2013 who received DET during hospital admission. We used multiple logistic regression and Cox proportional hazard models to determine the association between time from admission to DET placement and outcomes of severe disability at discharge (modified Rankin Scale score 4-5) and 30-day mortality after DET placement, adjusting for age, sex, co-morbidities, stroke type, stroke severity, intensive care or stroke unit admission, palliation, and hospital type. **Results:** 1,342 patients met our inclusion criteria. There was a lower hazard of 30-day mortality for each week in delay to DET placement (adjusted HR 0.89, 95%CI 0.80 to 0.99), but higher odds of severe disability (adjusted OR 1.36, 95%CI 1.14 to 1.62). Patients with DET placement within 1 week had the highest 30-day mortality compared to subsequent weeks (adjusted HR 1.59, 95%CI 1.05 to 2.4). **Conclusions:** Delayed DET placement after stroke is associated with lower 30-day mortality but greater disability. Thirty-day mortality was highest in those who received DET