recurrence at an average of 1.7 years after documented disease inactivity. Patients with generalized morphea experienced higher recurrence rates than those with linear morphea (HR: 3.03, 95% CI: 1.48–6.22), and those treated with UVA1 phototherapy had higher recurrence over those treated with methotrexate (HR: 2.33, 95% CI: 1.03–5.31). In patients with follow-up periods longer than 5 years (n = 50), disease recurrence was observed in 44% of patients and the majority of recurrence represented new activity in an area of pre-existing morphea (82%). DISCUSSION/SIGNIFICANCE OF IMPACT: This study highlights the previously under-studied dynamic long-term course of morphea, and identifies the clinical characteristics that predispose patients to having a relapsing-remitting course. We conclude that patients with morphea should be followed closely over time even in the absence of disease activity due to the potential for disease recurrence.

2003

Mixed meal effects of neprilysin inhibition

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OBJECTIVES/SPECIFIC AIMS: Test the hypothesis that neprilysin inhibition with sacubitril/valsartan will increase endogenous intact GLP-1 after a mixed meal compared with valsartan. METHODS/STUDY POPULATION: Adults 18–80 years with pre-diabetes or type 2 diabetes and elevated blood pressure. RESULTS/ANTICIPATED RESULTS: We anticipate higher intact GLP-1 area under the cure after the meal when subjects receive sacubitril/valsartan compared with valsartan. DISCUSSION/SIGNIFICANCE OF IMPACT: Neprilysin inhibition may be a target for anti-diabetes therapy by decreasing degradation of GLP-1.

2563

National dissemination of the accrual to clinical trials (ACT) network across the Clinical and Translational Science Award (CTSA) Consortium*

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OBJECTIVES/SPECIFIC AIMS: The ACT Network was developed by 46 members of the CTSA Program hubs in collaboration with NCATS to help investigators explore and validate feasibility of clinical studies in real-time using linked electronic health record data for cohort discovery. ACT is being disseminated nationally across the CTSA consortium. METHODS/STUDY POPULATION: Diffusion of Innovation Theory and Lean Start-Up principles inform dissemination strategies. Core materials were developed nationally and are being tailored to meet local CTSA dissemination norms. An advisory board, with expertise in communications, journalism, customer channel management, pharmaceutical commercialization and health IT entrepreneurship, is providing strategic advice to develop and refine dissemination strategies. Evaluation of dissemination methods will include network usage and web analytics for the ACT Network's interactive digital content and log-in portal, and surveys-interviews of ACT users using the RE-AIM implementation framework. RESULTS/ANTICIPATED RESULTS: Formative research identified ACT's primary value proposition for clinical researchers: "Explore patient populations in depth, in real time, from your desktop;" "Confirm study feasibility by iteratively testing and refining inclusion and exclusion criteria;" "Demonstrate feasibility in funding proposals and IRB submissions;" and "Identify collaborating sites for multi-site studies by searching for patients across the CTSA network." Early dissemination metrics, including number-type of registered users, queries performed, and web analytics, will be presented. DISCUSSION/SIGNIFICANCE OF IMPACT: Researchers nationwide face common barriers in accruing enough participants for clinical trials. The inability to identify the right number and type of people to participate often makes clinical trials slow and costly. Better cohort discovery at the protocol development phase is a necessary requirement. By end of 2018, the ACT Network will reach 60% of the CTSA consortium providing a new tool for investigators to improve the design and execution of clinical trials.

*Submitted on behalf of the ACT Network Research Team.

2428

Obstructive sleep apnea as an independent predictor of postoperative delirium and pain: An observational study of a surgical cohort

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OBJECTIVES/SPECIFIC AIMS: To study the role of OSA as an independent predictor of perioperative outcomes. METHODS/STUDY POPULATION: For this single-institution cohort study, we included data from patients who were enrolled into 1 of 3 prospective parent studies. All participants underwent inpatient surgeries, excluding neurosurgeries, which required general anesthesia and a postoperative stay of at least 1 day. Patients included in this study were assessed daily for postoperative delirium and pain severity as part of the parent studies. In the current study, determination of delirium diagnosis was based on the 3-minute Diagnostic Confusion Assessment Method (3D-CAM), and the Visual Analogue Pain Scale (VAS) was used for pain severity. Data on OSA diagnosis (determined by sleep study); OSA risk (determined by the STOP-Bang tool; snoring, tiredness, observed apnea, high blood pressure, body mass index > 35 kg/m^2, age > 50, neck circumference, male gender); and compliance with treatment were obtained from the preoperative assessment record. Participants were grouped into 1 of 3 categories: high risk of OSA (HR-OSA; including patients with a previous positive sleep study or STOP-Bang score ≥5); intermediate risk of OSA (IR-OSA; including patients with a STOP-Bang score of 3 or 4); and low risk of OSA (LR-OSA; including patients with a previous negative sleep study or STOP-Bang score <3). Candidate risk factors for delirium and pain were also extracted from this record. RESULTS/ANTICIPATED RESULTS: Logistic regression will be used to test whether OSA independently predicts postoperative delirium and linear regression to assess OSAs relationship to acute pain severity. We hypothesize that patients in the HR-OSA category will experience a higher incidence of postoperative delirium and greater postoperative pain severity. We also predict a step-wise increase in risk of these adverse outcomes when analyzing patients stratified by OSA risk (HR-OSA vs. IR-OSA vs. LR-OSA). For our secondary analyses, we anticipate these outcomes are modified by compliance with CPAP treatment. We believe patients with OSA who do not use prescribed CPAP will experience a higher incidence of postoperative delirium as well as increased pain severity. DISCUSSION/SIGNIFICANCE OF IMPACT: OSA is a common and frequently undiagnosed perioperative problem associated with altered pain processing and a high incidence of postoperative delirium. While likely providing stronger evidence of OSA's reported impact on postoperative delirium and pain, our findings might also help discern points of intervention for treatment and prevention. Since OSA's presumed impact poses challenges to clinicians and patients, prospective, randomized trials testing preventative or mitigating interventions are necessary. We hope to use these results to design such trials and clinical plans, with the goal of reducing postoperative delirium and acute postsurgical pain severity for the large number of patients at risk due to OSA.

2568

Pembrolizumab for patients with leptomeningeal disease from advanced solid tumors

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OBJECTIVES/SPECIFIC AIMS: Pembrolizumab is an anti-PD-1 immune checkpoint antibody that has demonstrated promising anti-tumor activity in patients with solid tumor malignancies, including patients with brain metastases from malignant melanoma and non-small cell lung cancer. Leptomeningeal disease (LMD) is a rare form of malignant spread to the central nervous system (CNS), that occurs in 2%–10% of patients with solid tumors, most commonly in breast cancer and non-small cell lung cancer. We propose an open-label phase II study of pembrolizumab in patients with LMD from advanced solid tumors

https://doi.org/10.1017/cts.2018.174 Published online by Cambridge University Press

(NCT03091478). This study aims to determine if pembrolizumab therapy can lead to a radiologic, cytologic or clinical response in the CNS, in patients with LMD. METHODS/STUDY POPULATION: Patients with pathologically confirmed advanced solid tumors, and either radiologic or cytologic evidence of LMD, will be identified at a single institution. Radiologic LMD will be defined as a >4 mm area of measurable LMD on gadolinium-enhanced MRI brain/total-spine; and cytologic LMD will be defined as the presence of malignant cells on CSF cytology. Patients will be excluded if they have: active autoimmune conditions that require immunosuppression, received radiation therapy to the only area of measurable LMD within 3 months of study enrollment, have an ECOG performance status <1. Once enrolled, patients will receive pembrolizumab 200 mg intravenously every 3-weeks, until disease progression or unacceptable toxicity. Patients will have CSF sample sampling, blood draws, radiologic imaging of the body (CT), brain/total-spine (gadolinium-enhanced MRI) pre-treatment, after 2 and after 4 cycles of therapy, for response assessment and correlative studies. The primary endpoint of the study is CNS response assessed at 12 weeks/after 4 cycles of pembrolizumab, defined either as radiologic response (reduction in size of LMD on gadolinium-enhanced MRI) and/or cytologic response (conversion of positive to negative CSF cytology on 2 consecutive samples) and/or clinical response. Secondary endpoints will include progression-free survival, overall survival, and safety. To explore the mechanisms by which pembrolizumab may affect LMD, we will assess dynamic changes in genomic and immunologic markers in the CSF and serum pre and post pembrolizumab using next-generation sequencing and multi-color flow cytometry, respectively. RESULTS/ANTICIPATED RESULTS: We will aim to accrue a total of 20 patients, allowing for a 10% drop-out rate, the final sample size will include 18 patients who have received at least 1 dose of pembrolizumab. CNS-response at 12 weeks will be assessed radiologically +/− cytologically, and the proportion of patients with CNS response and associated 95% confidence interval with be reported. CNS-progression-free survival and overall survival will be assessed using the Kaplan-Meier method. Cause of death will be recorded. Safety will be assessed as detailed above, and monitored as per an institutional Data Safety and Monitoring Plan. Exploratory endpoints will include genomic testing of tumor cells and cell-free DNA in CSF and serum, and immunologic studies of immune cells in CSF and serum at pre-defined timepoints. These data will be presented descriptively. We conservatively estimate that we will accrue 1 patient per month at our institution. Study duration will be approximately 24 months, allowing 18 months for accrual and 6 months for follow-up and data analysis. DISCUSSION/SIGNIFICANCE OF IMPACT: There are no currently FDA-approved therapies for patients with LMD from solid tumors. Anti-PD-1 immunotherapy is a promising class of agents, with known efficacy in patients with CNS metastatic disease, across tumor types. This study seeks to identify whether pembrolizumab may lead to CNS responses in patients with LMD. Additionally, genomic and immunologic analyses in CSF and blood pre and post-pembrolizumab may identify mechanisms by which immunotherapy affects the CNS in patients with LMD.

2137

Percentage of viable tumor Versus radiation treatment effect in surgical specimens is not associated with outcomes in recurrent glioblastoma

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OBJECTIVES/SPECIFIC AIMS: In patients with recurrent glioblastoma (GBM) who undergo a second surgery following standard chemoradiotherapy, histopathologic examination of the resected tissue often reveals a combination of viable tumor and treatment-related inflammatory changes. However, it remains unclear whether the degree of viable tumor Versus "treatment effect" in these specimens impacts prognosis. We sought to determine whether the percentage of viable tumor Versus "treatment effect" in recurrent GBM surgical samples, as assessed by a trained neuropathologist and quantified on a continuous scale, is associated with overall survival. METHODS/STUDY POPULATION: We reviewed the records of 47 patients with histopathologically confirmed GBM who underwent surgical resection as the first therapeutic modality for suspected radiographic progression following standard radiation therapy and temozolomide. The percentage of viable tumor Versus "treatment effect" in each specimen was estimated by one neuropathologist who was blinded to patient outcomes. RESULTS/ANTICIPATED RESULTS: After adjusting for other known prognostic factors in a multivariate Cox proportional hazards model, there was no association between the degree of viable tumor and overall survival (HR 0.83; 95% CI, 0.20–3.4; $p = 0.20$). DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that, in patients who undergo resection for recurrent GBM following standard first-line chemoradiotherapy, histopathologic quantification of the degree of viable tumor Versus "treatment effect" present in the surgical specimen has limited prognostic influence and clinical utility.

2016

Plasma microRNA markers of upper limb recovery following human stroke

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OBJECTIVES/SPECIFIC AIMS: MicroRNAs are small, non-coding RNAs that control gene expression by inhibiting protein translation. Preclinical studies in rodent stroke models suggest that changes in microRNA expression contribute to neural repair mechanisms. To our knowledge, no one has previously assessed microRNA changes during the recovery phase of human stroke. Our goal was to determine whether patients with significant upper limb recovery following stroke have alteration of neural repair-related microRNA expression when compared to those with poor recovery. METHODS/STUDY POPULATION: Plasma was collected at 19 days post-stroke from 27 participants with mild-moderate upper extremity impairment enrolled in the Critical Periods After Stroke Study. MicroRNA expression was assessed using TaqMan microRNA assays (Thermo Fisher Scientific). Good recovery was defined as ≥ 6 point change in the Action Research Arm Test (ARAT) score from baseline to 6 months. Bioinformatics analysis compared the plasma microRNA expression profiles of participants with good Versus poor recovery. Candidate biomarkers were identified after correcting for multiple comparisons using a false discovery rate <0.05. RESULTS/ANTICIPATED RESULTS: Eleven microRNAs had significantly altered expression in the good ($n = 22$) Versus poor ($n = 5$) recovery groups, with 2 showing increased expression—miR-371-3p and miR-520g, and 9 showing decreased expression—miR-449b, miR-519b, miR--581, miR-616, miR-892b, miR-941, miR-1179, miR-1292, and miR1296. Three of these could be implicated in neural repair mechanisms. Elevated miR-371-3p levels increase the likelihood that pluripotent stem cells will differentiate into neural progenitors. MiR-892b decreases levels of amyloid precursor protein, which has been implicated as a regulator of synapse formation. Finally miR-941, the only known human-specific microRNA, downregulates the CSPα protein which is involved in neurotransmitter release. DISCUSSION/SIGNIFICANCE OF IMPACT: This preliminary study suggests that circulating microRNAs in the plasma may help serve as biomarkers of neural repair and aid in understanding human neural repair mechanisms. If validated in larger studies with appropriate controls, these markers could aid in timing rehabilitation therapy or designing recovery-based therapeutics.

2196

Pre-treatment sleep disturbance as a risk factor for radiation therapy induced pain in 676 women with breast cancer

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OBJECTIVES/SPECIFIC AIMS: The purpose of the present secondary data analysis was to examine the effect of moderate-severe disturbed sleep before the start of radiation therapy (RT) on subsequent RT-induced pain. METHODS/STUDY POPULATION: Analyses were performed on 676 RT-naïve breast

https://doi.org/10.1017/cts.2018.174 Published online by Cambridge University Press