expression which makes it more susceptible to anti-PD-L1 antagonism and ADCC through avelumab therapy. **Methods:** This is a single center, phase 2, open label, add-on, single dose study of 156 weeks duration in patients receiving standard therapy for newly diagnosed GBM. In total 30 patients will be entered into the study within 3 weeks of finishing their last day of combined radiotherapy/temozolomide. The following are the results of the first interim analysis completed when the first eight patients completed 52 weeks or an end of study visit. **Results:** 24 patients have so far started therapy. There as been no unexpected treatment emergent adverse event (TEAE). Two patients transiently withheld therapy because of immune related TEAE's and none permanently. The objective response rate at week 52 for the first eight patients was 50% with 2 (25%) having a complete response and 1 (12.5%) a partial response. **Conclusions:** These preliminary results suggest that the addition of avelumab to standard therapy in patients with GBM is safe. Efficacy trends look promising.

Neurocritical Care

P.021

Esophageal cooling for hypoxic ischemic encephalopathy: a feasibility study

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Background: Targeted temperature management (TTM) is a recognized treatment to decrease mortality and improve neurological functionin hypoxic ischemic encephalopathy (HIE). An esophageal cooling device (ECD) has been studied in animal models but human data is limited. ECD appear to offer similar benefits to intravascular cooling catheters with potentially less risk to the patient. We studied whether the ECD could act as a substitute for intravascular cooling catheters. **Methods:** Eight ICU patients admitted following cardiac arrest who required TTM were enrolled prospectively. The primary outcome measures were timeliness of insertion, ease of insertion, user Likert ratings, time to achieve a target temperature of 36˚C and time target temperature was maintained within 0.5˚C of the 36˚C goal for 24 hours using an ECD. **Results:** Time to reach target temperature 0 min to 540 min. ECD appeared to be effective at maintaining a target temperature of 36˚C for most patients. In general, the catheter was easy to insert and use. **Conclusions:** For patients requiring TTM, use of an ECDadequately allowed for TTM goalsto be achieved and maintained. Overall user evaluationwas positive.

Neuromuscular Disease and EMG

P.022

Myasthenia gravis following dabrafenib and trametinib for metastatic melanoma

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Background: Inhibitors of BRAF and MEK, enzymes in the mitogen-activated protein kinase (MAPK) pathway, are now widely used in the treatment of metastatic melanoma. We report a case of acetylcholine receptor (AChR) antibody-positive myasthenia gravis developing after exposure to dabrafenib, a BRAF inhibitor, and trametinib, a MEK inhibitor. **Methods:** A 68-year-old man presented with dysarthria, dysphagia, cough, dyspnea, and fever. Examination revealed fatigable ptosis and proximal muscle weakness. He had started dabrafenib and trametinib for metastatic melanoma two weeks prior. He was diagnosed with myasthenia gravis and superimposed aspiration pneumonia. AChR antibodies were positive. Dabrafenib and trametinib were stopped. He improved rapidly with pyridostigmine alone, and remained free of myasthenic symptoms for the next two months. Another course of dabrafenib and trametinib was given, and seven weeks later, his myasthenic symptoms recurred. Pyridostigmine produced only partial improvement, and treatment with intravenous immunoglobulin and prednisone was initiated. **Results:** We are unaware of prior reports of an association between BRAF/MEK inhibitors and seropositive myasthenia gravis. The development of myasthenic symptoms twice after BRAF/MEK inhibitor exposure suggests that the association is more than coincidental. **Conclusions:** Myasthenia gravis may be a complication of treatment of melanoma with dabrafenib and trametinib. The mechanism by which this occurs is unknown.

P.023

Eculizumab shows consistent improvements across muscle groups in patients with AChR antibody-positive refractory myasthenia gravis

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Background: The physician-reported Quantitative Myasthenia Gravis (QMG) test was a key efficacy measure in REGAIN, a 26-week, phase 3, placebo-controlled study of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized MG. Ocular and generalized weakness have shown variable responses to therapies including prednisone and intravenous immunoglobulin/plasma exchange. Using the patient-reported MG Activities of Daily Living (MG-ADL) scale during REGAIN, eculizumab showed a consistent trend toward rapid and sustained improvement across bulbar, respiratory, limb and ocular domains. We analyzed the effect of eculizumab on bulbar, respiratory, gross motor and ocular domains during REGAIN, using the QMG test. **Methods:** QMG domain score changes to REGAIN week 26 were determined for patients with abnormal baseline scores. Repeated-measures analyses were performed for bulbar (swallowing/speech), respiratory (forced vital capacity),

gross motor (limb/axial motor items) and ocular (ocular/facial muscles) domains. **Results:** Eculizumab-treated patients showed improvements in all four QMG domain scores to week 26. Rapid, sustained improvements were demonstrated across all domains, with a trend toward significant differences between eculizumab and placebo (bulbar, p=0.0628; respiratory, p=0.0682; gross motor, p=0.0114; ocular, p=0.0017). The eculizumab safety profile was consistent with previous reports. **Conclusions:** Eculizumab demonstrated a consistent response across all QMG muscle domains. This aligns with previously reported MG-ADL findings with eculizumab. (NCT01997229).

P.024

Long-term use of patisiran in patients with hereditary transthyretin amyloidosis (hATTR): 12 month efficacy & safety data from a global open label extension (OLE) study

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Background: Hereditary transthyretin-mediated (hATTR) amyloidosis is a multi-systemic, heterogenous, life-threatening disease. Patisiran resulted in significant improvement in neuropathy and QoL at 18-months compared to placebo, and was generally well-tolerated in the Phase 3 APOLLO study. **Methods:** Multi-center, OLE study to evaluate the efficacy and safety of long-term patisiran dosing for ≤ 5 years in hATTR amyloidosis patients with polyneuropathy who have completed the APOLLO study (NCT02510261). Endpoints include safety, tolerability and long-term efficacy of patisiran. Measures of clinical benefit are the same endpoints used in APOLLO including changes in mNIS+7 composite neuropathy impairment score and QoL (Norfolk QoL-DN) **Results:** As of December 2017, 184 of 186 (99%) patients who completed APOLLO and 25 patients from the Ph 2 OLE study enrolled in the Global OLE study. Baseline data for 211(APOLLO/placebo, n=49; APOLLO/patisiran, n=137 and patisiran Ph 2 OLE, n=25) patients included: median age 61 years (26-84); 74% males; 46% V30M. Interim safety data and 12-month efficacy results will be presented. **Conclusions:** The global OLE study includes a diverse population of hATTR amyloidosis patients. Interim data will include the long-term safety and maintenance of effect in patients continuing on patisiran, as well as the impact of treatment with patisiran on patients previously treated with placebo.

P.025

APOLLO, a phase 3 study of patisiran for the treatment of hereditary transthyretin amyloidosis (hATTR): 18-month safety and efficacy in subgroup with cardiac involvement

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Background: Hereditary transthyretin-mediated (hATTR) amyloidosis a hereditary, multi-systemic and life-threatening disease resulting in neuropathy and cardiomyopathy. In the APOLLO study, patisiran, an investigational RNAi therapeutic targeting hepatic TTR production resulted in significant improvement in neuropathy and QoL compared to placebo and was generally well tolerated. **Methods:** APOLLO, a Phase 3 study of patisiran vs. placebo (NCT01960348) prespecified a cardiac subpopulation (n=126 of 225 total) that included patients with baseline left ventricular (LV) wall thickness ≥ 13mm and no medical history of aortic valve disease or hypertension. Cardiac measures included structure and function by electrocardiography, changes in NT-proBNP and 10-MWT gait speed. **Results:** At 18 months, patisiran treatment resulted in a mean reduction in LV wall thickness of 1 mm (p=0.017) compared to baseline, which was associated with significant improvements relative to placebo in LV end diastolic volume (+8.31 mL, p=0.036), global longitudinal strain (-1.37%, p=0.015) and NT-proBNP (55% reduction, p=7.7 x 10-8) (Figure 1). Gait speed was also improved relative to placebo (+0.35 m/sec, p=7.4 x 10-**9**). Rate of death or hospitalization was lower with patisiran. mNIS+7 results in the cardiac subpopulation will also be presented. **Conclusions:** These data suggest patisiran has the potential to halt or reverse cardiac manifestations of hATTR amyloidosis.

P.026

Response to eculizumab in patients with myasthenia gravis recently treated with chronic intravenous immunoglobulin

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Background: Chronic intravenous immunoglobulin (IVIg) is used to treat refractory myasthenia gravis (MG). This subgroup analysis evaluated response to eculizumab in patients receiving chronic IVIg before entry to REGAIN, a phase 3, randomized, double-blind, placebo-controlled study of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalized MG. **Methods:** IVIg was only permitted during REGAIN as rescue therapy; previously treated patients underwent a 4-week washout before randomization. Patients included in this analysis had received chronic IVIg ≥4 times in 1 year, with ≥1 dose within 6 months before REGAIN entry. Exacerbations and MG status changes were assessed. **Results:** Eighteen patients were evaluated; four experienced exacerbations (eculizumab-treated, 1/9; placebo-treated, 3/9). Clinically relevant improvements were larger with eculizumab than placebo, respect-