Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
assessing the efficacy and safety of AKCEA-TTR-LRx in hATTR-CM or wtATTR-CM patients receiving available background standard of care (SoC) therapy. Approximately 750 patients around the world with a history of HF due to ATTR-CM will be randomized 1:1 to receive either AKCEA-TTR-LRx 45 mg or placebo administered by SC injection once every 4 weeks. Key inclusion criteria include diagnosis of ATTR-CM by biopsy or positive PYP/DPD/HMDP scan, interventricular septum thickness >12 mm, NT-proBNP > 600 pg/mL, NYHA class I-III and 6-minute walk distance (6MWD) > 150 m. Key exclusion criteria include, platelet count < 125 x 10^9/L and urine protein/creatinine ratio > = 750 mg/g. Concomitant treatment with tafamidis as SoC for ATTR-CM is allowed. The study consists of a 120-week Treatment Period. Primary efficacy endpoint is the composite of cardiovascular (CV) mortality and recurrent CV clinical events at Week 120 study visit using the Andersen-Gill model. Secondary endpoints include the change from baseline in the 6MWD, KCCQ score, CV clinical events, CV death and all-cause of mortality at Week 120.

Conclusions: Despite recent advances, additional efficacious, safe and convenient treatment options for ATTR-CM are needed. The CAR-DIO-TTRansform trial is a large Phase 3 trial designed to evaluate the efficacy and safety of AKCEA-TTR-LRx compared to placebo in patients with ATTR-CM receiving available SoC therapy.

Results: APOLLO enrolled 225 patients worldwide with a mean age of 60.5 years, 74% male, and 43% with V30M transthyretin mutation. At baseline, patisiran and placebo groups had similar R-ODS, KPS, and Norfolk ADL scores. After 18 months, a higher proportion of patisiran-treated patients experienced no change/improvement in functional status and ADLs relative to placebo: R-ODS 49.3% vs 13.0% (odds ratio [OR] 6.5, 95% confidence interval [CI] 2.8 to 15.4), KPS 64.9% vs 42.9%, (OR 2.5, 95% CI 1.3 to 4.8), Norfolk ADL 56.2% vs 20.4% (OR 5.0, 95% CI 2.4 to 10.5).

Conclusions: In APOLLO, the largest randomized clinical study of patients with hATTR amyloidosis with polyneuropathy to date, patisiran preserved ability to perform ADLs and functional status for the majority of patients and demonstrated greater odds of stabilizing or improving these assessments compared to placebo.

Research

P011. Impact of Patisiran on Activities of Daily Living and Functional Status in hATTR Amyloidosis

MADELIN MERKEL, PharmD, DAVID ADAMS, MD,a SENDA AJROUD-DRISS, MD, b JOHN BERK, MD, c ALEJANDRA GONZALEZ-DUARTE, MD, d CECILIA HALE, PhD, e HOLLIS LIN, MS, f AMANDA PELTIER, MD, f OLE SUHR, MD, PhD, g IVALIO TOUROVNE, MD, h TARO YAMASHITA, MD, i

a Alnylam Pharmaceuticals, Cambridge, MA; b National Reference Center for FAP (NNERF)/ APHP/ INSERM U, Ile-de-France, France; c Northwestern University, Chicago, IL; d Boston University, Boston, MA; e Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán, Ciudad de México, Mexico; f Vanderbilt University Medical Center, Nashville, TN; g Umea University, Umeå, Sweden; h University Hospital Alexandrovska, Sofia, NA, Bulgaria; i Kumamoto University Hospital, Kumamoto, Japan.

Background: Hereditary transthyretin-mediated (hATTR) amyloidosis, a rare, multi-systemic, life-threatening disease, causes neurologic and cardiac dysfunction, leading to impaired functional status and declining ability to perform activities of daily living (ADLs).

Objectives: To analyze the impact of patisiran on ADLs and functional status in the Phase 3 APOLLO study.

Methods: APOLLO was a randomized, placebo-controlled study of patisiran in patients with hATTR amyloidosis with polyneuropathy (NCT01963048). ADL functional status assessments included: Rasch-built Overall Disability Scale (R-ODS), Karnofsky Performance Status (KPS), the ADL subdomain of Norfolk QOL-DN (Norfolk ADL). Post-hoc analyses quantified patients with no change/improvement in these assessments at 18 months.

Results: More than half of patients with hATTR amyloidosis with polyneuropathy had impaired functional status at baseline (125/225, 56%). Among 98 study participants with a baseline R-ODS score, 53 of 98 (54%) experienced no change/improvement in R-ODS at 18 months, 21 of 98 (21%) experienced improvement, and 24 of 98 (25%) experienced worsening. In APOLLO, the largest randomized clinical study of patients with hATTR amyloidosis with polyneuropathy to date, patisiran-treated patients experienced no change/improvement in functional status and ADLs relative to placebo: R-ODS 49.3% vs 13.0% (odds ratio [OR] 6.5, 95% confidence interval [CI] 2.8 to 15.4), KPS 64.9% vs 42.9%, (OR 2.5, 95% CI 1.3 to 4.8), Norfolk ADL 56.2% vs 20.4% (OR 5.0, 95% CI 2.4 to 10.5).

Conclusions: In APOLLO, the largest randomized clinical study of patients with hATTR amyloidosis with polyneuropathy to date, patisiran preserved ability to perform ADLs and functional status for the majority of patients and demonstrated greater odds of stabilizing or improving these assessments compared to placebo.
CVD. Psychosocial and biophysical outcomes from telehealth engagements are areas for further investigation.

Research

P013. BNP as a Predictor of Diuretic Nonadherence in 30-Day Heart Failure Readmissions

REBECCA MERAZ, KATIE FRANK, KATHRYN OSTEEN, PhD, RN, CMSRN, CNE, HENRY VIEJO, MSN, RN, NEA-BC, NANCY VISH, RN, PhD, NEA-BC

Background: Diuretic treatment effectively treats heart failure (HF), lowers brain natriuretic peptide (BNP), and can reduce hospital readmissions, yet approximately 50% of HF patients do not take medications as prescribed. Additionally, 25% of HF hospital readmissions are thought to be preventable and associated with imperfect adherence to prescribed medications. One barrier to solving this problem is the lack of an objective marker for identifying or gauging diuretic-taking habits in the HF patient. Better understanding of the impact of imperfect diuretic adherence on BNP provides insight into the significance of taking diuretics as prescribed to 30-day HF readmissions and the usefulness of BNP in identifying patients at-risk for diuretic nonadherence.

Objective: The purpose of this retrospective, exploratory investigation was to examine the association between diuretic nonadherence and BNP in those with a 30-day HF readmission and further explore the usefulness of BNP as an objective marker for diuretic adherence.

Methods: A retrospective review of electronic health records from 10 Texas hospitals between the years of 2014 and 2018 was conducted. We examined the association of nonadherence to BNP with three BNP-related variables: change in BNP from index hospitalization to readmission, percent change over time, and readmission BNP. We investigated the relationship of each with nonadherence and patient characteristics by performing backwards stepwise logistic regression to determine if one of the three BNP-related variables we considered is a superior objective marker of diuretic nonadherence. BNP could be useful in identifying patients at risk for diuretic nonadherence and a hospital readmission. Since medication-taking habits are modifiable, finding new ways to gauge diuretic adherence could reduce hospital readmissions and improve HF outcomes.

Results: Of the study sample (N=405), the medical records of 124 (31%) patients explicitly documented diuretic nonadherence at readmission. In final BIC-selected logistic regression models for predicting nonadherence in patients with a 30-day HF readmission, BNP-related variables were the only remaining predictors and were significantly associated with nonadherence; other variables concerning patient characteristics were excluded. The discrimination ability of these models was evaluated by calculating area under the curves (AUCs) and testing for differences among them with the DeLong method.

Conclusions: Results suggest that variables relating to patient characteristics are not as important as those relating to BNP for predicting diuretic nonadherence. Additionally, more investigation is warranted to determine if one of the three BNP-related variables we considered is a superior objective marker of diuretic nonadherence. BNP could be useful in identifying patients at risk for diuretic nonadherence and a hospital readmission. Since medication-taking habits are modifiable, finding new ways to gauge diuretic adherence could reduce hospital readmissions and improve HF outcomes.

Research

P014. Risk Factors for Cardiovascular Events In Hospitalized Patients with COVID-19

LYNN ROSER, PhD, RN, CIC, FAPIC, JIAPENG HUANG, MD, PhD, FASA, FASE, MAIYING KONG, PhD, TREVOR MCCUFIN, BSN, JAVANESE BURDELL, VIVI SALUNKHE, HARIDEEP SAMANAPELLY, NRM, QIAN XU

Background: Between 25%-50% of patients hospitalized with COVID-19 suffer cardiovascular events. Limited information is available to identify those at greatest risk for cardiac complications.

Objectives: Objectives were to analyze risk factors associated with cardiovascular events (CE); analyze whether risk factors and outcomes were influenced by race; and analyze survival differences among various groups.

Methods: This retrospective cohort study of 700 inpatients with COVID-19 was conducted at nine hospitals within a large urban midwestern city. Data was collected from March 9, 2020, to June 20, 2020. Inclusion criteria included all COVID-19 inpatients and excluded non-inpatients. Predictor variables included demographics, comorbidities, and current clinical data. The outcomes were heart failure (HF), deep-vein thrombosis, myocardial infarction, pulmonary edema, stroke, cardiomyopathy, myocarditis, reduced ejection fraction, cardiac arrhythmias, cardiogenic shock, and cardiac arrest. Pearson’s correlation coefficients were used to evaluate the correlation between different variables. Multiple logistics regression analyses were conducted to examine which variables predict cardiovascular events for the entire cohort, African American patients, and white patients, respectively. Mann-Whitney U, Chi-square, or Fisher’s exact tests were used to examine differences in groups with and without CE and Kaplan-Meier was conducted for survival comparisons between groups.

Results: Of 700 COVID-19 positive inpatients, 126 experienced cardiovascular events and 574 did not. The incidence of cardiovascular events in our sample population was 18%. As shown in Table 1, we found the following factors were highly associated with the odds of new-onset of CEs: advanced age in years, males, non-Hispanic African American, presence of comorbidities, and decreased saturation levels. Numerous laboratory values were significantly associated with the risk of CEs (Table 1). African Americans had greater odds of CEs in the presence of diabetes and cardiovascular comorbidities (p=0.008, p=0.014, respectively). However, multiple logistics analysis was used to examine the joint effect of the risk factors which suggested that lower serum albumin and neoplastic/immune compromised diseases count were highly associated with CEs for African American COVID-19 inpatients (p=0.001, p=0.044, respectively). SaO2/FiO2 ratio and cardiovascular comorbidities were significantly associated with CEs for white inpatients (p=<0.001, p=0.007, respectively).

As shown in Figure 1, Kaplan-Meier survival analysis revealed inpatients with CEs had a much higher mortality rate than those without CEs (45.2% vs. 8.7%). Median survival for patients with CEs was 18 days as opposed to 100 days for those that did not experience CEs. African Americans with CEs experienced higher mortality than those without CEs (43.9% vs. 7.8%). White COVID-19 inpatients’ mortality rates were 46.3% and 9.0% for those with and without CEs, respectively.