was lower in sQTc at 2.6 years (IQR 0.4-12.3) compared to 9.7 years (IQR 2.0-16.9) in all patients with ECGs ($p<0.00001$). All-cause mortality was increased for patients with xsQTc interval compared to those with sQTc above 300ms (14.9% vs. 9.4%, $p=0.003$). In regression analysis for mortality adjusting for demographics and total ECGs per patient, the presence of multiple sQTc ECGs was associated with increased mortality compared with single sQTc (OR 2.39, 95% CI 1.73-3.27, $p<0.0001$). Prior to 2010 when sQTc syndrome was first reported, 1 ECG written report included sQTc; after 2010 only 5.2% (171 of 3,272 ECGs) with final sQTc interval and 4.4% (4 of 90 ECGs) with final xsQTc included a written report of short QTc by the interpreting physician.
Conclusion: The presence of short QTc interval, particularly when seen on multiple ECGs, is associated with increased all-cause mortality but is not automatically reported. In addition to prolonged QTc, it may be important to note and report short QTc interval in the written ECG report.

PE-499663-003

SGK-1 INHIBITION WITH LQT-1213 SIGNIFICANTLY REDUCES THE QTCF IN PATIENTS WITH CONGENITAL LONG QT SYNDROME IN THE WAVE I, PART 2 STUDY

Philip T. Sager; Michael J. Ackerman; Saumya Das; Pirouz Shamszad; Dinesh Srinivasan; Douglas Wight; Alexandre Brkovic and Wojciech Zareba

Background: Serum glucocorticoid kinase 1 (SGK1) regulates cardiac ion channels and plays a role in maintaining heart rhythm and function. SGK1 inhibitors shorten genetic or drug-induced abnormally prolonged QTc values both in vitro and ex vivo. In previously reported results, treatment with a novel, potent inhibitor of SGK1 (LQT-1213) shortened the QTc in healthy subjects with dofetilide-induced QT prolongation (NCT05906732).
Objective: The WAVE I, Part 2 study evaluated the safety and efficacy of LQT-1213 in patients with LQT2 or LQT3 and persistent prolongation of their QTc while receiving standard of care therapy.
Methods: Adult subjects with either LQT2- or LQT3-causative mutations and a QTcF $\geq$ 480 msec were enrolled in the ongoing trial. On Day 1, subjects received placebo and on Days 2 through 4, received either a lower or higher dose of LQT-1213, TID. Triplicate ECGs were collected at pre-dose, 1, 2, 4, 6, 8, 10 and 12 hours on Days 1, 2, and 4 and analyzed by a core ECG laboratory. The primary objective was to evaluate the safety and tolerability of LQT-1213. Efficacy measures included ΔQTcF AUC analyses and time-matched ΔQTcF.
Results: Nine subjects with LQT2 and three subjects with LQT3 were enrolled. No drug-related SAEs, TEAEs, or TEAEs leading to study discontinuation were reported. No safety concerns were identified from results of labs, vital signs, physical examinations or ECGs; no meaningful effects on heart rate, PR/QRS intervals at either dose. In the higher dose group, ΔQTcF AUC analyses demonstrated statistically significant and clinically meaningful reductions in QTcF on Day 4 (-37.0 msec•hr ($p=0.01$) for AUC(2-6hr); -32.36 0 msec•hr ($p=.014$) for AUC (3-6 hr), and -44.6 msec•hr ($p=0.002$) for AUC(0-8hr)). The time matched ΔQTcF's achieved statistical significance at 3h (-16.1 msec, $p=0.04$), 4h (-9.1 ms, $p=0.08$) and 6h (-10.7 msec, $p=0.01$) on Day 4. Post-hoc analyses of ΔQTcF from maximum pre-dose QTcF to minimum post-dose QTcF were significant on Day 2 and Day 4 (-35.5 msec, $p=0.0047$, -37.7 msec, $p=0.0025$, respectively).
Conclusion: The SGK1 inhibitor LQT-1213 appeared safe, well-tolerated, and demonstrated a QT shortening dose response relationship in the WAVE I, Part 2 study. Clinically meaningful and statistically significant reductions in QTcF were observed in LQTS2/3 patients in the higher dose group after 7 doses of LQT-1213. These results support the development of LQT-1213 in future studies as a potential treatment for patients with congenital LQTS.

PE-499663-004

LONG-QT SYNDROME TYPE 2 (LQT 2) IN THE YOUNG: PRELIMINARY RESULTS OF AN INTERNATIONAL REGISTRY STUDY

Matthias Mueller; Anjan Batra; Charles I. Berul; Adam C. Kean; Stefan Kurath-Koller; Joanna Kwiatkowska; Martin J. LaPage; Ayelet Machtei; John Phillips; Anthony Pompa; Shubhayan Sanatani; Yekaterina Spivak; Marie Wilkin and Thomas Paul

Background: Data on LQT 2 is limited particularly in children and adolescents with regards to efficacy of û-blocker therapy and additional antiarrhythmic agents like mexiletine, impact of left cardiac sympathetic denervation (LCSD) as well as the usefulness of ICD implantation.
Objective: To improve knowledge on pediatric LQT 2 a retrospective international register study was set-up to establish contemporary data on diagnosis, management, and outcome of pediatric LQT 2.
Methods: Inclusion criteria: age $<$ 18 years at diagnosis, LQT 2 disease-specific genetic mutation. Data entry was accomplished via a web-based case report form (CRF) and managed using a custom-made database (secuTrial®).
Results: By the end of 11/2024, a total of 172 (female 59%, male 41%) patients were included into the database. Median age at diagnosis was 8 (range 0-18) years, median QTc was 0.48 (IQR 0.45-0.52). Symptoms were present in 51 (30%) individuals including syncope ($n=38$) and cardiac arrest ($n=13$). β-Blockers were prescribed initially in 161/172 (94%, non-selective in 138/161) and mexiletine in 6/172 (3.5%). A total of 11 patients remained untreated for various reasons. A pacemaker was implanted in 15 (9%), while 20 (12%) had an ICD implanted (for primary prevention $n=6$, secondary prevention $n=14$) and 10 had an AED (for primary prevention $n=8$, secondary prevention $n=2$). 4 patients had left cardiac sympathetic denervation (LSCD). During median follow-up of 5.5 years, 27/161 (17%) patients experienced symptoms (syncope $n=24$, cardiac arrest $n=3$) on β-blockers. 8 patients suffered an appropriate ICD-discharge. 109/172 participated in school sports without any cardiac event. At the last follow-up visit 169/171 patients were alive, a newborn baby died from sepsis after pacemaker implantation and a 23-year-old female suffered sudden cardiac death while on nadolol 0.3mg/kg.
Conclusion: Contemporary data show that mortality in the young LQTS patients on effective beta-blocker therapy was very low during mid-term follow-up. ICD and LCSD contributed to patients' survival. Participation in school sports was not associated with increased risk of sudden cardiac death.

PE-499663-005

PEDIATRIC OUT-OF-HOSPITAL CARDIAC ARREST SURVIVAL TO HOSPITAL ADMISSION: IN-HOSPITAL EVALUATION AND OUTCOMES

Carlos Lodeiro; Emily Grimes; Chelsea Boyd; Sara Stephens; Alexandra M. Menillo; Taylor S. Howard; Tam Dan N. Pham; Wilson W. Lam; Bryan C. Cannon; Santiago O. Valdés; Jeffrey J. Kim; Cameron Dezfulian and Christina Y. Miyake