Control Number:	21-LB-20783-ACC
Session Number:	**412**
Session Title:	**Featured Clinical Research III**
Session Time:	Monday, May 17, 2021, 12:30 pm - 1:45 pm
Presentation Number:	412-16
Topic 1:	Vascular Medicine
PatientsEnrolled:	264
PublishedAcronym:	RESCUE
PublishedNameofTrail:	Trial to Evaluate Reduction in Inflammation in Patients With Advanced Chronic Renal Disease Utilizin
TrialType:	Smaller study/randomized clinical trial (RCT)
Publishing Title:	Effects Of Interleukin-6 Inhibition With Ziltivekimab On Biomarkers Of Inflammation Among Patients At High Risk For Atherosclerotic Events
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Abstract Body:	**Background:** Interleukin-6 (IL-6) has emerged as a pivotal factor in atherothrombosis, but no large clinical outcomes trial of IL-6 inhibition has been conducted. Anticipating such a trial, we performed a phase II study to address if ziltivekimab, a fully human monoclonal antibody directed against the IL-6 ligand, safely and effectively reduces biomarkers of inflammation. We focused on patients with chronic kidney disease (CKD) and elevated high-sensitivity C-reactive protein (hsCRP), a group with high vascular risk where prior work in inflammation inhibition has shown efficacy for event reduction. **Methods:** In a randomized, double-blind trial, 264 participants with moderate to severe CKD and hsCRP >2 mg/L were allocated to placebo or subcutaneous ziltivekimab 7.5, 15 or 30 mg every 4 weeks. The pre-specified primary endpoint was change in hsCRP after 12 weeks of treatment, with additional biomarker and safety data collected over 24 weeks of treatment. **Results:** After 12 weeks, median hsCRP levels were reduced by 77%, 88% and 92% in the ziltivekimab 7.5, 15 and 30 mg groups, respectively, compared with 4% for placebo (all $p<0.001$ vs placebo); the corresponding proportions of individuals in these groups who achieved both a 50% reduction in hsCRP and on-treatment hsCRP levels <2 mg/L were 66%, 80% and 93% for ziltivekimab compared with 4% for placebo (all $p<0.001$ vs placebo). Effects were stable over the 24-week treatment period. Dose-dependent reductions were also observed for four additional inflammatory biomarkers (fibrinogen, serum amyloid A, haptoglobin and secretory phospholipase A2). Ziltivekimab was well tolerated and did not result in persistent neutropenia or thrombocytopenia, with minimal effect on hepatic enzymes and without clinically significant change in total cholesterol (C)/high-density lipoprotein-C ratio. **Conclusion:** In this phase II trial, ziltivekimab was effective at reducing multiple inflammatory biomarkers relevant to atherosclerosis without the adverse effects associated with other agents in its class. Based on these data, a large-scale phase III cardiovascular (CV) outcomes trial is planned to investigate the effect of ziltivekimab in patients at high CV risk.