薬剤により心不全患者のナトリウム利尿ペプチド濃度が改善する(LBCT 01)

SOCRATES-REDUCED：Vericiguatは増悪した慢性心不全患者のナトリウム利尿ペプチド濃度を改善する

SOCRATES-REDUCED Study: Vericiguat improves natriuretic peptide levels for patients with worsening chronic heart failure

初回解析で主要評価項目の達成はできなかったが、左室駆出率（LVEF）の低下した慢性心不全の増悪（WCHF）患者で1日10mgのvericiguatを投与された患者はプラセボ群に比べ、ＮＴ-ｐｒｏＢＮＰ低下およびＬＶＥＦの改善が大で、臨床イベントが少なかった。SOCRATES-REDUCEDは、LVEF<45%でWCHFイベント後4週以内の安定した患者を対象とした第II相用量設定試験であった。研究者らは、LVEFの低下したWCHF患者456人をプラセボまたはvericiguatを4種類の1日用量のうちのいずれかを12週間投与される群にランダムに割り付けた。初回解析において、ベースラインから12週後までのNT-proBNP値の変化は、統合vericiguat群とプラセボ群とで有意差はなかった。二次解析の結果から、vericiguatの用量が大きいほどNT-proBNP値低下が大きいという用量反応関係が示唆された。今回の用量設定のように、1日10mgまでのvericiguatは安全で12週後の血圧や心拍数には有意な影響がなかった。この結果は2015年American Heart Association学会で発表され、同時に*JAMA*に掲載された。

Full Text

Although the primary analysis of the primary end point was not achieved, compared to placebo, patients with worsening chronic HF and reduced left ventricular ejection fraction (LVEF) receiving vericiguat 10mg daily experienced a greater reduction in NT-proBNP, greater improvement in LVEF, and fewer clinical events. This *JAMA* study is being released to coincide with its presentation at the American Heart Association's Scientific Sessions 2015.

Worsening chronic heart failure (WCHF) is a major public health problem around the world. Despite an often rapid and substantial in-hospital improvement in HF signs and symptoms with standard therapy, approximately 25 percent of patients are rehospitalized within 30 days and 30 percent of patients may die within 1 year.

The SOCRATES-REDUCED trial was a phase II, dose-finding study of stable patients with LVEF<45% within 4 weeks of a WCHF event. This study, which included patients from across Europe, North America, and Asia, was conducted to determine the optimal dose and tolerability of the drug vericiguat to reduce elevated natriuretic peptide levels.

Mihai Gheorghiade, M.D., of the Northwestern University Feinberg School of Medicine, Chicago, and colleagues randomly assigned 456 patients with WCHF and reduced LVEF to receive placebo or 1 of 4 daily target doses of the medication vericiguat for 12 weeks.

Overall, 351 patients (77 percent) completed treatment with the study drug with valid 12-week N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and no major protocol deviation. In the primary analysis, change in NT-proBNP levels from baseline to week 12 was not significantly different between the pooled vericiguat group and placebo. The secondary analysis suggested a dose-response relationship, such that higher vericiguat doses were associated with greater reductions in NT-proBNP level. Rates of any adverse event were 77 percent and 71 percent among the placebo and 10-mg vericiguat groups, respectively.

Although the primary analysis of the primary end point was not achieved, compared to placebo, patients receiving vericiguat 10mg daily experienced a greater reduction in NT-proBNP, greater improvement in LVEF, and fewer clinical events. As titrated in this study, vericiguat doses up to 10 mg daily were safe and did not meaningfully influence blood pressure and heart rate at 12 weeks.

"Among patients with worsening chronic HF and reduced LVEF, compared with placebo, vericiguat did not have a statistically significant effect on change in NT-proBNP level at 12 weeks but was well-tolerated. Further clinical trials of vericiguat based on the dose-response relationship in this study are needed to determine the potential role of this drug for patients with worsening chronic HF," the authors write.

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