

## ベンペド酸は12週後のLDLコレステロールを低下させる (Abstract 19-LB-20667)

CLEAR:スタチンへの追加治療は高リスク患者における LDL コレステロール降下のもう 1 つの選択肢である

CLEAR: Statin add-on may offer another option for reducing LDL in high risk patients

スタチンに加えベンペド酸を併用した心筋梗塞または脳卒中の高リスク患者は、12 週後の LDL コレステロール値が有意に低かった、と American College of Cardiology's 68th Annual Scientific Session で発表された。12 週の治療後、この試験薬を投与された患者の LDL コレステロール値は、プラセボ群に比べ 17.4% 低かった。このコレステロール値低下は 52 週持続し、重篤な有害事象および筋肉関連副作用を含む有害事象に差はなかった。筆者らは、動脈硬化性心血管疾患の高リスク患者に対し、この薬剤が既存の治療への追加治療の選択肢となり得る、と述べている。

### Full Text

Patients at high risk for a myocardial infarction or stroke who took an investigational drug in addition to a statin had significantly lower LDL cholesterol after 12 weeks compared to similar patients who took a placebo in addition to statin therapy, according to research presented at the American College of Cardiology's 68th Annual Scientific Session.

LDL cholesterol levels in patients who received the investigational drug, known as bempedoic acid, were reduced by 17.4 percent after 12 weeks of treatment and the reduction was sustained at 52 weeks of treatment, compared with patients who received a placebo, with no differences in overall adverse effects, including serious adverse events and muscle-related side effects, said Anne C. Goldberg, MD, professor of medicine at Washington University School of Medicine in St. Louis and lead author of the study.

"These findings—taken together with other recently reported results of large randomized trials of bempedoic acid—indicate that this agent may add to the armamentarium of treatment options for high-risk patients with atherosclerotic cardiovascular disease whose LDL cholesterol remains uncontrolled despite taking a maximally tolerated statin," Goldberg said.

Studies have shown statins to be highly effective at lowering cholesterol levels and reducing the risk of a myocardial infarction or stroke. These drugs work primarily by blocking an enzyme that the liver uses to make cholesterol, but they also inhibit cholesterol production in muscles. Some patients develop muscle pain and must limit the statin dose they take, or in some cases, discontinue taking a statin to avoid this side effect. About 10 percent of patients taking high-dose statins experience muscle pain as a side effect, Goldberg said.

The Blood Cholesterol Guideline published in 2018 by the ACC and the American Heart Association recommends treating patients with atherosclerotic cardiovascular disease (ASCVD) with the highest tolerated dose of a statin, with the goal of reducing LDL cholesterol levels by at least 50 percent.

Bempedoic acid also blocks the liver from making cholesterol, but unlike statins it does not block cholesterol production in muscles. For this reason, Goldberg said, researchers think that bempedoic acid may be less likely than statins to cause muscle pain and thus may promote further reduction of LDL cholesterol levels in patients who must limit their statin doses or not take a statin at all because of this adverse effect.

A total of 779 patients were enrolled in the study. Their average age was 64 years and more than 60 percent were men. At study entry, all patients had LDL cholesterol levels of at least 100 mg/dL and were already taking the highest tolerated dose of a statin. A subset of 77 patients was not able to tolerate any dose of a statin.

In addition to ASCVD, 80 percent of the patients had high blood pressure and 30 percent had diabetes. Six percent had familial hypercholesterolemia, which causes high LDL cholesterol and elevates risk for a heart attack from an early age.

Patients were randomly assigned to take either bempedoic acid 180 mg tablet once a day or an identical placebo tablet once a day as an add-on to the statin they were already taking. Because this was a double-blind study, neither the patients nor their doctors knew which one they received. Two-thirds of the patients received the study drug and one-third took the placebo.

The study's primary endpoint was the percentage change in LDL cholesterol levels after 12 weeks. Patients continued to take the study medications for a year so that researchers could monitor the safety of bempedoic acid and the durability of treatment effects.

At 12 weeks, LDL cholesterol levels had declined to 97.6 mg/dL from an average of 119.4 mg/dL at study entry for patients taking bempedoic acid. Over the same period, LDL cholesterol levels among patients in the placebo group were essentially unchanged (122.8 mg/dL at 12 weeks vs 122.4 at study entry). In the subgroup of patients who were not taking a statin at study entry, LDL cholesterol levels were reduced by 22 percent at 12 weeks.

At one year, patients in the bempedoic acid group had an average LDL cholesterol level of 99.6 mg/dL, while for those in the placebo group the average was 116.9 mg/dL. Major adjudicated cardiovascular events (5-point MACE) were reported by 6.1 percent of patients taking bempedoic acid and by 8.2 percent of those taking the placebo, a non-statistically significant difference, Goldberg said. Rates of worsening diabetes were similar in the two groups.

"The effect of bempedoic acid was durable at one year and we observed no increase in adverse effects from the addition of bempedoic acid to statin therapy," Goldberg said.

Results of a randomized, double-blinded trial involving 2,230 patients, announced in May 2018, found that bempedoic acid reduced LDL cholesterol by 18.1 percent on top of maximally tolerated statin therapy at 12 weeks with no increase in adverse events compared with the placebo arm.

A global randomized, double-blinded, placebo-controlled trial is now underway to determine whether treatment with bempedoic acid decreases the risk of heart attacks, strokes and death from heart or blood-vessel disease in patients who can tolerate less than the lowest approved daily starting dose of a statin. This trial, which will enroll an estimated 12,600 patients in about 30 countries, is expected to be completed in 2022.

This study was funded by Esperion Therapeutics, Inc.

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