アリロクマブは家族性高コレステロール血症のアフェレーシスを減少させる(Abstract 3166)

ODYSSEY ESCAPE：PCSK9阻害薬は家族性高コレステロール血症におけるアフェレーシス治療の必要性を減少させる

ODYSSEY ESCAPE: PCSK9 inhibitor reduces need for apheresis treatment in familial hypercholesterolemia

家族性高コレステロール血症ヘテロ接合体患者は、PCSK9阻害薬アリロクマブを用いることで、高価で時間のかかるアフェレーシス治療の必要性を軽減またはなくすことすら可能となる。アリロクマブ治療患者はプラセボ群患者に比べ、アフェレーシスを75%減らすことができた（$p < 0.0001$）。実際、アリロクマブを使用した患者の63.4%がアフェレーシスを完全にやめることができ（プラセボでは0人）、92.7%は少なくとも半減した（プラセボ群では14.3%）。この第3相ODYSSEY-ESCAPEトライアルの結果は2016年ESC Congressで発表され、同時に*European Heart Journal*に掲載された。

Full Text

Patients who have heterozygous familial hypercholesterolemia (HeFH), a condition that causes abnormally raised low-density lipoprotein cholesterol (LDL-C) levels and premature cardiovascular disease, can significantly reduce or even eliminate their need for expensive and time-consuming apheresis treatments with the PCSK9 inhibitor alirocumab.

Results of the phase 3 ODYSSEY-ESCAPE trial, reported in a Hot Line session at ESC Congress 2016, "suggest a role for alirocumab in the overall management of patients with HeFH undergoing regular lipoprotein apheresis therapy, with the potential to avoid apheresis treatments or delay the requirement for such treatments," said the study's lead investigator Patrick M. Moriarty, MD, from the University of Kansas Medical Center, in Kansas City, KS, USA.

The findings, published simultaneously in The *European Heart Journal*, have exciting implications for HeFH patients, many of whom struggle with weekly apheresis treatments, he explained.

"Being able to reduce or eliminate apheresis would be a major breakthrough for these patients who spend $50,000 to $75,000 a year, and 3-4 hours every 1-2 weeks to clear their blood of excess LDL-C. If our results are confirmed in other studies this could mark a new era for patients with familial hypercholesterolemia who have uncontrolled cholesterol levels and resistance to normal medical management."

The study included 62 HeFH patients from 14 centers in the US and Germany, who were undergoing apheresis either weekly or every 2 weeks.

They were randomized to receive subcutaneous injections of either alirocumab 150 mg (n=41) or placebo (n=21) every 2 weeks for 18 weeks while still continuing their regular lipid-lowering medications (LLT).

Apheresis treatments during the study were scheduled over 2 phases: Until week 6, the rate was fixed according to the patient's established schedule, but was then adjusted between weeks 7 through 18 based on individual needs. If a patient's LDL-C had dropped by 30% or more since the start of the study, apheresis was skipped.

At the end of the study, the alirocumab-treated patients had a 75% greater reduction in apheresis compared to those on placebo (P<0.0001).

In fact, 63.4% of patients on alirocumab eliminated apheresis altogether (compared to none in the placebo group), and 92.7% avoided at least half of the procedures (compared to 14.3% in the placebo arm).

"Reasons why apheresis rates reduced with placebo are unclear, but may reflect individual variation in LDL-C values, perhaps due to changes in diet or adherence to LLT, the small sample size, and the fact that patients were in a supervised clinical trial," noted Dr. Moriarty.

Adverse events were generally not serious, and were similar in both groups (75.6% of alirocumab vs. 76.2% of placebo patients).

"In the future, lipoprotein-apheresis centers may now add alirocumab to a patient's LLT and possibly not have to treat them with apheresis or at least treat them less often," predicted Dr. Moriarty. "Since the drug has already been approved for this patient population (HeFH and high CVD risk) it can be now considered part of standard care for these patients intolerant to other LLT. Both patients and health care providers will all be pleased to know there is potentially easier, more efficient, and less expensive means of treating dyslipidemia in these patients."

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