# 直接的なレニン阻害と心不全

## ALOFTスタディの結果、臨床的に使用可能な初めての経口直接的レニン阻害薬は既存の薬剤で最適に治療されている心不全患者に有望であることが示唆された

ALOFT study suggests that the first clinically available oral direct renin inhibitor has promise for patients with heart failure treated optimally with current drugs

臨床的に使用可能な初めての経口直接的レニン阻害薬aliskirenの有効性、忍容性、および安全性を評価したALOFT（ALiskiren Observation of heart Failure Treatment）スタディの結果、この薬剤が、アンジオテンシン変換酵素阻害薬またはアンジオテンシン受容体拮抗薬およびβ遮断薬で最適に治療されている心不全患者に有望であることが示された、とESCで発表された。この3ヵ月のスタディでは、現在または過去に高血圧を有し血漿中のBNPが100pg/mLを超えているクラスII-IVの心不全患者302人を組み入れた。患者は既に最適の治療をされているかまたは、禁忌のため前述の薬剤を使用していない者に限られた。プラセボと比較しaliskirenは3つの有効性の指標：血漿NT-pro BNP、血漿BNP、尿中アルドステロンをそれぞれ25%、25%、21%低下させた。Aliskirenは過剰な血圧低下や腎障害を引き起こさず、忍容性は良好であった。

## Full Text

The ALOFT (ALiskiren Observation of heart Failure Treatment) study, which evaluated tolerability and safety of the first clinically available oral direct renin inhibitor, shows the drug may benefit patients with heart failure who are already optimally treated with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker and beta-blocker, according to a presentation at the annual meeting of the European Society of Cardiology.

Direct renin inhibitors block the renin-angiotensin-aldosterone system at its first and rate-limiting step. As a result, all downstream products in the cascade are suppressed; additionally, the direct inhibitors are specific for the system. Both properties differentiate these new medications from angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

In the ALiskiren Observation of heart Failure Treatment study (ALOFT), 302 patients with New York Heart Association class II-IV heart failure with current or prior hypertension and plasma B-type natriuretic peptide concentration > 100 pg/mL were enrolled in nine countries. Patients had to be optimally treated with an angiotensin converting enzyme inhibitor or angiotensin receptor blocker and beta-blocker, unless contraindicated or not tolerated. Patients were studied for three months.

Although primarily a safety and tolerability study, a variety of efficacy measurements were made. The first three of these were to study the effect of aliskiren compared with that of placebo, on N terminal pro BNP, BNP and aldosterone.

Compared with placebo, aliskiren reduced three parameters significantly: plasma NT-pro BNP by 25 percent, plasma BNP by 25 percent, and urinary aldosterone by 21percent.

There was also a favorable change in Doppler-echocardiographic measure of left ventricular filling pressure. Aliskiren was well tolerated and there was no significant excess of hypotension or renal dysfunction.

Thus, this first sizeable, placebo-controlled trial with aliskiren, showed favorable neurohumoral and other effects in otherwise optimally treated patients with heart failure.