

## Aliskirenと左室肥大

ALLAYトライアルの結果、直接的レニン阻害薬aliskirenの高血圧を有する過体重患者における左室肥大軽減作用はロサルタンと同等であることが示された

ALLAY trial finds that direct renin inhibitor aliskiren is as effective as losartan in reducing left ventricular hypertrophy in overweight patients with hypertension

高血圧を有する過体重患者におけるaliskirenの左室肥大軽減作用はロサルタンと同等であることが示された、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiologyで発表された。36週間にわたるALLAYトライアルでは比較的控制の良好な高血圧患者でbody mass indexが $25\text{kg/m}^2$ より大きい患者460人を、aliskiren 1日300mg（154人）、ロサルタン1日100mg（152人）、またはaliskiren 300mgとロサルタン 100mg併用投与群（154人）に無作為に割り付けた。全ての患者は血圧が目標値に達するように治療された。左室心筋量は36週までに全ての群の患者において有意に改善した。心筋重量減少は数の上では併用群で大きかったが、その差は統計学的に有意ではなかった。筆者らは、より長期の治療を行うかコントロールの不良な高血圧患者に対して治療を行えば、併用療法により心筋重量軽減効果がより有意に認められる可能性があるが、この仮説を検証するさらなる研究が必要であろう、と述べている。

### Full Text

The direct renin inhibitor aliskiren is as effective as losartan in reducing left ventricular hypertrophy in overweight patients with hypertension, according to a late-breaking clinical trial presented at the meeting of the American College of Cardiology.

The ALLAY (The ALiskiren Left Ventricular Assessment of Hypertrophy) Trial, conducted at 77 centers in eight countries, examined whether aliskiren, alone or in combination with losartan, was at least as effective as losartan in reducing hypertrophy in this patient population.

After screening 1,086 patients, 460 patients with a body mass index greater than  $25\text{ kg/m}^2$  were randomized to one of three treatment arms: aliskiren 300 mg daily (154 patients), losartan 100 mg daily (152 patients), or aliskiren 300 mg daily plus losartan 100 mg daily (154 patients), with all patients treated to blood pressure targets. Treatment with the study drug was continued for 36 weeks.

Researchers compared changes in left ventricular mass index as assessed by cardiovascular magnetic resonance imaging between baseline and 36 weeks. The researchers also looked at changes in left ventricular volumes, 24-hour ambulatory blood pressure and electrocardiographic voltage during the same 36-week period.

Aliskiren was as effective as losartan in reducing left ventricular mass, which improved significantly in all treatment groups after nine months of therapy. The degree of left ventricular mass reduction was numerically greater in the combination arm, but it failed to reach statistical significance.

Aliskiren, either alone or in combination with losartan, was very well tolerated with no differences in adverse events between groups and a very low level of adverse events. There were no increases in hyperkalemia, hypotension or renal dysfunction in patients receiving aliskiren either alone or in combination.

"Aliskiren inhibits the renin-angiotensin-aldosterone axis at the beginning of the cascade. It is likely that patients would derive many of the same benefits from inhibiting the renin angiotensin system at this step as they do with inhibition at more proximal steps in the system," said Scott Solomon, MD, of Brigham and Women's Hospital and Harvard Medical School, and lead author of the study.

"Moreover, inhibiting the renin-angiotensin-aldosterone (RAAS) system with ACE inhibitors or angiotensin receptor blockers results in reflexive rises in plasma renin activity. This provides a rationale for combining a renin inhibitor with another inhibitor of the renin-angiotensin-aldosterone system, as aliskiren has been shown to reduce plasma renin activity either alone or when combined with other RAAS-blocking drugs. Because treatment of hypertension can be difficult, physicians and patients will benefit from additional agents that can not only lower blood pressure, but can affect the end-organ damage that hypertension causes."

"These data suggest that aliskiren, which is the first orally active direct renin inhibitor and is currently approved for treatment of hypertension, is as effective as an angiotensin receptor blocker for reducing left ventricular mass. Along with other recently reported studies with aliskiren showing incremental benefits in reducing abnormal protein excretion in the urine (proteinuria) in diabetic patients and improvements of indicators of heart function in heart failure patients, these data suggest that aliskiren is efficacious for end-organ protection, beyond just blood pressure reduction."

The patients in this study had relatively well-controlled hypertension and thus the overall degree of blood pressure lowering observed was moderate.

"It is conceivable that treating patients with higher blood pressures or for a longer period of time would have resulted in greater left ventricular mass reduction with the combination of aliskiren plus an angiotensin receptor blocker, but this remains to be determined in future studies," he concluded.

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