治験薬は血管形成術中の心筋傷害を軽減する（Abstract＃13-LB-15976）

SELECT ACS: InclacumabはNSTEMI患者のPCI後の心筋傷害を軽減する

SELECT ACS: Inclacumab reduces myocardial damage after PCI in patients with NSTEMI

治験中の抗炎症薬inclacumabの単回投与は血管形成術中の心筋傷害を軽減するとのスタディ結果が第62回American College of Cardiology学会で発表され、同時に*Journal of the American College of Cardiology*に掲載された。SELECT ACS第Ⅱ相試験は非ST上昇心筋梗塞（NSTEMI）を発症した患者530人（年齢中央値61歳）を対象とした。患者は、20mg/kgのinclacumab、5mg/kgのinclacumabまたはプラセボを血管形成術の1時間前に投与される群にランダムに割り付けられた。研究者らはトロポニンIおよびCK-MBを用いて心筋傷害を評価した。20mg/kgの inclacumabを投与された患者においてはプラセボ投与患者と比較し、16時間後のトロポニンI値が22.4%（*P* =0.066）そして24時間後のトロポニンI値が24.4%（*P* =0.05）低かった。CK-MB値はプラセボと比較し、16時間後に16.3%（*P* =0.088）そして24時間後に17.4%（*P* =0.055）低かった。血管形成術後24時間の時点で、プラセボ群では18.3%でCK-MBが 正常上限の3倍以上（多くの臨床試験で血管形成術後心筋梗塞を定義するのに用いる閾値）に上昇していた。これと比べ高用量のinclacumab投与患者におけるその割合は8.9%であった（*P* =0.051）。5mg/kgの用量は有効性のエンドポイントにおいて有意な効果は示さなかった。

Full Text

A single dose of an investigational anti-inflammatory drug, inclacumab, reduced myocardial damage during angioplasty in a study presented at the American College of Cardiology's 62nd Annual Scientific Session and simultaneously in the *Journal of the American College of Cardiology.*

In this trial, researchers compared a single dose of inclacumab administered one hour before angioplasty with a placebo. Inclacumab is a human monoclonal antibody that blocks p-selectin, a molecule found in platelets and the cells that line blood vessels. P-selectin is activated in response to inflammation, which can ultimately lead to tissue damage. The study met its primary endpoint: decrease in levels of troponin I, a protein found in the bloodstream when heart damage has occurred, after angioplasty.

"Our hypothesis was that by using the p-selectin antagonist inclacumab, we'd be able to demonstrate vascular benefit," said Jean-Claude Tardif, M.D., director of the Research Centre at the Montreal Heart Institute, professor of medicine at the University of Montreal and the study's lead investigator.

The SELECT-acute coronary syndrome phase II trial involved 530 patients with a median age of 61 experiencing a type of heart attack called non-ST-elevation myocardial infarction or NSTEMI. Patients were randomized to receive an infusion of inclacumab at 20 mg/kg, inclacumab at 5 mg/kg or placebo one hour before angioplasty.

Researchers measured heart damage using two standard molecular markers: troponin I and CK-MB. These markers are used clinically to diagnose myocardial infarction (MI). They were measured at baseline and at eight, 16 and 24 hours after PCI. The co-primary endpoints were the change in troponin I at 16 hours and 24 hours.

In patients receiving 20 mg/kg of inclacumab, troponin I levels dropped 22.4 percent more at 16 hours (P =0.066) and 24.4 percent more at 24 hours (*P* =0.05), compared with patients on placebo. CK-MB levels dropped 16.3 percent more at 16 hours (*P* =0.088) and 17.4 percent more at 24 hours (*P* =0.055), compared with patients on placebo.

Also, at 24 hours after angioplasty, 18.3 percent of patients on placebo had CK-MB increases of more than three times the upper limit of normal, a threshold that many clinical trials use to define a post-angioplasty MI. This compared with 8.9 percent of patients who received the higher dose of inclacumab (*P* =0.051).

The 5 mg/kg dose of inclacumab had no significant effects on the cardiac markers.
Researchers also measured p-selectin levels to see if they correlated with changes in CK-MB and troponin I. Levels did not drop significantly in the group that received 5 mg/kg inclacumab. However, levels dropped 19.2 percent with the 20 mg/kg inclacumab dose, compared with placebo (*P* =0.0002).

"It was exciting to see that a single administration of inclacumab would yield clinical benefit," Dr. Tardif said.

The researchers analyzed a subgroup of patients who were not taking antiplatelet drugs called glycoprotein 2b3a inhibitors. These are given to some patients to prevent blood clots but can increase the risk of bleeding. In patients not taking 2b3a inhibitors, those who received the 20 mg/kg dose of inclacumab experienced a 36 percent decrease in troponin I at 24 hours (P =0.008 compared with placebo).

"If we're able to confirm these results in potential future studies, this drug could become part of the therapeutic armamentarium in modern cardiology," Dr. Tardif said. "You could use this drug more widely, in all patients coming in with heart attacks, although that would require additional large studies."

The trial was sponsored by Hoffman-La Roche, Ltd. Dr. Tardif's institution has received financial support from Hoffman-La Roche.