

## 心筋梗塞後のlosmapimod投与により改善は認めなかった (LBCT 410-14)

LATITUDE-TIMI 60: 抗炎症薬は心筋梗塞後の重大な心血管イベントリスクを低下させない  
LATITUDE-TIMI 60: Anti-inflammatory drug does not reduce risk of major cardiovascular events following myocardial infarction

急性心筋梗塞(MI)で入院した患者において、抗炎症薬losmapimodは12週間の治療期間中の重大な心血管イベントの再発リスクを減少させなかった、と第65回American College of Cardiology年次集会で発表され、同時にJAMAに掲載された。第3相LATITUDE-TIMI 60トライアルにおいて、主要評価項目(心血管死、MI、または緊急冠動脈血行再建術を要する重症再発性心筋虚血の複合評価項目)が12週までに発現したのは、プラセボ群で7%であったのに対し、losmapimod群では8.1%であった。重篤な有害事象の発現率は、losmapimod群で16%であり、プラセボ群では14.2%であった。

### Full Text

Michelle L. O'Donoghue, M.D., M.P.H., of Brigham and Women's Hospital, Boston, and colleagues evaluated the efficacy and safety of the anti-inflammatory drug losmapimod on cardiovascular outcomes in patients hospitalized after a heart attack. The study was published online by JAMA to coincide with its presentation at the American College of Cardiology's 65th Annual Scientific Session.

Inflammation stimulated by the enzyme p38 mitogen-activated protein kinase (MAPK) is implicated in atherogenesis and plaque destabilization. Pilot data in a phase 2 trial in patients with non-ST elevation myocardial infarction (NSTEMI) indicated that the p38 MAPK inhibitor losmapimod lessens inflammation and may improve outcomes.

In this phase 3 trial (LATITUDE-TIMI 60 trial), Dr. O'Donoghue and colleagues randomly assigned patients who had been hospitalized with an acute MI and had at least 1 additional predictor of cardiovascular risk to either twice-daily losmapimod (n = 1,738) or matching placebo (n = 1,765) on a background of guideline-recommended therapy. Patients were treated for 12 weeks and followed up for an additional 12 weeks. The study was conducted at 322 sites in 34 countries. Part A of the trial consisted of a group (n = 3,503) to provide an initial assessment of safety and exploratory efficacy before considering progression to part B (approximately 22,000 patients).

Among the 3,503 patients in part A, the primary end point (a composite of cardiovascular death, MI, or severe recurrent ischemia requiring urgent coronary revascularization with the principal analysis specified at week 12) occurred by 12 weeks in 123 patients treated with placebo (7 percent) and 139 patients treated with losmapimod (8.1 percent). The on-treatment rates of serious adverse events were 16 percent with losmapimod and 14.2 percent with placebo.

The authors write that the results of this exploratory efficacy study did not justify proceeding to a larger efficacy trial in the existing patient population.

"In this trial, losmapimod did not reduce the risk of recurrent major adverse cardiovascular events through 12 weeks of treatment in patients hospitalized with acute MI. Furthermore, there was no evidence that losmapimod reduced the incidence of any secondary outcomes including all-cause mortality. Therefore, our findings do not support a strategy of p38 MAPK inhibition with losmapimod in patients hospitalized with MI."

"Because inflammation is believed to play a key role in atherogenesis, there remains intense interest to identify an anti-inflammatory therapeutic that will reduce the risk of cardiovascular events. However, because inflammation acts along multiple redundant and interconnected pathways, the identification of an appropriate target may be difficult, and it is challenging to predict clinical efficacy prior to phase 3 testing."

This trial was funded by GlaxoSmithKline.

## ACC2016特集

[News01]  
脳画像が扁桃体の活性と心臓発作のリスクを関連付ける

[News02]  
心疾患患者においてうつ病は予後不良と関連している

[News03]  
心疾患疑いの症状は男女で差がない

[News04]  
午睡はメタボリック症候群のリスクを上昇させる

[News05]  
バイスタンダーによるCPRは生存率向上および神経学的転帰が良好であることと関連がある

[News06]  
マンモグラムは心疾患の新たなスクリーニング法となり得る

[News07]  
スタチンの広範な使用がスタディにより支持された

[News08]  
中等度リスクの患者においてTAVRは手術に代わる妥当な代替療法である

[News09]  
PCSK9阻害薬はスタチン不耐性患者のコレステロール値を低下させる

[News10]  
心臓検査における性差

[News11]  
Evacetrapibトライアルは早期中断された

[News12]  
肥満手術の血糖値に対する効果は時間が経過しても持続する

[News13]  
幹細胞治療は心不全の転帰を改善する

[News14]  
院外心停止に対する抗不整脈薬投与が疑問視される

[News15]  
ステント留置を遅らせても臨床的有益性は示さなかった

[News16]  
心筋梗塞後のlosmapimod投与により改善は認めなかった

[News17]  
クライオアブレーションは高周波アブレーションに匹敵する

[News18]  
CABGは心不全患者の寿命を延長させる