

抗凝固薬による出血に対する迅速かつ有効な中和剤(Abstract 5718)

ANNEXA-4: 予備試験の結果において第Xa因子阻害剤は抗凝固作用を迅速に軽減した

ANNEXA-4: Factor Xa reversal agent quickly reduces anticoagulant activity in preliminary results

生命を脅かす可能性のある抗凝固作用を抑制するようデザインされた中和剤は、迅速に作用し忍容性は非常に良好であった、と現在進行中のANNEXA-4スタディの中間解析結果が2016年ESC Congressで発表され、同時に*New England Journal of Medicine*に掲載された。スタディ対象患者は、直接または間接fXa阻害剤投与後、18時間以内に急性大出血を来し緊急の中和作用を必要とした。リバロキサバン投与患者では、静注終了時にはfXa阻害活性がベースラインから89%低下しており、アピキサバン投与患者では同様に93%低下した。12時間後の臨床的止血効果は、79%の患者において"良から優"と評価された。

Full Text

A specially designed antidote to reverse acute, potentially life-threatening anticoagulant-related bleeding worked quickly, and was well-tolerated according to interim results of the ongoing ANNEXA-4 study.

Andexanet alfa reduced anticoagulant activity by roughly 90% within half an hour among patients with acute major bleeding while receiving a factor Xa (fXa) inhibitor, resulting in "excellent or good" hemostasis at 12 hours in most subjects, reported lead investigator Stuart J. Connolly, MD, from McMaster University, in Hamilton Ontario, Canada.

The **AN**dexanet Alfa, a **N**ovel Antidote to the Anticoagulation **E**ffects of **FXa** Inhibitors (ANNEXA-4) study was presented at ESC Congress 2016, with simultaneous publication in *The New England Journal of Medicine*.

"Andexanet is the first specific agent designed for reversal of factor X inhibitors. Although it has been shown to reduce anti-fXa activity in volunteers, until now we did not have experience in acutely bleeding patients. In these patients andexanet reduced the anticoagulant effect of the factor Xa inhibitors and was associated with effective hemostasis in most patients," according to Dr. Mark Crowther, ANNEXA-4 co-principal investigator, also from McMaster University.

The interim results include 67 patients, mean age 77 years, who required urgent reversal of acute major bleeding within 18 hours of receiving either a direct (apixaban, rivaroxaban, edoxaban) or indirect (enoxaparin) fXa inhibitor.

The primary site of bleeding was gastrointestinal 49% of patients, and intracranial in 42%.

For ethical reasons, the study was not randomized, and all patients received andexanet – first in an immediate bolus over 15-30 minutes, followed by a 2-hour infusion. Dosing was based on which fXa inhibitor they had been exposed to, and when.

Patients were assessed at baseline, end-of-bolus, and end of the 2-hour infusion, as well as at 4, 8, and 12 hours, and 3 and 30 days post-infusion.

Among 47 patients included in the efficacy assessment, there was an 89% decrease in anti-fXa activity from baseline to end-of-bolus for those exposed to rivaroxaban (n=26), and a corresponding 93% reduction for those exposed to apixaban (n=20).

At 12 hours, clinical hemostatic efficacy was rated as "good to excellent" in 79% of patients.

Thrombotic events occurred in 18% of subjects during 30-day follow up. "This rate of events is not unexpected considering the thrombotic potential of the patients and the fact that in most of them anticoagulation was discontinued at the time of bleeding and not restarted," said Dr. Connolly.

"This preliminary report of the ongoing ANNEXA-4 study shows us that andexanet rapidly reverses anti-factor Xa activity in acutely bleeding patients and this is associated with excellent or good hemostasis in most."

The study was funded by Portola Pharmaceuticals. Both Dr. Connolly and Dr. Crowther have received research support and fees for consulting and lecturing from Portola Pharmaceutical Co.

Conference News

[News 01]

新規経口抗凝固薬はワルファリンと比べても遜色はない

[News 02]

Nebivololはアントラサイクリン心毒性を予防する

[News 03]

非虚血性心不全におけるICDの延命効果は示されなかった

[News 04]

N-アセチルシステインはMI後の状態を引き上げる

[News 05]

CPAP治療による心血管系の有益性はない

[News 06]

幹細胞静脈内投与の期待されるベネフィット

[News 07]

心臓再生療法のトライアルが新たな知見をもたらす

[News 08]

短期間の抗血小板薬2剤併用療法は有効である

[News 09]

除細動前の抗凝固薬による新たな治療選択肢

[News 10]

冠動脈分岐部病変に対するステント留置技術の比較

[News 11]

STEMIにおいてプラスグレレルとticagrelorの有効性は同等である

[News 12]

機能的画像検査の広範な使用が推奨される

[News 13]

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

[News 14]

伏在静脈グラフトにおいて薬剤溶出ステントはより有効である

[News 15]

光干渉断層法による有益性は小さい

[News 16]

抗凝固薬による出血に対する迅速かつ有効な中和剤