Integrilin Reduces CD-40L Acutely In Patients Undergoing Peripheral Vascular Interventions: Results of the INFLAME Trial

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**ABSTRACT**

Background: Acute inflammatory responses have been described following percutaneous coronary and peripheral vascular interventions (PVI). Gp2b/3a inhibitors have been shown to attenuate this inflammation rise in the coronary patient, but data in patients undergoing PVI is lacking. In INFLAME we hypothesized that integrilin reduces inflammation during PVI when administered in a dose similar to the one approved for coronary interventions (ESPRIT dosing).

**METHODS**

This study is a single center, randomized, open-label study of i.v. integrilin (ESPRIT dosing) and unfractionated heparin (UFH) (60 Units per kg, target ACT 200-300 sec) versus UFH alone (100 Units per kg, target ACT 300-400 sec) in patients undergoing elective iliac and infrapopliteal interventions. Patients were excluded if they had a contraindication to the use of integrilin or were unable to take oral antiplatelet drugs. Patients with thrombocytopenia, creatinine>2.0, undergoing renal interventions, or had a recent cardiac or peripheral intervention within the past one month of randomization were excluded. The primary endpoint of the study was the changes in markers of inflammation (CD-40L, hs-CRP) and thrombosis (F1.2) in the integrilin-UFH group (n=21) versus the UFH group alone (n=21). Baseline markers were obtained after achieving optimal ACT in each group and immediately prior to balloon dilation. Markers were then assayed post dilation at 30 minutes, 2 hours, 18 hours, 48 hours and seven days. The natural logarithmic transformation was used to decrease the level of skewness of the distribution of CD-40L, hs-CRP, and F1.2.

**RESULTS**

After adjusting for baseline values, the Mean ± SE difference in CD-40L (log scale) between the integrilin-UFH group and the UFH group alone was significant at 30 minutes post intervention (-0.628 ± 0.273, 95% CI [-1.182, -0.074], p=0.0274) with the integrilin group reduced CD-40L more significantly than UFH. No statistical differences were seen at the remaining sampling points post intervention for CD-40 L. Also, differences between the two groups were not significant for hs-CRP and F1.2 markers, despite a significant increase in hs-CRP at 48 hours post intervention. Integrilin inhibited 98% of platelets (range 92-100%) after the second bolus administration.

**CONCLUSIONS**

Eptifibatide-UFH combination reduced CD-40L significantly at 30 minutes post balloon inflation during PVI when compared to UFH alone. Future studies are needed to determine whether the acute reduction of CD-40L with the adjunctive use of eptifibatide post PVI will result in a reduction of clinical events in this population group.