BMC Pharmacology

Meeting abstract

The aptamer ARC1779 is a potent and specific inhibitor of von Willebrand Factor-mediated *ex vivo* platelet function in ST-elevation and non-ST-elevation acute myocardial infarction

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from 14th Scientific Symposium of the Austrian Pharmacological Society (APHAR)
Innsbruck, Austria. 21–22 November 2008

Published: 5 November 2008

BMC Pharmacology 2008, **8**(Suppl 1):A54 doi:10.1186/1471-2210-8-S1-A54

This abstract is available from: http://www.biomedcentral.com/1471-2210/8/S1/A54

Background

ARC1779 is an aptamer which blocks the A1 domain binding of the von Willebrand Factor (vWF) A1 domain to platelet glycoprotein (GP) Ib receptors. vWF is increased in the elderly and in the setting of AMI, as reflected in higher vWF levels in circulation and in increased shear-dependent platelet function as measured by the platelet function analyzer (PFA-100) and cone and plate analyzer (IMPACT). Conventional therapy of AMI partially reduces platelet activation and aggregation, but does not address excessive vWF activity or platelet adhesion.

Methods

We studied the *ex vivo* dose response curves for ARC1779 on PFA-100 and IMPACT platelet function tests, agonist-induced platelet aggregation, and vWF ristocetin cofactor activity (vWF:RiCO; free A1 domain sites) of patients with AMI on standard treatment including aspirin and clopidogrel (n = 40), young (n = 20) and elderly controls (n = 20).

Results

AMI patients displayed ~2-fold increased plasma levels of VWF:RiCO as compared to controls. Nevertheless, the IC_{50} and IC_{100} indicate that comparable ARC1779 concentrations were needed in AMI patients and controls to suppress vWF-dependent platelet plug formation under high sheer rates (IC_{50} and IC_{100} for CADP-CT in hirudinized blood: ~1.6 to ~2.8 μg/mL (IC_{50}) and ~2.9 to ~3.9 μg/mL (IC_{100})). Concomitant anti-platelet therapy (aspirin and clopidogrel) in AMI patients could be responsible for this finding. In contrast to GPIIb/IIIa antagonists, ARC1779 did not inhibit platelet aggregation by ADP, collagen or arachidonic acid as measured by impedance aggregometry at concentrations (10 μg/mL) that fully inhibited vWF-dependent platelet function.

Conclusion

ARC1779 potently and specifically inhibits vWF activity and vWF-dependent platelet function, even in the setting of AMI where vWF activity is increased.