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Proof of concept for the anti-von Willebrand factor aptamer ARC1779 in patients with acute thrombotic thrombocytopenic purpura (TTP)

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Background

TTP has a high morbidity and mortality rate despite current standard therapy comprising plasma exchange (PEX). The aim of this prospective, open-labeled clinical trial was to test the safety and efficacy of the anti-von Willebrand factor aptamer ARC1779 added to PEX in patients with acute TTP.

Methods

Seven patients with acute idiopathic TTP received continuous i.v. infusions of ARC1779 (0.001–0.002 mg/kg/min) on top of standard PEX therapy until remission of TTP was induced, or for 14 days, whichever occurred first. ARC1779 concentrations were quantified by a high-performance liquid chromatography/ultraviolet assay, ARC1779 blockade of vWF A1 domains was evaluated with an ELISA kit (REAADS vWF Activity ELISA Test Kit, Corgenix Inc., Westminster, CO, USA), and platelet function was assessed with the platelet function analyzer (PFA-100).

Results

Patients responded to ARC1779 with a rise in platelet counts. One diabetic, hypertensive, elderly patient died on day 6 of myocardial infarction (judged as related to TTP and unrelated to the study drug). In the remaining patients, platelet counts fully normalized after 5 days in one, after 72 hours in another, and within 48 hours in two further patients. ARC1779 was well tolerated and did not induce bleeding in any patient despite severe thrombocytopenia.

Conclusions

ARC1779, given as an add-on to plasma exchange therapy, effectively blocked vWF-platelet binding in idiopathic TTP patients and this was associated with a rapid increase in platelet counts. Whether ARC1779 will improve clinical outcome of TTP patients will be tested in a currently ongoing phase II study.