CASE STUDY: Using human blood vessels to determine dose and time-dependent activity of a novel therapy for renal and vascular diseases

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Background

Proteon Therapeutics Inc. is a privately held biopharmaceutical company developing novel, first-in-class pharmaceuticals to address the medical needs of patients with renal and vascular diseases.

The company is leveraging a unique understanding of tissue remodeling to develop a pipeline of proprietary therapeutics. Proteon Therapeutics' first drug candidate (PRT-201) is in development as a persistent local vasodilator for the improvement of blood flow following vascular surgery procedures.

The Company's initial clinical focus is vascular access for hemodialysis. PRT-201 has received both FDA fast-track and orphan drug designations for hemodialysis vascular access indications.

Collaborations with Biopta

Proteon Therapeutics has collaborated with Biopta for over three years, during which time Biopta's human tissue-based test systems have created dose-response relationships for PRT-201 that have helped inform clinical trial designs and have provided basic information on the activity of PRT-201 in human blood vessels.

Importantly, Biopta's extensive network of tissue suppliers has also allowed the exact type of blood vessels that will ultimately be treated in patients, to be tested functionally *in vitro.* One of the major benefits of this approach is that it allows a much wider range of application times and drug concentrations than is practical *in vivo*.

The Science

Vascular tissue contains abundant elastin that contributes to vessel compliance. PRT-201 is a recombinant human type I pancreatic elastase that has been shown to cleave elastin fibers resulting in increased vessel lumen diameter in animals.

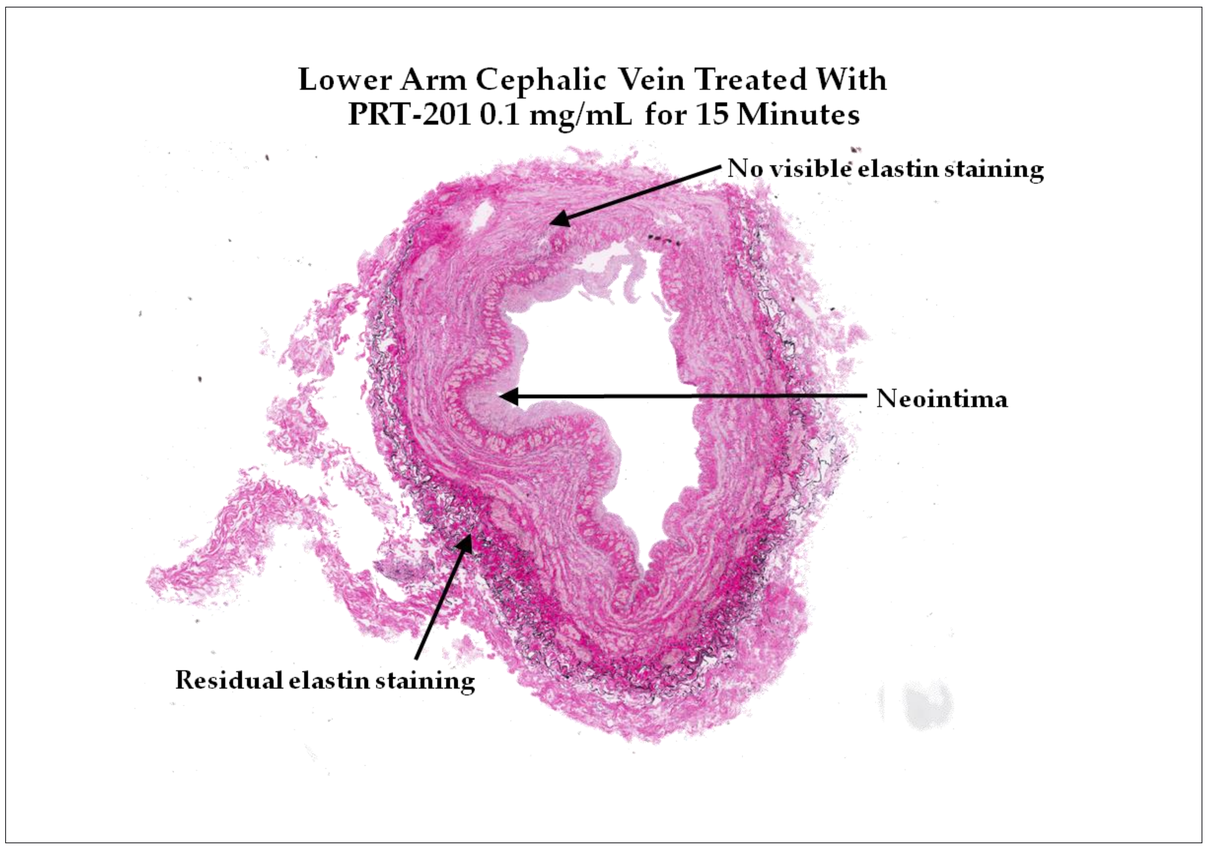
The purpose of the *ex vivo* studies was to determine the elastin content of veins commonly used in hemodialysis access surgery and establish the relative sensitivity of these veins to elastin removal by PRT-201.

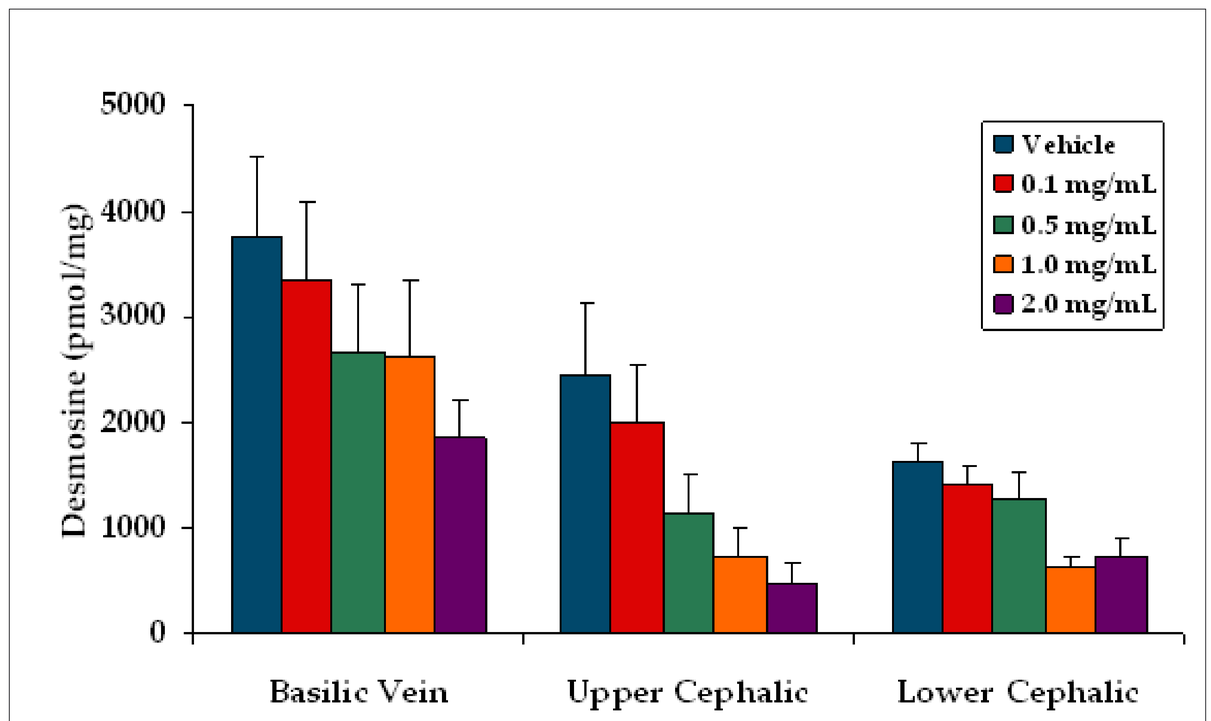
Human upper arm basilic (BV), upper arm cephalic (UAC) and lower arm cephalic (LAC) veins were dissected post mortem from both right and left arms of 3 donors and then cut into rings approximately 2 mm in length. Rings were incubated in the absence or presence of PRT-201 at 37ºC. Elastin content was estimated by quantifying desmosine, a protein cross-link unique to elastin. At baseline, elastin content was greatest in BV and least in LAC rings. In all vein ring types, PRT-201 removed elastin in a time- and concentration-dependent manner (see figure 1 below).

Benefits to Proteon Therapeutics

The present study allowed Proteon Therapeutics to better understand the effects of their drug in relevant human blood vessels.

Steven Burke, M.D., Senior Vice President and Chief Medical Officer of Proteon Therapeutics, said ***"Biopta has provided Proteon with high quality data in human tissue to guide dose selection for human clinical trials. The information has been extremely valuable in demonstrating the potential benefit of PRT-201 in patients needing hemodialysis access or treatment of peripheral arterial disease. The information has and will continue to be an important part of our nonclinical data for regulatory submissions."***





PRT-201 decreased desmosine (elastin) in a concentration and time-dependent manner in all three vein types. Upper arm cephalic veins were most sensitive to PRT-201, reaching > 50% desmosine reduction at a lower PRT-201 concentration and an earlier time point

Summary

In summary, human tissues are a powerful and cost-effective method to predict new drug activity.

If you are interested in how human tissue research can de-risk and accelerate your development, please contact us via:

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