BASIC SCIENCE, ANIMAL MODELS AND PRECLINICAL STUDIES (TCTAP A-023 TO TCTAP A-024)

TCTAP A-023

5-Oxymethyluracil Stimulate Neoangiogenesis in Postinfarction Cardiosclerosis Model in Rabbits

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BACKGROUND To study the effectiveness of pyrimidine-5-oxymethyluracil as a neoangiogenesis stimulator by determining the density of the vascular network and structural changes of the left ventricle in a postinfarction cardiosclerosis model in rabbits.

METHODS The study was conducted on 53 male chinchilla rabbits weighing 2.0-2.5 kg, in which a postinfarction myocardium model was reproduced by ligation of the anterior descending artery at the border of the initial and middle parts. 4 weeks after the operation, all animals were divided into 2 groups as follows: the experimental group (27 animals) received orally 5-oxymethyluracil drug at a dose of 25 mg/1 kg of live weight 3 times a day for 14 days, the control group also consisted of 26 rabbits. Animals were removed from the experiment by Arduan overdosing 2 weeks after the end of the drug administration.

Histological sections were stained with hematoxylin-eosin and pyrofuxin according to Van Gieson. The borderline zone with the scar was evaluated. In each preparation, in five consecutive fields of view with an increase of x400, the number of all vessels was counted, that is arterioles, capillaries, venules, veins and sinuses. Dilation of the left ventricle was assessed by heart sections. The photographed slices were subjected to the Adobe Photoshop computer program. Dilation of the left ventricle was calculated as the ratio of the area of the left ventricular lumen to the area of the myocardium of both ventricles. The results of the left ventricular dilation index were calculated from three sections and the average values were represented.

RESULTS The density of the vascular network and the left ventricular dilation index in groups of animals with and without 5-oxymethyluracil therapy 2 weeks after the end of the drug administration, M± σ is shown in Table 1. (p - statistical significance of the differences between the control and main groups was calculated using single-factor analysis of ANOVA variance).

Indicators	Group		p
	Control, n =26	Main, n=27	
Number of vessels in one field of view (×400)	4.92±1.26	9.40±1.19	<0.0001
LV dilation index, rel. units	0.23±0.07	0.19±0.05	0.0055

CONCLUSION The representative of pyrimidines-5-oxymethyluracil leads to a significant increase in the density of the vascular network in the zone on the border of postinfarction cardiosclerosis by 91% and prevents the remodeling of the left ventricle in the postinfarction cardiosclerosis model in rabbits (the left ventricular dilation index in the main group is 17.2% lower than in the control group).

TCTAP A-024

Hemodynamic Analysis of New Version Mirage Bioresorbable Scaffold and Metallic Ultimaster Stent: A New Era Begins With Shear Stress Analysis in Stent Assessment

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BACKGROUND Optical Coherence Tomography (OCT) based computational fluid dynamic (CFD) studies have provided enormous information for coronary flow behaviors at a detailed level that cannot be attainable using experimental techniques. Stent implantation causes local flow disruptions which can end up in thrombus formation and exuberant neointimal hyperplasia. Restoring vasomotricity and cyclic strain makes bioresorbable scaffold (BRS) glamorous in front of metallic stents. After unprecedented results from Absorb, with circular thinner struts, Mirage seems flashing as an alternative door to knock. In this exploratory analysis, the aim was to compare *hemocompatibility* of Mirage using physiologically realistic CFD techniques using preclinical models.

METHODS We analyzed data from Yucatan mini pigs implanted with 3x18 mm Ultimaster metallic stent (strut thickness:85 μm) (n=6) and 3×18 mm Mirage Bioresorbable scaffold (BRS) (strut thickness: 105 μm) (n=6). In Ultimaster group, 6 coronary arteries were implanted with a single Ultimaster stent in three animals. In Mirage group, six coronary arteries were implanted with a single Mirage BRS in six animals. Study protocol was approved by the Institutional Animal Care and Use Committee of the testing facility (AccelLAB Inc., Canada) and were in compliance with the Canadian Council on Animal Care regulations. Animal husbandry, medication administration, and stent implantation were performed according to standards. OCT was performed before and after scaffold implantation in all treated coronary arteries, using a frequency-domain OCT system (C8-XR OCT Intravascular Imaging System; St. Jude Medical, USA). Coronary artery reconstruction was conducted implementing a validated methodology. In x-ray angiographic and OCT images, the anatomical landmarks (i.e., side branches) and the radiopaque markers identified both on angiography and OCT, were used to define the scaffolded segment and proximal-distal native vessel segments. In the region of interest (ROI), the OCT images portraying the scaffolded and the proximal-distal non-scaffolded native vessel segments were identified and analyzed at a 100-micron (μm) interval. Two post-procedure end-diastolic angiographic images with at least 25o-angle difference showing the ROI with the table in the isocenter were selected. In these images, the luminal borders were delineated for ROI and processed to extract the luminal centerline which was then used for 3D luminal center line of the ROI. The borders of flow area identified on OCT images were then mounted perpendicularly onto the luminal centerline. Following 3D reconstruction of the coronary arteries, endothelial shear stress (ESS) was quantified using Newtonian steady flow simulation in each cross-section in 5-degree subunit (sector) of the circumferential luminal surface in CFD models. Mixed effects models have been implemented for statistical analysis.