Title of the project: Study of cardioprotective effects of ACE-inhibitor, dexrazoxane and its novel derivatives against chronic anthracycline cardiotoxicity in rabbits.

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Summary of 2017 results

Title of the presentation:

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Inhibitors of angiotensin-converting enzym (ACEi) are often used to treat cardiac dysfunction induced by anthracycline (ANT) anticancer drugs. Several recent experimental and clinical studies have proposed that they could also serve as cardioprotectants preventing induction of cardiac damage when used prophylactically. Unfortunately, neither of the studies included significant follow-up without ACEi to establish whether these drugs are able to provide true long-lasting cardioprotection similarly like dexrazoxane or they merely modulate the clinical manifestation of the cardiotoxicity symptoms. The present experimental study was undertaken to clarify this point. Chronic ANT cardiotoxicity was induced in rabbits by daunorubicin (DAU, 3 mg/kg, once weekly for 10 week DAU). The combination group received daily perindopril (PER) in two doses (0.1 and 0.05 mg/kg, selected from previous experiments) orally in drinking water. The treatment started one week before 1st DAU dose and continued till the last DAU dose. At the end of the treatment period (11th week), the animals were randomized for the termination of the experiment and for 3 week drug-free follow up (FU). Vast majority of evaluated parameters (mortality, LV function, histological, biochemical and molecular data) suggested marked improvement induced by ACEi during whole treatment period. However, most of the data showed gradual deterioration during drug-free FU period; the increase of ACEi dose did not have a positive impact on this finding. These data are clearly different from those we have previously obtained with clinical cardioprotectant dexrazoxane, but it remained unclear whether this trend would continue further or not. Hence, in other set of experiments, which are currently underway, we have performed the same study with significantly longer (11 week) FU. The FU period was scheduled to be either completely drug free or with continued ACEi treatment with drug withdrawal 3 weeks before the end of the study. Supported by GAUK 680216.

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