## 7 Summary


**Effects of the $A_1$-adenosine receptor antagonist SLV320 on the progression of interstitial myocardial fibrosis in a model of 5/6-nephrectomized rats**

Patients with kidney disease have a high burden of cardiovascular illness. Uremic cardiomyopathy contains left-ventricular hypertrophy, myocardial interstitial fibrosis and myocardial infarction. Atherosclerosis and anemia are also components.

The treatment of the cardiovascular complications in patients with end-stage renal disease is so far unsatisfactory; these complications are the leading cause of death in this population.

Myocardial interstitial fibrosis is one of the main components of uremic cardiomyopathy and can cause impaired diastolic elasticity, malfunction in cardiac conduction, as well as ischemia with subsquent myocardial infarction.

Adenosine is an endogene-produced nucleoside that occurs in any living cell. In addition to its manifold functions in cellular metabolism this nucleoside plays an important role as a signal transductor in the cardiovascular system.

Via the $A_{2b}$-adenosine receptor, adenosine influences the collagen- and protein-synthesis in cardiofibroblasts.

SLV320 is a selective $A_1$-adenosine receptor antagonist. In this study the effects of SLV320 on the progression of the interstitial myocardial fibrosis in an organism with experimental renal failure were investigated.

The 5/6-nephrectomy model with rats was selected. Young male Sprague-Dawley rats were 5/6-nephrectomized in two steps. Animals for control groups were sham operated: both kidneys were decapsulated. Animals were then randomly divided into groups and given the substance SLV320 or a placebo.

At the end of 12 weeks animals were killed and their hearts and kidneys, or what was left of the kidney, were extracted and preserved in formaldehyde.

Chemical blood tests proved chronic renal failure in the 5/6-nephrectomized rats.

Increased myocardial interstitial fibrosis was found in uremic animals. Enhanced plasma-activity of the enzymes CK, ALT and AST was also found.

Interstitial myocardial fibrosis was significantly reduced in SLV320-treated uremic rats when compared with those that were untreated. Moreover, the plasma-activity of the muscle enzymes was significantly decreased.

The antifibrotic effect of SLV320 may offer a chance to treat an important component of uremic cardiomyopathy. More studies are necessary to clarify whether the effect on the enzymes is independent or dependent on the antifibrotic effect.

The molecular mechanisms with which SLV320 works must be investigated in order to make possible its therapeutic use in the treatment of uremic cardiomyopathy.