**Introduction:** Introduction: Inflammation and angiogenesis are hallmarks of rheumatoid arthritis (RA) that contribute largely to the formation of pannus tissue and joint destruction in patients suffering from RA. We have recently shown that intravenously applied cationic liposomes target efficiently angiogenic endothelial cells in the synovial vasculature of rheumatoid joints and therefore may also serve as potent vehicles for systemic drug delivery and therapy in RA.

Therefore the aim of our study was to demonstrate that EndoTAG-1® (paclitaxel formulated in cationic liposomes) is effectively delivered to the synovial vasculature of knee joints from arthritic mice after systemic application. Furthermore to quantify the anti-angiogenic and anti-inflammatory properties of EndoTAG-1® in the inflamed joints of murine models of RA and to compare the therapeutical efficacy of EndoTAG-1® to Taxol® (paclitaxel in Cremophor EL).

**Materials and Methods:** Methods: Targeting of fluorescently labelled cationic liposomes (LipoRed) and of fluorescently labelled drug oregon-green paclitaxel included in cationic liposomes (EndoOGT) to the synovial vasculature in mice with antigen-induced arthritis (AIA) was analysed by intravital microscopy. Density of functional vessels and adhesion of fluorescently labelled platelets or leukocytes were determined after treatment with EndoTAG-1®. Mice with developing or established collagen type II-induced arthritis (CIA) were treated with EndoTAG-1®. Paws and/or knees were subjected to clinical scoring and histopathological analysis. At the end of the treatment serum levels of the pro-inflammatory cytokines IL-6 and KC as well as the acute phase protein SAA were determined.

**Results:** Results: Enrichment of LipoRed was observed in the vascular bed of the pannus of the diseased joints of CIA animals. EndoTAG-1® treatment of CIA mice with developing or in established disease showed a strong attenuation of the course of the disease as well as a potent anti-inflammatory effect. Histological analysis of knee or paw sections demonstrated a dramatic reduction of the pannus and infiltration of inflammatory cells. Serum levels of the inflammatory cytokines IL-6 and KC and SAA were reduced after treatment with EndoTAG-1® compared with Taxol® and the control group.

AIA mice are characterized by a severe inflammatory reaction induced after immunisation of these mice with methylated BSA and specific delivery of the antigen in the knee. Enrichment of EndoOGT at the synovial vasculature of AIA mice was observed when compared with healthy mice. Treatment of AIA mice with EndoTAG-1® concomitant to disease induction showed a complete remission of the course of the disease as shown by a significant decrease of clinical scores [Image_1] compared to both control and Taxol® treated groups. A complete inhibition (98%) of neo-vascularisation was observed in the synovial vasculature of mice with AIA that were treated with EndoTAG-1® whereas Taxol® alone showed only 50% inhibitory effect. Rolling and adhesion of platelets were reduced to 53% (paclitaxel 5%) and 98% (paclitaxel 57%), respectively [Image_2].

**Discussion:** Discussion: Our in vivo data clearly demonstrates that anti-angiogenic and anti-inflammatory activity of EndoTAG-1® contribute to the therapeutical efficacy of this drug in RA. Notably, therapeutic efficacy with EndoTAG-1® was superior to Taxol®. This strongly suggests that systemic delivery of cationic liposomes is very well suited to enrich compounds to rheumatoid joints for therapy and could be a promising treatment option for RA.