



# UNIVERSITÀ DEGLI STUDI DI MILANO

DIPARTIMENTO DI SCIENZE FARMACOLOGICHE  
E BIOMOLECOLARI - DiSFeB

*Direttore: Prof.ssa Monica DiLuca*



Milano, February 02, 2023

Dear Society's Award Committee,

I would like to nominate myself for the “Young Investigator Award for outstanding publications” for the paper entitled “The HDL mimetic CER-001 improves renal function in inherited LCAT deficiency by remodeling plasma lipoproteins and reducing kidney lipid deposits”, published in *Journal of Internal Medicine*.

This manuscript describes the effects of treatment with the HDL mimetic CER-001 in a patient affected by familial LCAT deficiency, a rare recessive disorder of HDL metabolism with no cure. The hypothesis that CER-001 would be beneficial in LCAT deficiency came from our study in a mouse model of disease, showing that treatment corrects the dyslipidemia and more importantly limits renal damage (PMID: 33309714). The results reported in the present manuscript show that CER-001 had beneficial effects on plasma lipoproteins, specifically reducing the abnormal nephrotoxic lipoprotein X. Moreover, despite the extremely compromised renal status of the patient and the quite short duration of treatment, CER-001 was able to slow renal function decline. To identify the mechanisms responsible for the beneficial effects of the drug, we have carried out in vitro experiments with renal cells incubated with patient's plasma collected at different time points. The experiments very strikingly show that plasma collected at baseline leads to cholesterol accumulation in cells, which is significantly reduced when serum collected after CER-001 treatment is used in vitro. Moreover, CER-001 was able in vitro to rescue cholesterol accumulation induced by patient's plasma in podocytes. All these data provide important insights into the mechanism of renal protection by CER-001, which is double: (i) remodeling of plasma lipoproteins thus reducing their nephrotoxicity; and (ii) direct efflux of cholesterol from renal cells.

Our data support the potential use of CER-001 to delay renal disease in Familial LCAT Deficiency, and possibly in other renal disorders characterized by lipid deposit.

I hope this will be considered.

With kind regards,

Chiara Pavanello