	Pool of alirocumab 75/150mg[a] vs ezetimibe (with statins)[b]	Pool of alirocumab 75/150mg[a] vs placebo (with statins)[c]	Pool of alirocumab 150mg vs placebo (with statins)[d]
Alirocumab (n) and Control (n)	Alirocumab (669) vs Control (436)	Alirocumab (693) vs Control (350)	Alirocumab (1601) vs Control (815)
LDL-C, baseline, mmol/L [mg/dL]	2.8 vs 2.7 [109.3 vs 105.0]	3.3 vs 3.4 [129.1 vs 129.9]	3.3 vs 3.2 [126.0 vs 125.4]
LDL-C, absolute level at W24, mmol/L [mg/dL][e]	1.4 vs 2.2 [53.7 vs 83.9]	1.7 vs 3.5 [64.6 vs 133.7]	1.3 vs 3.2 [50.9 vs 121.8]
LDL-C, absolute change to W24, mmol/L [mg/dL][e]	-1.4 vs -0.6 [-53.9 vs -23.6]	-1.7 vs 0.1 [-64.8 vs 4.3]	-1.9 vs -0.1 [-74.9 vs -4.0]
LDL-C, % change to W24[ef]	-48.9 vs -19.3*	-48.6 vs 4.2*	-60.4 vs 0.5*
LDL-C, % change to W12[eg]	-49.2 vs -22.3*	-44.5 vs 4.1*	-
% pts reaching LDL-C goal at W24[h]	78.0 vs 52.4*	75.2 vs 6.4*	79.0 vs 8.4*
Other lipids (% change to W24)			
Apo B[e]	-38.6 vs 15.9*	-40.2 vs 1.0*	-52.2 vs 0.7*
Non-HDL-C[e]	-41.1 vs 17.8*	-41.7 vs 4.7*	-51.1 vs 0.4*
Lp(a)[i]	-27.1 vs -5.3*	-25.0 vs -7.7*	-29.1 vs -4.0 *
Fasting TGs[i]	-13.0 vs -11.2	-8.9 vs 1.4*	-15.3 vs 1.7*
HDL-C[e]	8.1 vs 0.8*	6.6 vs -1.0*	4.1 vs -0.4*
Apo A1[e]	5.6 vs -0.6*	4.0 vs -1.0*	4.1 vs 1.2*

TG=triglyceride; W=week.
All patients in pool of alirocumab vs placebo and ODYSSEY COMBO II were receiving background of maximally tolerated statin ± other LLT; patients in ODYSSEY OPTIONS studies were on commonly used statin doses.
Intent to treat analysis.
[a]Dose was increased from 75 to 150 mg at W12 if W8 LDL-C was ≥1.8 or ≥2.6 mmol/L (depending on CV risk);
[b]Pool of ODYSSEY COMBO II + OPTIONS I + OPTIONS II (NCT01644188 , 01730040, 01730053);
[c]Pool of ODYSSEY COMBO I + FH I + FH II (NCT01644175, 01623115, 01709500);
[d]Pool of ODYSSEY LONG TERM and HIGH FH (NCT01507831, 01617655); [e]LS means from mixed effect model with repeated measures; [f]Primary endpoint for all studies; [g]Only shown for studies with dose increase;
[h]LDL-C goals: LDL-C <1.8 mmol/L (<70 mg/dL, very high risk) or <2.6 mmol/L (<100 mg/dL, high risk); multiple imputation followed by logistic regression; [i]Multiple imputation followed by robust regression. *p<0.0001.

EAS-0710.
GENE THERAPY FOR LIPOPROTEIN LIPASE DEFICIENCY (LPLD): FINAL RESULTS OF 3 PROSPECTIVE GENE THERAPY CLINICAL STUDIES AND 1 RETROSPECTIVE CLINICAL EVENTS ANALYSIS

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Aim: To present final results from 3 prospective gene therapy clinical studies in LPLD, as well as a retrospective analysis of the incidence of disease-related clinical events in the same subjects.

Methods: 27 subjects received 3 different dosages of a LPL gain-of-functiongene cassette packaged into an AAV1 vector ($1x10^{11}$, $3x10^{11}$,and $1x10^{12}$ gene copies/kg) via IM administration to the leg musculature, with or without immune-suppressants. Duration of the 3 prospective studies was 1-5 years. At a median post-treatment follow up of 6 years, an independent, blinded committee analyzed the incidence of pre- vs post-treatment disease-related clinical events (pancreatitis/acute abdominal pain events consistent with pancreatitis).
Results: Expression of LPL protein in muscle biopsies was substantiated using immunohistochemistry (N=17subjects tested; post-treatment range 10- 52 weeks). Similarly, post-prandial clearance of chylomicrons improved significantly compared to baseline (N=5subjects tested; post-treatment range 14-52 weeks). Strikingly, the incidence of post-treatment disease-related clinical events decreased by 40 to 60% compared to an equivalent period prior to the gene therapy. Parallel reductions in hospitalizations and ICU stays were also observed. The most common AE was a local reaction following IM injections. Two deaths have occurred, both unrelated to gene therapy.
Conclusion: A gene therapy treatment approach in LPLD has resulted in sustained expression of the transgene proteinand improved chylomicron clearance. A marked decrease in post-treatment incidence of disease-related clinical events and hospitalizations/ICU stays has been demonstrated. Additional natural history and outcomes data are currently being collected via a world-wide registry for LPLD patients (GENIALL).

Late breaking session: basic and translational research on atherosclerosis

EAS-0869.
TARGETED MOLECULAR IMAGING AND CELL HOMING IN CARDIOVASCULAR DISEASE VIA ANTIBODY-SORTAGGING

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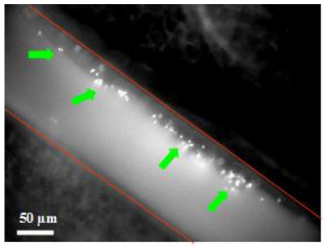
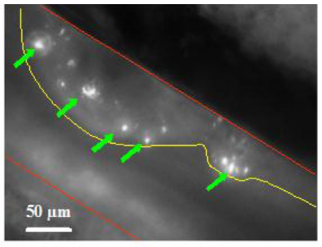


scFv-nanoparticles (white) bound to a small thrombus in a mouse mesenteric artery



scFv-CHO cells (white) bound to a thrombus in a mouse mesenteric vein

Aim: Targeting of contrast agents to unstable atherosclerotic plaques offers the potential to identify such plaques before rupture, allowing suitable interventions and thus avoiding myocardial infarction and death. Similarly, homing of stem cells to disease sites increases the efficacy of regenerative cell therapy while reducing the number of cells required. Currently, targeting can be achieved via chemical conjugation to specific antibodies, which typically results in the loss of antibody functionality and in severe cell damage. An ideal conjugation technique should ensure retention of antigen binding activity and functionality of the targeted biological component (e.g. stem cells). Here we report a novel, gentle, robust, highly reproducible, and site-specific coupling method utilizing the *Staphylococcus aureus* sortase A enzyme to conjugate a single-chain antibody (scFv), anti-GPIIb/IIIa-scFv, to nanoparticles and cells for molecular imaging and stem cell homing in cardiovascular disease.
Methods and results: The conjugation procedure involves chemical and enzyme-mediated coupling steps. The scFv was successfully conjugated to iron oxide magnetic particles (IOMPs), and to model cells. The bioactivity of the scFv after coupling was preserved. The targeting of scFv-coupled cells and nanoparticles to activated platelets was strong and specific as demonstrated in in-vitro static adhesion assays, in a flow chamber system under shear stress and in mouse intravital microscopy. **MR imaging of** atherothrombosis using scFv-IOMPs was also demonstrated in-vitro and in-vivo.
Conclusions: This unique biotechnological approach provides a versatile and broadly applicable tool for procuring targeted regenerative cell therapy as well as targeted molecular imaging in cardiovascular, inflammatory diseases and beyond.