Press release 5

***** Embargoed until 15:00 GMT, March 23, 2015*****

83rd Annual Congress of the European Atherosclerosis Society (EAS)
March 22-25, Glasgow, Scotland, UK

Clinical Latebreaker: High intensity statin therapy does not affect LDL cholesterol lowering with the PCSK9 inhibitor alirocumab

- **In this analysis of more than 4,000 patients, lowering of low-density lipoprotein (LDL) cholesterol with alirocumab was not influenced by background high intensity statin therapy**

LDL cholesterol is the proven lipid target for preventing heart disease and stroke (cardiovascular disease). Inhibitors of PCSK9 (proprotein convertase subtilisin/kexin type 9), a protein which plays a key role in regulating plasma levels of LDL cholesterol, are novel treatments that have been shown to consistently lower LDL cholesterol by 50-60 percent in high cardiovascular risk patients.

However, it is well known that statins also increase plasma PCSK9 concentration. *'In patients treated with high-intensity statins compared with non-high intensity statins, higher plasma PCSK9 levels could be expected, and this could potentially reduce the efficacy of the same dose of PCSK9 inhibitor. This hypothesis was tested in this analysis of six alirocumab trials in more than 4,000 patients,'* commented lead author, Professor Michel Krempf, Head of the Department of Endocrinology, Metabolic Diseases and Nutrition, University Hospital of Nantes, France.

The analysis[1] included 4,166 patients receiving background treatment with a maximally tolerated dose of high intensity statin or non-high intensity statin.[1] Five trials also allowed for non-statin lipid-lowering treatment. All patients were at high cardiovascular risk (18% with heterozygous familial hypercholesterolaemia, inherited high cholesterol). Patients received alirocumab injection (75 mg increasing to 150 mg every 2 weeks if the LDL cholesterol goal was not achieved, or 150 mg every-2 weeks), placebo or the cholesterol absorption inhibitor ezetimibe, in addition to background statin treatment.

Background high intensity statin treatment did not influence the LDL cholesterol lowering response to alirocumab. The least square mean reduction in LDL cholesterol ranged from 47 to 62 percent reduction on high intensity statin treatment versus 35 to 61 percent in those not on high-intensity statin therapy. In the largest trial in this analysis, ODYSSEY LONG TERM (n=2,310 patients), treatment with alirocumab reduced LDL cholesterol by 62 percent in

patients on high intensity statin therapy compared with 61 percent in patients who were not.

A separate analysis evaluated LDL cholesterol goal attainment in eight Phase 3 trials in patients at high cardiovascular risk on statin treatment with or without other lipid-lowering therapy.[2] Patients in these trials were allocated to treatment with alirocumab (75 mg every 2 weeks increasing to 150 mg every 2 weeks at week 12 if LDL cholesterol levels were above guideline-recommended LDL cholesterol goal at week 8, or 150 mg every 2 weeks), placebo or ezetimibe.

At Week 24, alirocumab reduced LDL cholesterol from baseline by 49 percent (75/150 mg every 2 weeks) and by 60 percent with 150 mg every 2 weeks ($p<0.0001$). Across the trials, 75-79 percent of patients achieved LDL cholesterol goal (<1.8 or <2.6 mmol/L).

In both analyses, alirocumab was generally well tolerated. Local injection site reactions, influenza and pruritus were the most common adverse events among alirocumab-treated patients. Commenting on both trials, Professor Anthony Wierzbicki, Consultant in Metabolic Medicine/Chemical Pathology, Guy's and St Thomas' Hospital NHS Trust, London, UK said: '*These data provide further support for the efficacy of PCSK9 inhibitors in significantly lowering LDL cholesterol consistently across all categories of patients and previous therapeutic regimens without any evidence of increased treatment-emergent adverse events.'*

These data add to growing evidence suggesting a future role for these novel treatments to improve the management of patients at high risk of heart attack or stroke who commonly do not achieve LDL cholesterol targets despite best treatment including high intensity statins.

More information:

This latebreaker session will be held on **Monday 23 March, 15:00-16:30.**

Contact:

EAS Press Officer	**EAS Administration Executive**
Dr. Robert Cramb	**Dr. Carmel Hayes**
+44 121 371 5962/+44 7973186206	+46 31 724 27 95 / +46768 61 00 51
Email: Rob.Cramb@uhb.nhs.uk	Email: office@eas-society.org

References

1. Krempf M, Bergeron J, Elassal J, Minini P, Miller K, Kastelein JJP. Efficacy of alirocumab according to background statin intensity and other lipid-lowering therapy in heterozygous

familial hypercholesterolemia or high CV risk populations: Phase 3 subgroup analyses. EAS Congress Glasgow, 22-25 March, 2015. Abstract EAS-0493 45.
[Monday 23 March, 15:00-16:30]

2. Farnier M, Gaudet D, Valcheva V, Minini P, Miller K, Cariou B. Efficacy of alirocumab in heterozygous familial hypercholesterolemia or high CV risk populations: Pooled analyses of eight Phase 3 trials. EAS Congress Glasgow, 22-25 March, 2015. EAS-0563 45.
[Workshop: FH and severe hyperlipidemias. Tuesday 24 March, 15:00-16:30]

Links to references for Editors:

Kotseva K, Wood D, De Bacquer D, De Backer G, Rydén L, Jennings C, Gyberg V, Amouyel P, Bruthans J, Castro Conde A, Cífková R, Deckers JW, De Sutter J, Dilic M, Dolzhenko M, Erglis A, Fras Z, Gaita D, Gotcheva N, Goudevenos J, Heuschmann P, Laucevicius A, Lehto S, Lovic D, Miličić D, Moore D, Nicolaides E, Oganov R, Pajak A, Pogosova N, Reiner Z, Stagmo M, Störk S, Tokgözoğlu L, Vulic D; on behalf of the EUROASPIRE Investigators. EUROASPIRE IV: A European Society of Cardiology survey on the lifestyle, risk factor and therapeutic management of coronary patients from 24 European countries. Eur J Prev Cardiol. 2015 Feb 16. pii: 2047487315569401. [Epub ahead of print]. PUBMED link: http://www.ncbi.nlm.nih.gov/pubmed/25687109

Catapano AL, Reiner Z, De Backer G, Graham I, Taskinen MR, Wiklund O, Agewall S, Alegria E, Chapman M, Durrington P, Erdine S, Halcox J, Hobbs R, Kjekshus J, Filardi PP, Riccardi G, Storey RF, Wood D; European Society of Cardiology (ESC); European Atherosclerosis Society (EAS). ESC/EAS Guidelines for the management of dyslipidaemias The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS). Atherosclerosis 2011;217:3-46. PUBMED link: http://www.ncbi.nlm.nih.gov/pubmed/21882396

END