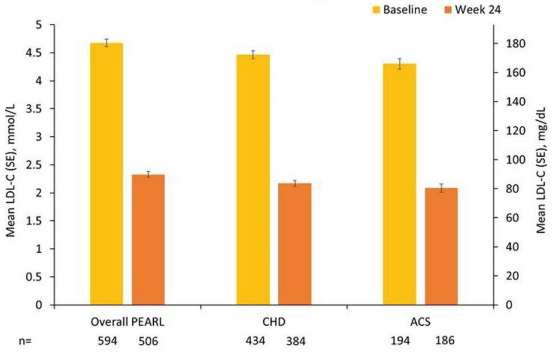
mg/dl×hour vs. 238 mg/dl×hour, p<0.05, respectively), whereas, those of heterozygous carriers were comparable to those with heterozygous FH.
Conclusions: Our results indicate that post-prandial lipoprotein metabolism in sitosterolemia appeared to be impaired, leading to their elevation in serum sterol levels. (UMIN Clinical Trials Registry number, UMIN000020330)

P5382
PEARL, a non-interventional study on real-world use of alirocumab in German clinical practice: final study and cardiovascular subgroup data

K.G. Parhofer[1], B. Von Stritzky[2], W.D. Paar[2]. *[1]University of Munich, Medical Department IV - Grosshadern, Munich, Germany; [2]Sanofi-Aventis Deutschland GmbH, Medical Department, Berlin, Germany*

Background: The updated 2017 ESC/EAS Task Force guidance recommends that PCSK9 inhibitors should be considered for patients with atherosclerotic cardiovascular (CV) disease who are not adequately treated with maximally tolerated statins.
Purpose: The PEARL (Prospektive Nicht-Interventionelle Studie zur Erfassung der WirksAmkeit und VeRträgLichkeit des PCSK9-Inhibitors PRALUENT) study assessed efficacy and safety of the PCSK9 inhibitor alirocumab (ALI) in patients with hypercholesterolaemia in a real-world setting. Here, we present data from the overall PEARL population and from those with coronary heart disease (CHD) or acute coronary syndrome (ACS).
Methods: PEARL was an open, prospective, multicentre, non-interventional study conducted in Germany. Enrolled patients (n=619) had LDL-C >1.81 or 2.59 mmol/L (70 or 100 mg/dL; depending on CV risk) despite maximal tolerated non-ALI lipid-lowering therapies (LLTs), and subsequently received ≥1 dose of ALI 75 or 150 mg every 2 weeks (Q2W) prior to study enrolment. All patients received ALI. ALI dose was adjusted based on physicians' clinical judgment throughout the study (duration: 24 weeks). Data were documented based on case report forms. The primary efficacy endpoint was LDL-C reduction from baseline (LDL-C prior to ALI therapy) to Week 24.
Results: Most patients (72.4%) had a history of CHD and 33.0% were post-ACS. Overall, 45.3% were statin intolerant (unable to tolerate ≥2 statins) and 27.6% were partially statin intolerant (unable to tolerate sufficient statin dose to reach treatment target). Before the start of ALI therapy, 23.5% of patients were on statin therapy only, 47.8% were on LLT (ezetimibe, fibrates and/or bile acid sequestrants) combined with statin, 10.1% were on non-statin LLT combination therapy and 1.9% were on other LLTs; no information was available for 16.7%. In total, 13.7% of patients with CHD and 16.7% with ACS received >1 statin. Overall, initial ALI dose was 75 mg Q2W in 72.9% of patients and 150 mg Q2W in 24.5%, with similar percentages observed for patients with CHD (72.2% and 25.3%, respectively) and ACS (74.3% and 23.8%). Week 24 LDL-C levels are presented in Figure 1. Least-squares mean percentage changes from baseline to Week 24 in LDL-C were –48.6% for all patients, –50.0% for those with CHD and –50.4% for those with ACS. During the study, 20.4% of all patients received dose increase from 75 mg to 150 mg Q2W and 4.0% had a dose decrease from 150 mg to 75 mg Q2W. Similar percentages were seen for patients with CHD (20.5% and 1.8%, respectively) and ACS (19.8% and 2.0%). Treatment-emergent adverse events were reported in 10.3% of patients, with myalgia (7.3%) the most common; 13.4% of patients discontinued therapy.
Conclusions: PEARL showed that, in a real-world setting, ALI significantly reduced LDL-C levels in patients with high CV risk, including those with CHD and ACS. ALI efficacy and safety were consistent with those observed in the ODYSSEY Phase 3 programme.
Funding Acknowledgements: Sanofi and Regeneron Pharmaceuticals, Inc.

Figure 1. Mean LDL-C at baseline and Week 24 for the overall PEARL study population, patients with CHD and patients with ACS (ITT analysis)



ACS, acute coronary syndrome; CHD, coronary heart disease; ITT, intention-to-treat; LDL-C, low-density lipoprotein cholesterol; SE, standard error

P5383
Risk for major adverse cardiovascular events estimated by the TIMI Risk Score for Secondary Prevention TRS2P in patients with coronary artery disease did not impact lipid lowering treatment in clinica

A.K. Gitt[1], D. Lautsch[2], D. Lautsch[2], M. Horack[3], M. Horack[3], C.A. Baxter[4], C.A. Baxter[4], G. De Ferrari[5], G. De Ferrari[5], J. Ferrieres[6], J. Ferrieres[6]. *[1]Herzzentrum Ludwigshafen, Cardiology and Stiftung Institut f. Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany; [2]MSD, Vienna, Austria; [3]Institut f. Herzinfarktforschung Ludwigshafen, Ludwigshafen am Rhein, Germany; [4]Merck & Co., Inc., Kenilworth, United States of America; [5]University of Pavia, Pavia, Italy; [6]Toulouse Rangueil University Hospital (CHU), Toulouse, France*. On behalf of DYSIS-Study Group

Background: Patients suffering from cardiovascular disease are at high risk for future thromboembolic events. The recently proposed TIMI Risk Score for Secondary Prevention (TRS2P) provides an important tool to determine the individual patients' risk for major adverse cardiovascular events (MACE). Little is known if the risk for future MACE might impact the intensity of lipid-lowering treatment and LDL-C target achievement.
Methods: The CHD cohort of DYSIS II included patients from 17 countries of Asia (India, Indonesia, the Philippines, Singapore, South Korea, Taiwan, and Vietnam), Europe (Belgium, France, Greece, Ireland, Italy, and Russia), and the Middle East (Jordan, Lebanon, Saudi Arabia, and the United Arab Emirates) aged ≥18 and with a complete fasting lipid profile. LDL-C goal (<70 mg/dL) attainment and kind of LLTs was documented. We classified the patient population using the TRS2P and examined the quality of care of lipid-lowering treatment (% LDL-C<70mg/dl target achievement) dependent on the risk for MACE. TRS2P can easily be calculated using simple clinical parameters (1 point for each: chronic heart failure, hypertension, age≥75y, diabetes, prior stroke, prior CABG, PAD, eGFR<60, Smoking).
Results: Of the 5370 patients with coronary artery disease 29.3% were at low risk (TRS2P 0/1pts), 37.2% at intermediate risk (TRS2P 2pts) and 33.5% at high risk (TRS2P≥3pts). There were no significant differences in the mean daily dosage of statin treatment or the additional use of ezetimibe between the risk groups. The overall LDL-C-target achievement was 29.0% in the overall population. Patients at high risk (TRS2P≥3pts) were only little more likely to achieve LDL-C target <70mg/dl as compared to intermediate or low risk.
Conclusion: In patients with chronic coronary artery disease treated with statins the risk for future MACE measured with the TRS2P score did not impact the choice or lipid lowering treatment in clinical practice.
Funding Acknowledgements: MSD

P5384
Changes in LDL cholesterol one month after acute coronary syndrome: prognostic implications

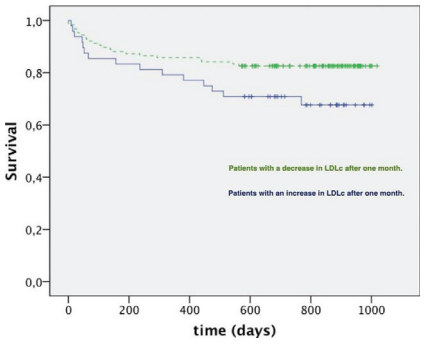
L. Alvarez Roy, T.F. Benito-Gonzalez, M. Rodriguez Santamarta, E. Martinez Paz, E. Tundidor Sanz, L. Garcia Bueno, C. Lezcano Pertejo, G. Flores Vergara, I. Iglesias Garriz, F. Fernandez Vazquez. *Hospital of Leon, Cardiology, Leon, Spain*

Background: Many patients experience increased LDL cholesterol one month after acute coronary syndrome (ACS) despite proper treatment.
Objective: We investigated the clinical implications of an increase in LDL cholesterol one month after ACS.
Methods: We included 174 consecutive patients admitted to our hospital for ACS. Blood LDL cholesterol was measured on admission and one month after the index ACS. Patients who experienced increased LDL one month after ACS were

Abstract P5383 – Table 1

	DYSIS II CHD study arm n=5370	0* n=107 (2.0%)	1* n=1466 (27.3%)	2* n=1995 (37.2%)	3* n=1160 (21.6%)	4* n=441 (8.2%)	5–9* n=201 (3.7%)	P-value[1]
Age [years]	65.6±10.8	61.6±11.5	63.4±11.2	65.4±10.7	66.8±10.4	68.8±9.8	71.0±9.2	<0.0001
Females	21.5% (1155/5370)	12.1% (13/107)	18.1% (265/1466)	21.9% (437/1995)	24.7% (286/1160)	24.7% (109/441)	22.4% (45/201)	<0.0001
Previous MI	55.0% (2875/5230)	33.3% (35/105)	56.2% (814/1449)	54.6% (1067/1955)	52.9% (590/1116)	59.4% (247/416)	64.6% (122/189)	<0.05
Previous PCI or CABG	80.5% (4295/5338)	78.5% (84/107)	77.6% (1133/1460)	77.8% (1535/1973)	83.7% (968/1157)	89.1% (392/440)	91.0% (183/201)	<0.0001
Diabetes mellitus	40.3% (2166/5370)	0.0% (0/107)	1.6% (23/1466)	43.6% (870/1995)	66.6% (773/1160)	74.1% (327/441)	86.1% (173/201)	<0.0001
Chronic renal failure	9.6% (516/5370)	2.8% (3/107)	2.1% (31/1466)	5.0% (100/1995)	13.5% (157/1160)	28.3% (125/441)	49.8% (100/201)	<0.0001
Treated with statin	92.6% (4974/5370)	78.5% (84/107)	92.1% (1350/1466)	92.3% (1842/1995)	94.2% (1093/1160)	94.6% (417/441)	93.5% (188/201)	<0.001
Statin + Ezetimibe	10.4% (560/5370)	11.2% (12/107)	10.0% (147/1466)	10.7% (213/1995)	10.9% (126/1160)	9.3% (41/441)	10.4% (21/201)	0.98
Statin dose (calculated in Atorvastatin, mg/day)	25±19, n=4960	21±13, n=84	26±20, n=1346	25±18, n=1835	25±18, n=1091	25±18, n=417	23±14, n=187	0.54
LDL (mg/dl)	87.7±31.5, n=5370	91.6±36.5, n=107	89.2±31.0, n=1466	87.0±30.1, n=1995	87.7±32.8, n=1160	85.3±32.6, n=441	87.4±35.2, n=201	<0.01
LDL <70 mg/dl	29.0% (1557/5370)	28.0% (30/107)	26.8% (393/1466)	28.6% (570/1995)	29.7% (345/1160)	34.7% (153/441)	32.8% (66/201)	<0.01
Distance to target (LDL <70mg/dl)	31.0±27.3, n=3813	35.5±33.5, n=77	31.2±27.3, n=1073	29.8±25.4, n=1425	31.6±28.8, n=815	31.5±28.5, n=288	34.3±30.0, n=135	0.88

allocated to group I; the remaining patients were allocated to group D. The endpoint of the study was the composite of death of any cause and hospitalization for cardiovascular causes.
Results: Forty-eight patients (28%) experienced increased LDL concentrations (group I). These patients were older (70±12 years vs. 65±12 years, p=0.017), often diabetics (33% vs. 18%, p=0.024) and more likely to have taken lipid-lowering medications before the ACS (63% vs. 29%, p<0.0001). The diagnosis of myocardial infarction was less frequent in group I (64% vs. 80%). The percentage of patients with LDL cholesterol below 70 mg/dL one month after ACS was higher in group I (67% vs. 44%, p=0.009). After a median follow-up of 799 days, Kaplan-Meier curves showed a striking difference in the time to the first primary event (p=0.051). However, the multivariable Cox regression analysis and the joint frailty model to assess recurrent events, revealed no significant differences between groups.



Kaplan-Meier curves.

Conclusion: Although increased LDL one month after ACS is often thought to indicate a poor prognosis, we report that this finding is not associated with outcome after correcting for confounding variables.

P5385
Apoliprotein E genotypes and very long-term outcomes: an unexpected finding regarding diabetes incidence

C. Ferreira[1], M. Oliveira-Santos[1], R. Costa[2], J. Milner[1], R. Baptista[1], P. Dias[2], J. Moura[2], M. Pego[1]. *[1]University Hospitals of Coimbra, Cardiology A, Coimbra, Portugal; [2]University Hospitals of Coimbra, Internal Medicine A, Coimbra, Portugal*

Background: The apolipoprotein E (ApoE) locus and its three common alleles determine six isoforms; the E4 allele is associated with increased cardiovascular (CV) risk, compared with wild-type E3/E3 carriers. Additionally, controversy exists whether these polymorphisms have impact on cancer and diabetes mellitus (DM) incidence.
Purpose: We aimed to investigate the impact of ApoE genotype on CV outcomes, cancer and DM incidence and mortality rate in a Southern European cohort of patients.
Methods: We prospectively included 463 patients treated at the Lipidology Clinic from 1994 to 2007. All patients were genotyped regarding the ApoE locus and were followed for a median (interquartile range) time of 15.1 (12.3–17.4) years. Patients with CV events prior to the first visit were excluded (n=19), as well as patients with E4/E2 genotype (n=8) due to conflicting effects on outcomes. The primary endpoint was a composite of CV mortality, acute myocardial infarction and stroke. The secondary endpoints included all-cause mortality, DM and cancer.
Results: The most prevalent allele was ApoE3 (283 homozygotes), followed by ApoE4 (102 carriers) and ApoE2 (51 carriers). Demographic data was similar between the three groups except for age (p<0.05) and blood pressure (p<0.05). The 10-year CV mortality rate was 1.4%, yielding an intermediate-low risk considering the SCORE CV risk; at follow-up was 1.6%. At 10-year follow-up, no differences were found regarding the primary endpoint incidence for ApoE4 carriers (HR 1.08 (0.45–2.58), p=0.87) or ApoE2 carriers (HR 0.95 (0.28–3.24), p=0.93) versus the wild-type ApoE3. At follow-up, still no significant differences were found for ApoE4 or ApoE2 carriers versus the wild-type ApoE3 (p=0.687 and p=0.89, respectively). DM incidence at follow-up in ApoE3 and ApoE4 carriers (33.5% and 34.4%, respectively) was significantly lower compared to ApoE2 carriers (52.4%, p=0.017). The age-adjusted odds ratio for DM in ApoE2 patients was 1.9 (1–3.78, p=0.049), versus non-ApoE2 carriers. The cancer incidence at follow-up in wild-type ApoE3 carriers was 9.6% and in ApoE4 was 6.8%. Although not reaching statistical significance (p=0.37), ApoE2 carriers had a higher cancer incidence (14.7%). All cause-mortality at follow-up was 9.9%, with no differences found between the three ApoE groups (p=0.52).
Conclusion: In a large, prospective, Mediterranean cohort of patients treated with lipid-lowering therapy with a very long-term follow-up, no interaction was found between ApoE genotypes and CV outcomes, cancer risk or mortality. Interestingly, we found a 2-fold DM incidence in ApoE2 carriers.

P5386
Lipoprotein subclasses and their associations with physical activity, cardiorespiratory fitness and adiposity in Norwegian schoolchildren: the active smarter kids study

P.R. Jones[1], O.M. Kvalheim[2], G.K. Resaland[3], S.A. Anderssen[1], U. Ekelund[1]. *[1]Norwegian School of Sport Sciences, Department of Sports Medicine, Oslo, Norway; [2]University of Bergen, Department of Chemistry, Bergen, Norway; [3]Western Norway University of Applied Sciences, Faculty of Teacher Education and Sports, Sogndal, Norway*

Background: Physical activity (PA), cardiorespiratory fitness (CRF) and adiposity are associated with certain lipoproteins. Research in adults has shown that these associations are not consistent across lipoprotein subclasses.
Purpose: To examine cross-sectional associations in children between objectively measured PA and sedentary time (SED), CRF and adiposity with a number of biomarkers of lipoprotein metabolism.
Methods: We included 1055 healthy fifth-grade (mean age 10.2 yrs) Norwegian schoolchildren (47.4% females). Total PA (tPA), PA intensity (light (LPA); moderate-vigorous (MVPA)), and SED were assessed using triaxial accelerometery. We used the 20-m shuttle run test to assess CRF, and waist circumference to measure abdominal adiposity. We quantified 31 measurements of lipoprotein metabolism including subclass concentrations, and particle size of three major classes (VLDL, LDL, HDL) using nuclear magnetic resonance spectroscopy. We used linear regression (median regression for skewed data) models adjusted for age, sex, sexual maturity and socioeconomic status (standard model). Additional tPA, PA intensity and CRF models were adjusted for adiposity, and additional adiposity models were adjusted for moderate-vigorous PA (MVPA) and CRF separately. An isotemporal substitution regression model quantified associations of replacing 30 minutes LPA or SED with 30 minutes MVPA. We applied a false discovery rate (FDR) adjustment to p-values of each regression model.
Results: Adiposity was significantly associated with all 31 biomarkers in the tPA and MVPA-adjusted models, and 29 biomarkers following adjustment for CRF. CRF was associated with each of the 31 biomarker measures in the standard model and 22 in the adiposity-adjusted model. Total PA, MVPA, LPA and SED were associated with 10, 18, 0 and 5 of the 31 biomarkers, respectively (standard model). The number of significant associations were attenuated after adjusting for adiposity (10, 12, 0, and 0), respectively. Substituting 30 minutes of SED or LPA for MVPA revealed significant associations with 22 and 21 biomarkers, respectively. Following adjustment for adiposity, 10 and 12 associations, respectively remained statistically significant (p<0.05).
Conclusion: CRF is associated with a number of markers of lipoprotein metabolism independent of adiposity. PA, especially of higher intensity, is associated with some of these biomarkers independent of adiposity. Substituting time spent sedentary or in LPA for MVPA shows favourable associations with these biomarkers. This suggests that improving cardiorespiratory fitness and increasing physical activity of at least moderate intensity may favourably affect lipoprotein metabolism in healthy children. Future work should replicate these findings in other cohorts and determine the clinical significance of differences in these biomarkers.
Funding Acknowledgements: The Research Council of Norway

P5387
LDL cholesterol, apolipoprotein B, lipoprotein(a), apolipoprotein CIII and triglyceride lowering by MGL-3196, a thyroid hormone beta selective agonist, in a 12 week study in HeFH patients

J.J.P. Kastelein[1], I.C. Klausen[2], G.K. Hovingh[1], E. Heggen[3], R. Taub[4], G. Langslet[5]. *[1]Academic Medical Center, Vascular Medicine, Amsterdam, Netherlands; [2]Regional Hospital Viborg, Cardiology, Viborg, Denmark; [3]Oslo University Hospital, Preventive Cardiology, Oslo, Norway; [4]Madrigal Pharmaceuticals, Conshohocken, PA, United States of America; [5]Oslo University Hospital, Lipidklinikken, Oslo, Norway*

Background and aims: MGL-3196 is a liver-directed, orally active, selective THR-beta agonist studied in a Phase 2 clinical trial in 116 patients with proven heterozygous familial hypercholesterolemia (HeFH). In Phase 1 studies MGL-3196 reduced LDL-cholesterol (LDL-C), triglycerides (TG) and lipoprotein(a) (Lp(a) and reduced ALT at 12 weeks in Phase 2 NASH patients with baseline elevated ALT. The primary endpoint was reduction in LDL-C compared with placebo and secondary endpoints included effects on additional lipids and lipoproteins.
Methods: MGL-3196–06 is a 12 week multicenter, randomized, double blind, placebo controlled trial in HeFH patients not at LDL-C target on maximally tolerated statins. Patients received MGL-3196 100 mg or placebo once daily (in a 2:1 ratio) in addition to their LDL-C lowering regimen. Based on blinded Week 2 PK, MGL-3196 patients continued on 100 mg or a dose of 60 mg from Week 4–12.
Results: Baseline characteristics: age 57.3; male 52.3%; atorvastatin 80mg, 37.1%; rosuvastatin 20/40 mg 37.1%; moderate or no statin, 25.9%; ezetimibe, 71.6%. MGL-3196 treated patients (intention-to-treat) achieved highly significant (p<0.0001) LDL-C and Lp(a) lowering compared with placebo (Table). LDL-C lowering reached 28.5% compared to placebo in the prespecified group of MGL-3196-treated patients on moderate dose/no statins. Triglyceride (TG) (25–31%) apolipoprotein CIII (Apo CIII) (24%) and ApoB (18.0–20.3%) lowering were observed (p<0.0001). MGL-3196 was well-tolerated. Seven patients did not com-