Of the 12 presentations at the three Hotline sessions of the 26th European Congress of Cardiology, held in Munich, Germany, 27 August–1 September 2004, nine will be summarized here, as the other three have been published in the mean time: the ACTION trial (Lancet 2004;364:849–57), the INTER-HEART study (Lancet 2004;364:937–52) and the A to Z trial (JAMA 2004;292:1307–16). The authors of this summary collected the information given during the presentation of the studies and, therefore, this report only shows preliminary results.

During the first Hotline session, two new studies on prevention and medical treatment were presented.

Dr. T. Lüscher from Zürich, Switzerland presented the ENCORE-2 study: a randomized, placebo-controlled, angiographic and intravascular ultrasound (IVUS) trial, in which the 18–24 months effects of nifedipine gastrointestinal therapeutic system (GITS) 30–60 mg once daily was investigated. In patients with stable angina, a coronary stenosis less than 40% was studied for coronary endothelial function by an intracoronary acetylcholine test and for atheroma volume by IVUS, both at baseline and follow-up. The trial was originally designed to study the effect of cerivastatin and nifedipine GITS, but due to the withdrawal of cerivastatin only the effect of nifedipine was studied. In total, 226 patients were randomized; both groups received lipid lowering medication according to the current guidelines.

The percentage decrease in vasoconstriction over time measured as changes in mean luminal diameter in response to acetylcholine was significantly greater in patients receiving nifedipine as compared to placebo (18.3% and 6.9%, respectively, \( p = 0.0007 \)). The percentage change in atheroma volume showed an increase, but did not differ significantly between nifedipine and placebo (+3.2% and +5.4%, respectively, \( p = 0.59 \)).

This study showed a significant nifedipine induced improvement in acetylcholine-induced vasoconstriction reflecting an improvement of endothelial function, but no significant changes in atheroma volume. These results are in concordance with the outcomes of the ACTION trial with 8000 patients (see above), where less coronary events were observed with the drug in mild stable angina.

Dr. L. van Gaal from Antwerp, Belgium presented the one-year results of the RIO-EUROPE trial: a randomized double-blind placebo-controlled trial comparing rimonabant, a selective cannabinoid receptor 1 (CB1) blocker of the endocannabinoid system, to placebo. In obesity this physiological system, which acts centrally and peripherally to regulate body weight and metabolic processes, is overactivated leading to excessive food intake, accumulation of fat and nicotine dependency.

In total, 1507 obese non-diabetic patients with a mean BMI of 36.6 kg/m² and a mean age of 45 years (80% women, 40% hypertension, 60% dyslipidaemia and 40% metabolic syndrome) were randomized in three parallel groups (rimonabant 5 mg once daily, rimonabant 20 mg once daily or placebo). All patients were on a stringent hypo-calorific diet of 600 kcal/day.

The primary endpoint was absolute weight change at one year, which was significantly greater in patients receiving rimonabant 5 and 20 mg (−3.4 kg for 5 mg, \( p = 0.002 \), −6.6 kg for 20 mg, \( p < 0.001 \), and −1.8 kg for placebo). Furthermore, 39% of the patients treated with rimonabant 20 mg/day lost more than 10% of their initial body weight (\( p < 0.001 \) vs. placebo) compared to 15.3% using 5 mg/day (\( p = \text{ns} \)) and 12.4% in the placebo group. Secondary endpoints such as difference in waist...
circumference, HDL cholesterol, triglycerides, insulin resistance and metabolic syndrome according to the ATP III-criteria improved significantly in the rimonabant 20 mg group. The effect of the improvement of lipid parameters seemed, at least in part, independent of the weight loss. Discontinuation of the medication due to adverse effects was seen in 14.5% of the participants with the highest dose of rimonabant, compared to 9.2% receiving placebo; no relevant cardiovascular side effects were seen.

This selective CB1-blocker is an effective drug for weight loss and seems promising in the prevention of cardiovascular events. Long-term results, side effects and effects on clinical endpoints are eagerly awaited.

The topics of the second Hotline session were acute coronary syndromes and medical treatment of heart disease.

Dr. R. de Winter from Amsterdam presented a multicentre trial from the Netherlands: the ICTUS study, in which 1201 patients (mean 62 years; 75% male) with acute chest pain without ST-elevation, an elevated cardiac troponin T and either ischaemic electrocardiographic changes (>60% of the patients) or a documented history of coronary artery disease were investigated within 24 h of presentation. This high-risk group was randomized to an early invasive treatment (coronary angiography and PCI within 48 h after randomization or CABG as soon as possible) or a selective invasive strategy (initially treated medically according to current guidelines and angiography and revascularization only in case of refractory angina or ischaemia on pre-discharge exercise testing).

All patients received clopidogrel and abciximab in case of early or selective invasive PCI.

In the invasive group, 97% of patients underwent angiography and 73% PCI at a mean of 19 h after randomization, whereas in the selective invasive group these figures were 67% and 47%, respectively, at a mean of 11 days. The combined primary endpoint death, myocardial infarction (MI) and revascularization for ACS was not significantly different between both strategies (21.7% and 20.4%, respectively, p = 0.59). Mortality did not significantly differ either and was surprisingly low (2.2% for early invasive vs. 2.0% for selective invasive, p = 0.86). New or recurrent MI favoured the selective invasive treatment group significantly (14.6% for early invasive vs. 9.4% for selective invasive, p = 0.006), but re-hospitalization for ACS was lower in the early invasive group (7.0%) vs. 10.9% in the selective invasive group (p = 0.017). At one year follow-up there was no significant difference in anginal status between the groups.

In the ICTUS trial, an early invasive strategy in pre-specified troponin positive patients was not superior to a selective invasive strategy. The overall mortality was very low, which is potentially attributable to an optimized medical treatment.

In the JUMBO-TIMI 26 trial Dr. S. Wiviott from Boston, USA studied the platelet ADP receptor blocker prasugrel in a dose-ranging safety study in comparison to clopidogrel in patients scheduled for PCI. In total, 904 low risk patients underwent elective PCI (41% with ACS) were randomized 3:1 to prasugrel in increasing dosages (loading dose 40 mg i.v./maintenance dose 7.5 mg once daily; loading dose 60 mg i.v./maintenance dose 10 mg once daily, and loading dose 60 mg i.v./maintenance dose 15 mg once daily) or standard clopidogrel (loading dose 300 mg orally/maintenance dose 75 mg daily). Eventually 99% of the patients underwent PCI with stenting (54% drug eluting stent) and 70% received GPIIb/IIIa blockers.

With respect to the primary endpoint, significant bleeding according to the TIMI criteria at 30 days follow-up, there was no significant difference between combined prasugrel groups vs. clopidogrel (1.7% prasugrel vs. 1.2% clopidogrel p = 0.77). In the prasugrel groups there was no dose-dependent effect seen. Death, MI, stroke, clinical target vessel thrombosis and severe recurrent ischaemia non-significantly favoured prasugrel (7.2% prasugrel vs. 9.4% in clopidogrel, p = 0.31) without a dose-response effect.

In the aim to develop platelet-inhibitors with higher potency and less inter-patient variability, prasugrel showed to be as safe as clopidogrel. Clinically significant differences in efficacy have to be established in the future by the TRITON TIMI-38 megatrial.

Dr. S. Hohnloser from Frankfurt, Germany presented two multi-centre, placebo-controlled trials on the efficacy and safety of 400 mg b.i.d. dronedarone, a new non-iodinated derivate of amiodarone, in the prevention of recurrent atrial fibrillation or flutter: the European EURIDIS study and the African–Australian–American ADONIS trial. In 1237 patients with a documented paroxysm of atrial fibrillation or flutter in the last three months (612 in EURIDIS and 625 in ADONIS) and with sinus rhythm for at least 1 h at randomization, were randomized to 400 mg b.i.d. dronedarone (n = 828) and placebo (n = 409). None of the patients had severe heart failure or previous ventricular rhythm and conduction disorders.

Time to the first adjudicated recurrence of atrial arrhythmia at one year was the primary endpoint: in EURIDIS the dronedarone relapse was 66% at a mean of 96 days vs. 77% at a mean of 41 days in the placebo group: RR (95%CI) 0.78 (0.64–0.95). In ADONIS, dronedarone relapse was 59% at a mean of 158 days vs. 70% for placebo at a mean of 59 days: RR (95%CI) 0.72 (0.59–0.89). As a secondary endpoint, dronedarone decreased symptomatic arrhythmia recurrence only borderline significance in both trials. The ventricular response rate at recurrence was significantly lower in both studies favouring dronedarone: in EURIDIS 102 beats per minute on dronedarone vs. 118 on placebo, p < 0.0001, and in ADONIS these figures were 105 vs. 117, respectively, p < 0.001.

The treatment emergent adverse events (TEAE) were 9.7% on dronedarone vs. 7.1% on placebo. No excess of death, pro-arrhythmic effects or dysthyroidy was seen.

Dronedarone showed a prolonged time to recurrence of atrial fibrillation and flutter and a lower ventricular rate at recurrence. The rate of prevention of recurrence with dronedarone was rather disappointing. It has a good safety and average tolerability profile at one-year follow-up. Comparison to existing anti-arrhythmic agents and
more safety data especially at long term follow-up are needed.

The SENIORS-study presented by Dr. A. Coats from Sydney, Australia is a randomized double-blind multi-centre placebo-controlled study in 2128 elderly patients (mean age 76 years; 63% male) with clinical congestive heart failure (mean LVEF 36%; 40% NYHA class 3 and 4) randomized to the β-blocker nebivolol, titrated to a maximum dose of 10 mg in 16 weeks, or placebo. The patient population was treated with ACE-inhibitors in 83% of cases and an aldosterone antagonist in 26%. The mean achieved dose was 7.7 mg for nebivolol and 8.5 mg for placebo. The maximum dose was achieved in 65% in the nebivolol group and 76% in the placebo group.

At 36 months follow-up, the combined primary endpoint of all-cause mortality and cardiovascular admission was significant better for nebivolol as compared to placebo (31.1% and 35.3%, respectively, \( p = 0.04 \)). All-cause mortality at 36 months did not differ significantly (15.8% on nebivolol and 18.1% on placebo, \( p = 0.214 \)).

In concordance with other studies demonstrating beneficial effects on mortality and hospitalization of β-blockers in patients with heart failure, this was also seen in this study specifically aimed at an elderly population.

The third Hotline Session presented three studies on inflammation in coronary disease.

Dr. C. Cannon from Boston, USA presented the antibiotic phase of the PROVE IT-TIMI 22. Previous studies have found *Chlamydia pneumoniae* a risk factor for cardiovascular events. This randomized multi-centre placebo-controlled trial studied the effect of long-term usage of quinolone therapy to placebo on clinical outcomes. In total, 4162 patients stabilized for 10 days of acute coronary syndrome received gatifloxacin 400 mg daily for 10 days a month (mean exposure 1.6 years) or placebo.

The combined primary endpoints of all-cause mortality or major cardiovascular events at 30 months of follow-up did not significantly differ (23.7% on gatifloxacin and 25.1% on placebo, \( p = 0.41 \)). Subgroup analyses and the hs-CRP over time showed no statistical significant differences and the outcomes were independent of the baseline antibody titre to *C. pneumoniae*.

Like other studies on antibiotics for coronary disease, no risk reduction in cardiovascular events was again found despite long-term treatment.

Dr. S. Wright from Rochester, USA presented the PRINCESS-trial. In this multi-centre double-blind placebo-controlled trial, 3605 patients with acute coronary syndromes admitted within 6 h of symptoms were randomized to cerivastatin 0.4 mg/day for three months within 48 h from symptom onset or placebo, regardless of baseline lipid values. After three months, both groups received cerivastatin 0.4–0.8 mg/day.

Because of the withdrawal of cerivastatin, the trial was prematurely ended. The endpoint analysis was set at 4.5 months follow-up, which was reached by 44% of the patients. The composite primary endpoint rate of death, MI, stroke, hospitalization for unstable angina or heart failure was not significantly different between the groups. A significant lipid profile improvement was achieved.

Interestingly, in this prematurely stopped, underpowered study on early initiation of lipid therapy, a non-significant early separation of clinical outcome curves was observed.

Dr. J. Grayston from Seattle, USA presented the randomized placebo-controlled double-blind multi-centre, antibiotic ACES-trial. The effect of azithromycin 600 mg once weekly for one year on cardiovascular events in 4012 patients with stable documented coronary artery disease was studied.

After four years of follow-up the composite endpoint of cardiovascular death, non-fatal MI, coronary revascularization procedure and hospitalization for unstable revascularization procedure and hospitalization for unstable angina did not differ between the antibiotic and placebo (22.3% and 22.4%, respectively, \( p = ns \)). All-cause death was not significantly different either (7.1% on azithromycin and 6.6% on placebo, \( p = ns \)). The outcomes were independent of the baseline antibody titre to *C. pneumoniae*. Gastrointestinal adverse events were the most frequent findings in the antibiotic therapy group.

In concordance with PROVE-IT and other earlier antibiotic-trials no clinical effect can be observed from antibiotic treatment in acute, nor chronic, cardiovascular disease.