between quality indicators and hard outcomes were tested using Cox regression adjusting for confounding, reporting hazard ratios (HR) with 95% confidence intervals.

**Results:** Lipid and albuminuria-lowering treatment status were associated with a lower risk of the composite outcome (HR = 0.77 [0.67, 0.88]; HR = 0.75 [0.59, 0.94]). Glucose-lowering treatment status was associated with a lower risk of the composite outcome only in patients with an elevated HbA1c level (HR = 0.72 [0.36, 0.93]). Blood pressure-lowering treatment status was not associated with a risk of the composite outcome. Treatment intensification with glucose lowering but not with lipid-, blood pressure-, and albuminuria-lowering drugs was also associated with a lower risk of the composite outcome (HR = 0.73 [0.60, 0.89]).

**Conclusion:** Treatment quality indicators measuring lipid- and albuminuria-lowering treatment status are valid quality measures because they predict a lower risk of cardiovascular events and mortality in patients with diabetes. The quality indicator measuring glucose-lowering treatment status should only be used for restricted populations with elevated HbA1c levels. Intriguingly, the tested indicators measuring blood pressure-lowering treatment status and treatment intensification with lipid-, blood pressure-, and albuminuria-lowering drugs did not predict patient outcomes. These results question whether all of the currently used and proposed treatment indicators are valid to judge health care and economics.

**Disclosure of Interest:** None declared.

**OC025—REVERSAL STRATEGY IN ANTAGONIZING THE P2Y12-INHIBITOR TICAGRELOR**

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**Introduction:** Patients on antiplatelet therapy have a higher incidence of bleeding complications and reversal of antiplatelet drug effects is an important issue at trauma or emergency departments. For old and conventional anticoagulants, reversal strategies are established. However, there is no experience or recommendation how to antagonize the reversible and highly effective P2Y12-inhibitor ticagrelor and how to restore platelet function after ticagrelor dosing. The aim of the study was to describe an ex vivo model to reverse the effects of ticagrelor and to estimate the optimal quantity of platelet transfusions required to normalize platelet aggregation.

**Patients (or Materials) and Methods:** To normalize platelet aggregation, increasing amounts of autologous platelet-rich plasma (PRP) were added ex vivo to hirudin-anticoagulated blood which was obtained 3 hours after the administration of ticagrelor, by spiking PRP into blood at ratios of 1:10, 1:5, and 1:3. Platelet aggregation was assessed by whole blood multiple electrode aggregometry (MEA; Multiplate®). For interpretation of aggregation, we defined a cutoff level of 40 A.U. as the lower limit of the range. Volunteers above this level were considered to exhibit normal platelet reactivity. Nonparametric tests were used and statistical comparisons were performed with the Friedman ANOVA, and the Wilcoxon test for post hoc comparisons. A 2-tailed P value < 0.05 was considered significant.

**Results:** The strategy to reverse the effect of ticagrelor was tested in 20 healthy volunteers. A clear dose-response was obtained after spiking whole blood with increasing amounts of PRP. After addition of PRP at a ratio of 1:10, platelet aggregation increased to 31 ± 14 A.U. When assuming that 1 apheresis platelet concentrate (200 mL) typically contains a minimum of 2 × 1011 platelets, the ratio of 1:10 corresponds to 0.5 unit of apheresis platelet concentrates. A ratio of 1:5—equivalent to 1 unit of platelet concentrates—increased ADP induced platelet aggregation to 41 ± 14 A.U. Platelet aggregation increased further to 48 ± 18 A.U. following the addition of PRP at a ratio of 1:3, which corresponds to 1.5 units of platelet concentrates. All comparisons were significant at P < 0.01.

**Conclusion:** Platelets dose-dependently improve ex vivo platelet aggregation of subjects after a loading dose of 180 mg of ticagrelor. It is estimated that >2 units of apheresis platelet concentrates will be necessary to completely restore baseline platelet aggregation in the majority of patients. Point-of-care platelet function tests may be suitable tools to verify this concept in emergency patients and to estimate the extent of the reversal and de-risk on an individual patient’s level.

**Disclosure of Interest:** None declared.
OC026—IMPACT OF CIRCULATING LEVELS OF INTERLEUKIN-17 AND CARDIOVASCULAR OUTCOMES IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Introduction and Background: IL-17 pathway is being clinically targeted in immune-mediated diseases, most of which are associated with a significant cardiovascular risk. We investigated the relationship between serum levels of IL-17 and the risk of cardiovascular events in patients with acute myocardial infarction.

Patients (or Materials) and Methods: We used data from patients enrolled in the prospective, multicenter French registry of acute ST elevation or non-ST-elevation myocardial Infarction (Fast-MI, NCT00673036). Of the 374 centers in France that treated patients with acute MI, 223 (60%) participated in the registry. Among these, 100 centers recruited 1029 patients who contributed to a serum bank. Their baseline characteristics were comparable to the overall population of the registry. Written informed consent was provided by each patient. More than 99% of patients were Caucasian. Two-year follow-up was >98% complete.

Results: Serum levels of IL-17 were associated with the risk of all-cause death and recurrent MI at 2 years, with levels of IL-17 below the median indicative of a worse outcome. The impact of IL-17 remained significant after adjustment for known cardiovascular risk factors, CRP, and treatments including statins: hazard ratio (HR) = 1.40 (1.03–1.91); P = 0.03. IL-17 inhibited mononuclear cell adhesion to endothelium and reduced endothelial VCAM-1 expression. Patients with low (below the median) IL-17 levels and high (above the median) soluble VCAM-1 (sVCAM-1) levels were at particularly increased risk of death and MI: adjusted HR = 2.22 (1.32–3.75) compared with the high IL-17/low sVCAM-1 group (P = 0.002).

Conclusion: Low serum levels of IL-17 are associated with a higher risk of major cardiovascular events in Caucasian patients with acute MI. Our results raise possible concern about the use of inhibitors of IL-17 pathway in clinical settings associated with a high cardiovascular risk.


OC027—DUAL REUPTAKE INHIBITOR MILNACIPRAN AND SPINAL PAIN PATHWAYS IN FIBROMYALGIA PATIENTS: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Aims: To determine the activity of the dual-reuptake inhibitor milnacipran (MLN) at the spinal level in patients with fibromyalgia who are drug naïve, and to evaluate its effects in terms of nociception, spinal reflexes, and pain processing in fibromyalgia patients.

Methods: One hundred and seventy-seven (39 placebo, 38 milnacipran all doses) of 80 randomized patients were available for analysis. The absence of influence of sex on the NFR surprisingly contrasted with the dose-dependent analgesic effect observed in MLN-treated patients with an adjusted change difference of –18.4 mm (–30.9; –5.8) in pain reduction between placebo and the maximum dosage (200 mg) MLN groups (P = 0.02). Unchanged depression and anxiety scores confirmed the predominant selectivity of the analgesic effect of MLN on nociceptive pain pathway.

Results: Seventy-seven (39 placebo, 38 milnacipran all doses) of 80 randomized patients were available for analysis. The absence of influence of sex on the NFR surprisingly contrasted with the dose-dependent analgesic effect observed in MLN-treated patients with an adjusted change difference of –18.4 mm (–30.9; –5.8) in pain reduction between placebo and the maximum dosage (200 mg) MLN groups (P = 0.02). Unchanged depression and anxiety scores confirmed the predominant selectivity of the analgesic effect of MLN on nociceptive pain pathway. Self-reported questionnaires consistently reflected the positive effects of MLN on quality of life and psychological well-being. Odds ratio 5.1 for PGIC responders (ie, much/very much improved) was significantly in favor of MLN (P = 0.04).

Conclusion: Milnacipran has a predominantly supraspinal analgesic effect as evidenced by the significant clinical benefits and the absence of changes in the nociceptive spinal reflex threshold. Higher dose was associated with higher pain reduction. Reported analgesia was independent of patients’ emotional status.

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OC028—A NEW PHARMACEUTICAL FORM OF PARACETAMOL: EFFICACY OF TRANSMUCOUS BUCCAL PARACETAMOL IN ACUTE PAIN PATIENTS

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Objective: To determine the efficacy and safety of a new buccal formulation of paracetamol (acetaminophen) versus an oral formulation in the treatment of acute pain.

Methods: A double-blind, randomized, parallel-group study comparing the new buccal formulation of paracetamol to an oral formulation in patients with acute pain. Patients received a single dose of either the buccal or oral formulation of paracetamol. Pain scores and adverse events were recorded at baseline, 30 minutes, and 60 minutes after dosing.

Results: Seventy-seven (39 placebo, 38 milnacipran all doses) of 80 randomized patients were available for analysis. The absence of influence of sex on the NFR surprisingly contrasted with the dose-dependent analgesic effect observed in MLN-treated patients with an adjusted change difference of –18.4 mm (–30.9; –5.8) in pain reduction between placebo and the maximum dosage (200 mg) MLN groups (P = 0.02). Unchanged depression and anxiety scores confirmed the predominant selectivity of the analgesic effect of MLN on nociceptive pain pathway. Self-reported questionnaires consistently reflected the positive effects of MLN on quality of life and psychological well-being. Odds ratio 5.1 for PGIC responders (ie, much/very much improved) was significantly in favor of MLN (P = 0.04).

Conclusion: Milnacipran has a predominantly supraspinal analgesic effect as evidenced by the significant clinical benefits and the absence of changes in the nociceptive spinal reflex threshold. Higher dose was associated with higher pain reduction. Reported analgesia was independent of patients’ emotional status.

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