Update on Prasugrel

Optimising Therapy after ACS / PCI

Christoph Kaiser
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Universitätsspital Basel

Take Home Message

Recommendations for antithrombotic treatment in patients with NSTE-ACS undergoing PCI

Recommendations	Class[a]	Level[b]	Ref[c]
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B	812,825

Recommendations for antithrombotic treatment in patients with STEMI undergoing primary PCI

Recommendations	Class[a]	Level[b]	Ref[c]
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B	812

2014 ESC-Guidelines on myocardial revascularization

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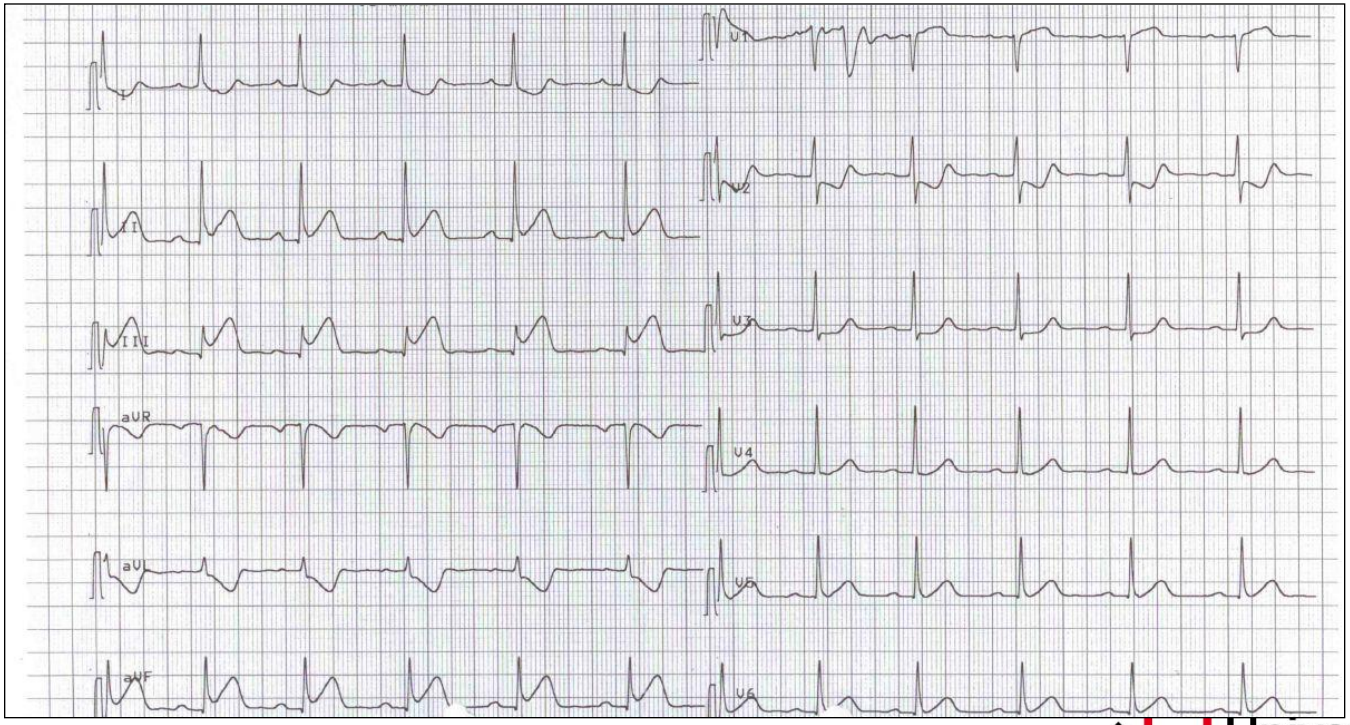
An example….

R.E, male, 30.09.1928

Day 1: acute inferior MI



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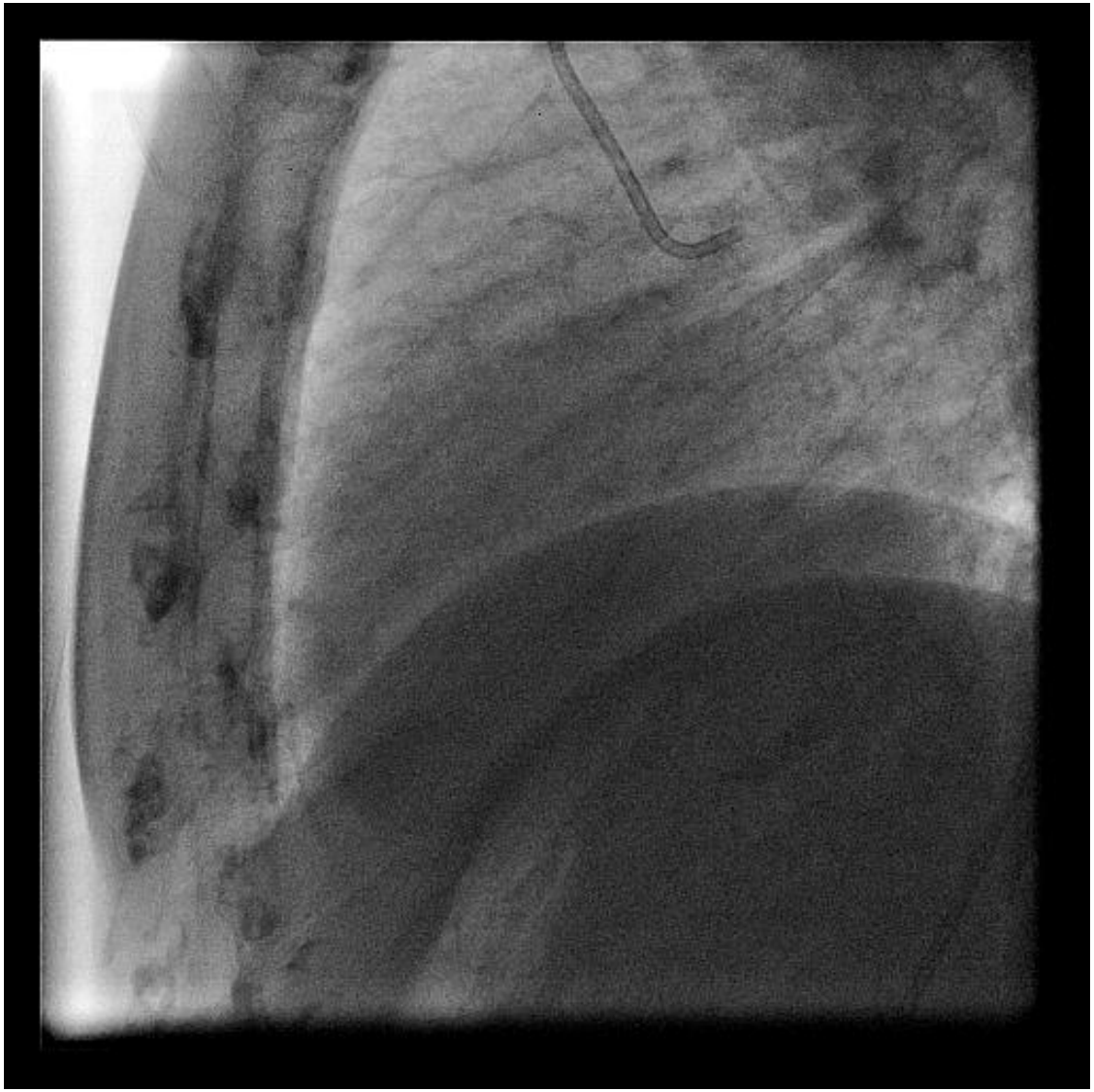

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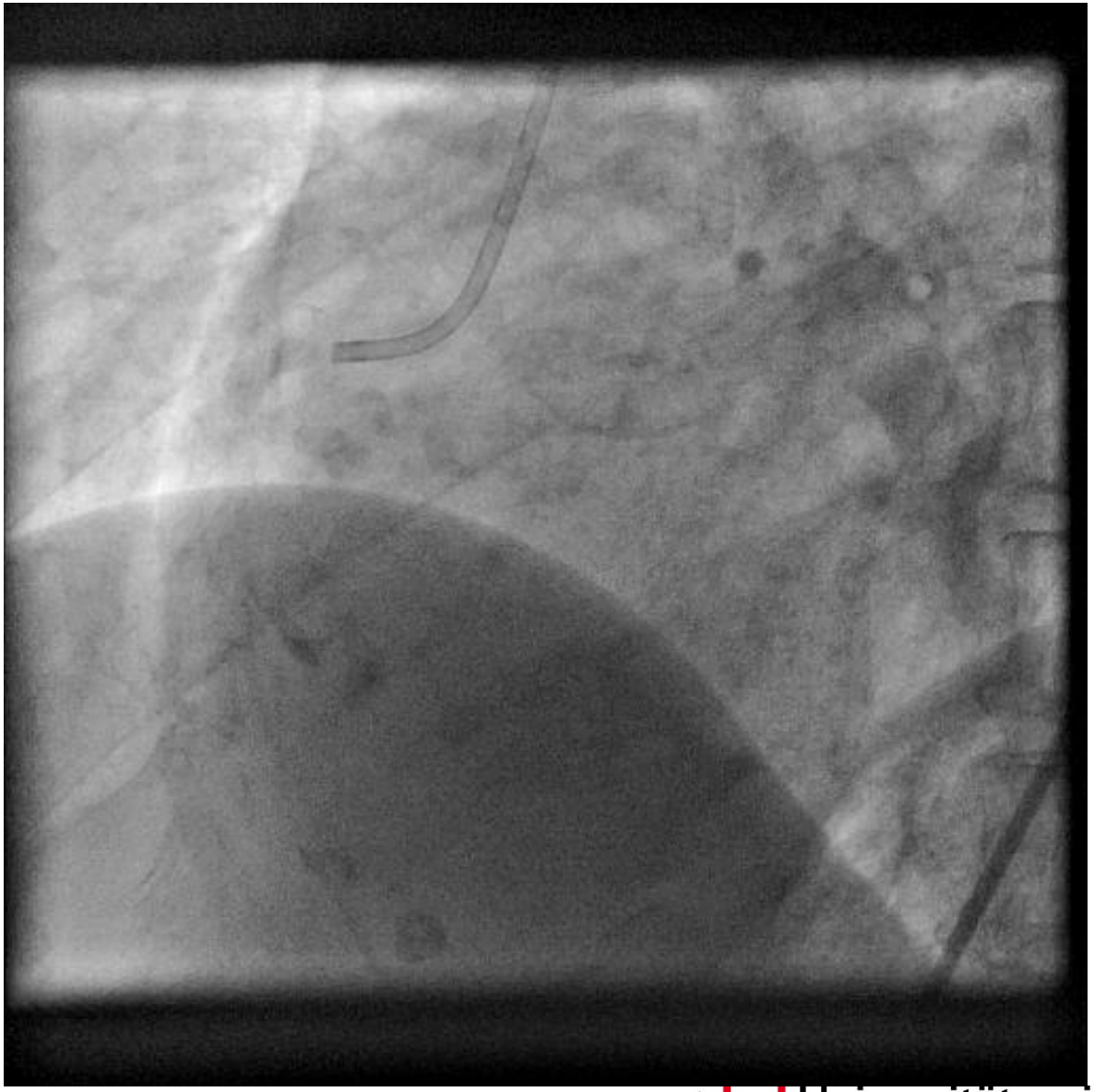
Reo-Pro Bolus

5000 IU Heparin

Thrombusaspiration

3 BMS (3.0 18/28/22mm



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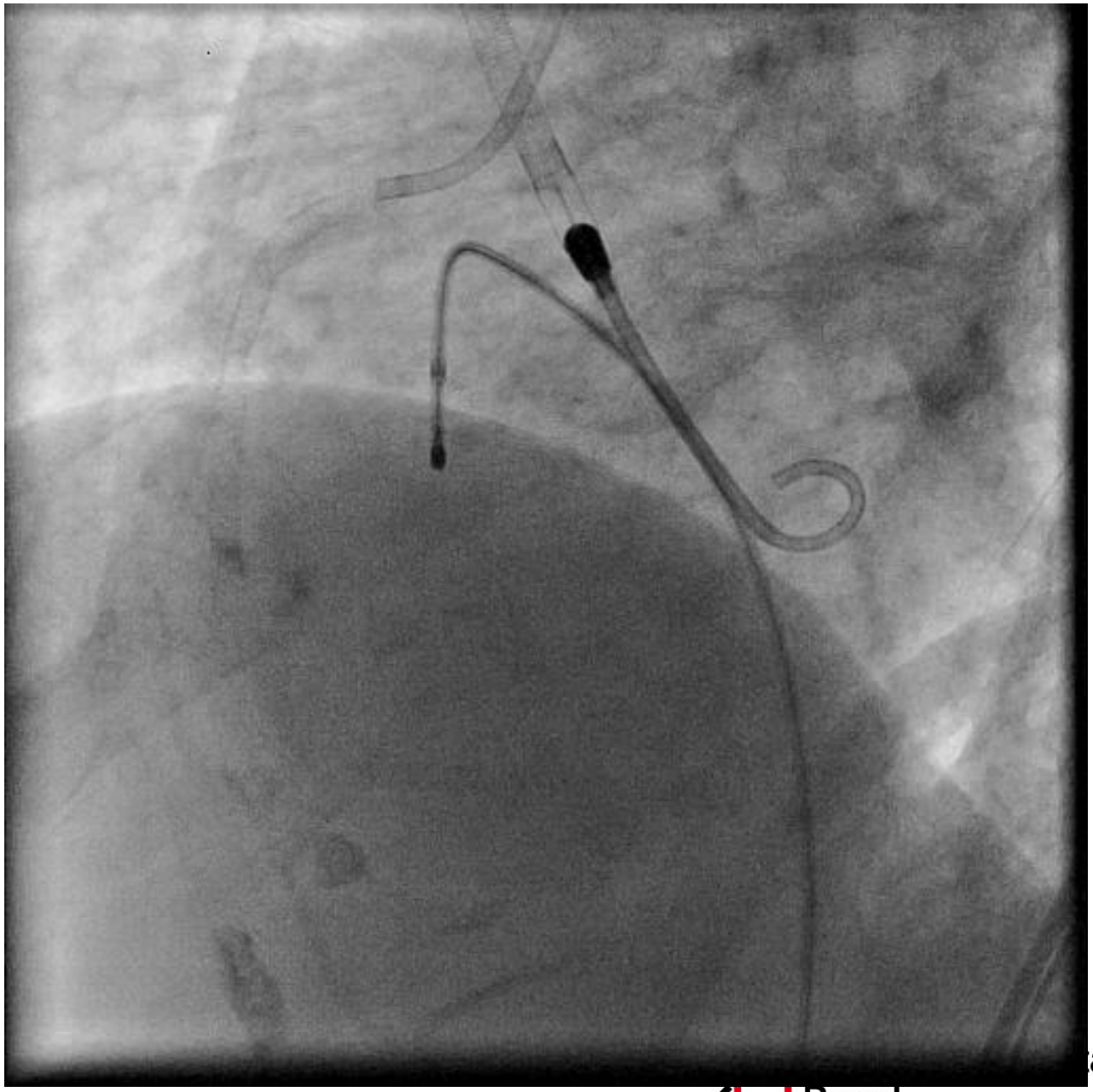
Final result

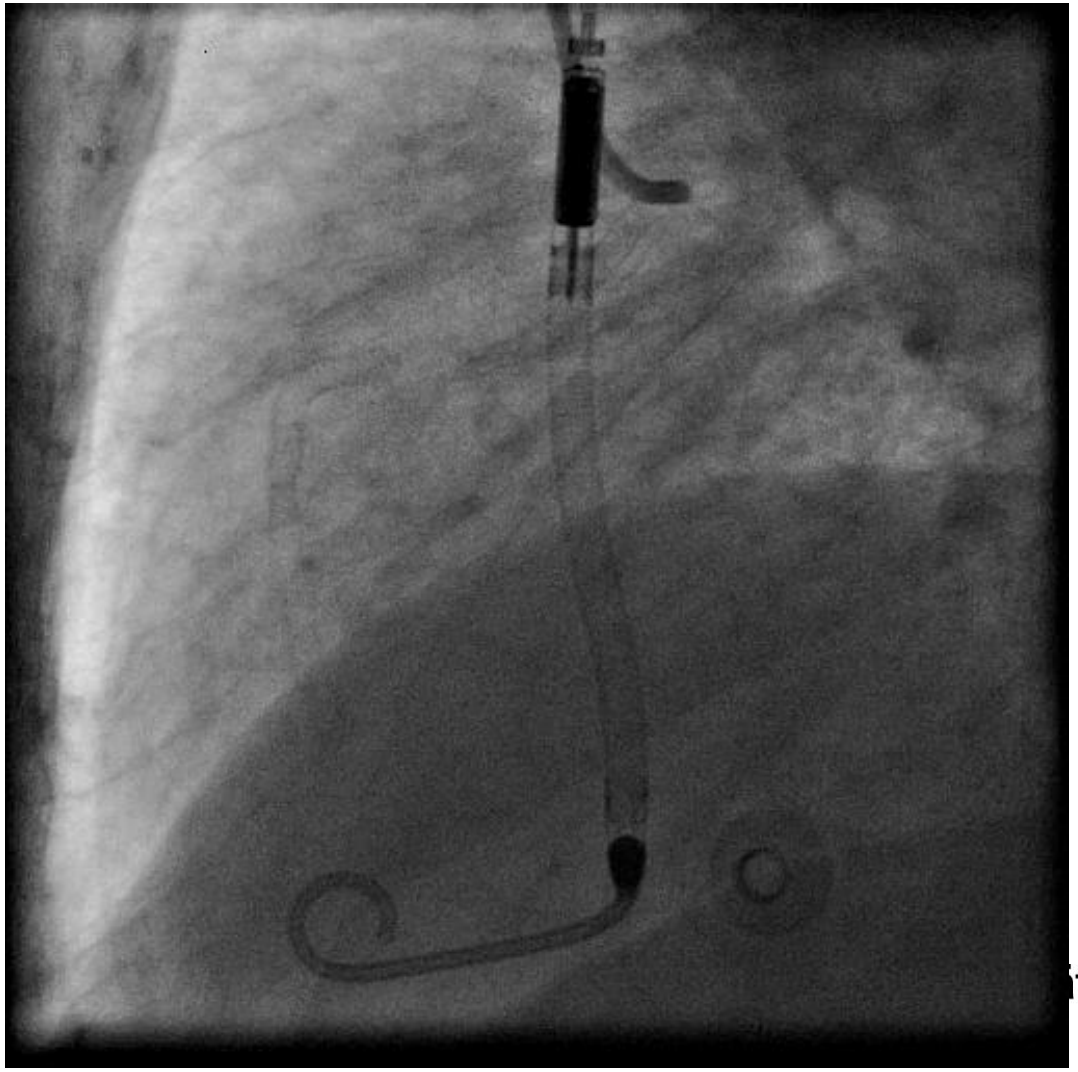
Patient stable with Impella



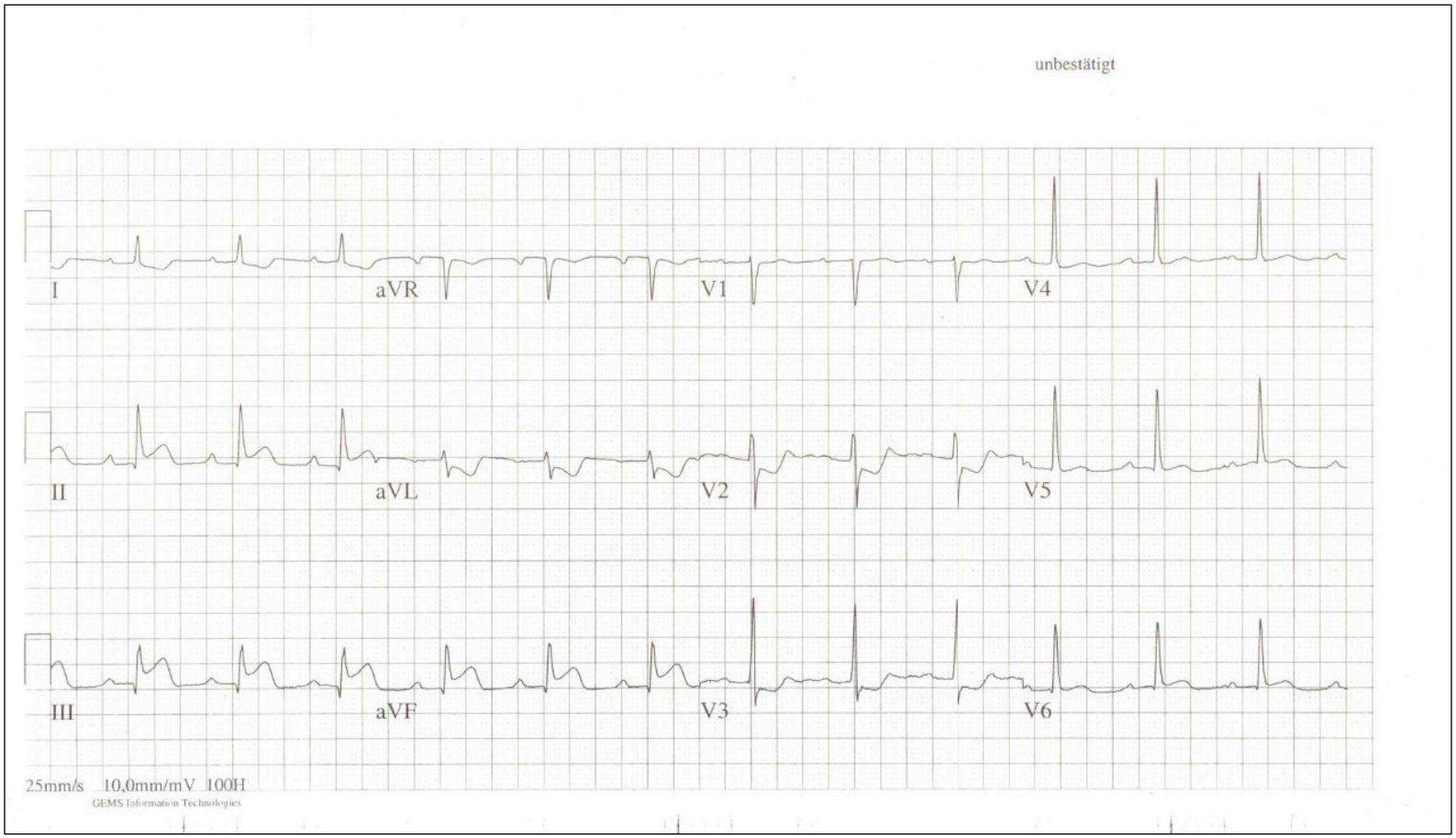
Day 5: **Echo: LVEF 60%, Hypokinesia inferior , PCI LAD**
Pre-Treatment: Heparin, ASS, Clopidogrel

RCA: open

BMS 3,0/18 mm



Day 9: Sudden onset of angina



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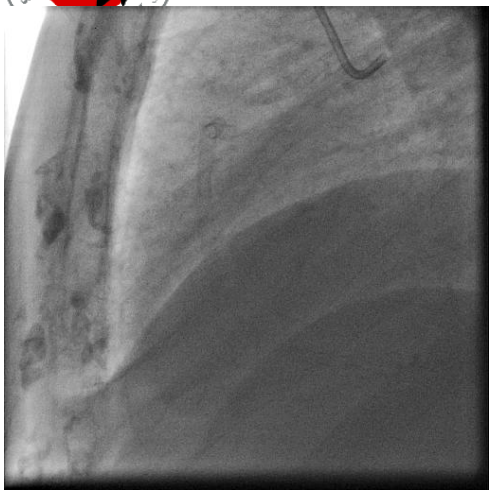
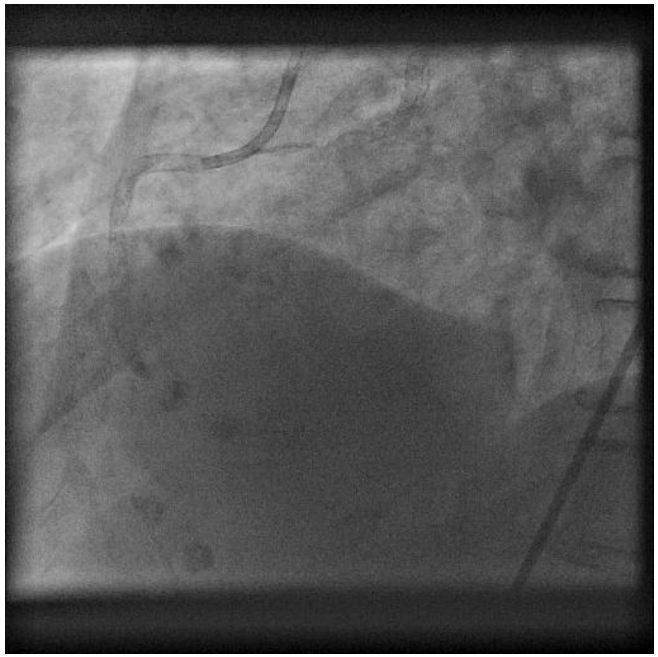
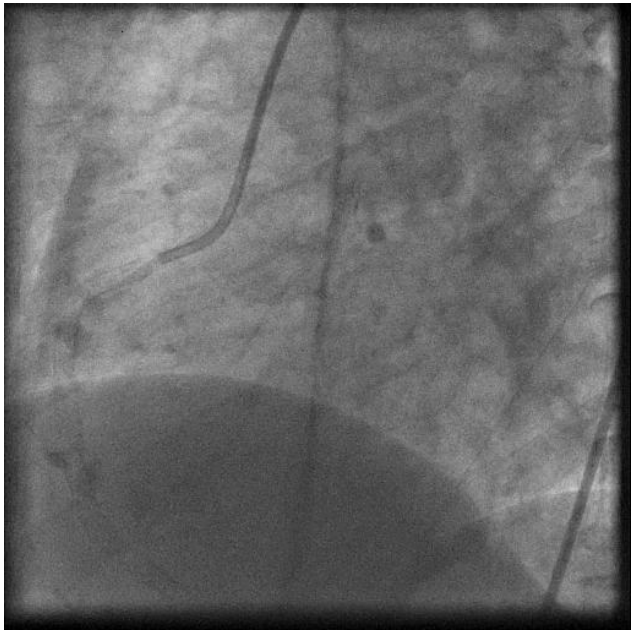
Day 9: Sudden onset of angina





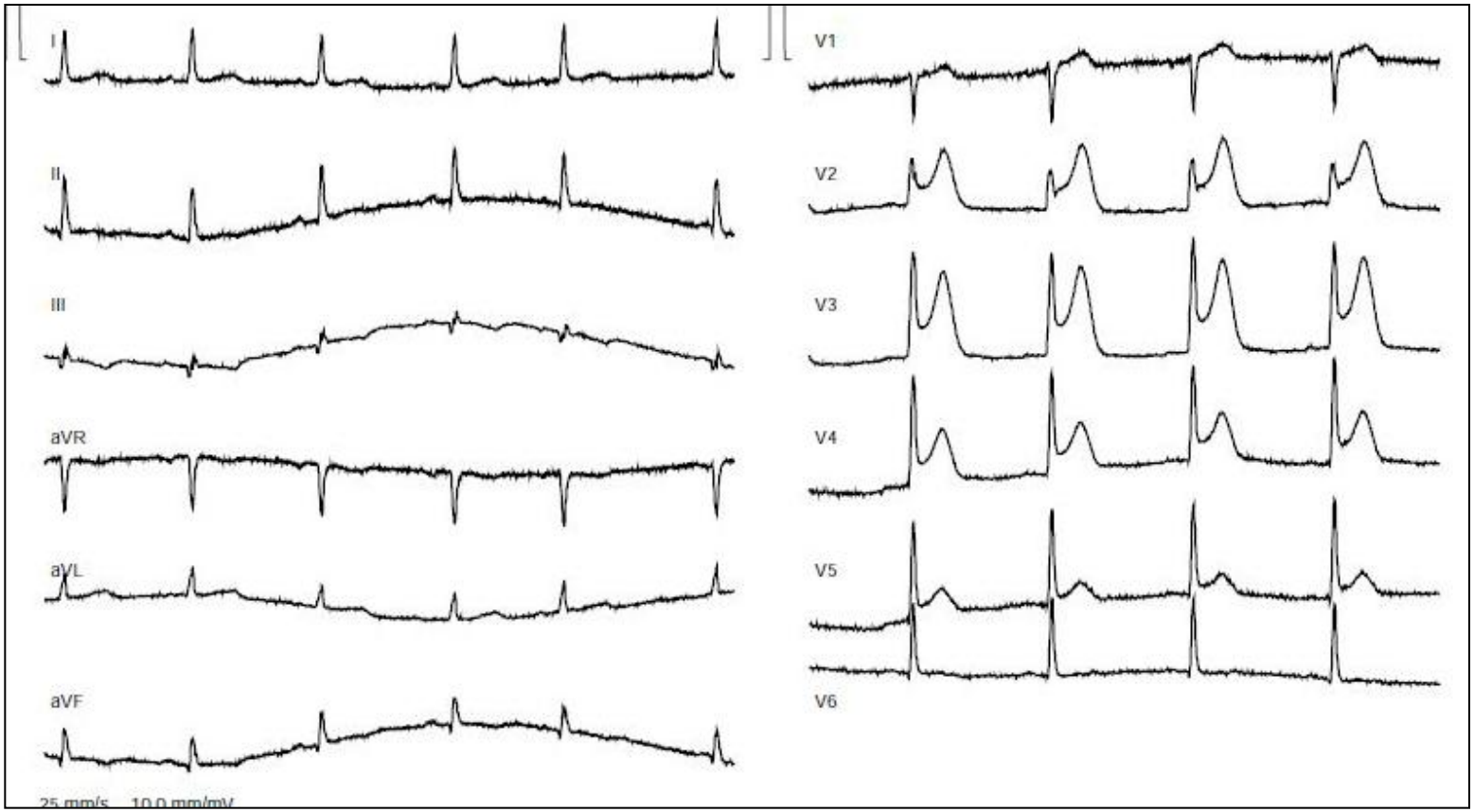


LAD open

RCA with Stent thrombosis

Tirofiban, Thrombusaspiration, 1 BMS

Day 11: Sudden onset of angina



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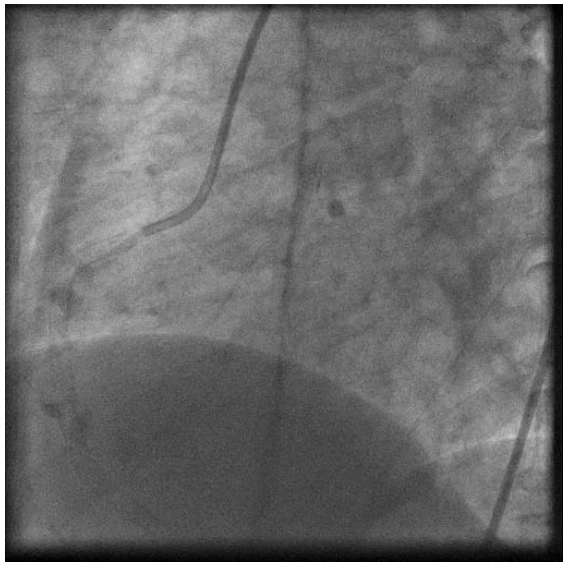
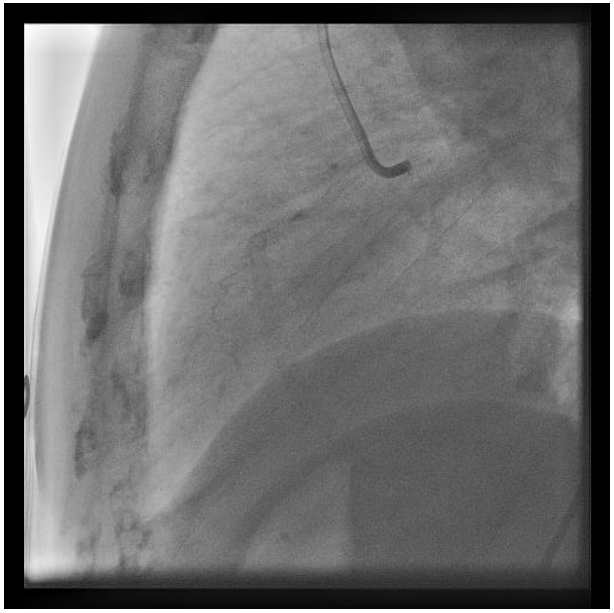
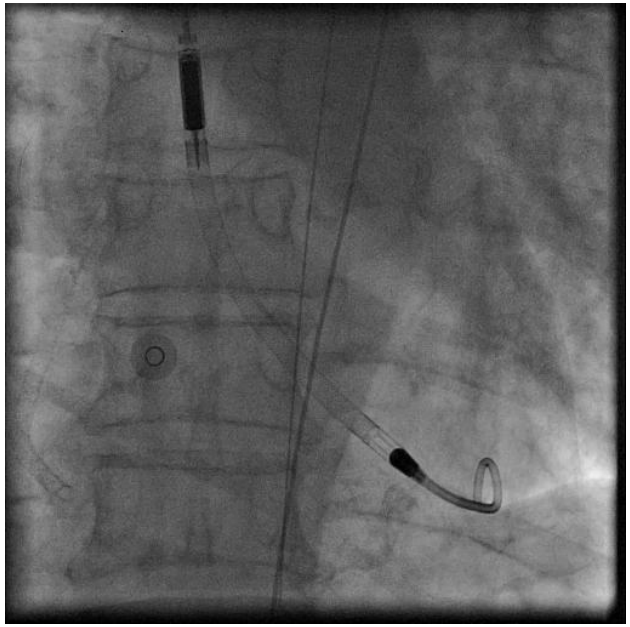
Day 11: Sudden onset of angina







RCA open

LAD with Stent thrombosis

Heparin, Thrombusaspiration, 1 BMS

Day 13: LVEF 40%, Hypokinesia inferior and lateral, akinesia apical

Multiplate® platelet function analysis - V2.01-Build.16 UniSpital Basel / Hämostaselabor

Patienten ID :21617917

Testname :ADPtest (TI-Blut), Version 1

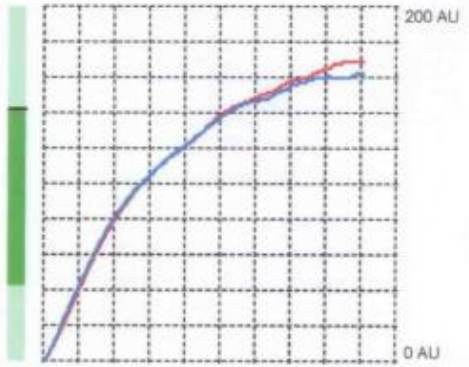
Messung gestartet :22. Nov. 2009, 09:19:56

Area under the Curve :1065 AU*min. (321 - 1059)

Aggregation :RUO: 166.9 AU

Velocity :RUO: 27.1 AU/min.

Base=1526/1494 Ag=170.3/163.5 Vel=26.6/27.7 AUC=1070.0/1061.0 CC=0.999 Abbr. from mean=0.422%



Patienten ID :21617917

Testname :ASPItest (TI-Blut), Version 1

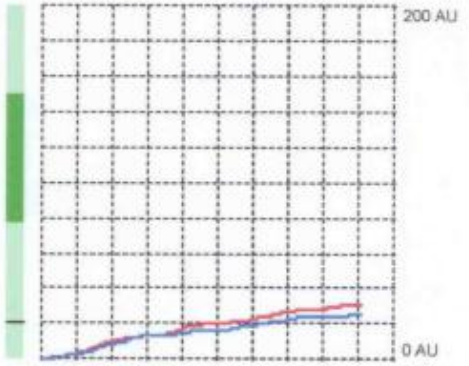
Messung gestartet :22. Nov. 2009, 09:20:15

Area under the Curve :150 AU*min. (583 - 1128)

Aggregation :RUO: 28.5 AU

Velocity :RUO: 4.3 AU/min.

Base=1514/1511 Ag=30.8/26.3 Vel=4.7/3.9 AUC=162.0/138.0 CC=0.995 Abbr. from mean=8.000%



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Prasugrel & Ticagrelor: Effective in patients with ACS & PCI (at the price of an increased bleeding risk)

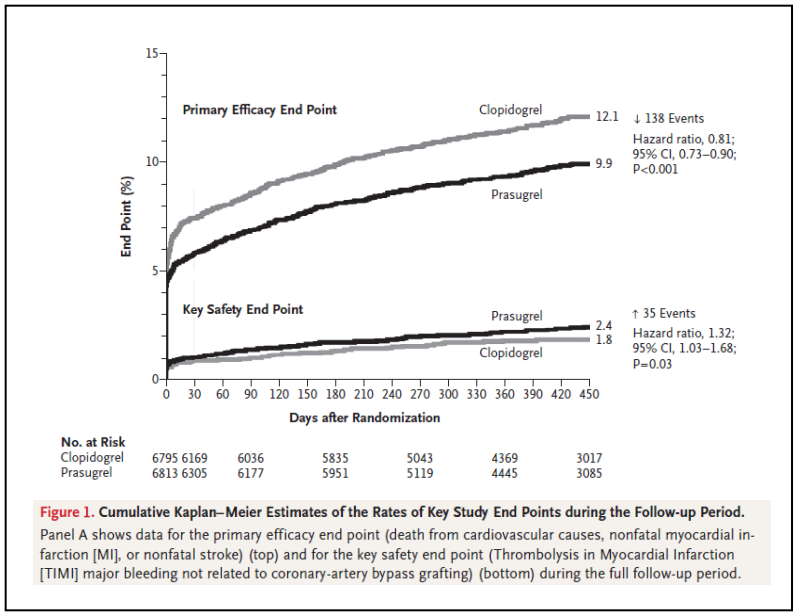

Figure 1. Cumulative Kaplan–Meier Estimates of the Rates of Key Study End Points during the Follow-up Period.
Panel A shows data for the primary efficacy end point (death from cardiovascular causes, nonfatal myocardial infarction [MI], or nonfatal stroke) (top) and for the key safety end point (Thrombolysis in Myocardial Infarction [TIMI] major bleeding not related to coronary-artery bypass grafting) (bottom) during the full follow-up period.

Wiviott S et al. N Engl J Med 2007;357:2001-15

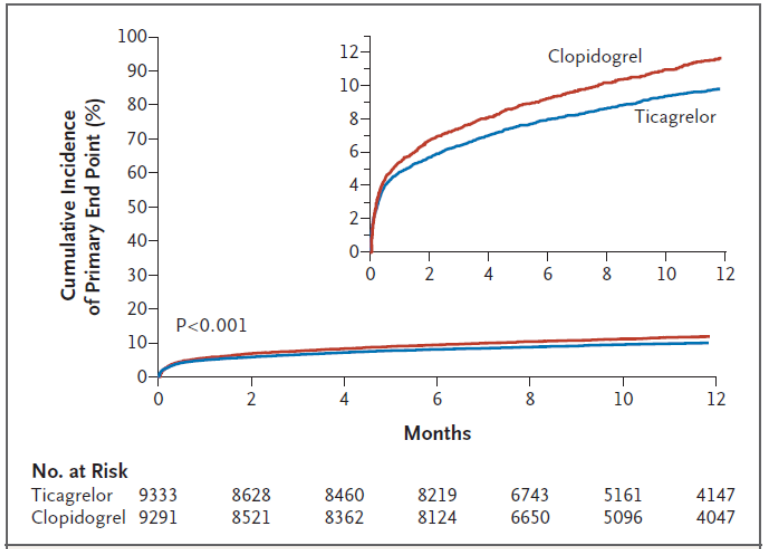

Figure 1. Cumulative Kaplan–Meier Estimates of the Time to the First Adjudicated Occurrence of the Primary Efficacy End Point.
The primary end point — a composite of death from vascular causes, myocardial infarction, or stroke — occurred significantly less often in the ticagrelor group than in the clopidogrel group (9.8% vs. 11.7% at 12 months; hazard ratio, 0.84; 95% confidence interval, 0.77 to 0.92; P<0.001).

Wallentin L et al. N Engl J Med 2009:361:1-13

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Treatment options in ACS & PCI

KISS

Keep It Safe and Simple

1. ASS & Prasugrel (once daily)

or

2. ASS & Ticagrelor (twice daily)

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Prasugrel :
Effective in patients with STEMI & PCI

n=3'534

	Clopidogrel	Prasugrel	Hazard ratio (95% CI)	p	Number needed to treat (95% CI)*
Efficacy endpoints					
Primary endpoint (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke)					
All STEMI cohort	166 (9·5%)	115 (6·5%)	0·68 (0·54–0·87)	0·0017	35 (24–84)
Primary PCI	101 (8·2%)	79 (6·6%)	0·80 (0·60–1·08)	0·1440	..
Secondary PCI	65 (12·3%)	36 (6·4%)	0·50 (0·34–0·76)	0·0008	17 (12–35)
Key secondary endpoint (cardiovascular death, non-fatal myocardial infarction, non-fatal urgent target vessel revascularisation)					
All STEMI cohort	155 (8·8%)	118 (6·7%)	0·75 (0·59–0·96)	0·0205	48 (29–283)
Primary PCI	91 (7·4%)	81 (6·8%)	0·92 (0·68–1·24)	0·5710	..
Secondary PCI	64 (12·1%)	37 (6·6%)	0·53 (0·35–0·79)	0·0016	18 (13–41)
Cardiovascular death or myocardial infarction	154 (8·8%)	109 (6·2%)	0·70 (0·55–0·90)	0·0042	39 (26–113)
Cardiovascular death	41 (2·4%)	25 (1·4%)	0·61 (0·37–1·00)	0·0469	109 (68–24758)
All-cause death	45 (2·6%)	28 (1·6%)	0·62 (0·39–0·99)	0·0445	103 (63–5470)
Myocardial infarction	123 (7·0%)	87 (4·9%)	0·70 (0·53–0·92)	0·0106	49 (31–189)
Stroke	16 (0·9%)	7 (0·4%)	0·43 (0·18–1·06)	0·0585	..
Urgent target vessel revascularisation	33 (1·9%)	22 (1·3%)	0·66 (0·39–1·14)	0·1329	..
Stent thrombosis					
All STEMI cohort	39 (2·4%)	19 (1·2%)	0·49 (0·28–0·84)	0·0084	81 (57–262)
Primary PCI	28 (2·5%)	12 (1·1%)	0·44 (0·22–0·87)	0·0144	71 (51–297)
Secondary PCI	11 (2·2%)	7 (1·3%)	0·60 (0·23–1·54)	0·2804	..
Safety endpoints					
TIMI major bleeding unrelated to CABG surgery					
All STEMI cohort	23 (1·3%)	17 (1·0%)	0·74 (0·39–1·38)	0·3359	..
Primary PCI	18 (1·5%)	14 (1·2%)	0·80 (0·40–1·60)	0·5238	..
Secondary PCI	5 (1·0%)	3 (0·5%)	0·56 (0·13–2·35)	0·4223	..
TIMI life-threatening bleeding	10 (0·6%)	10 (0·6%)	0·99 (0·41–2·39)	0·9919	..
TIMI major or minor bleeding unrelated to CABG surgery	57 (3·3%)	52 (3·0%)	0·91 (0·62–1·32)	0·6170	..
Net clinical outcome					
Death, myocardial infarction, stroke, TIMI major bleeding unrelated to CABG surgery†	187 (10·7%)	130 (7·4%)	0·69 (0·55–0·86)	0·0009	31 (21–70)

Rates (%) are expressed as Kaplan-Meier failure estimates. See figure 1 for numbers of patients in the clopidogrel, prasugrel, All STEMI, primary PCI, and secondary PCI cohorts. Except where specifically indicated, all endpoints refer to the All STEMI cohort. All p values are unadjusted for multiple comparisons. *Number needed to treat only provided for p<0·05. †With the exception of all-cause death, the other elements of this composite endpoint are non-fatal events.

Table 2: **Major efficacy and safety endpoints at 30 days**

Montalescot G et al. Lancet 2009; 373:723-31

Prasugrel : Effective in patients with NSTE-ACS

n=10’074

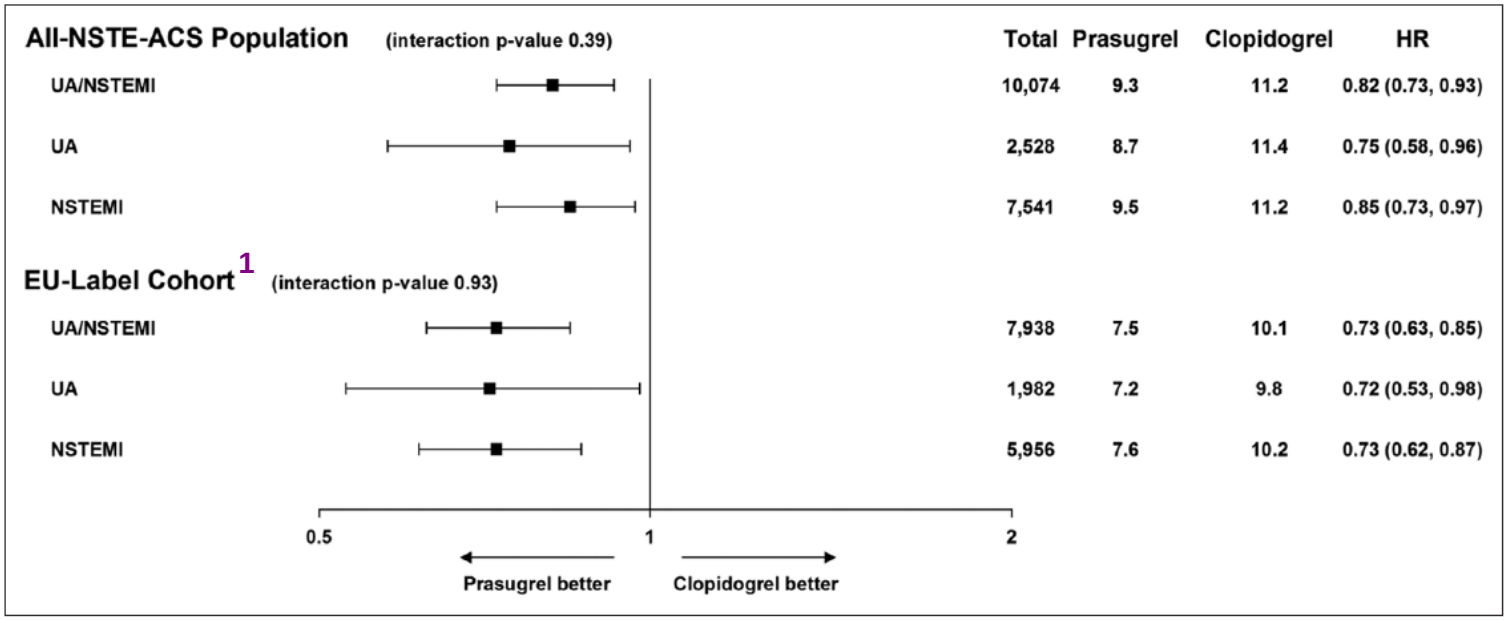

Figure 2. Hazard ratios (HRs) and rates of the primary endpoint in all included patients and in the selected subgroups. See text for details. ACS: acute coronary syndrome; MI: myocardial infarction; NSTEMI: non-ST elevation MI; STEMI: ST elevation MI; UA: unstable angina.

[1] **excluding patients with history of stroke/TIA, body weight <60kg and age ≥ 75 years**

De Servi S et al. Eur Heart J Acute Cardiovasc Care. 2014;3:363-72

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Prasugrel : Effective in patients with NSTE-ACS

n=10’074

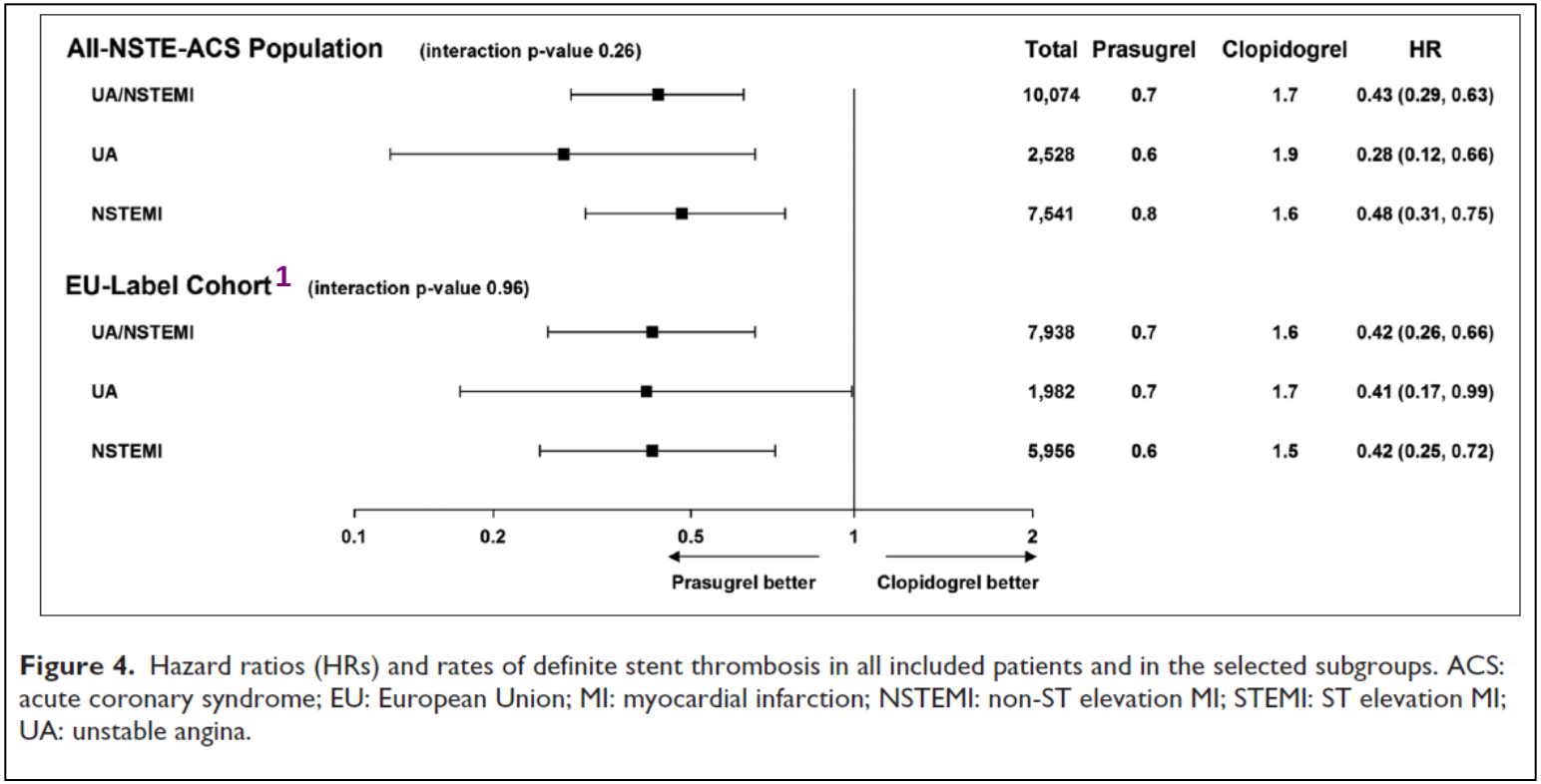

Figure 4. Hazard ratios (HRs) and rates of definite stent thrombosis in all included patients and in the selected subgroups. ACS: acute coronary syndrome; EU: European Union; MI: myocardial infarction; NSTEMI: non-ST elevation MI; STEMI: ST elevation MI; UA: unstable angina.

[1] **excluding patients with history of stroke/TIA, body weight <60kg and age ≥ 75 years**

De Servi S et al. Eur Heart J Acute Cardiovasc Care. 2014;3:363-72

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Prasugrel : Effective in patients with NSTE-ACS

n=10’074

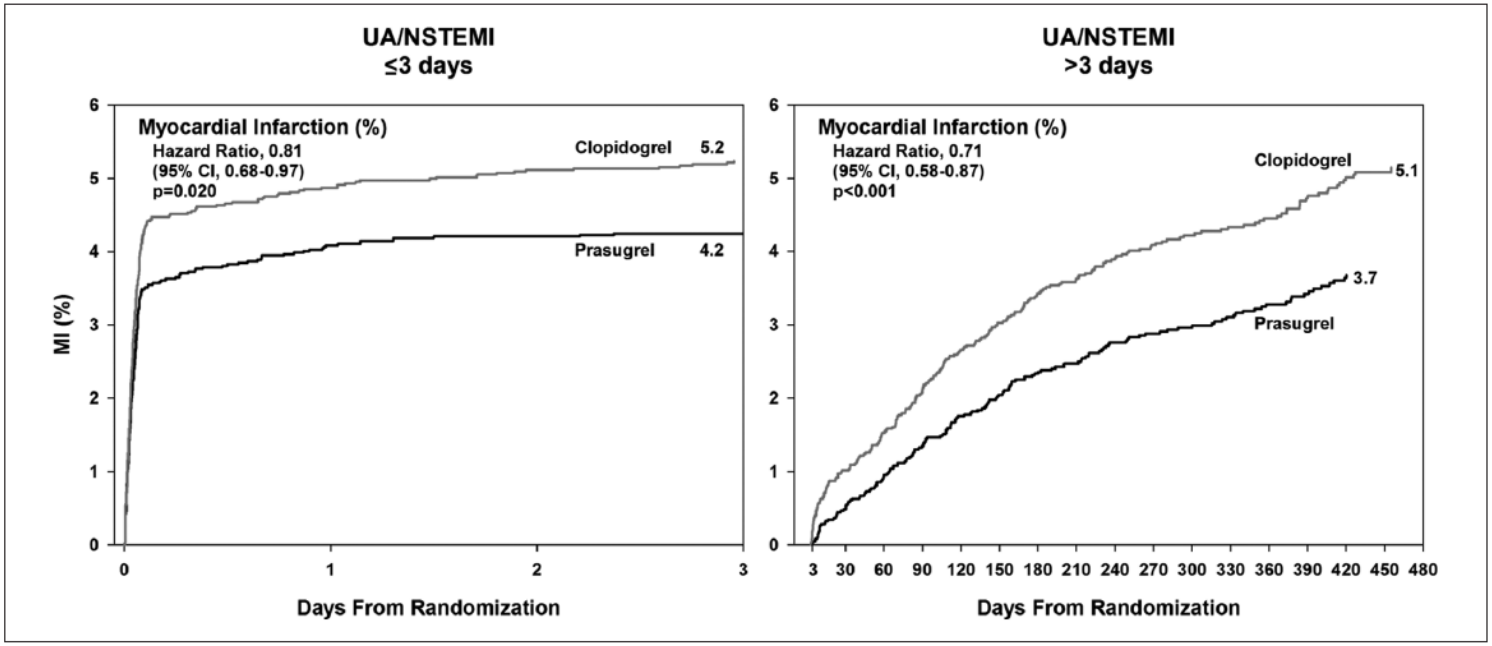

Figure 3. Landmark analysis showing the cumulative Kaplan–Meier estimates of myocardial infarction rates in the all-non-ST elevation (NSTE)-acute coronary syndrome (ACS) population during the follow up period. Data are shown from the time of randomisation until the end of day 3 (left), and from day 4 to day 450 (right). MI: myocardial infarction; UA: unstable angina.

De Servi S et al. Eur Heart J Acute Cardiovasc Care. 2014;3:363-72

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Prasugrel : Effective in patients with NSTE-ACS

n=10’074

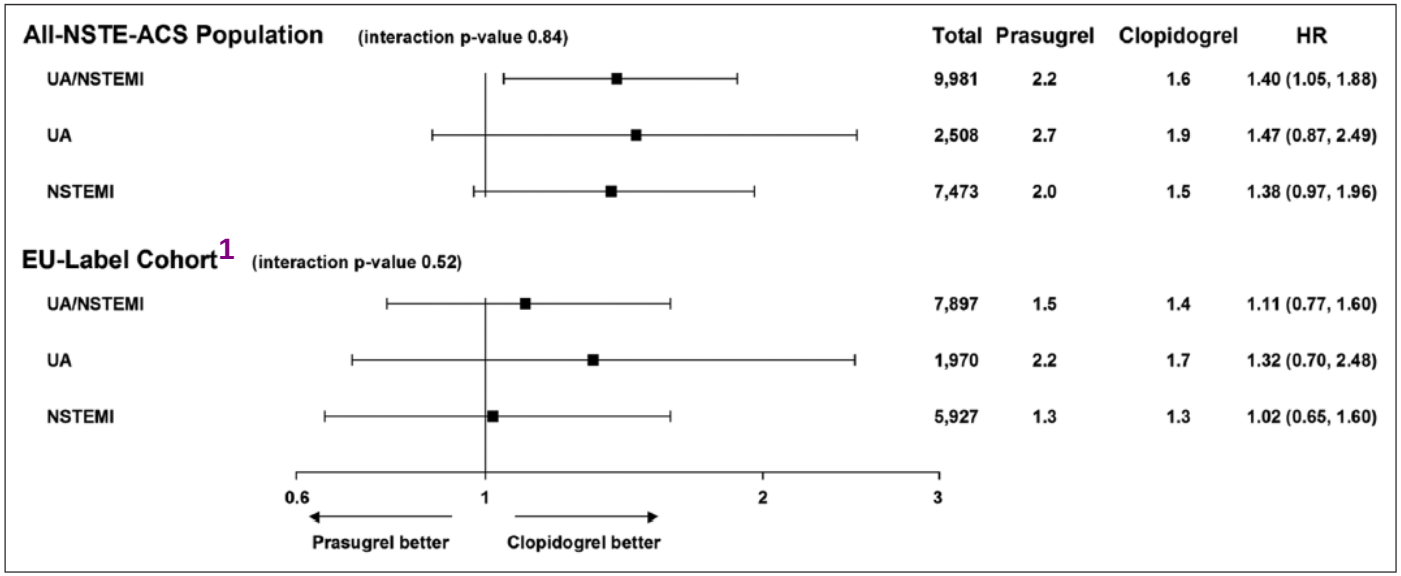

Figure 5. Hazard ratios (HRs) and rates of non-coronary artery bypass graft (CABG) related Thrombolysis In Myocardial Infarction (TIMI) major bleeding in all included patients and in the selected subgroups. ACS: acute coronary syndrome; EU: European Union; NSTEMI: non-ST elevation MI; STEMI: ST elevation MI; UA: unstable angina.

[1] **excluding patients with history of stroke/TIA, body weight <60kg and age ≥ 75 years**

De Servi S et al. Eur Heart J Acute Cardiovasc Care. 2014;3:363-72

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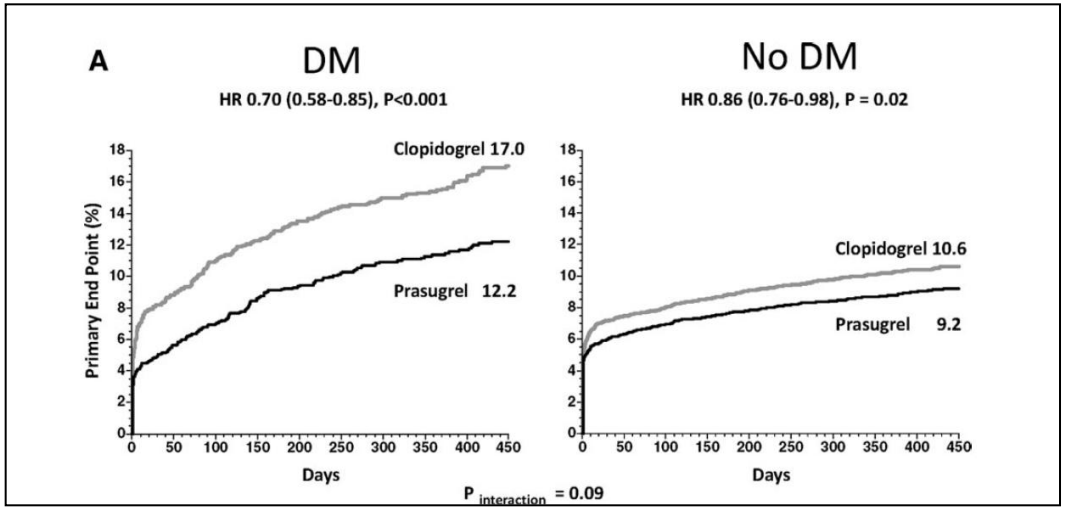
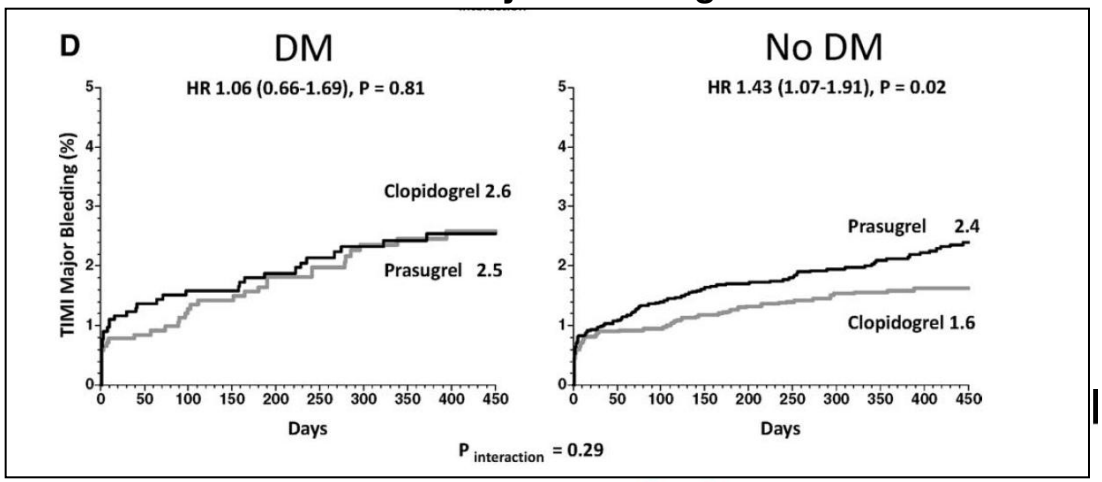
Prasugrel : Effective in patients with Diabetes

Primary endpoint



DM: n= 3'146
No DM: n= 10'462

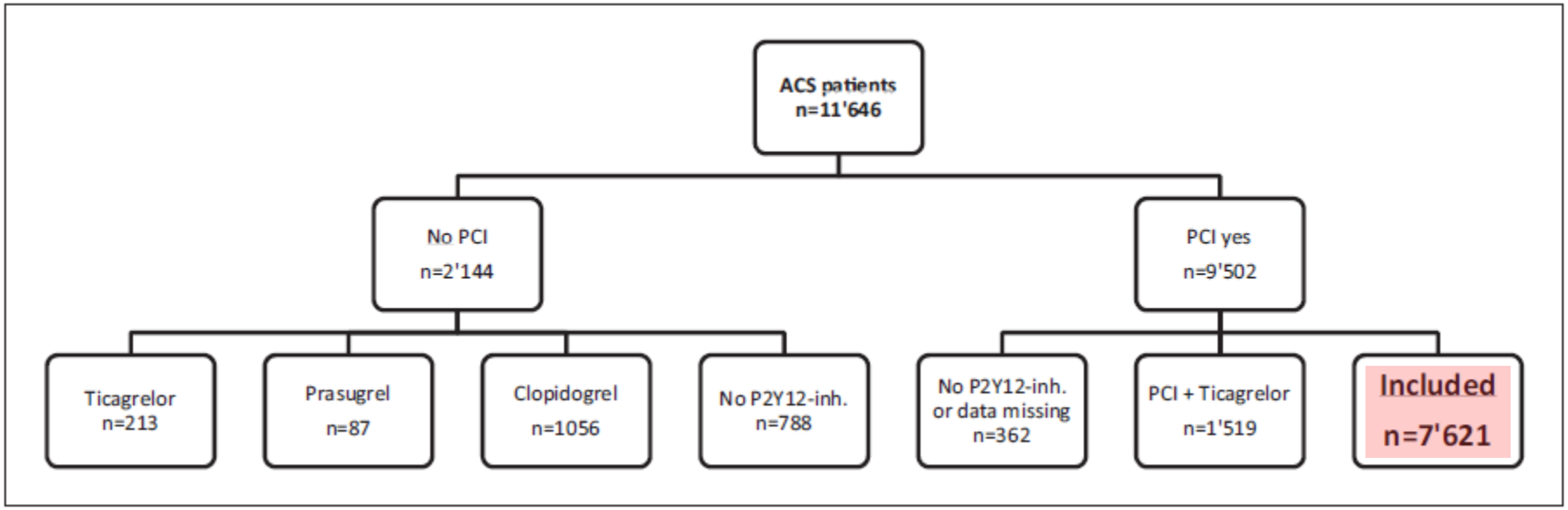
TIMI major bleeding



Wiviott, Circulation 2008;118:1626-36

Prasugrel : Real world experience in Switzerland

AMIS-Plus 2010-2013



Kurz, Eur Heart J Acute Cardiovasc Care 2015

Prasugrel: n= 2'891
Clopidogrel: n= 4'730

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Prasugrel : Real world experience in Switzerland

AMIS-Plus 2010-2013

Table 2. Independent predictors of hospital mortality in acute coronary syndrome (ACS) patients treated by percutaneous coronary intervention (PCI).

	OR (95% CI)	*p*-value
Prasugrel vs clopidgrel	0.50 (0.29–0.86)	0.013
Age, per additional year	1.04 (1.02–1.06)	<0.001
Killip>2	7.99 (4.84–13.2)	<0.001
Charlson score>1	1.89 (1.19–2.99)	0.007
Prehospital resuscitation	9.35 (5.38–16.3)	<0.001

CI: confidence interval; OR: odds ratio.

Table 3. Outcomes at hospital discharge in the matched population.

	Prasugrel (*n*=2301)	Clopidogrel (*n*=2301)	OR (95% CI)	*p*-value
Composite of death, MI, stroke/TIA (%)	69 (3.0)	99 (4.3)	0.69 (0.50–0.94)	0.019
Death (%)	41 (1.8)	72 (3.1)	0.56 (0.38–0.83)	0.004
Recurent MI (%)	18 (0.8)	17 (0.7)	1.06 (0.55–2.06)	0.87
Stroke/TIA (%)	12 (0.5)	14 (0.6)	0.86 (0.40–1.86)	0.64
Bleeding events (%)	94 (4.1)	65 (2.8)	1.47 (1.06–2.02)	0.020
Length of hospital stay, days, median (IQR)	4 (2–6)	4 (2–7)	NA	<0.001[a]

CI: confidence interval; IQR: interquartile range; MI: myocardial infarction; OR: odds ratio; TIA: transient ischemic attack.
[a]Mann-Whitney test.

Kurz, Eur Heart J Acute Cardiovasc Care 2015

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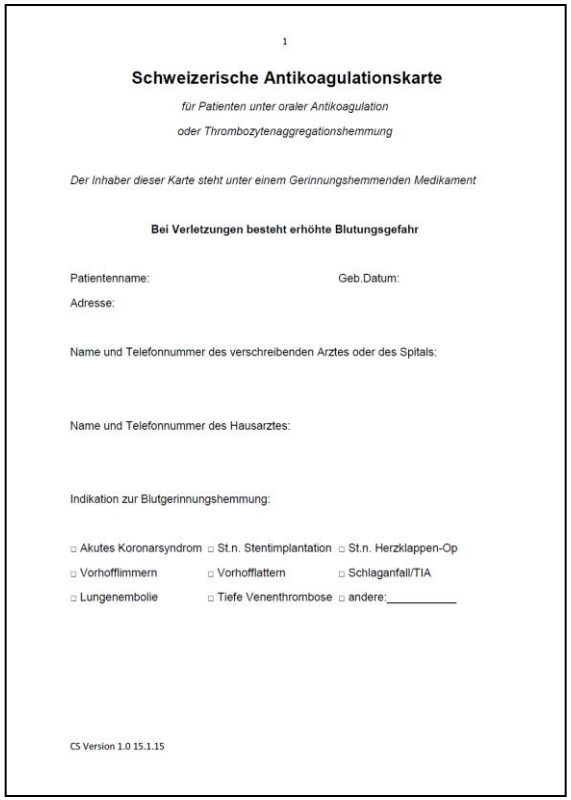
Swiss anticoagulation card: Available this summer !



1

Schweizerische Antikoagulationskarte

für Patienten unter oraler Antikoagulation

oder Thrombozytenaggregationshemmung

Der Inhaber dieser Karte steht unter einem Gerinnungshemmenden Medikament

Bei Verletzungen besteht erhöhte Blutungsgefahr

Patientenname: Geb.Datum:

Adresse:

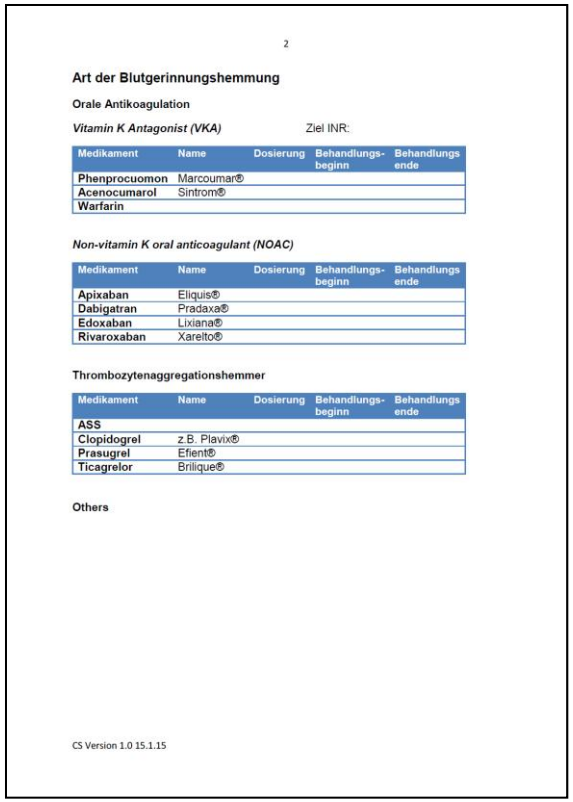
Name und Telefonnummer des verschreibenden Arztes oder des Spitals:

Name und Telefonnummer des Hausarztes:

Indikation zur Blutgerinnungshemmung:

□ Akutes Koronarsyndrom □ St.n. Stentimplantation □ St.n. Herzklappen-Op
□ Vorhofflimmern □ Vorhofflattern □ Schlaganfall/TIA
□ Lungenembolie □ Tiefe Venenthrombose □ andere:_____

CS Version 1.0 15.1.15



2

Art der Blutgerinnungshemmung

Orale Antikoagulation

Vitamin K Antagonist (VKA) Ziel INR:

Medikament	Name	Dosierung	Behandlungs-beginn	Behandlungs ende
Phenprocuomon	Marcoumar®			
Acenocumarol	Sintrom®			
Warfarin				

Non-vitamin K oral anticoagulant (NOAC)

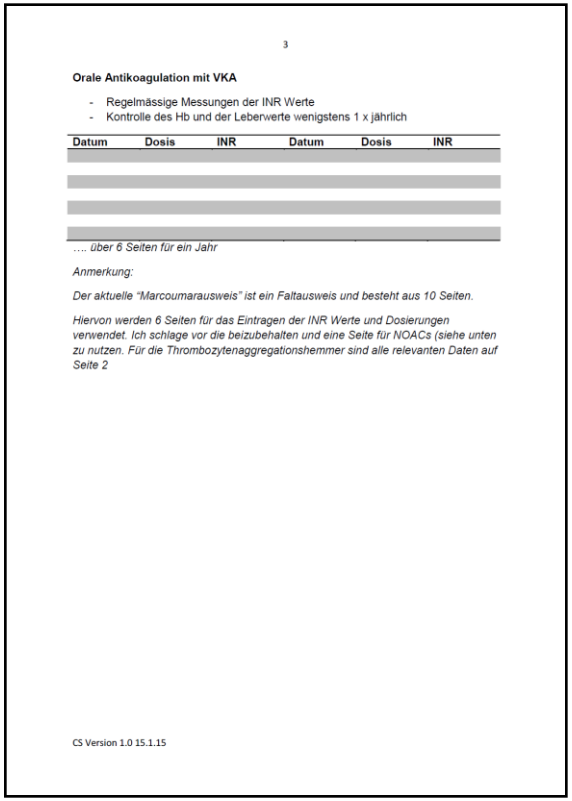
Medikament	Name	Dosierung	Behandlungs-beginn	Behandlungs ende
Apixaban	Eliquis®			
Dabigatran	Pradaxa®			
Edoxaban	Lixiana®			
Rivaroxaban	Xarelto®			

Thrombozytenaggregationshemmer

Medikament	Name	Dosierung	Behandlungs-beginn	Behandlungs ende
ASS				
Clopidogrel	z.B. Plavix®			
Prasugrel	Efient®			
Ticagrelor	Brilique®			

Others

CS Version 1.0 15.1.15



3

Orale Antikoagulation mit VKA

- Regelmässige Messungen der INR Werte
- Kontrolle des Hb und der Leberwerte wenigstens 1 x jährlich

Datum	Dosis	INR	Datum	Dosis	INR

…. über 6 Seiten für ein Jahr

Anmerkung:

Der aktuelle "Marcoumarausweis" ist ein Faltausweis und besteht aus 10 Seiten.

Hiervon werden 6 Seiten für das Eintragen der INR Werte und Dosierungen verwendet. Ich schlage vor die beizubehalten und eine Seite für NOACs (siehe unten zu nutzen. Für die Thrombozytenaggregationshemmer sind alle relevanten Daten auf Seite 2

CS Version 1.0 15.1.15

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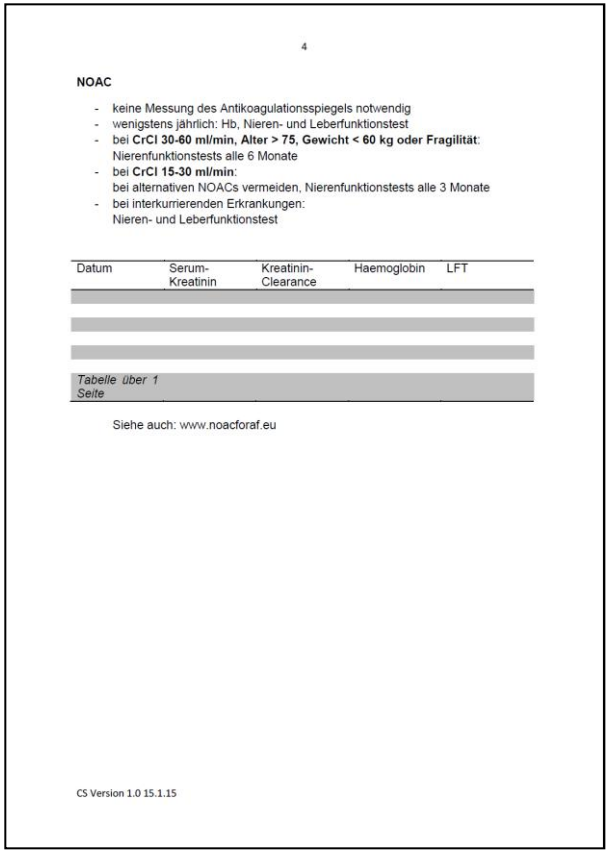
Swiss anticoagulation card: Available this summer !



4

NOAC

- keine Messung des Antikoagulationsspiegels notwendig
- wenigstens jährlich: Hb, Nieren- und Leberfunktionstest
- bei **CrCl 30-60 ml/min, Alter > 75, Gewicht < 60 kg oder Fragilität**: Nierenfunktionstests alle 6 Monate
- bei **CrCl 15-30 ml/min**: bei alternativen NOACs vermeiden, Nierenfunktionstests alle 3 Monate
- bei interkurrierenden Erkrankungen: Nieren- und Leberfunktionstest

Datum	Serum-Kreatinin	Kreatinin-Clearance	Haemoglobin	LFT
Tabelle über 1 Seite				

Siehe auch: www.noacforaf.eu

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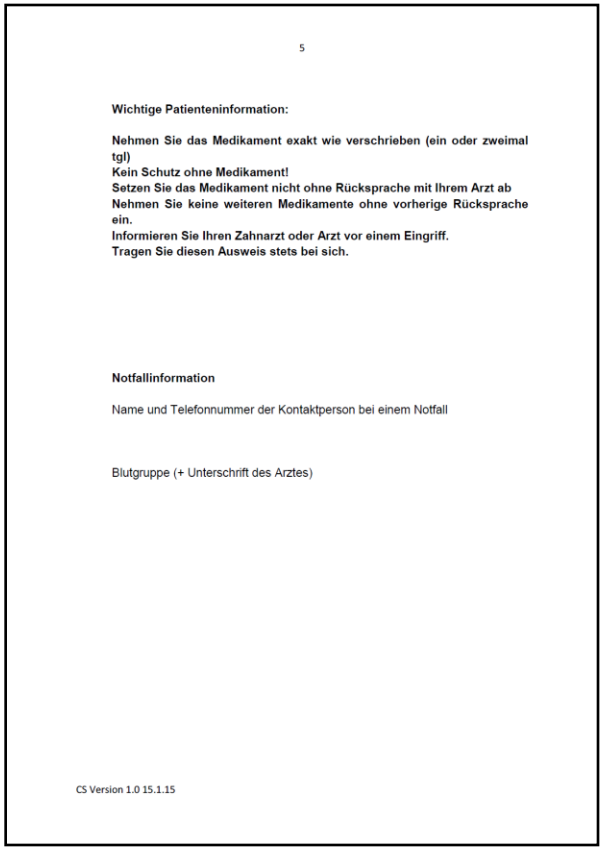

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Wichtige Patienteninformation:

Nehmen Sie das Medikament exakt wie verschrieben (ein oder zweimal tgl)
Kein Schutz ohne Medikament!
Setzen Sie das Medikament nicht ohne Rücksprache mit Ihrem Arzt ab
Nehmen Sie keine weiteren Medikamente ohne vorherige Rücksprache ein.
Informieren Sie Ihren Zahnarzt oder Arzt vor einem Eingriff.
Tragen Sie diesen Ausweis stets bei sich.

Notfallinformation

Name und Telefonnummer der Kontaktperson bei einem Notfall

Blutgruppe (+ Unterschrift des Arztes)

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Universitätsspital Basel

Thank you for your attention

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