

Clinical Implications

: Ticagrelor in “Real-World” Practice

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Case I

➤ **M/44**

➤ **Ant. Wall STEMI(3VD), Killip class 3, EF=30%**

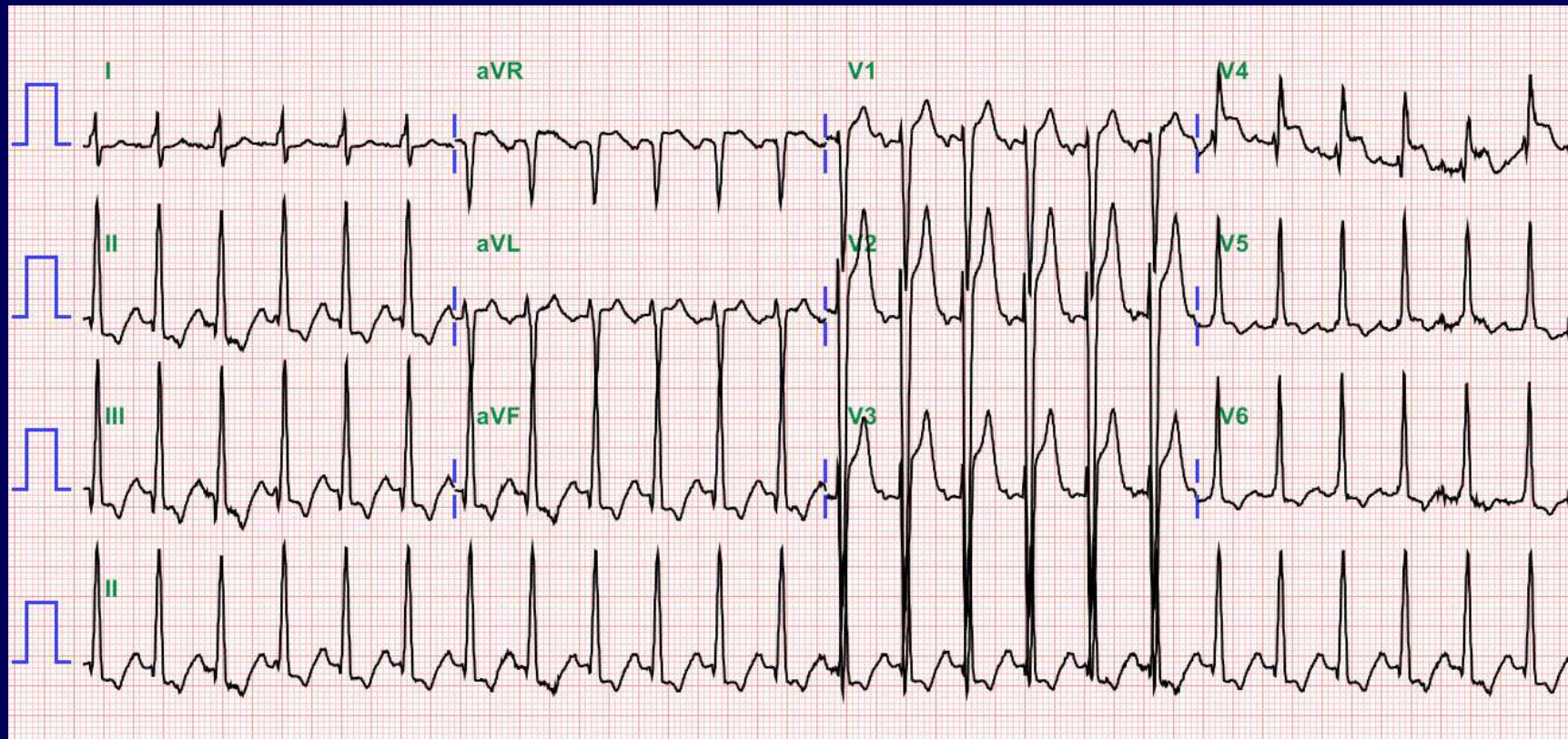
➤ C/C Chest pain & orthopnea

➤ P/Hx HTN, Current smoking, Epilepsy, Mental retardation

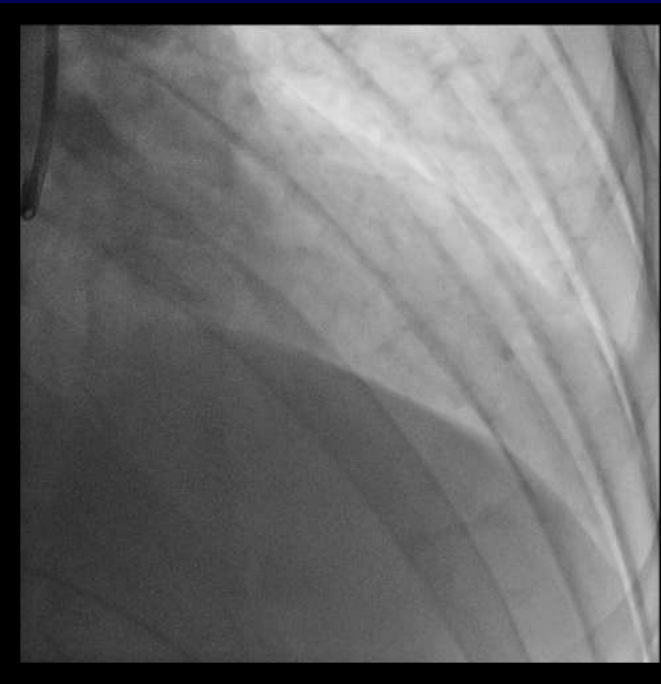
➤ Antiplatelet agent : Loading (Clopidogrel 600 mg)

→ Clopidorel 75 mg qd

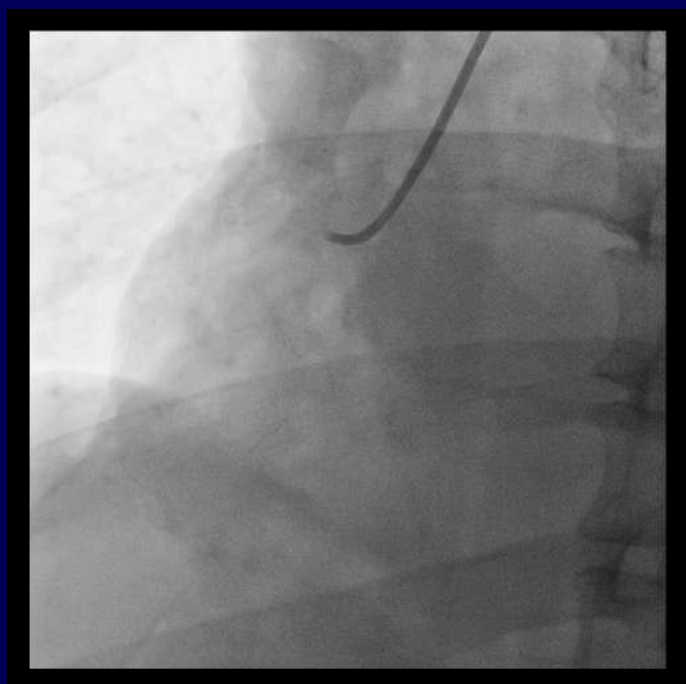
EKG – Initial admission



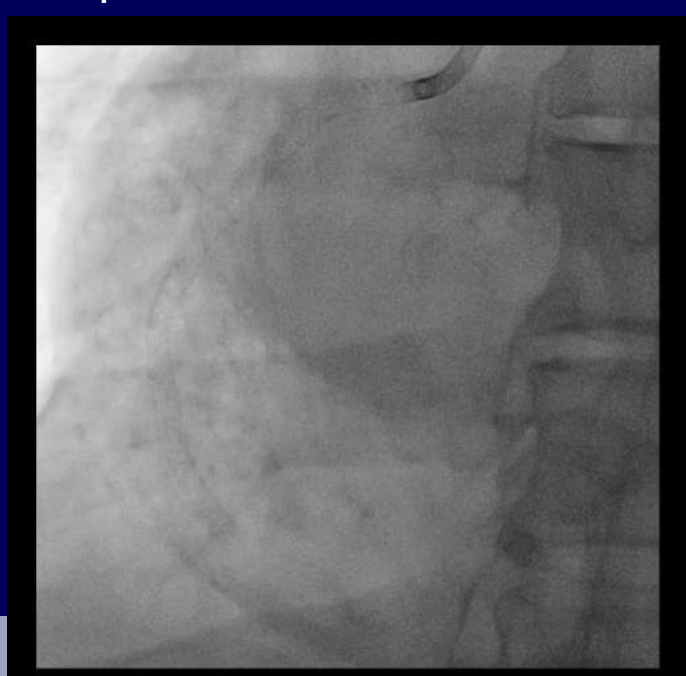
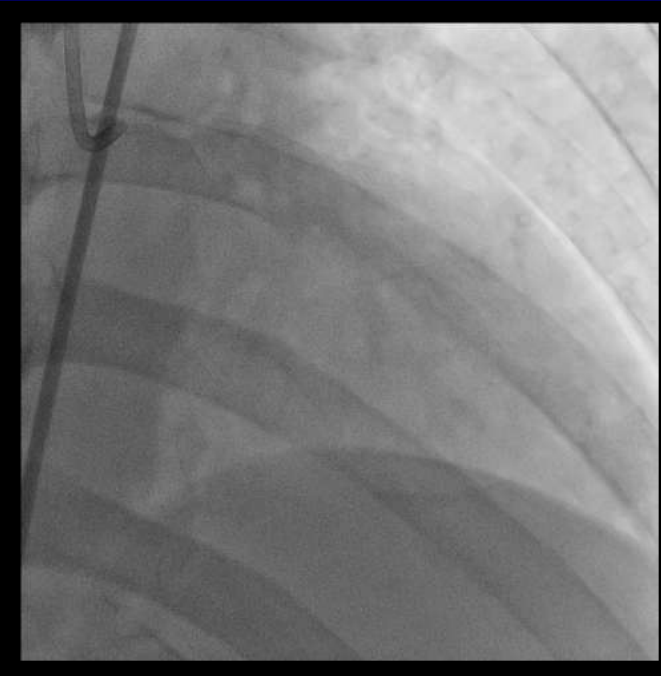
Initial admission



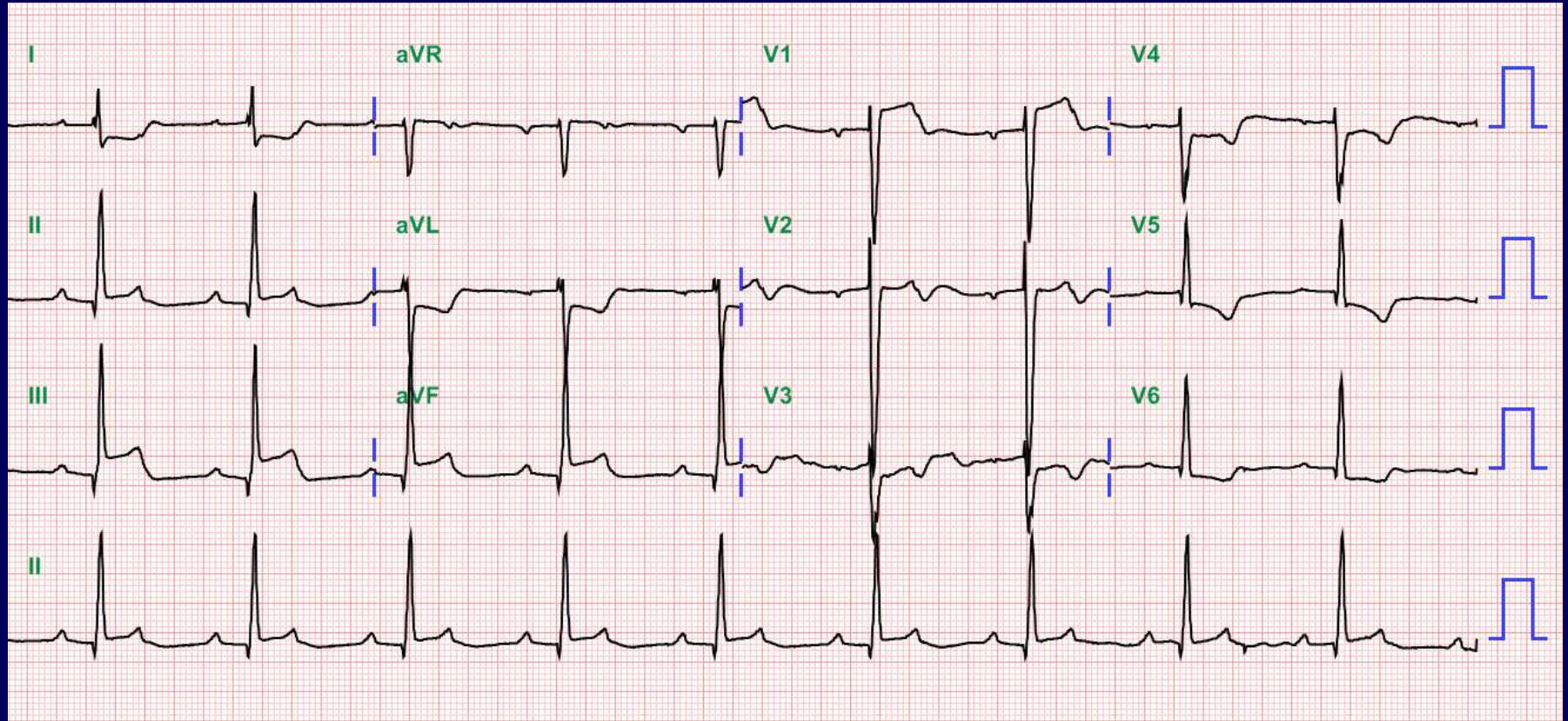
Xience prime 2.75/38mm



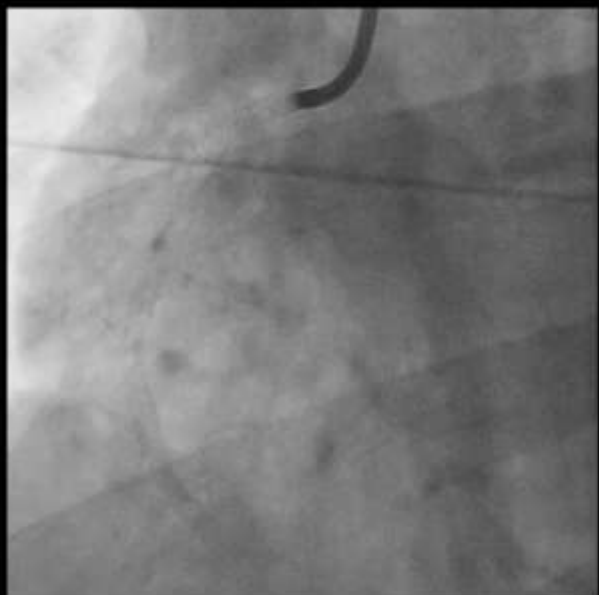
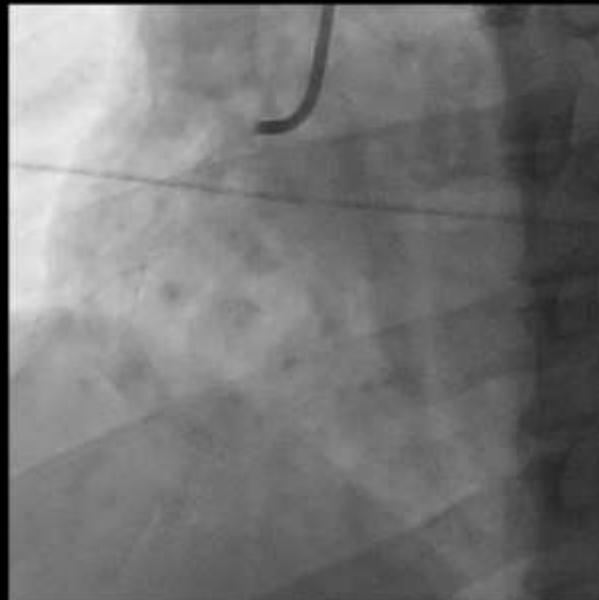
Xience prime 3.0/38mm + 2.75/38mm



EKG, 5 days after the staged PCI



Stent thrombosis : 5 days after initial PCI



Platelet Drug Response Assay (Aspirin)

529 [<550 , ARU] : Aspirin responder

Platelet Drug Response Assay (P2Y12)

229 [PRU]

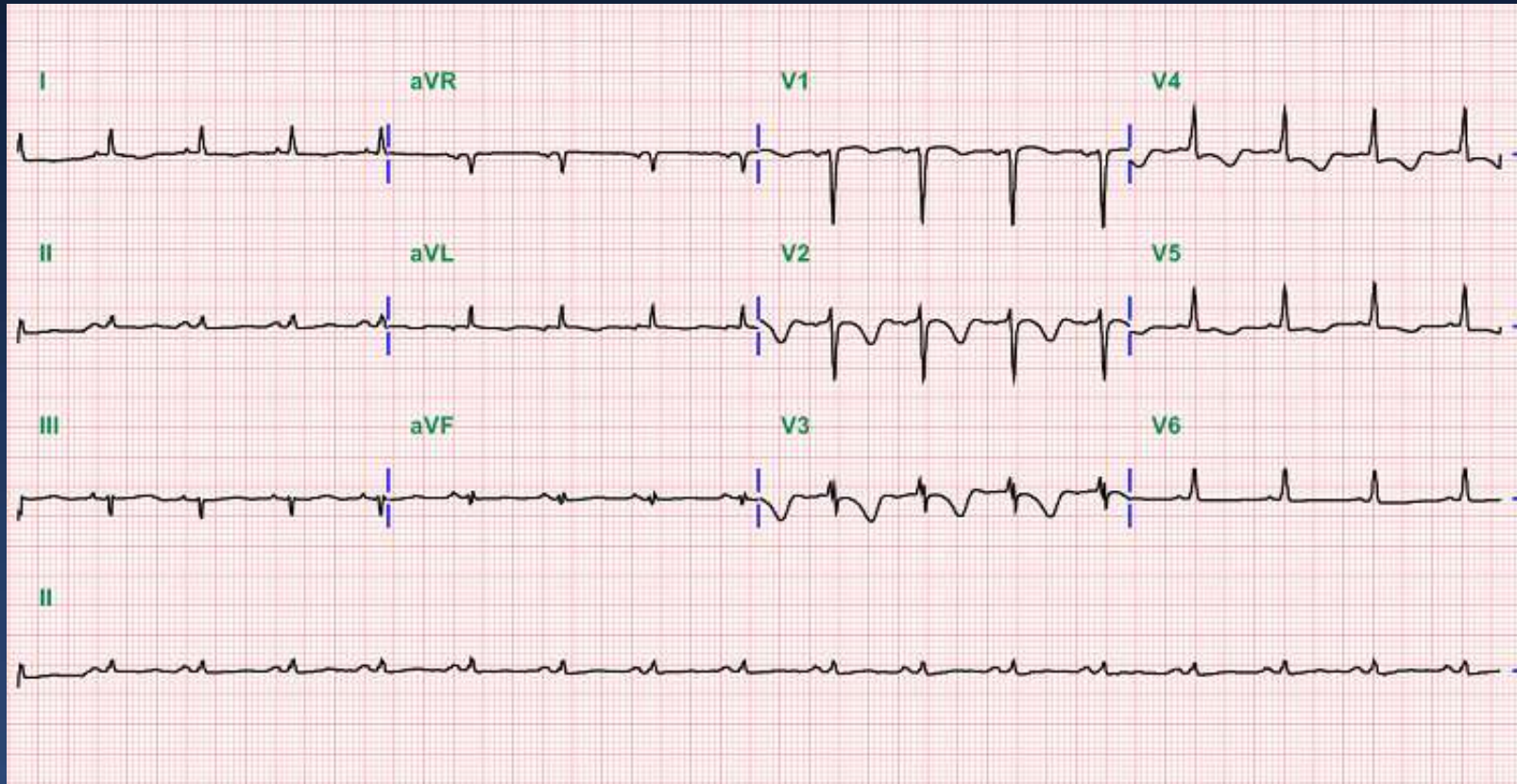
Which OAP next?

- Ticagrelor?
- Prasugrel?

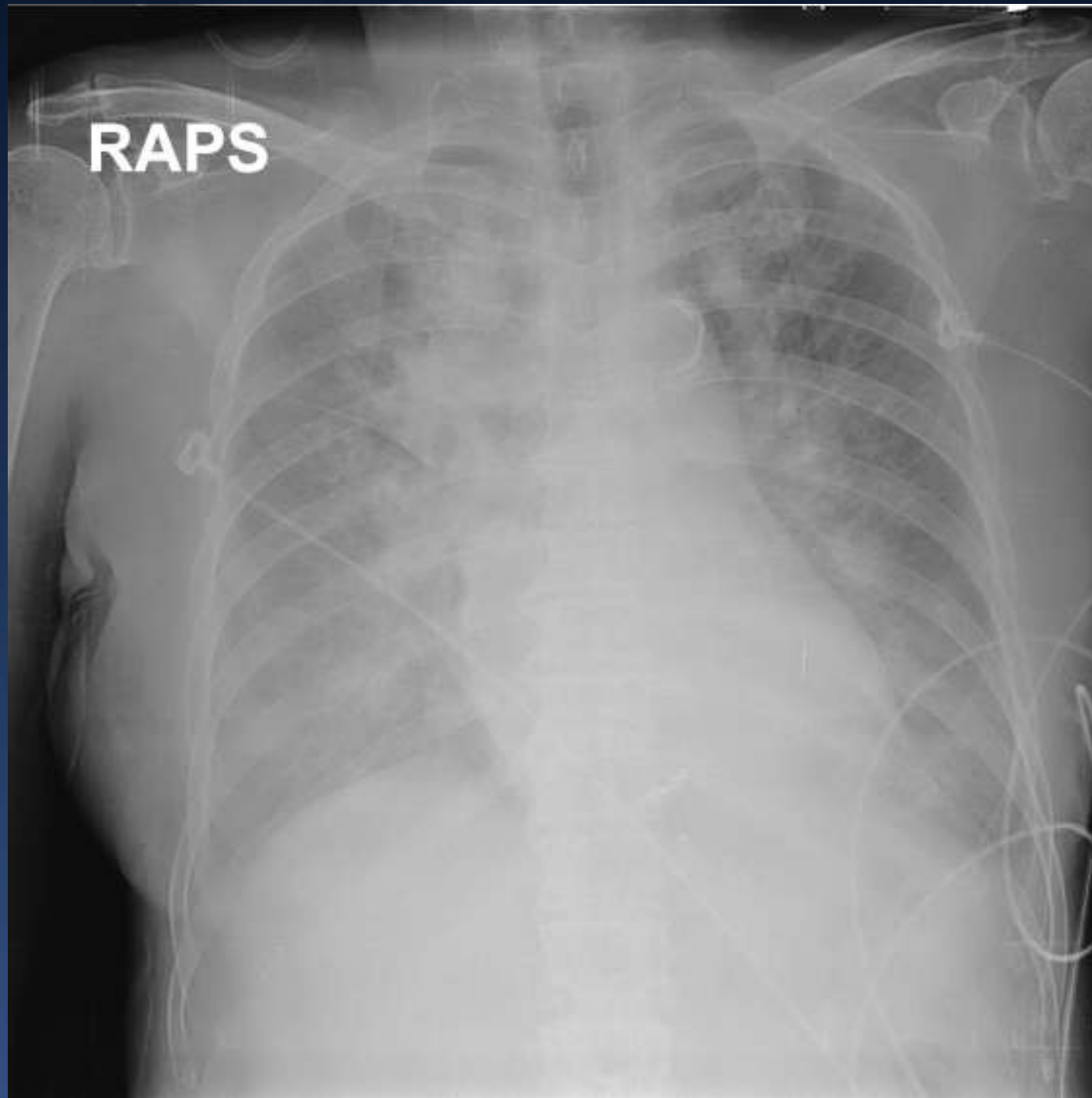
Case 2

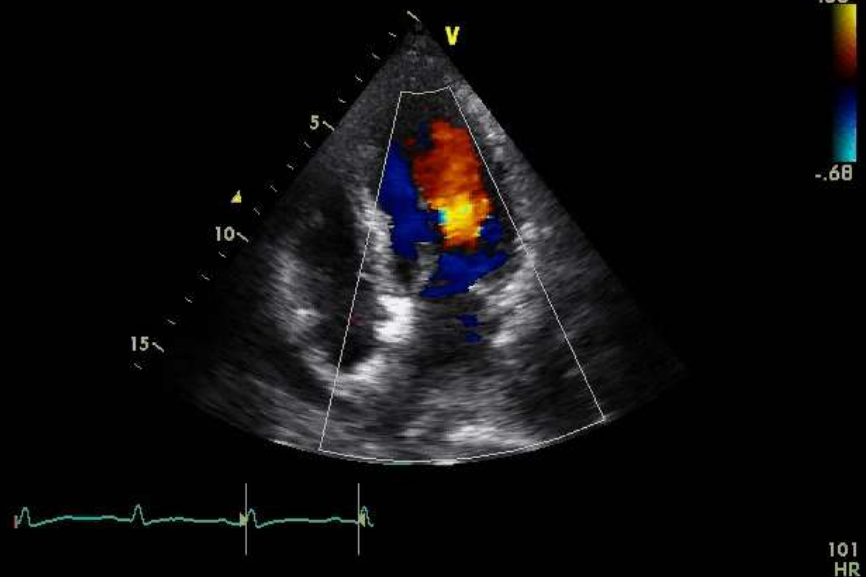
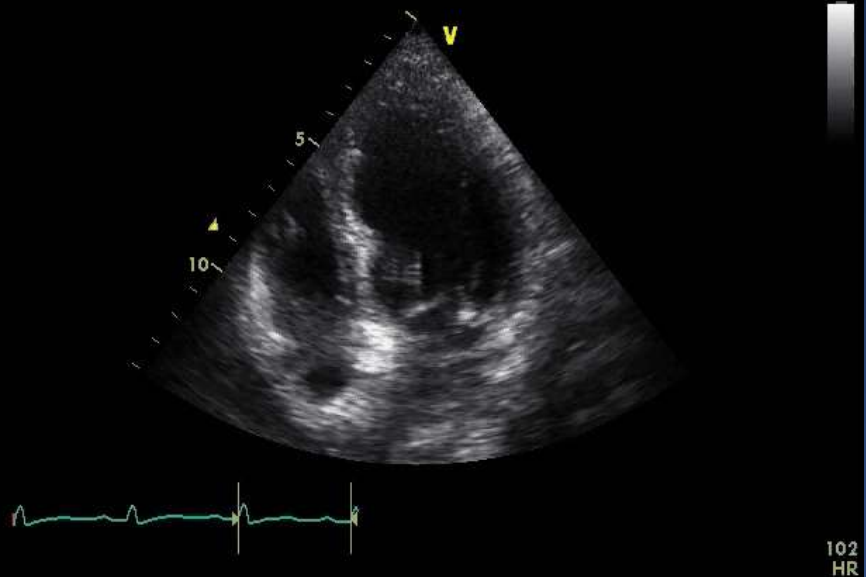
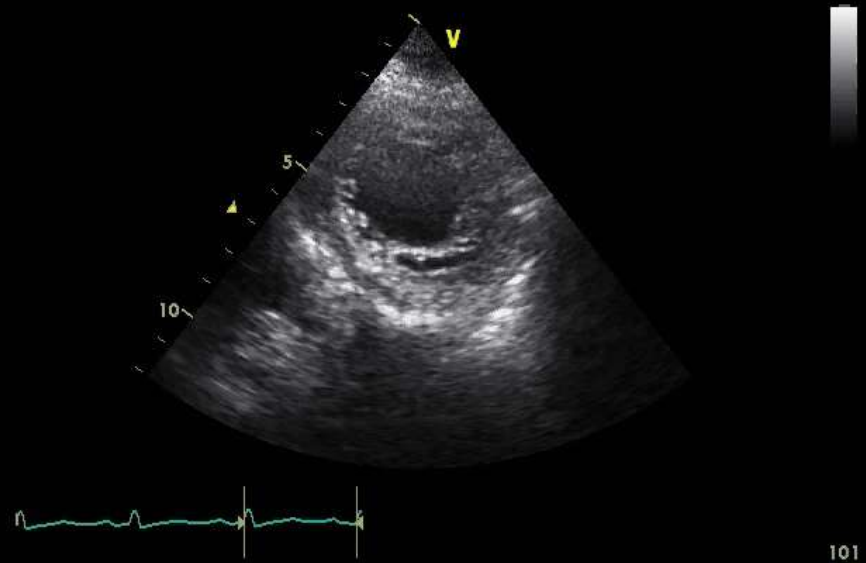
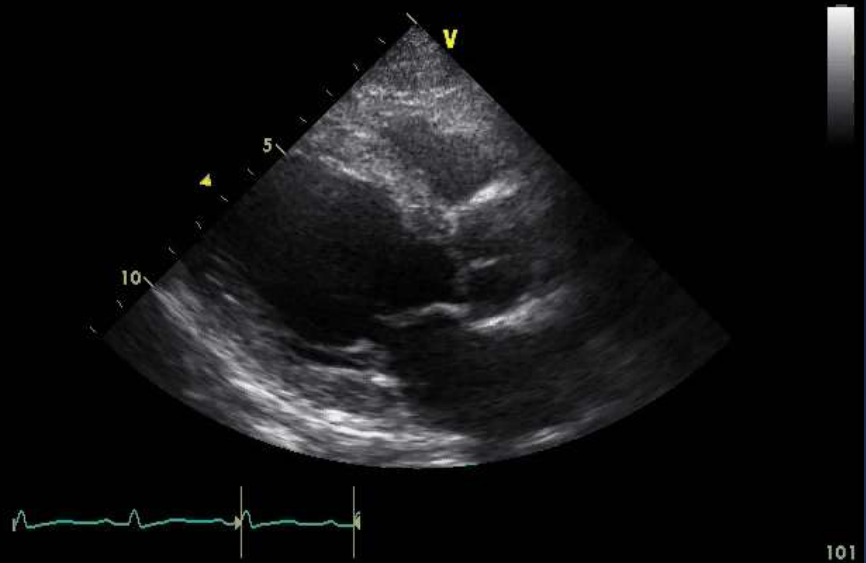
- ✓ F/77
- ✓ “Resting chest pain” since 6 hrs ago
- ✓ DM/HTN(+/+), Dyslipidemia(+), Smoking(-), Family Hx.(-)
- ✓ Current medication
 - Linagliptin 5mg + Metformin 500mg,
Losartan 50mg, Rosuvastatin 10mg

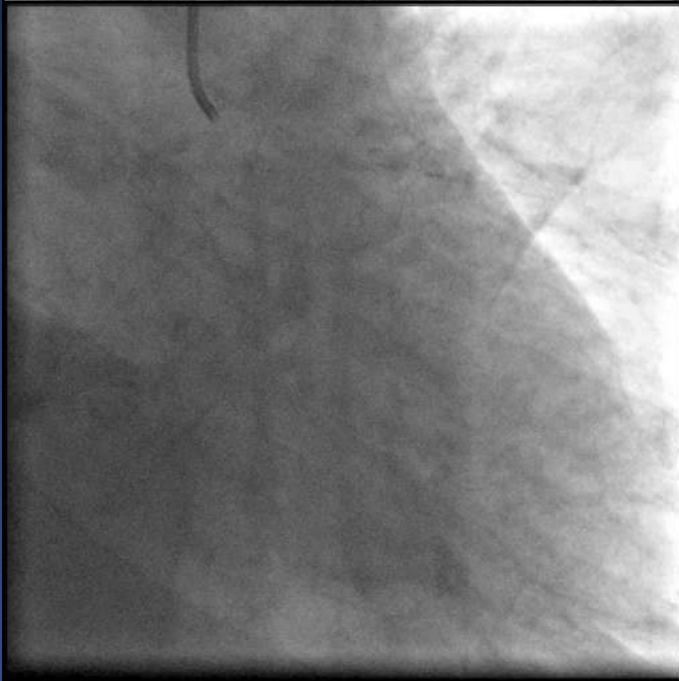
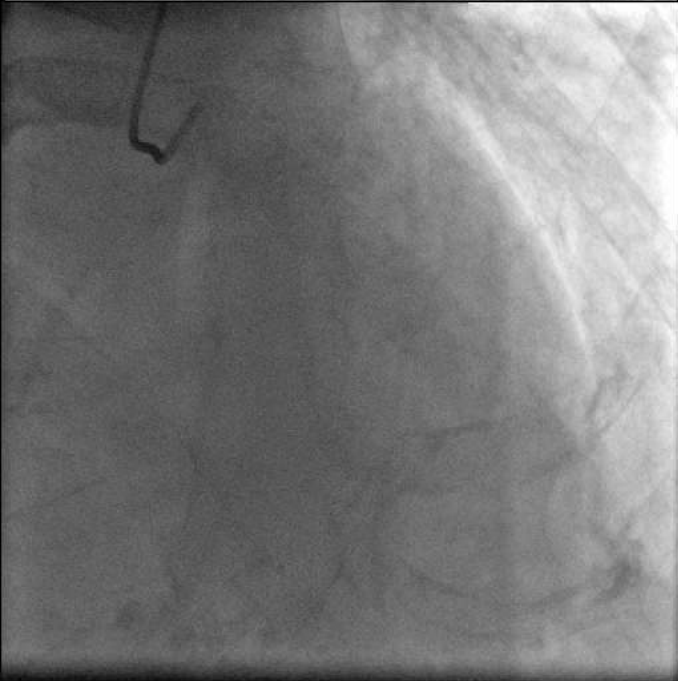
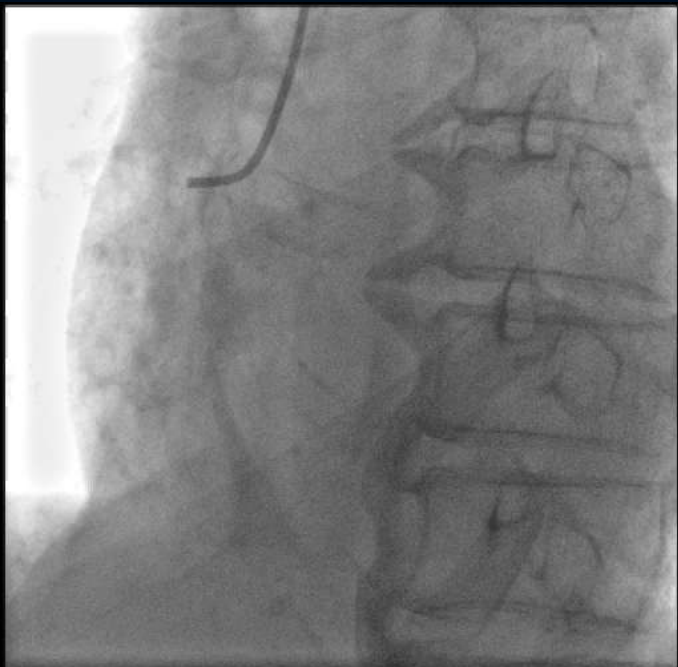
ECG

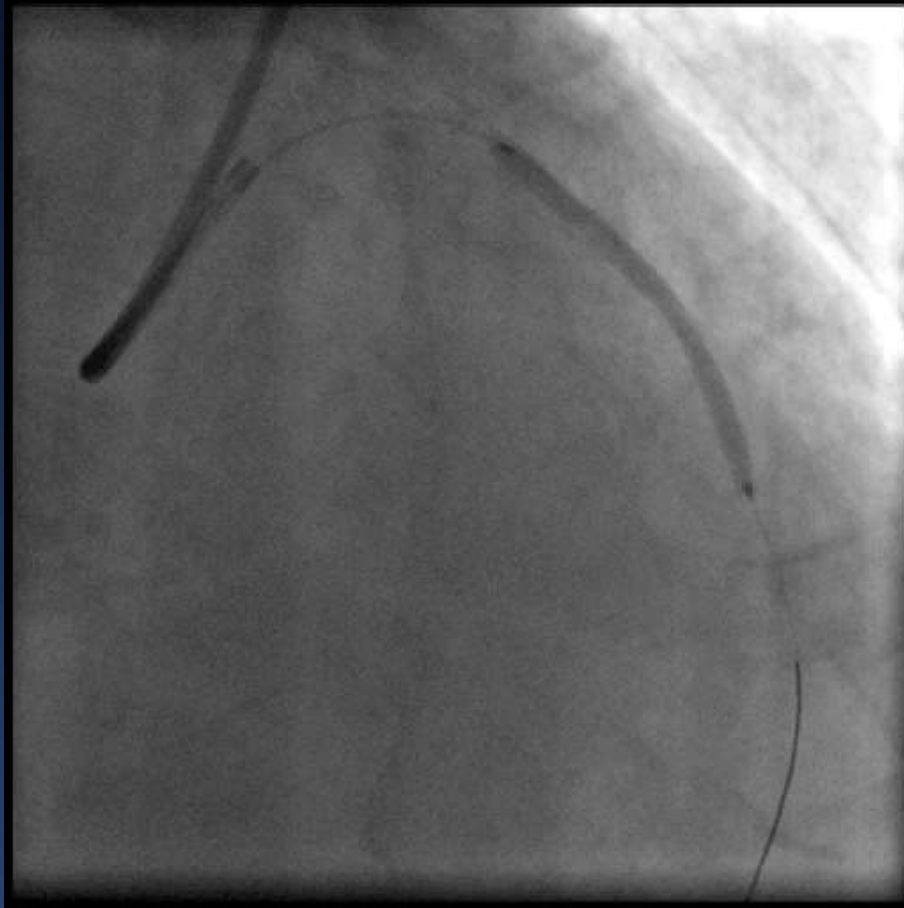


Chest X-ray





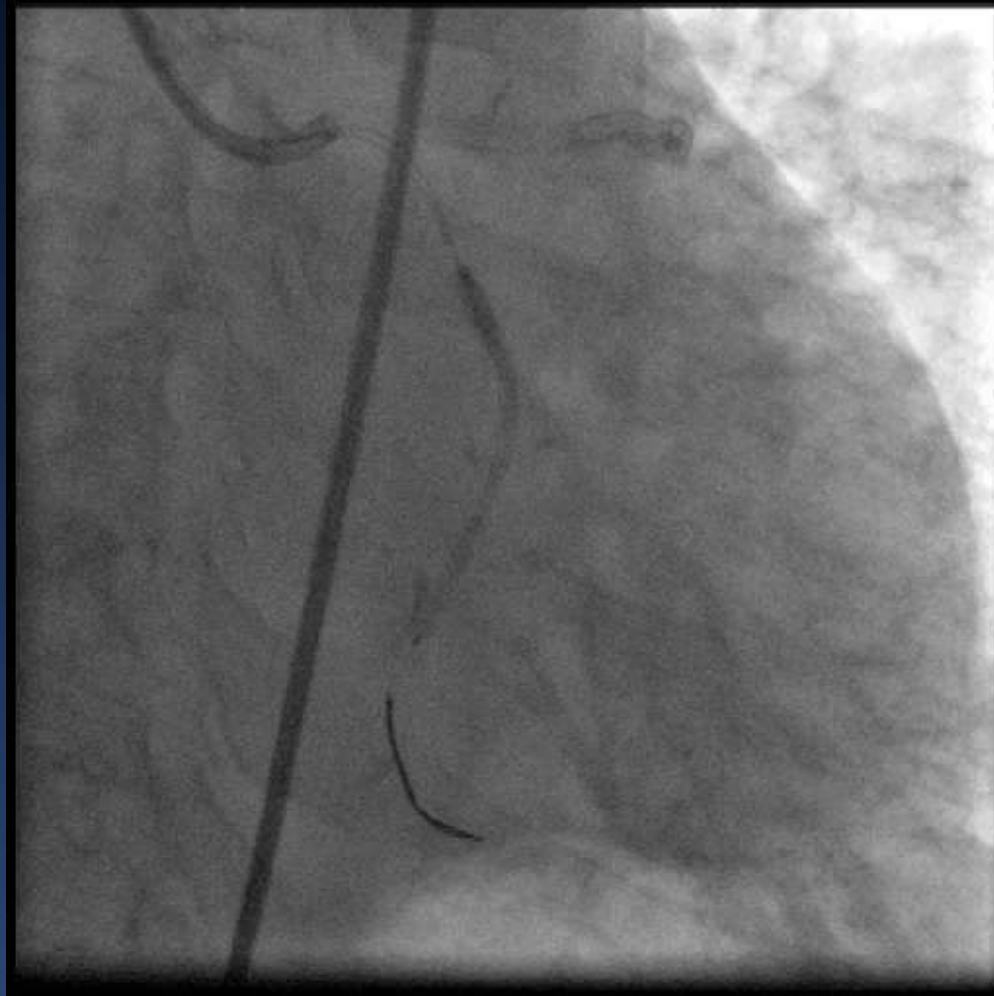




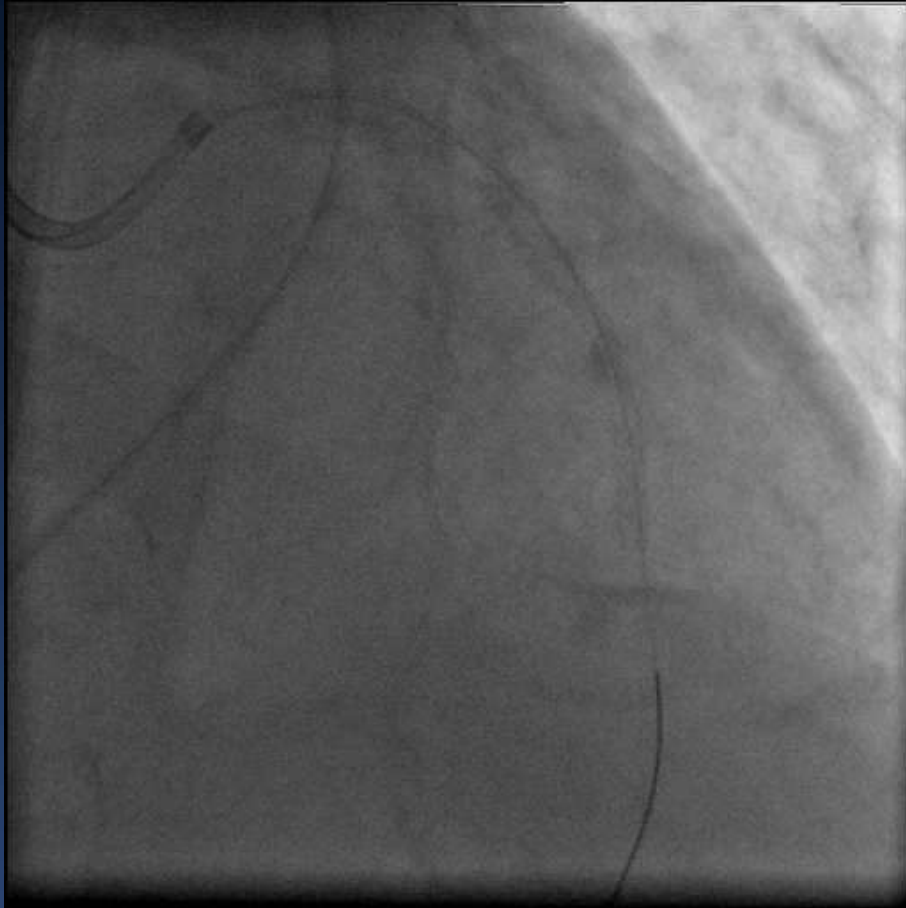
Xience Prime 2.5/38mm (mLAD)



Xience Prime 2.75/23mm (pLAD)



Xience Prime 2.5/38mm (mLCX)



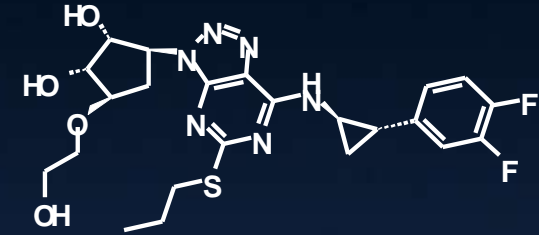
Final Angiography

Which ADP receptor blocker?

- Type 2 DM, NSTEMI,
- Long stent length
- Heavy atheroma burden in coronary trees

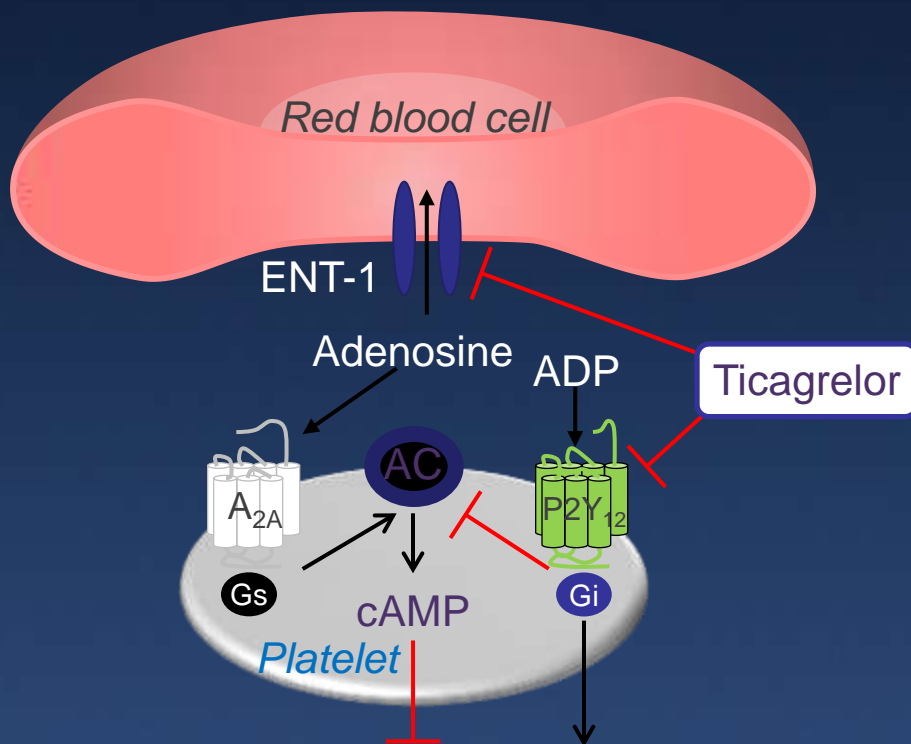
1. Clopidogrel?
2. Ticagrelor?
3. Praugrel?

Ticagrelor works via a dual pathway



	CPTP Cyclo-pentyl-triazolo-pyrimidine e (ticagrelor)	Thienopyridines (ticlopidine, clopidogrel, prasugrel)
Platelet pathway (P2Y ₁₂)	<ul style="list-style-type: none"> • Direct acting • 24-hour systemic po potential • Reversibly binding 	<ul style="list-style-type: none"> • Pro-drugs • Minimal systemic potential • Covalently binding • More efficient generation of active metabolite with prasugrel than an clopidogrel
Adenosine pathway (ENT-1)	<ul style="list-style-type: none"> • Inhibition of ENT-1 providing enhanced local adenosine response 	<ul style="list-style-type: none"> • No known effect

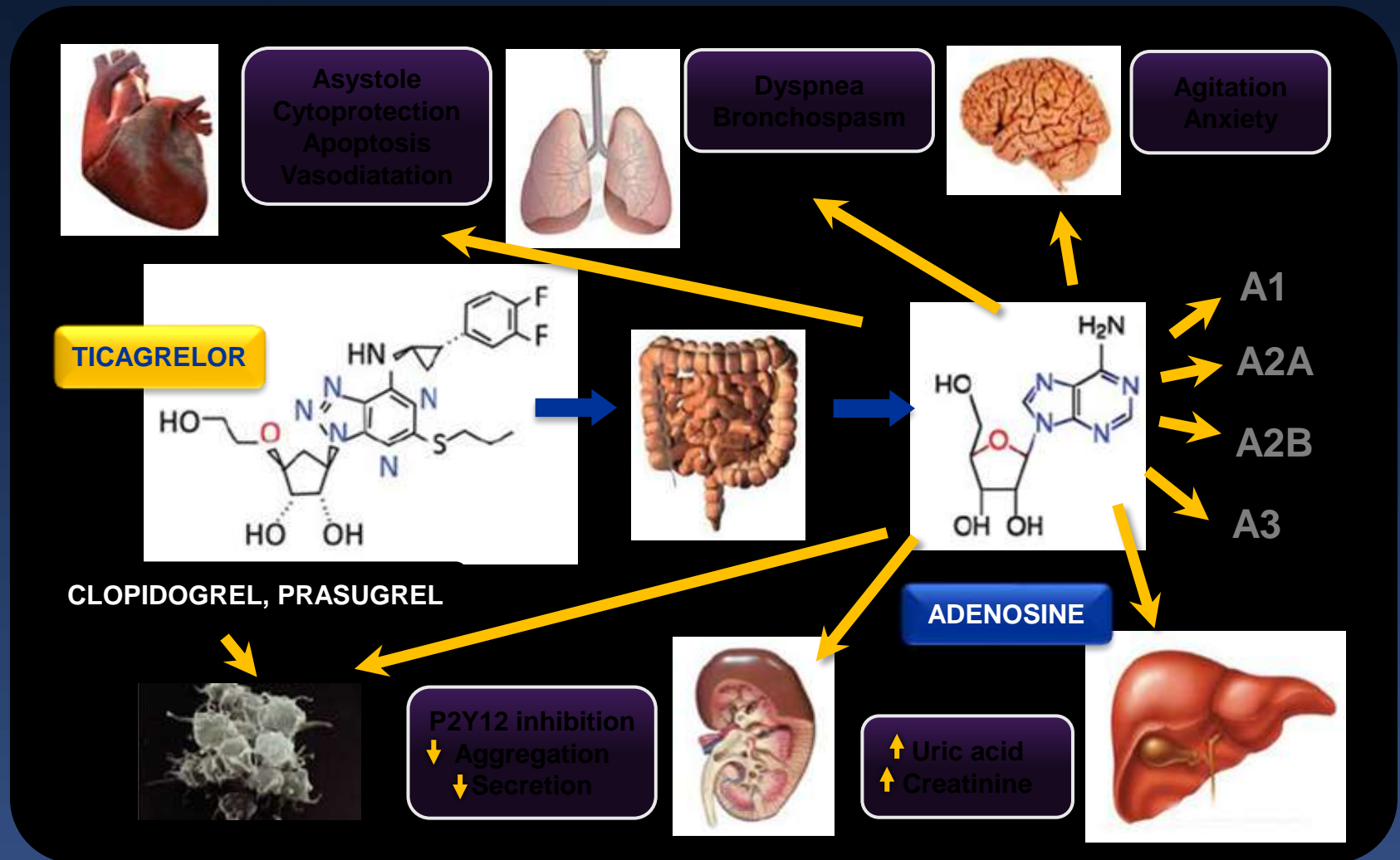
Ticagrelor inhibits ENT-1 transporter and enhances adenosine response



- Inhibition of ENT-1 transporter^{1,2,3}
 - Enhanced local adenosine response may result in:*
 - ✓ Additional inhibition of platelet aggregation/activation¹
 - ✓ Cardioprotection⁴
 - ✓ Vasodilation^{3,5,6}
 - ✓ Modulation of inflammation
 - ✓ Dyspnoea⁵

1. Nylander S, et al. *J Thromb Haemost* 2013;11:1867–1876.
2. Armstrong D, et al. *J Cardiovasc Pharmacol Ther*; In press.
3. van Giezen JJJ, et al. *J Cardiovasc Pharmacol Ther* 2012;17:164–172.
4. Wang K, et al. *Thromb Haemost.* 2010;104:609-17.
5. Wittfeldt A, et al. *J Am Coll Cardiol* 2013;61:723–727.
6. Alexopoulos D, et al. *Circ Cardiovasc Interv* 2013;19:5121–5126.

Possible role of adenosine in CV mortality benefit and dyspnea



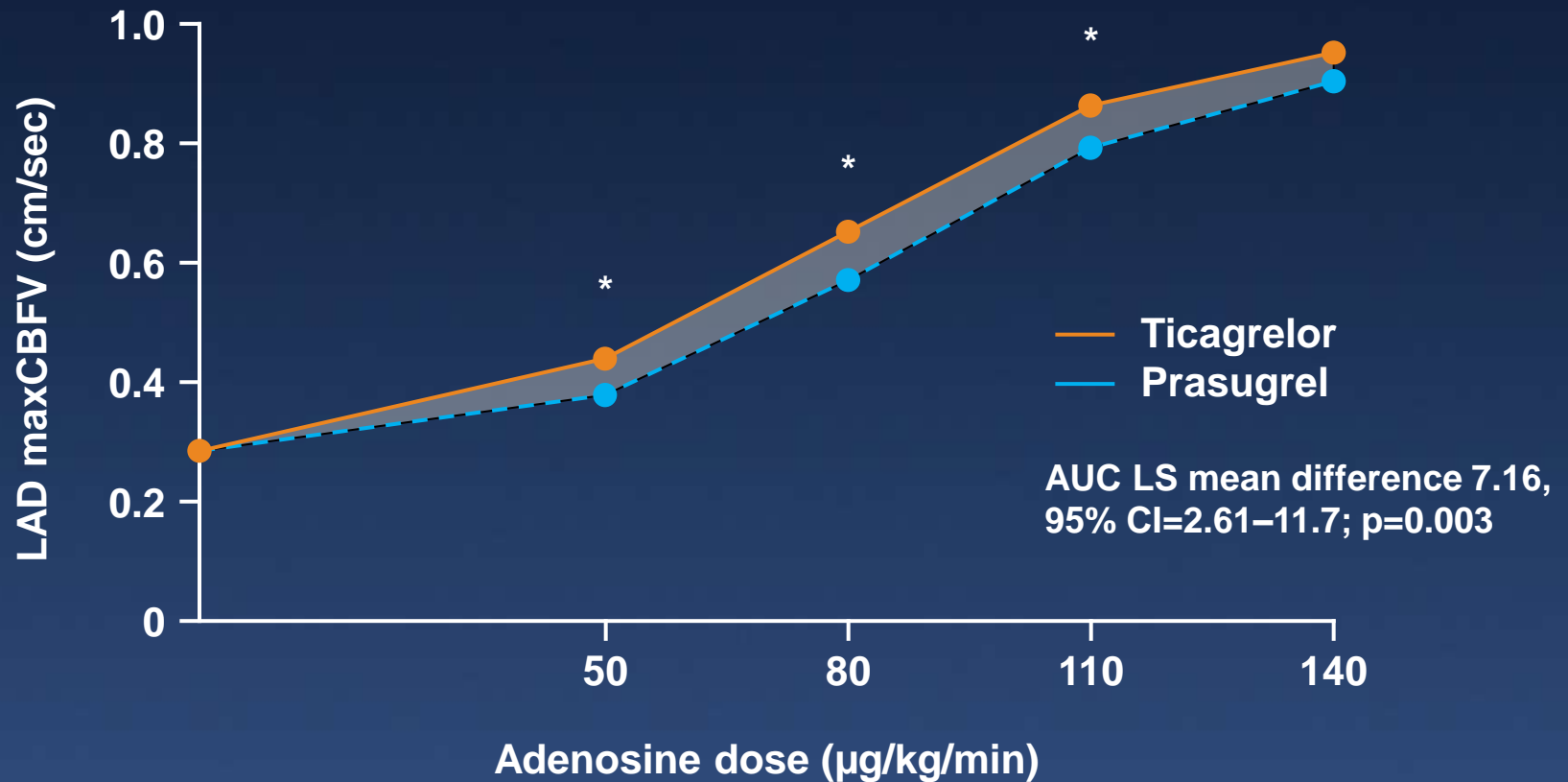
Ticagrelor enhances adenosine-induced coronary vasodilatory responses in Humans

Ticagrelor Enhances Adenosine-Induced Coronary Vasodilatory Responses in Humans

Ann Wittfeldt, MD,* Håkan Emanuelsson, MD, PHD,† Gunnar Brandrup-Wognsen, MD, PHD,*†
J. J. J. van Giezen, PHD,† Jenny Jonasson, PHD,† Sven Nylander, PHD,† Li-Ming Gan, MD, PHD*†
Göteborg and Mölndal, Sweden

- 40 healthy male
- Ticagrelor 180mg LD vs. placebo
- Coronary blood flow velocity (CBFV) ; measured by Doppler Echo

Ticagrelor increases adenosine-induced CBFV in NSTEMI-ACS patients relative to prasugrel



*Significantly higher ratio of LAD maxCBFV/bCBFV for ticagrelor vs. prasugrel.

AUC, area under the curve; CBFV, coronary blood flow velocity; CI, confidence interval; LAD, left anterior descending artery; LS, least squares;

NSTEMI-ACS, non-ST-segment elevation acute coronary syndromes.

Alexopoulos D, et al. *Circ Cardiovasc Interv* 2013;6:277–283.

Key summary

- Ticagrelor is the first, oral direct-acting P2Y₁₂ receptor antagonist working through a dual pathway
- Ticagrelor is only antiplatelet agent proving CV mortality benefit compared to clopidogrel
- Ticagrelor may have pleiotropic anti-atherosclerotic actions beyond platelet inhibition, however further investigation is required for its explanation

Thank you for your attention!