



Anti-Platelet İlaç Direnci ve Laboratuvar

Dr. Deniz İlhan Topcu

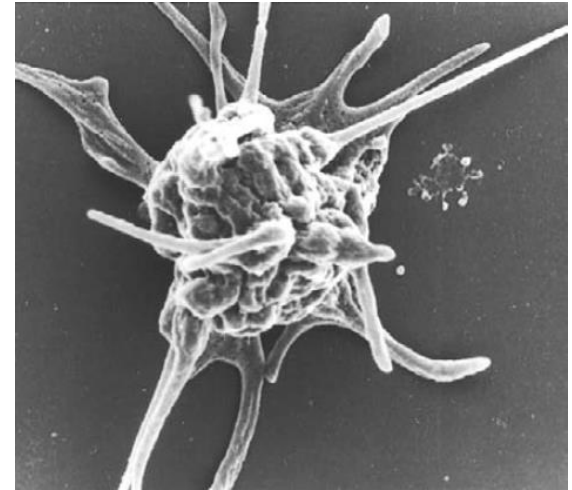
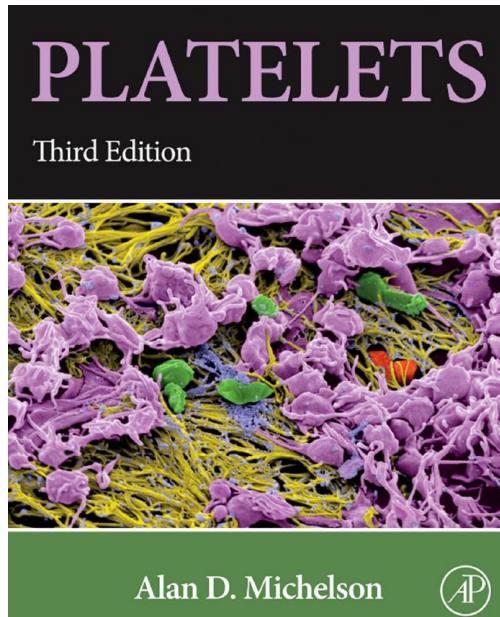
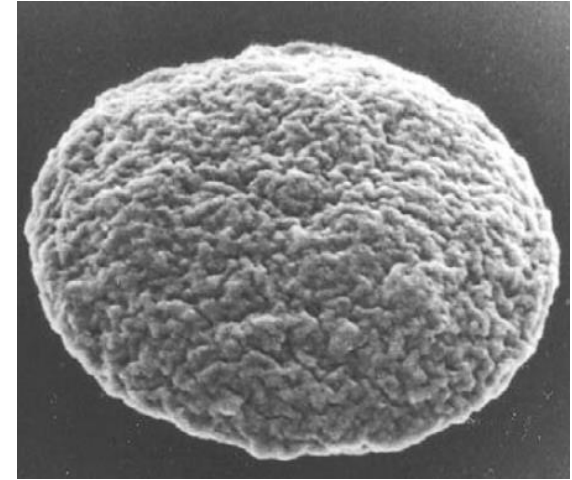


**BAŞKENT
ÜNİVERSİTESİ**

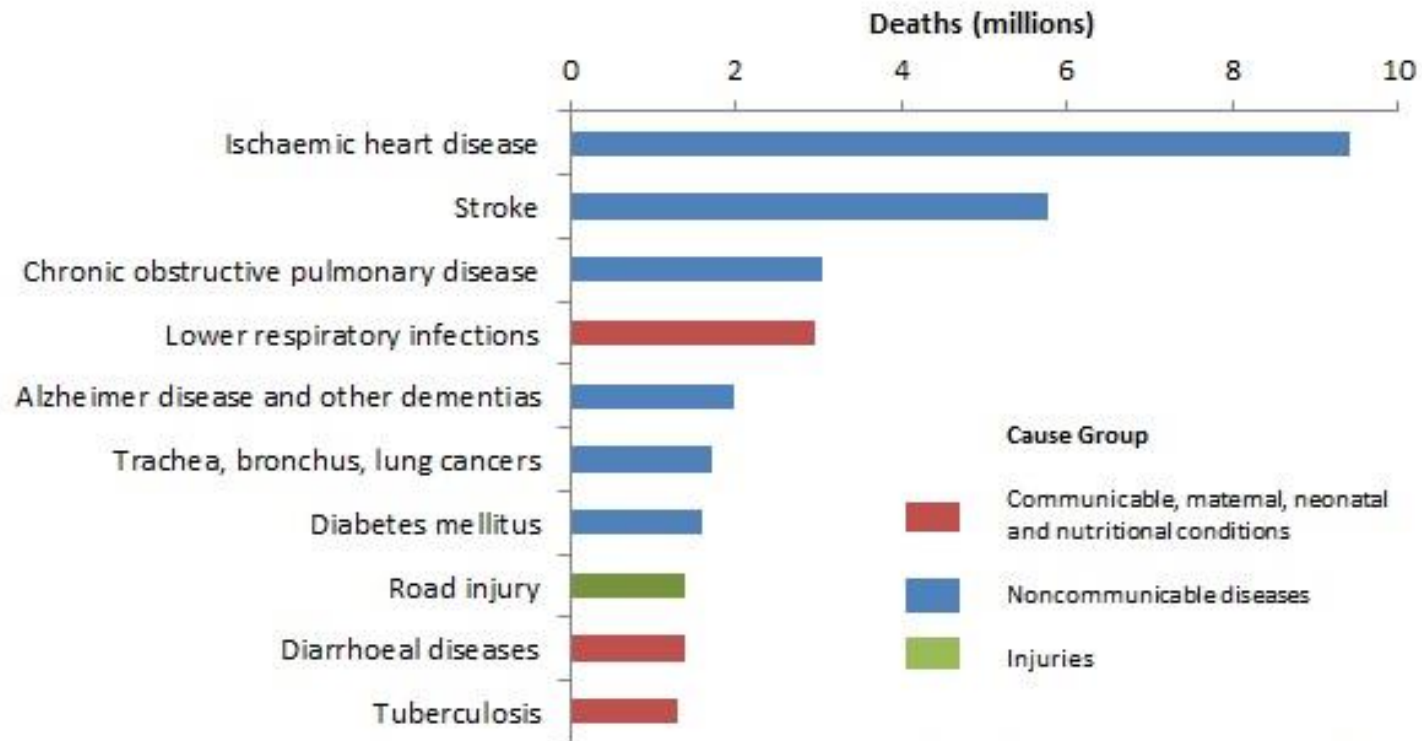
Plateletler

Osler 1873, 1874

Bizzozero....1881, 1882



Top 10 global causes of deaths, 2016



Source: Global Health Estimates 2016: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2016. Geneva, World Health Organization; 2018.



Antitrombotik İlaçlar

- Antikoagülan İlaçlar
- Anti-Platelet (Antitrombositik) İlaçlar
- Fibrinolitik (Trombolitik) İlaçlar



Neden Anti-Platelet Tedavi?

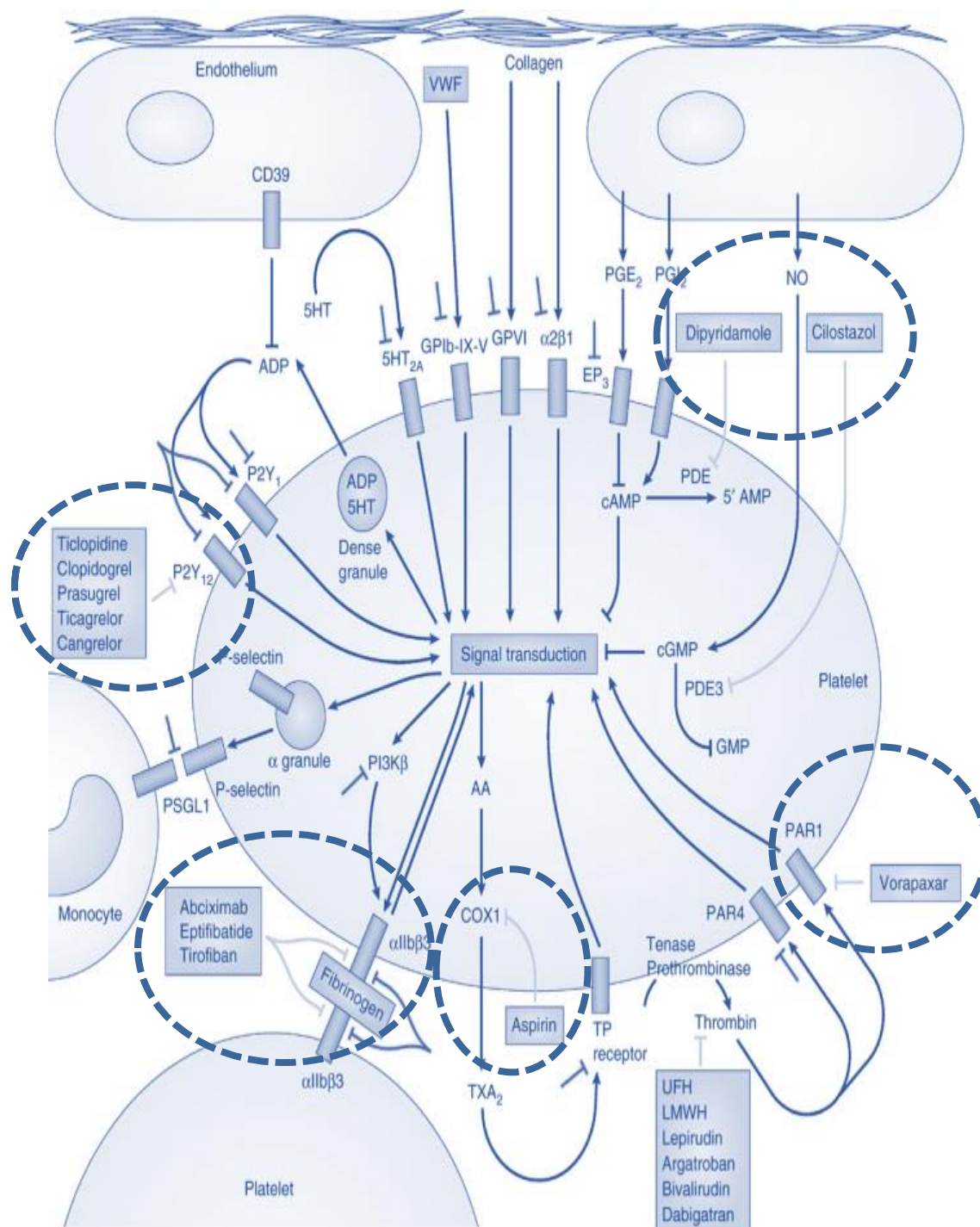
1. Acute coronary syndrome
2. Post Percutaneous coronary intervention with stenting percutaneous coronary intervention (PCI)
3. Mechanical heart valves in combination with warfarin
4. Acute Ischemic stroke
5. Post percutaneous intervention of peripheral arterial disease
6. Device closure such as post ASD closure for at least six months
7. Stable angina
8. Post-coronary artery bypass grafting surgery
9. Essential thrombocytosis
10. Primary prevention of coronary artery disease
11. Prevention of colon cancer
12. Kawasaki disease
13. Acute rheumatic disease
14. Post PDA device closure for the first six months
15. Acute pericarditis
16. Atrial fibrillation with a CHAD2SVASc score of 1
17. Primary prevention of venous thromboembolism
18. Ischaemic stroke
19. Transient ischaemic attack



Agent	Structure	Administration	Mechanism	Indication	
Aspirin	Acetylsalicylic acid	Oral	COX-1 inhibition	CAD, PAD, CVD, CABG, CEA, coronary and peripheral stents	1
Ticlopidine	Thienopyridine	Oral	P2Y ₁₂ inhibition	CVD, coronary stents	
Clopidogrel	Thienopyridine	Oral	P2Y ₁₂ inhibition	Prior MI, stroke or symptomatic PAD, as monotherapy; ACS or coronary stenting, in combination with aspirin	
Prasugrel	Thienopyridine	Oral	P2Y ₁₂ inhibition	ACS patients undergoing PCI with stenting, in combination with aspirin	
Ticagrelor	Triazolopyrimidine	Oral	P2Y ₁₂ inhibition	ACS patients, in combination with aspirin	2
Cangrelor	Adenosine triphosphate analog	Intravenous	P2Y ₁₂ inhibition	P2Y ₁₂ inhibitor naïve PCI patients	
Abciximab	F _{ab} fragment of mouse human chimeric antibody 7E3	Intravenous	GPIIb-IIIa inhibition	PCI	
Tirofiban	Non-peptide mimetic based on RGD	Intravenous	GPIIb-IIIa inhibition	ACS, PCI	
Eptifibatid	KGD-containing cyclic heptapeptide	Intravenous	GPIIb-IIIa inhibition	ACS, PCI	3
Vorapaxar	Tricyclic himbacine derivative	Oral	PAR-1 inhibition	Prior MI, PAD	4

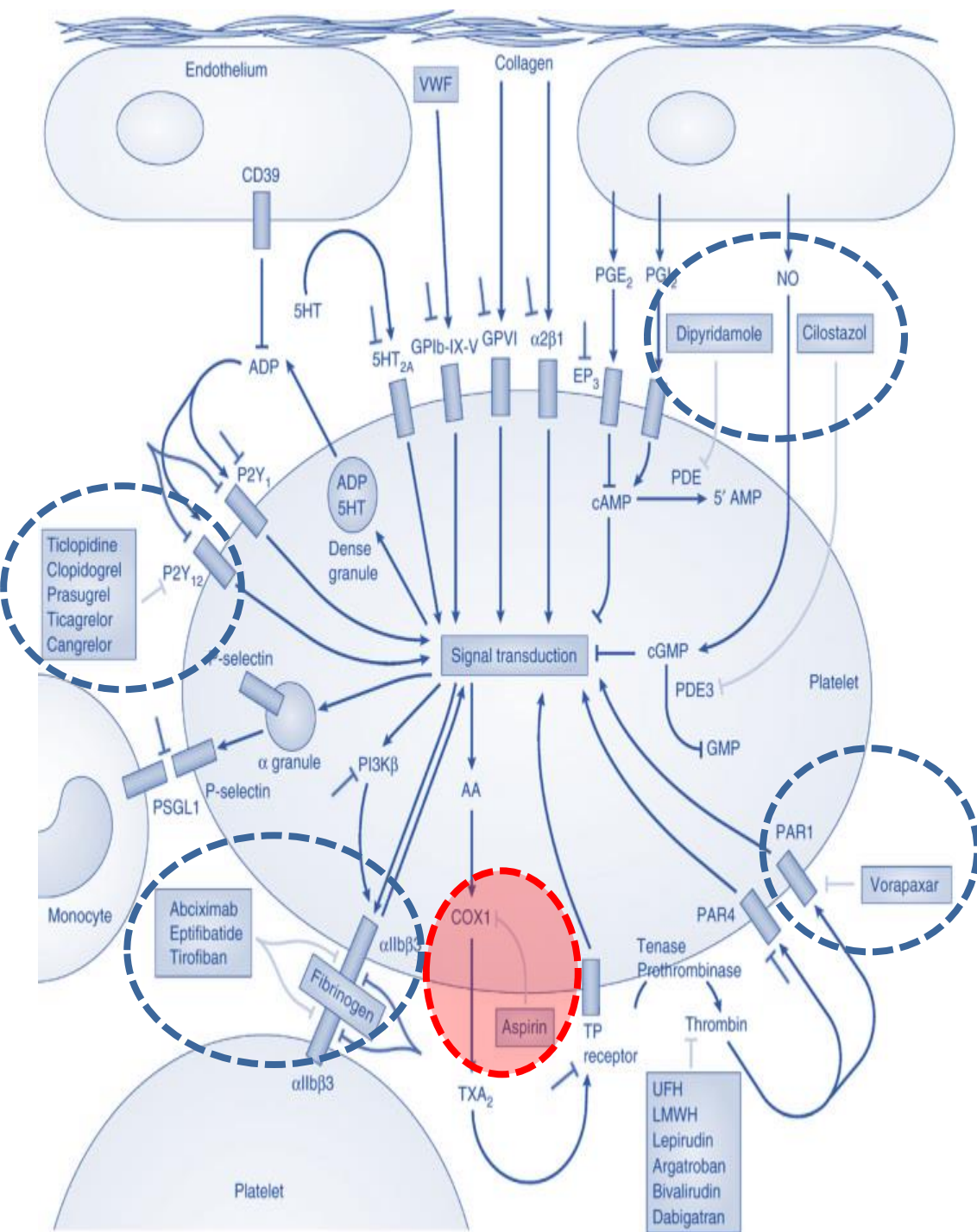
ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CEA, carotid endarterectomy; CAD, coronary artery disease; COX-1, cyclooxygenase-1; CVD, cerebrovascular disease; GPIIb-IIIa, glycoprotein IIb-IIIa; KGD, Lys-Gly-Asp; MI, myocardial infarction; PAD, peripheral artery disease; PAR-1, protease-activated receptor-1; PCI, percutaneous coronary intervention; RGD, Arg-Gly-Asp.





Nat Rev Drug
 Discov. 2010
 Feb;9(2):154-69.

1. Aspirin



2. ADP P2Y₁₂ reseptör antagonistleri

Oral Thienopyridinler:

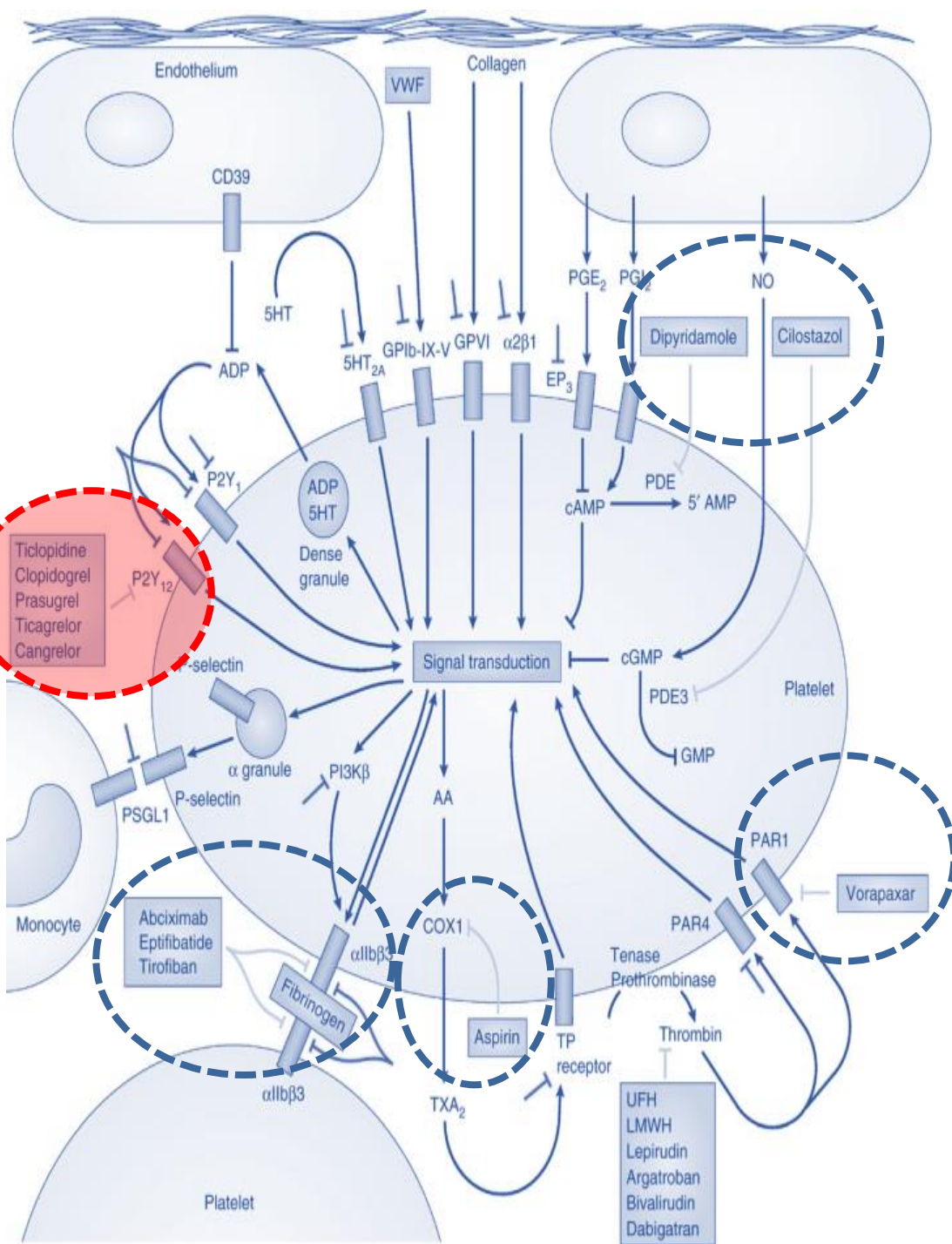
Ticlopidine
Clopidogrel
Prasugrel

Oral Triazolopyrimidin:

Ticagrelor
(aspirin ile birlikte)

I.V. Modifiye ATP türevi

Cangrelor

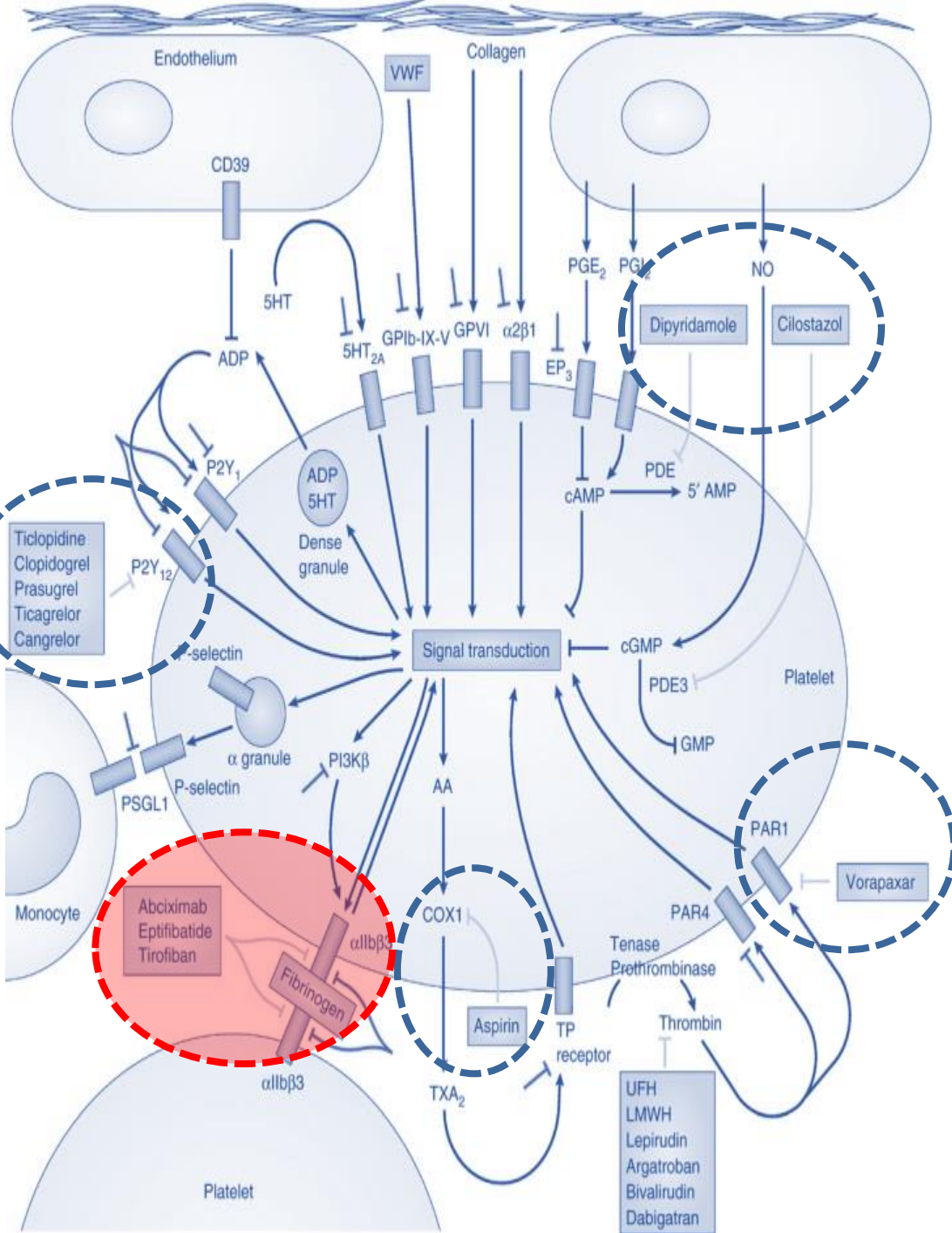


3. Glikoprotein Platelet İnhibitorleri

GPIIb-IIIa (α IIb β 3)

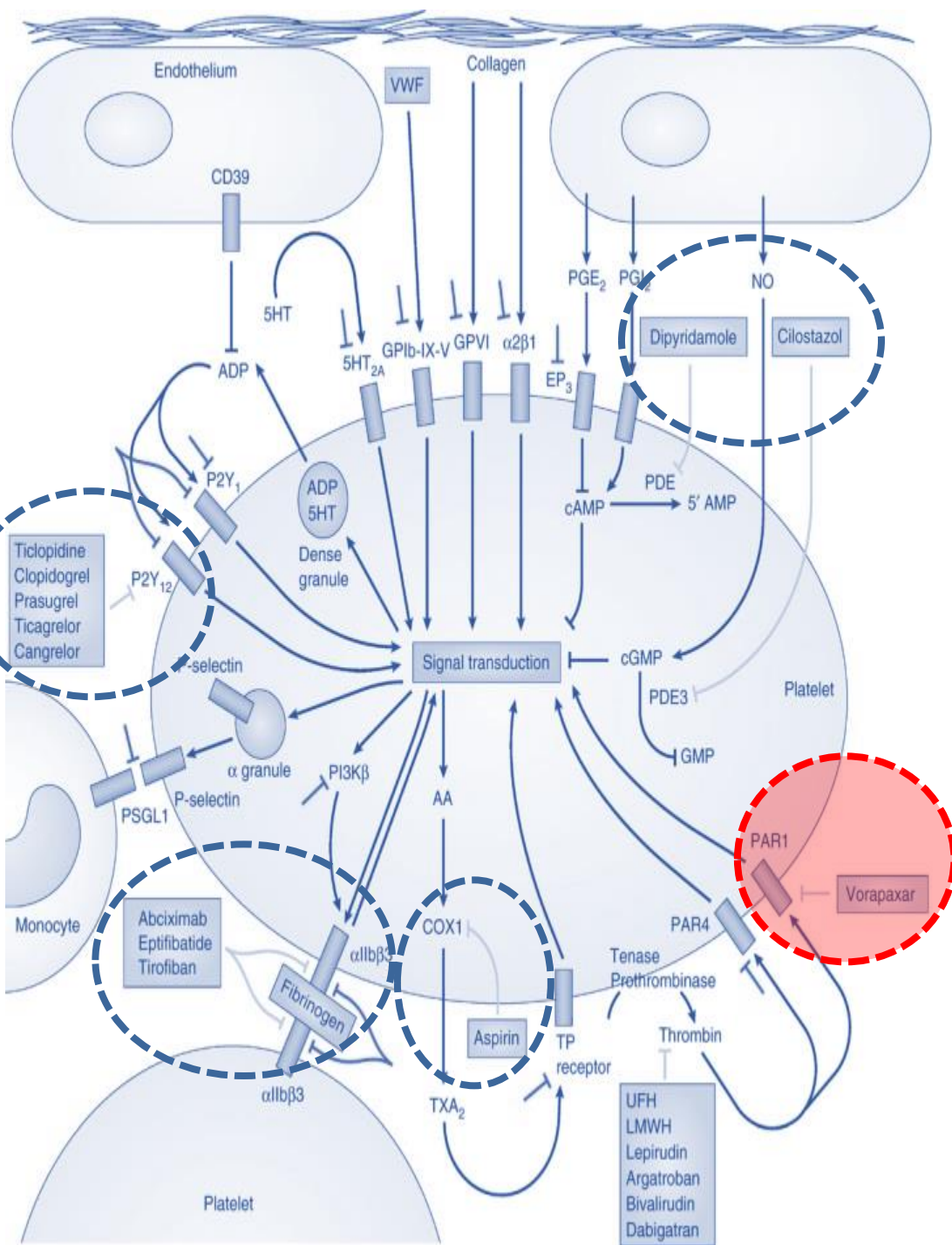
Abciximab
Eptifibatide
Tirofiban

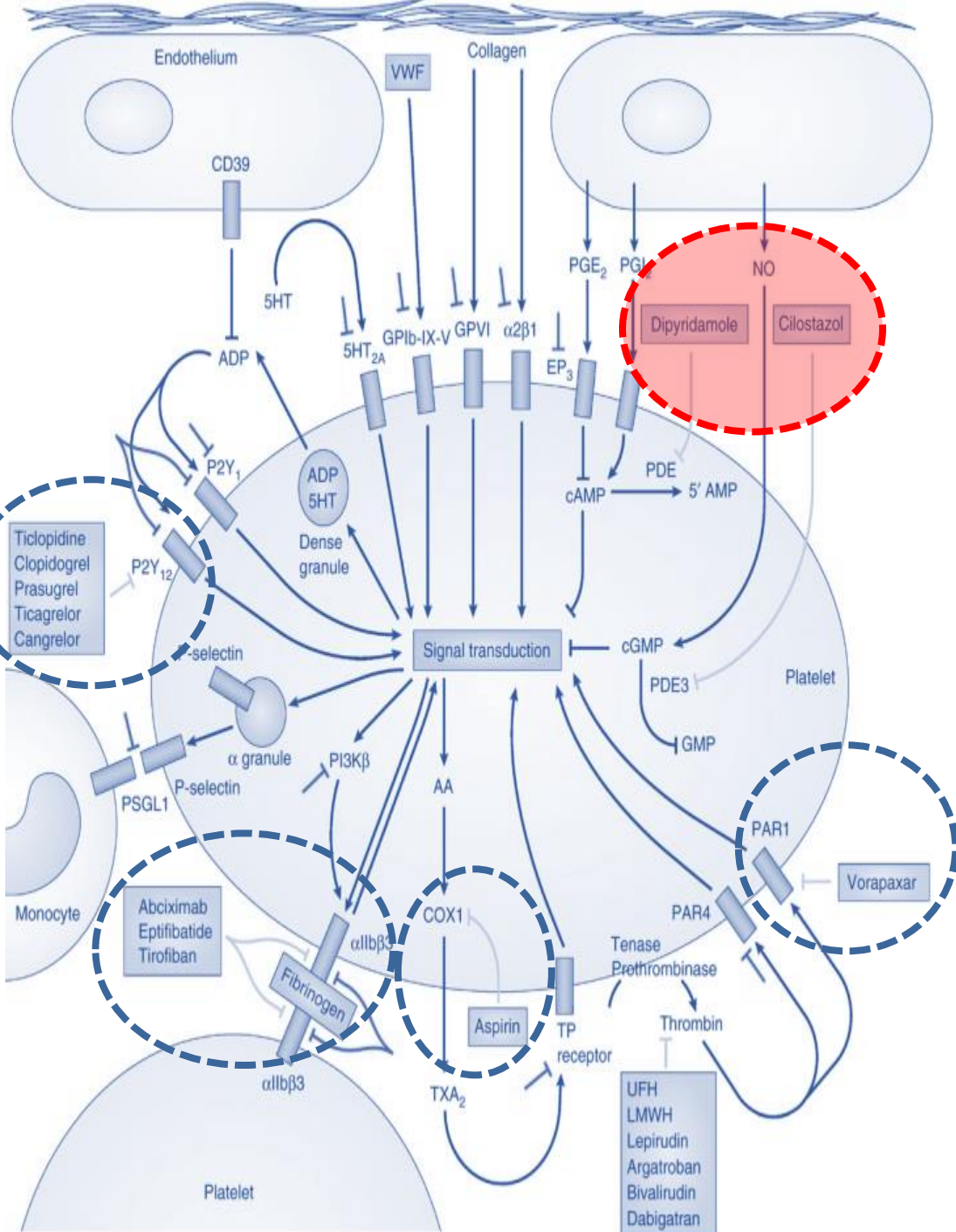
- Uygulama sonrası hızlıca aktive plateletlerde fibrinojen reseptörünü bloke ederler.
 - Platelet – platelet agregasyonunu inhibisyonu
- Kısa $t_{1/2}$ 10 dakika - 2.5 saat
- Özellikle AKS tedavisinde kullanılırlar



4. Protease-activated Receptor-1 Antagonistleri

Voraxapar





5. Fosfodiesteraz İnhibitörleri

Dipyridamole

Cilostazol (VD etkisi)

LABORATUVAR – NE ZAMAN?



! Laboratuvar değerlendirmesi rutin önerilmiyor **mu** ???

– ESC2017 kılavuzu

For these reasons, neither platelet function testing nor genetic testing can be recommended for tailoring DAPT. It may be considered in specific situations (e.g. patients suffering from recurrent adverse events) if the results may change the treatment strategy. This is the case for patients undergoing CABG who are exposed to DAPT (see Chapter 5).





– ACC / AHA 2016 Kılavuzu

guideline (9,14). To date, no RCT has demonstrated that routine platelet function testing or genetic testing to guide P2Y₁₂ inhibitor therapy improves outcome; thus, the routine use of platelet function and genetic testing is not recommended (Class III: No Benefit).



State-of-the-Art Review

Updated Expert Consensus Statement on Platelet Function and Genetic Testing for Guiding P2Y₁₂ Receptor Inhibitor Treatment in Percutaneous Coronary Intervention

Dirk Sibbing MD, MHBA^{a, b, *}  , Daniel Aradi MD, PhD^{c, *}, Dimitrios Alexopoulos MD^d, Jurrien ten Berg MD^e, Deepak L. Bhatt MD, MPH^f, Laurent Bonello MD^g, Jean-Philippe Collet MD^h, Thomas Cuisset MDⁱ, Francesco Franchi MD^j, Lisa Gross MD^{a, b}, Paul Gurbel MD^k, Young-Hoon Jeong MD^l, Roxana Mehran MD^{m, n}, David J. Moliterno MD^o, Franz-Josef Neumann MD^p, Naveen L. Pereira MD^q, Matthew J. Price MD^r, Marc S. Sabatine MD, MPH^s ... Dominick J. Angiolillo MD, PhD^j  

Highlights

- Different P2Y₁₂ inhibitors have enabled physicians to contemplate individualized treatment regimens.
- In selective scenarios, PFT and genotyping may be used as optional tools for guiding treatment.
- Further studies on DAPT deescalation and escalation are needed to refine existing treatment options.



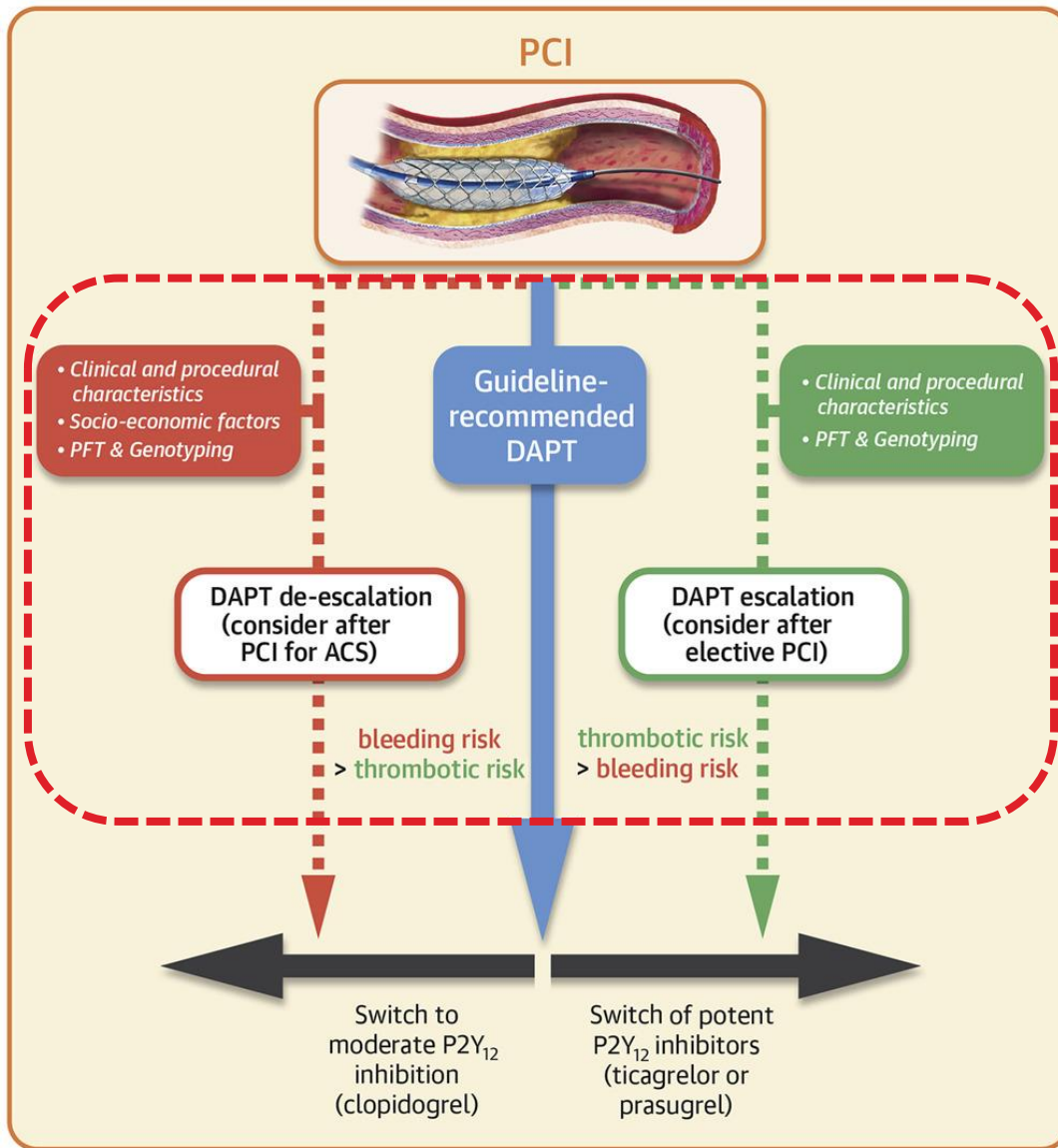
State-of-the-Art Review

Updated Expert Consensus Document on P2Y₁₂ Receptor Inhibition

Dirk Sibbing MD, MHBA^{a, b, *}, Jean-Philippe Collet MD^h, Thomas A. Manouk MD^{c, d, e}, Franz-Josef Neumann MD^{f, g}, Roxana Mehran MD^{m, n}, David J. Angiolillo MD, PhD^{j, k, l}

Testing for Guiding

Dirk Sibbing MD, MPH^f, Laurent Bonello MD^g, Jean-Philippe Collet MD^h, Roxana Mehran MD^{m, n}, David J. Angiolillo MD, PhD^{j, k, l}



Laboratuvar – Ne zaman?

① Kanama riski

② ilaç kullanımına rağmen trombotik olay



İlaç Kullanımına Rağmen Trombotik Olay

- «resistance» / «direnç»
- «non-responders»
- «poor responders»
- «**high on-treatment platelet reactivity**» (HTPR) :
refer to lack of therapeutic levels of inhibition of a drug as measured by a well-validated assay that has acceptable sensitivity and specificity for the particular drug effect



Laboratuvar – Ne zaman?

«Sonuçlar tedavi stratejisini yönlendirecekse»
Kişiselleştirilmiş Tedavi



Antiplatelet Tedavi Etkinliği Değerlendirilmesi

- Antiplatelet İlaç Dozunun Ayarlanması
 - Antiplatelet İlaç Türünün Seçimi
- Antiplatelet İlaç Tür ve Dozunun Seçimi



Amaç

Platelet inhibisyonu için
«**terapötik aralık**»
belirlemek

Analiz



Platelet Fonksiyon Testi



Trombosit Fonksiyon Değerlendirmesi

Platelet fonksiyonu nasıl gösterilebilir?

- Platelet Aktivasyonun Belirteçleri
- Platelet Agregasyonunun Gösterilmesi
- Platelet Turnover Belirteçleri



Platelet Aktivasyonun Belirteçleri

Aktivasyonun gösterilmesi için 3 farklı yaklaşım

1. Platelet granüllerinden serbestleşen maddelerin ölçümü
 - **ELISA** ile P-selectin düzeylerinin ölçülmesi
2. Platelet yüzeyine ekprese edilen belirteçlerin ölçümü
 - **Flowsitometri**
 - Platelet platelet – lökosit agregat yüzeyinde ekprese edilen P-selectin
 - **VASP**
3. Plateletler tarafından sentezlenen metabolitler:
 - **ELISA** ile serum **thromboxane B2** ölçümü
 - İdrar **11-dehydrothromboxane B2** ölçümü



Platelet Aktivasyonun Belirteçleri

Aktivasyonun gösterilmesi için 3 farklı yaklaşım

1. Platelet granüllerinden serbestleşen maddelerin ölçümü
 - ELISA ile P-selectin düzeylerinin ölçülmesi
2. Platelet yüzeyine ekprese edilen belirteçlerin ölçümü

Aspirin

11-Dehydro Thromboxane B2

Aspirin responsive

≤1500 pg 11-dehydro thromboxane B2/mg creatinine



Aspirin resistant

>1500 pg 11-dehydro thromboxane B2/mg creatinine

- VASP

3. Plateletler tarafından sentezlenen metabolitler:

- ELISA ile serum thromboxane B2 ölçümü
- İdrar 11-dehydrothromboxane B2 ölçümü



Platelet Aktivasyonun Belirteçleri

Aktivasyonun gösterilmesi için 3 farklı yaklaşım

1. Platelet granüllerinden serbestleşen maddelerin ölçümü
 - **ELISA** ile P-selectin düzeylerinin ölçülmesi
2. Platelet yüzeyine ekprese edilen belirteçlerin ölçümü
 - **Flowsitometri**
 - Platelet platelet – lökosit agregat yüzeyinde ekprese edilen P-selectin
 - **VASP**
3. Plateletler tarafından sentezlenen metabolitler:
 - **ELISA** ile serum **thromboxane B2** ölçümü
 - İdrar **11-dehydrothromboxane B2** ölçümü



Platelet Agregasyonunun Gösterilmesi

- Işık Transmisyon Agregometri(LTA)
- Platelet Function Analyzer PAF-100/200
- Impedans agregometri
- Thromboelastografi
 - Thromboelastogram
 - Platelet Mapping System
 - ROTEM Platelet Test
- Flow cytometry
- «VerifyNow»
- Plateletworks
- Impact-R
- In Vivo Platelet Aggregation izlenmesi



Study	N	Method	Patient Group	Outcome	Conclusion
Blindt et al. [113]	99	VASP LTA	PCI	stent thrombosis (ST) (6 months)	VASP was an independent predictor of ST.
Bonello et al. [114]	144	VASP	PCI	MACE (6 months)	VASP has a very high negative predictive value, it can predict postprocedural MACE.
Breet et al. [115]	1069	LTA VerifyNow PlateletWorks IMPACT-R PFA-100	Elective PCI	MACE (1 year)	PlateletWorks, LTA, VerifyNow and Innovance P2Y were significantly associated with the primary end point.
Buonamici et al. [116]	804	LTA (ADP induced platelet aggregation)	PCI+ DES implantation	stent thrombosis (6 months)	Nonresponsiveness to clopidogrel is a strong independent predictor of ST.
Cuisset et al. [117]	598	LTA (ADP induced platelet aggregation) VASP	PCI (ACS)	ST (30 days)	ST patients had greater ADP induced aggregation but only a trend toward greater platelet reactivity index.
Hochholzer et al. [118]	802	LTA (ADP induced platelet aggregation)	elective PCI	MACE (1 month)	Platelet aggregation immediately before elective stenting correlated with early outcome.
Geisler et al. [119]	1019	LTA (ADP induced platelet aggregation)	PCI	stent thrombosis (3 months)	Early but not late ST was influenced by residual platelet aggregation.
Gori et al. [120]	746	LTA (ADP, AA and collagen induced platelet aggregation)	PCI, DES	stent thrombosis, ST+death (6 months)	Dual non-responsiveness to aspirin and clopidogrel identifies patients at a very high risk of ST and death.
Migliorini et al. [121]	215	LTA (ADP induced platelet aggregation)	PCI, DES	stent thrombosis, cardiac death	HRPR after 600 mg clopidogrel is a strong marker of increased risk of cardiac death and ST.
Marcucci et al. [122]	683	VerifyNow P2Y12	PCI (ACS)	MACE (1 year)	HRPR to ADP is able to detect patients at risk of death and nonfatal MI.
Price et al. [123]	380	VerifyNow P2Y12	PCI+DES implantation	MACE (6 months)	HRPR was associated with post-discharge events.
Siller-Matula et al. [124]	416	MEA ADP VASP	PCI	stent thrombosis (6 months)	MEA predicts stent thrombosis better than the VASP phosphorylation assay.
Szapáry et al. [125]	100	LTA (ADP induced platelet aggregation)	Stroke or TIA	ischemic stroke, myocardial infarction, critical limb ischaemia (1 year)	Patients who were clopidogrel resistant at baseline had a significantly higher rate of ischemic events compared to clopidogrel responders.



Study	Patients	Methods	Association with Bleeding
Campo et al. [126]	PCI patients (<i>n</i> = 300)	VerifyNow	Low on-clopidogrel platelet reactivity was associated with bleeding events. 1 month on-clopidogrel platelet reactivity better discriminates bleeding complications than at baseline.
Chen et al. [127]	Patients treated with clopidogrel ≤ 6 days before CABG (<i>n</i> = 45)	LTA (ADP-induced platelet aggregation) PFA-100	<40% pre-heparin ADP-induced aggregation predicted in 92% severe bleedings requiring transfusion.
Cuisset et al. [128]	NSTEMI +PCI (<i>n</i> = 597)	VASP ADP induced platelet aggregation	Risk of TIMI major and minor bleeding was significantly higher in hyperresponders to antiplatelet therapy.
Michelson et al. [129]	ACS + PCI (<i>n</i> = 125)	VASP	Significant association of reduced VASP PRI with the occurrence of hemorrhage event
Mokhtar et al. [130]	PCI patients (<i>n</i> = 346)	VASP	VASP index was significantly higher in patients who suffered a non-CABG related TIMI bleeding compared to patients without bleeding.
Parodi et al. [131]	PCI patients treated with prasugrel and aspirin (<i>n</i> = 45)	LTA (ADP induced platelet aggregation)	Low residual platelet reactivity and female gender were independent predictors of bleeding events.
PEGASUS-PCI [132]	PCI (<i>n</i> = 416)	MEA, VASP, CPA, PFA-100	The incidence of major bleedings was numerically higher in patients with an enhanced vs. poor response to clopidogrel assessed by MEA.
Rahe-Meyer et al. [77]	cardiac surgery (<i>n</i> = 60)	MEA	Near-patient platelet aggregation may allow the identification of patients with enhanced risk of platelet concentrate transfusion, both pre-operatively and upon arrival on the ICU.
Ranucci et al. [76]	cardiac surgery, thienopyridine treatment (<i>n</i> = 87)	MEA ADP	MEA ADP test was associated with postoperative bleeding and platelet transfusion.



Işık Transmisyon Agregometri

- Platelet fonksiyonlarının değerlendirilmesinde kullanılan turbidimetrik metod (altın standart)
- Platelet zengin plazma (PRP)

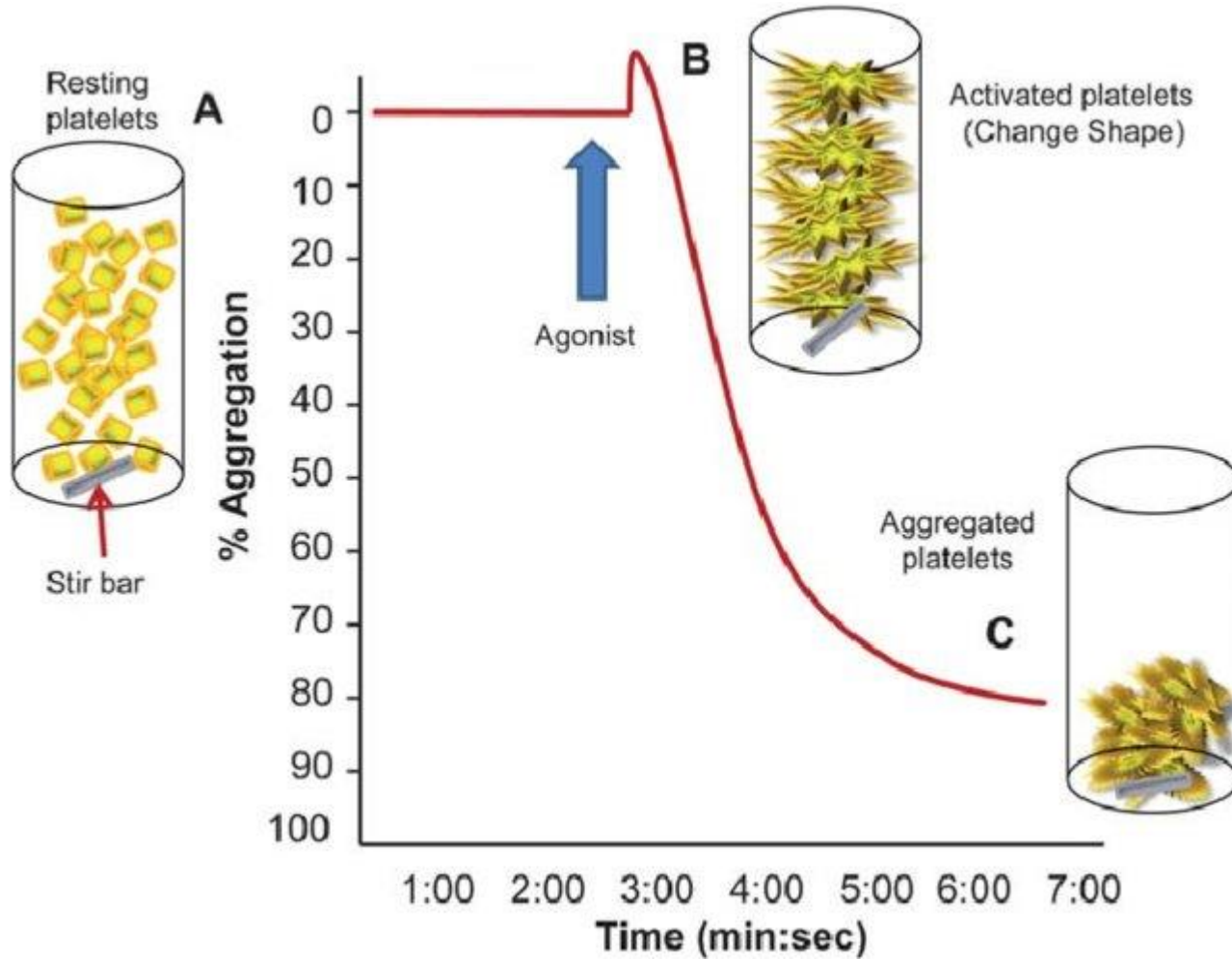
PRP + agonist = *agregasyon*



Türbiditede azalma / Transmittans artışı



Işık Transmisyon Agregometri



Işık Transmisyon Agregometri

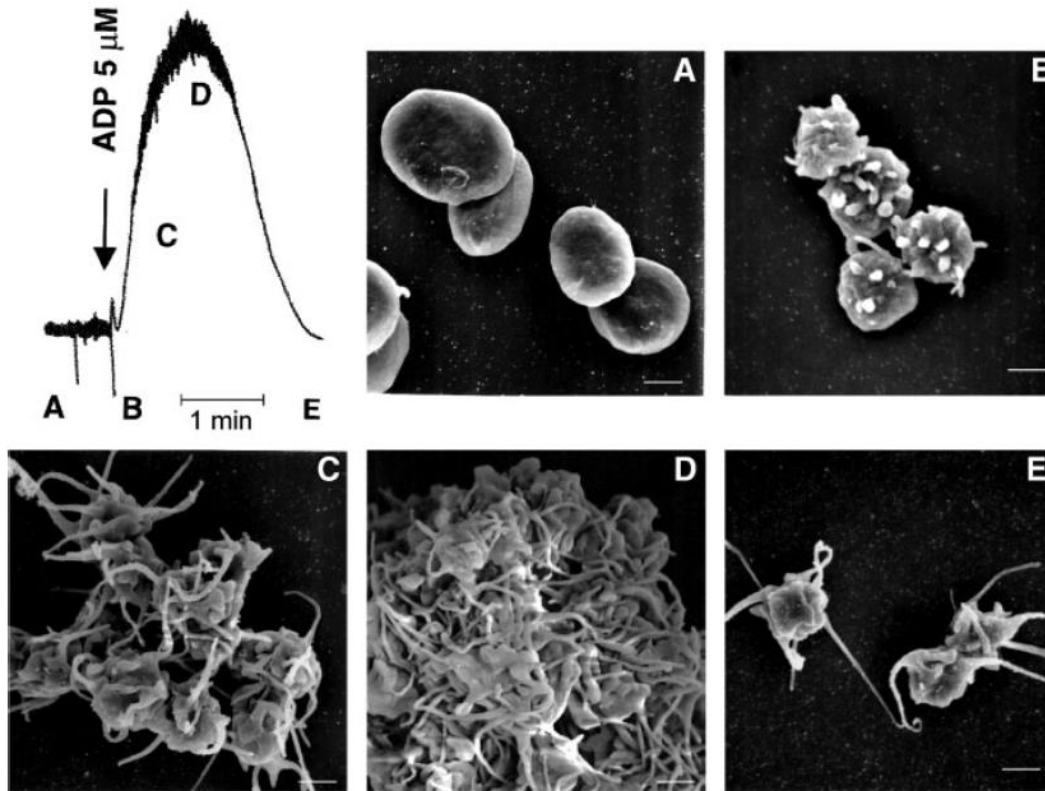


Fig. 1 Morphological changes of washed platelets during adenosine diphosphate (ADP)-induced aggregation. An aggregation response was obtained by stimulating platelets with 5 μM ADP (arrow). The platelets were fixed at different time points and their surface features were visualized by scanning electron microscopy. (A) Discoid cells in the resting state. (B) Formation of early pseudopods (7 seconds). (C) Full shape change and first platelet-platelet interactions (20 seconds). (D) Large platelet aggregates (45 seconds). (E) Isolated platelets after disaggregation (3 minutes). Bars = 1 μM. (Reproduced with permission from: Cazenave et al.⁴⁶ Copyright [2004] Humana Press Inc.)



Impedans Agregometri

- Multiple Electrode Aggregometry
 - Tam kan örneği (Hirudin)



Platelet + agonist = ***agregasyon***

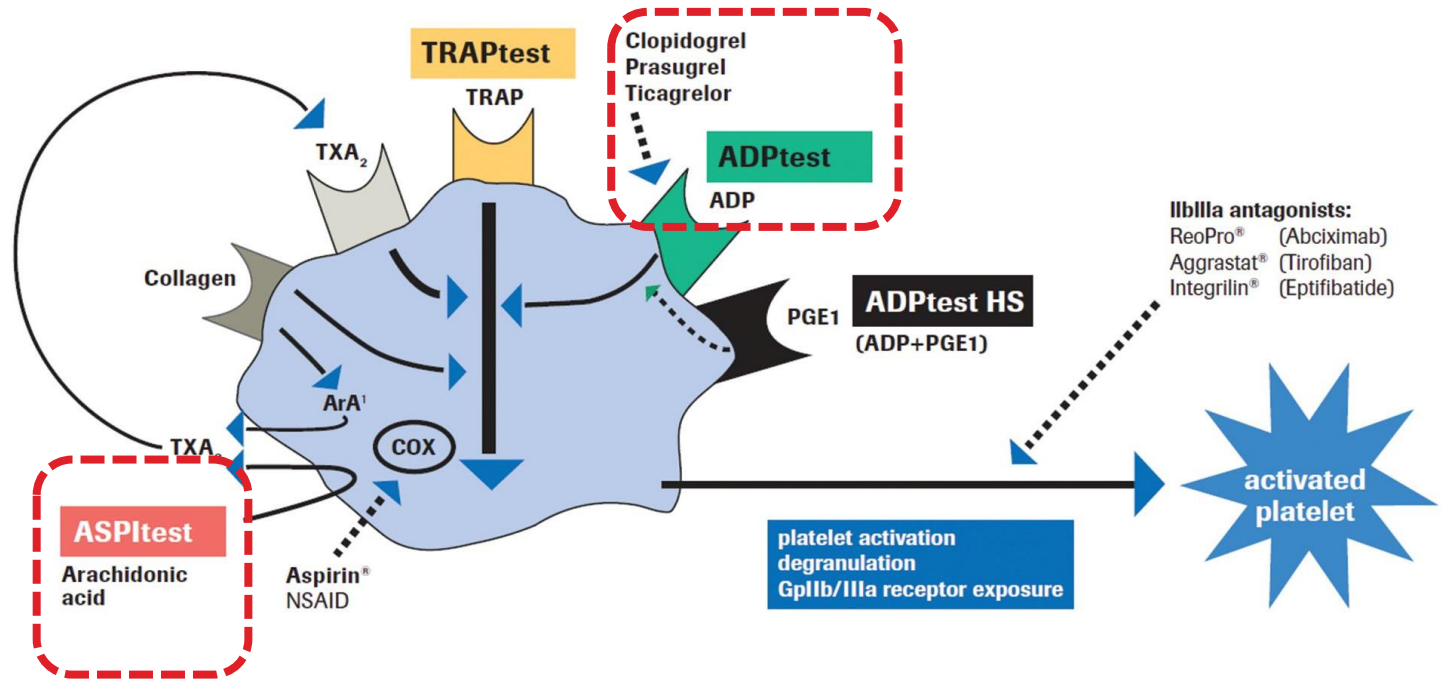


Impedans artışı

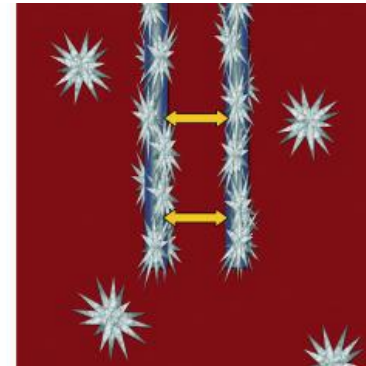
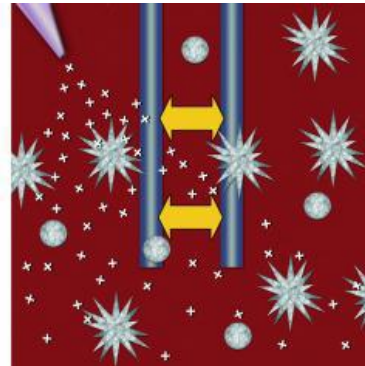
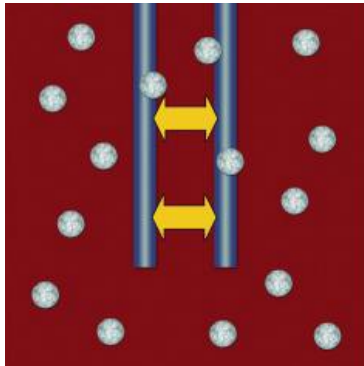
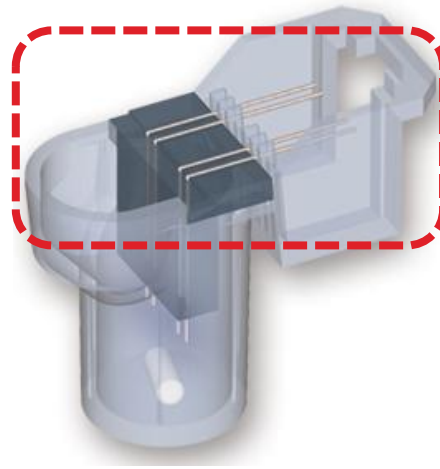


Multiplate Agonistler

—▶ Activation
 - - - -▶ Inhibition
¹ release of arachidonic acid

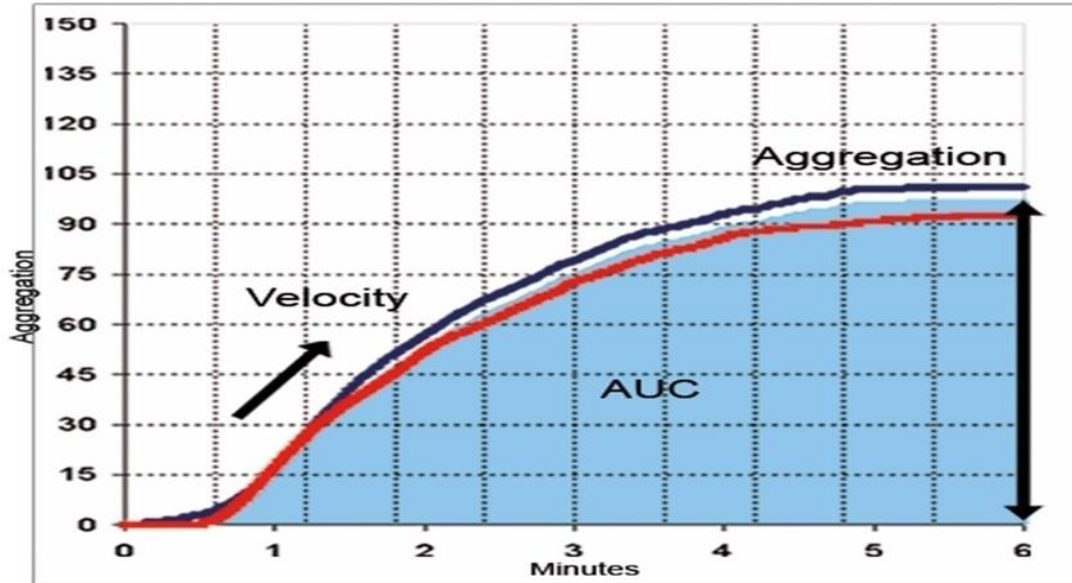


Multiplate Elektrot

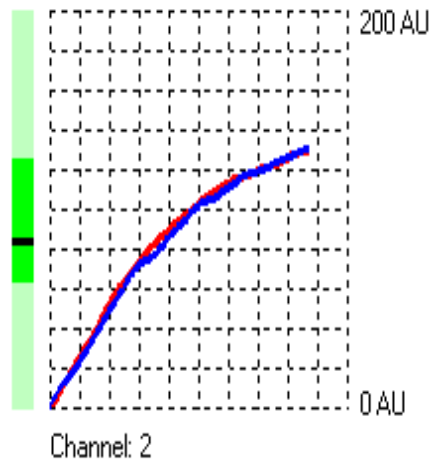


Multiplate Raporlama

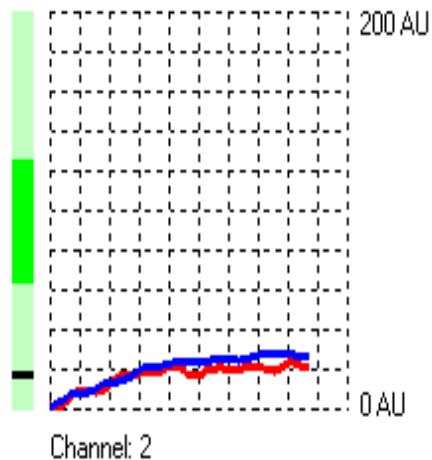
- İmpedans artışı, «**arbitrary aggregation unit**» (AU) çevrilir ve zamana karşı grafiklenir.



Multiplate ADPtest



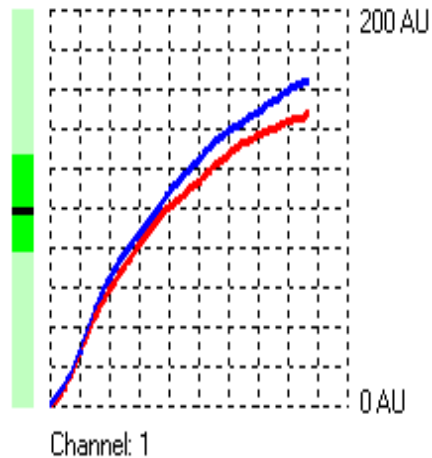
Patient ID : m.....
 Test name : ADPtest (TI blood), V1
 Start of test : 07. Jan. 2012, 05:33:13 (Measurement duration 6:00 min.)
 Area under the curve : 761 AU*min. (569 - 1130)
 Aggregation : RUO: 129.0 AU
 Velocity : RUO: 15.9 AU/min.
 Difference from mean : 1.051 %
 Correlation coefficient : 0.999



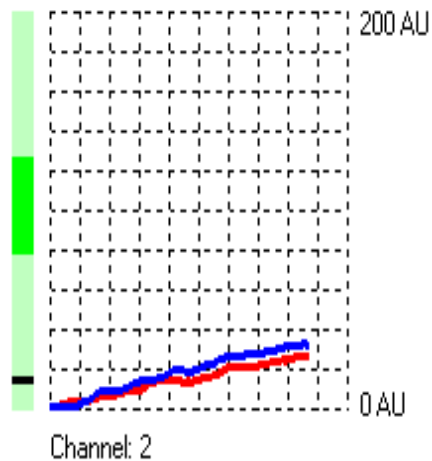
Patient II
 Test name : ADPtest (TI blood), V1
 Start of test : 02. Jan. 2012, 11:21:50 (Measurement duration 6:00 min.)
 Area under the curve : 158 AU*min. (569 - 1130)
 Aggregation : RUO: 25.5 AU
 Velocity : RUO: 6.7 AU/min.
 Difference from mean : 9.148 %
 Correlation coefficient : 0.946



Multiplate ASPItest



Patient ID :
 Test name : ASPItest (TI blood), V1
 Start of test : 14. Jan. 2012, 05:05:53 (Measurement duration 6:00 min.)
 Area under the curve : 897 AU*min. (706 - 1148)
 Aggregation : RUO: 154.9 AU
 Velocity : RUO: 22.5 AU/min.
 Difference from mean : 4.401 %
 Correlation coefficient : 0.999



Patient ID :
 Test name : ASPItest (TI blood), V1
 Start of test : 03. Jan. 2012, 05:08:57 (Measurement duration 6:00 min.)
 Area under the curve : 138 AU*min. (706 - 1148)
 Aggregation : RUO: 29.3 AU
 Velocity : RUO: 5.0 AU/min.
 Difference from mean : 11.913 %
 Correlation coefficient : 0.990



VerifyNow



- Hasta başı cihazı (POCT)
- Tam kan örneği

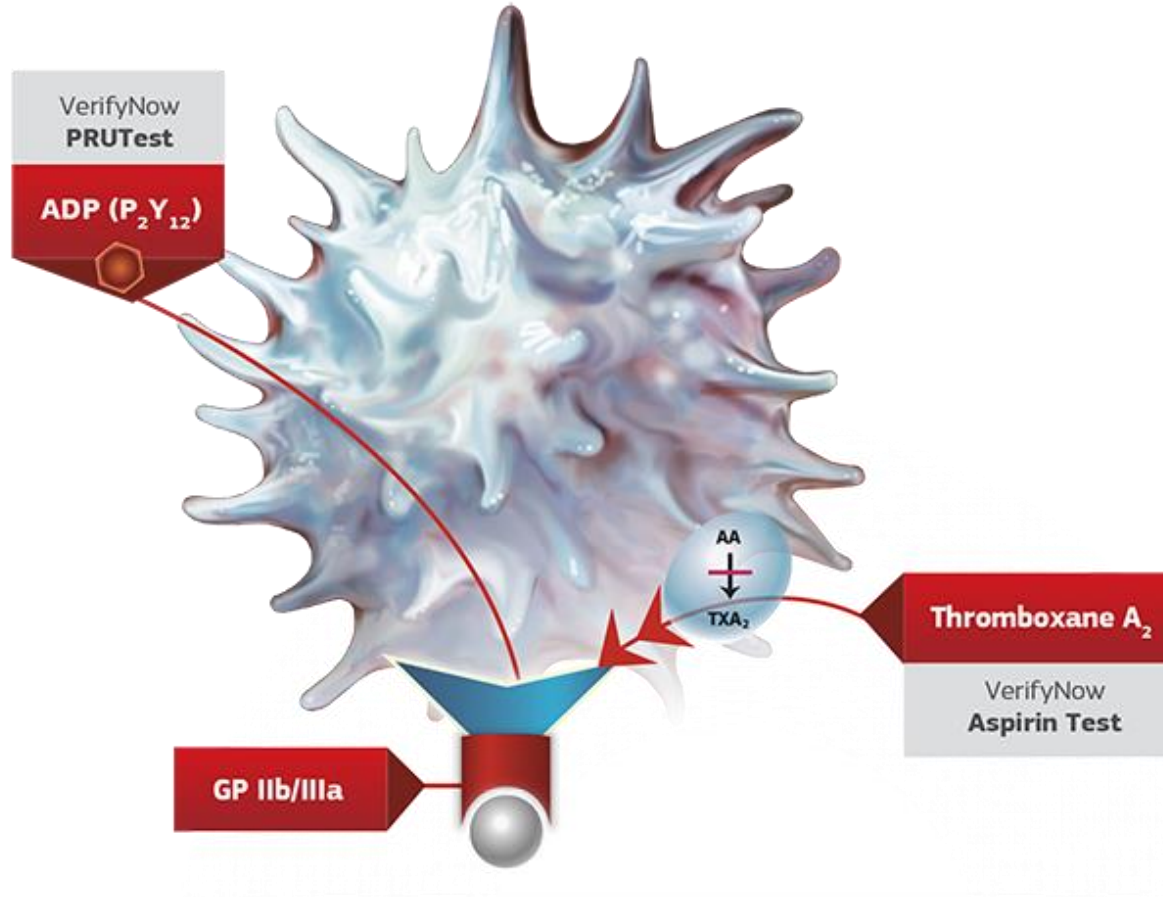
Fibrinojen kaplı boncuk +
Platelet + agonist = **agregasyon**



Transmitans artışı



VerifyNow Agonistler



VerifyNow Raporlama

$$\% \text{ Inhibition} = \frac{(\text{BASE-PRU})}{\text{BASE}} \times 100$$

Aspirin

- ≥ 550 ARU - Platelet dysfunction consistent with aspirin has not been detected
- < 550 ARU - Platelet dysfunction consistent with aspirin has been detected

Clopidogrel

- $\text{PRU} \leq 208$ represents specific evidence for the presence of a pharmacodynamic antiplatelet effect of a P2Y12 inhibitor. $\text{PRU} \leq 208$ is associated with reduced rates of thrombosis and increased rates of bleeding due to the presence of the P2Y12 inhibitor effect.
- $\text{PRU} < 95$ is associated with the highest risk for major bleeding.



Vasodilator-Stimulated Phosphoprotein (VASP)

- Flow sitometrik ölçüm
- Sitratlı Tam Kan

Örnek + PGE1

Örnek + PGE1 + ADP



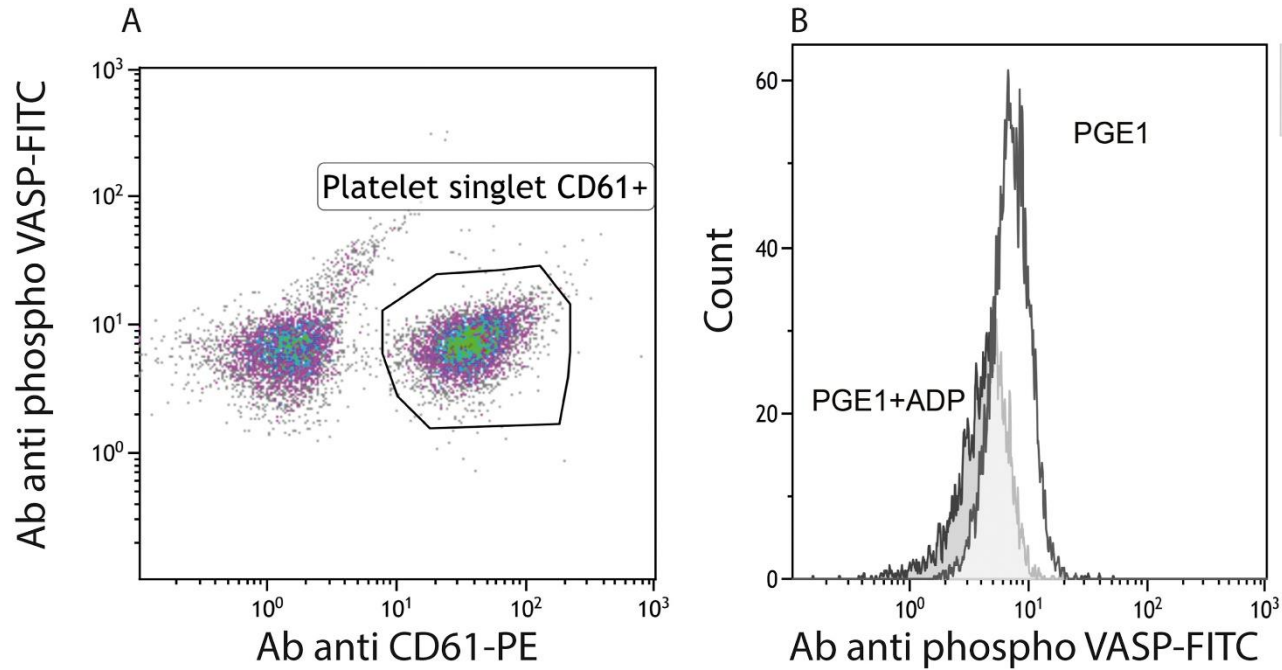
Platelet Reactivity Index (PRI)

$$PRI = \left[\frac{(\text{MFI}_{(\text{PGE1})} - \text{MFI}_{(\text{PGE1}+\text{ADP})})}{\text{MFI}_{\text{PGE1}}} \right] \times 100$$



VASP

PLT VASP/P2Y12 Healthy volunteer



YÖNTEMLERİN PERFORMANSI



Tekrarlanabilirlik – Aspirin

Test (units) (agonist)	Median and range (baseline) Healthy individuals	Median and range (on aspirin) Healthy individuals	Median and range (on aspirin) CAD patients	Effect size fold: median (min-max)	CV _{duplicate measurements} (baseline, %) Healthy individuals	CV _{duplicate measurements} (on aspirin, %) healthy / patients	CV _{day-to-day} (on aspirin, %) healthy / patients
LTA (%) (AA 1.0 mM)	85 (76–105)	8.5 (2.5–60)	12.5 (3.5–67)	10.5	5	19 / 17	37 / 31
MEA (AU min) (AA 0.5 mM)	574 (461–976)	44 (20–79)	62 (21–219)	11.8	8	46 / 46	12 / 24
MEA (AU min) (AA 0.75 mM)	551 (434–889)	67 (24–245)	98 (12–336)	8.8	12	41 / 37	23 / 37
VerifyNow® (ARU) (AA)	662 (653–670)	425 (395–524)	433 (350–533)	1.5	0.4	3 / 3	3 / 3
PFA-100® (sec) (C-EPI)	113 (83–146)	289 (118–301)	279 (79–301)	2.2	8	16 / 27	11 / 10



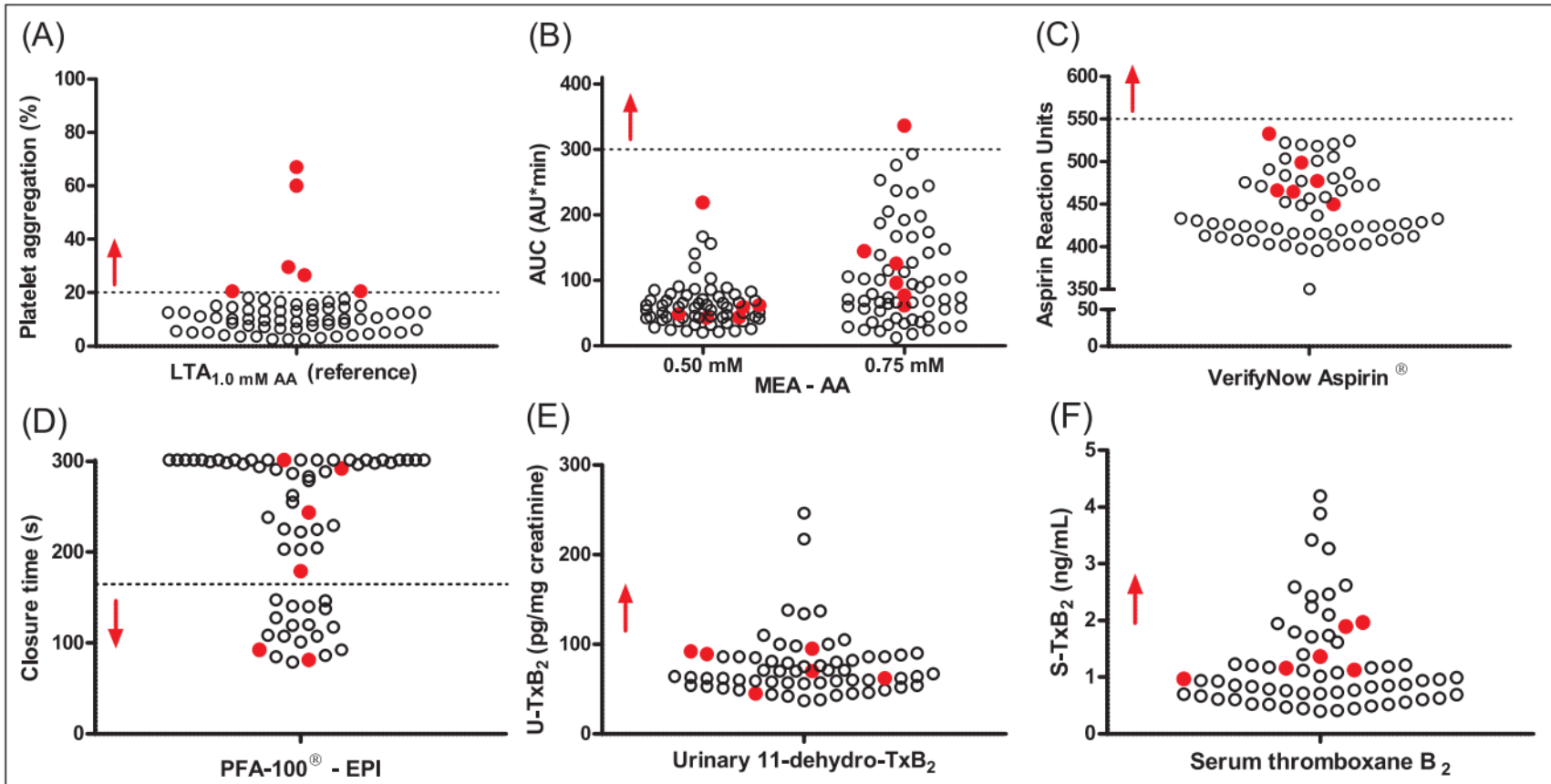
Metot Karşılaştırma – Aspirin

	LTA	MEA		Point-of-care tests		TxA metabolites	
	AA 1.0 mM	AA 0.5 mM	AA 0.75 mM	VerifyNow®	PFA-100® (C-EPI)	U-TxM	S-TxB ₂
LTA							
AA 1.0 mM	1.00	0.22	0.36*	0.43*	-0.56	0.12	0.02
MEA							
AA 0.5 mM	-	1.00	0.65*	-0.05	-0.16	0.00	-0.39*
AA 0.75 mM	-	-	1.00	0.32*	-0.43*	-0.08	-0.21
Point-of-care tests							
VerifyNow®	-	-	-	1.00	-0.33*	0.09	0.41*
PFA-100® (EPI)	-	-	-	-	1.00	-0.16	0.00
TxA metabolites							
U-TxM	-	-	-	-	-	1.00	-0.05
S-TxB ₂	-	-	-	-	-	-	1.00

*P < 0.05. AA, arachidonic acid; C-EPI, collagen-epinephrine; LTA, light transmission aggregometry; MEA, multiple electrode aggregometry; S-TxB₂, serum thromboxane B₂; U-TxM, Urinary 11-dehydro-thromboxane B₂.



Metot Karşılaştırma – Aspirin



Metot Karşılaştırma – Clopidogrel

Table 1 Correlation (95% confidence interval) between platelet function tests at baseline

Platelet function test	LTA ADP 20 μ M	WBA ADP 5 μ M	WBA ADP 20 μ M	PFA-100 [®]	VerifyNow [®] P2Y ₁₂
LTA ADP 5 μ M	0.766 ^a (0.679–0.832)	0.229 ^a (0.049–0.394)	0.326 ^a (0.153–0.479)	0.102 (–0.081 to 0.279)	0.167 (–0.067 to 0.383)
LTA ADP 20 μ M		0.249 ^a (0.070–0.412)	0.309 ^a (0.135–0.465)	0.076 (–0.107 to 0.254)	0.134 (–0.100 to 0.354)
WBA ADP 5 μ M			0.732 ^a (0.635–0.806)	–0.197 ^a (–0.366 to –0.016)	0.052 (–0.181 to 0.280)
WBA ADP 20 μ M				0.036 (–0.147 to 0.216)	0.006 (–0.225 to 0.237)
PFA-100 [®]					–0.020 (–0.212 to 0.250)

^aCorrelation is significant at $P < 0.05$.



Genetik Testler

- Single Nucleotide Polymorphisms (SNP)
 - CYP P-450 enzim sistemi: **CYP2C19**
 - Intestinal efflux transporter pump P-glycoprotein: **ABCB1**
- MicroRNAs (miRs)



Genetik Testler

Tek Nokta Mutasyonu


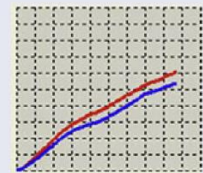
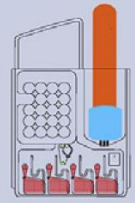
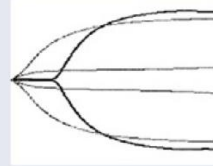
- CYP2C19 genotipine göre sınıflama
 - Ultrarapid metabolizers
 - Extensive metabolizers
 - Intermediate metabolizers
 - Poor metabolizers



POSTANALİTİK


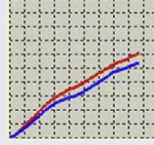
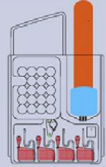
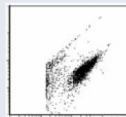
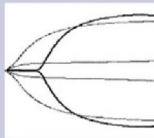


Platelet Araşidonik Asit Uyarımının İnhibisyonunun İzlenmesi

Test	Principle	Readout	
Light transmission aggregometry	Decreased turbidity of aggregated versus nonaggregated platelets		% aggregation
Multiple electrode aggregometry	Whole blood impedance aggregometry		Aggregation units (AU) or area under the curve of AU (AUC × min)
VerifyNow aspirin assay	Co-aggregation of fibrinogen-coated beads with platelets in whole blood		ARU (aspirin reaction units)
Thromboelastogram PlateletMapping	Platelet-dependent increase in clot strength		MA (maximum amplitude, mm)



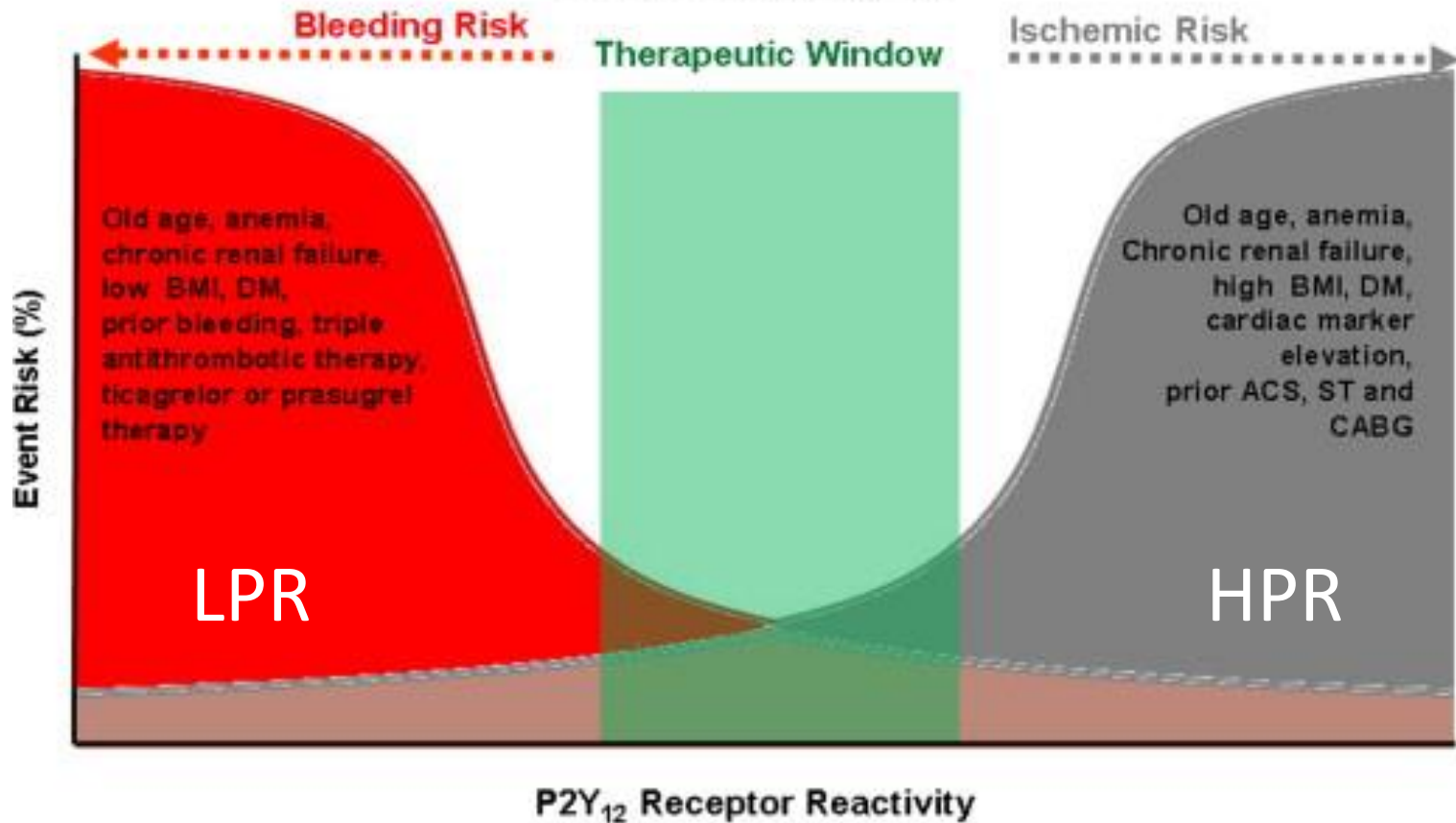
Platelet ADP Uyarımının İnhibisyonunun İzlenmesi

Test	Principle	Readout	
Light transmission aggregometry	Decreased turbidity of aggregated versus nonaggregated platelets		% aggregation
Multiple electrode aggregometry	Whole blood impedance aggregometry		Aggregation units (AU) or area under the curve of AU (AUC × min)
VerifyNow P2Y ₁₂ assay	Co-aggregation of fibrinogen-coated beads with platelets in whole blood		PRU (P2Y ₁₂ Reaction Units)
VASP (vasodilator-stimulated phosphoprotein)	Changes in VASP phosphorylation measured by flow cytometry		PRI (platelet reactivity index)
Thrombelastogram PlateletMapping	Platelet-dependent increase in clot strength		MA (maximum amplitude, mm)



Kılavuz Önerileri

<85 VerifyNow-PRU >208
 <16% VASP-PRI >50%
 <19 MEA-AU >46
 <31 TEG-MA_{ADP} (mm) >47



Sonuç

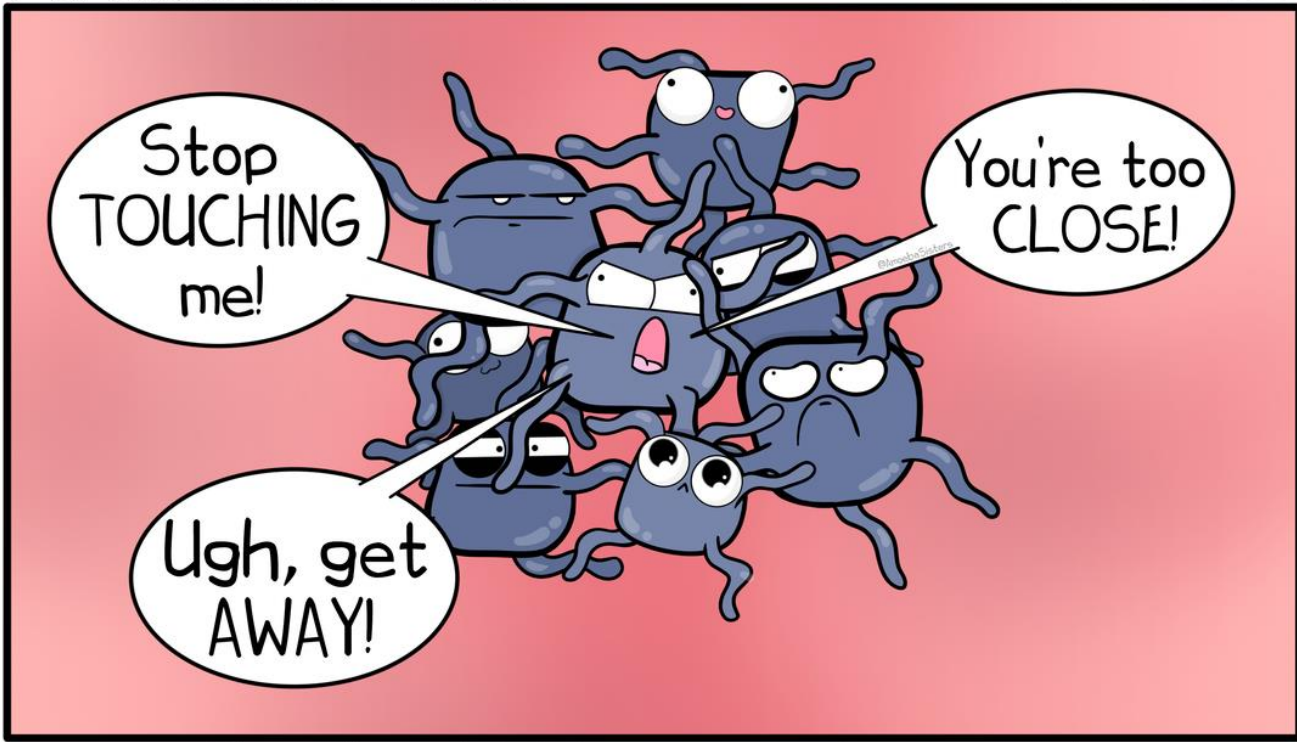
- Clopidogrel ilaç etkinliğinin izlenmesinde standardizasyon sağlayan yöntemlerin kullanılması önemli
- Clopidogral etkinliği tedavi süresince değişebilir



Sonuç

- Kişiselleştirilmiş tedavi için kullanım önerileri artmakta
 - ▶ Laboratuvar test sayısında artış (?)
- Raporda, kullanılan yöntemlere göre kılavuz önerilerinin verilmesi önemli





The other platelets were starting to wonder if Harry had chosen the wrong career.

