Antifoszfolipid szindróma

Prof. Dr. Kiss Emese

Reumatológiai és Immunológiai Klinika

SEMMELWEIS
EGYETEM 1769

Aktuális klasszifikációs rendszer
ACR/EULAR2023

Aktuális terápiás ajánlás
(EULAR 2019, 2023 revízió)

Egyéb kezelési lehetőségek a patogenezis alapján

Klasszifikációs kritériumok

Antifoszfolipid szindróma

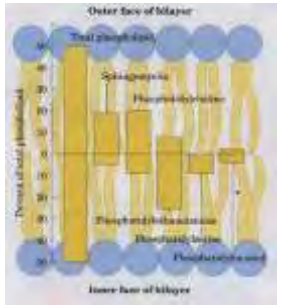
Sapporo: Wilson WA: Arthritis Rheum 42: 1309-1311,1999
**Sydney: Miyakis S: J Thromb Haemost 4: 295-306, 2006*

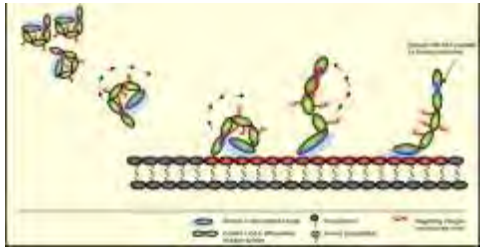
Artériák
Vénák
Mikovaszkulatúra
(Konfirmáció:
Képalkotó, szövettan)

LA,
aKL IgG, IgM,
ab2GPI IgG, IgM*
(12 hét különbséggel ismételten is, kp/magas titerben pozitív*)

Thrombosisok

aPL AT-ek





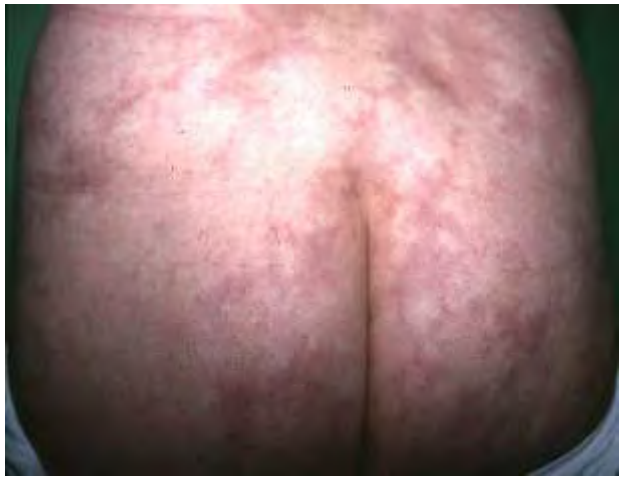
Terhességi patológia

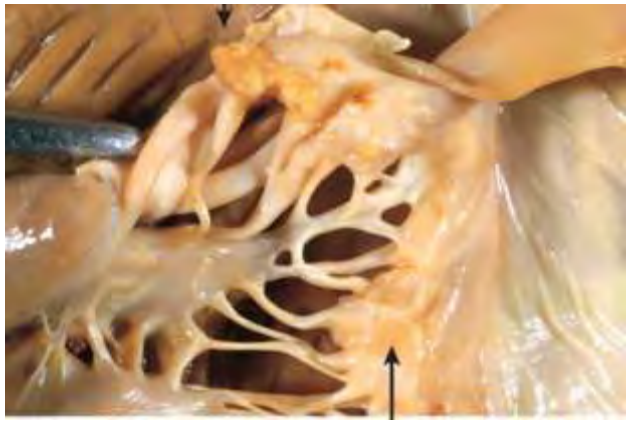
- A lakosság 1%-át érinti. Átlagos életkor 31 év.
- Gyakorisága: MVT-ben 10%, MI-ban 11%, stroke-ban 14%.
- Recidiv trombótikus esemény: 20%.
- High risk csoportban 45%.
- Stroke mortalitás 13%. (életkor átlag 42 év)
- CAPS: 1%, mortalitása 53% (33%).

Habituális abortusz (≥3)
Koraszülés
Halvaszülés
Egyéb (eclampsia)

ANTIFOSZFOLIPID ANTITESTEKHEZ TÁRSULÓ EGYÉB TÜNETEK

- Livedo reticularis, livedo racemosa
- Valvulopathia
- Non-stroke idegrendszeri események
  - epilepsia, chorea,
  - myelitis transversa, migren,
  - multi-infarct dementia
- Hematológiai manifesztációk
  - AIHA, ITP, TTP,
- Bőrtünetek:
  - Lábszárfekély
  - Livedo reticularis
  - Necrotizáló vasculitis
  - Livedoid vasculitis
  - Thrombophlebitis
  - Anetoderma
  - Degos-like léziók
- Asepticus osteonecrosis
- Raynaud jelenség
- Pulmonalis hypertensio





http://lupusimages.com/browser/detail/2577/libman-sacks-endocarditis-of-the-mitral-valve-in-sle

Az APS új 2023-as ACR/EULAR klasszifikációs kritériumai

Klinikai	Laboratóriumi
Domain 1 Macrovascular (venous thromboembolism)	Domain 7 aPL test by coagulation-based functional assay (LA)
Domain 2 Macrovascular (arterial thrombosis)	Domain 8 aPL test by solid phase-based assay (aCL, ab2GPI IgG/IgM)
Domain 3 Microvascular	
Domain 4 Obstetric	
Domain 5 Cardiac valve (thickening, vegetation)	
Domain 6 Haematology (thrombocytopenia)	

2023 ACR/EULAR antiphospholipid syndrome classification criteria

Medha Barbhaiya,[1] Stephane Zuily,[2] Ray Naden,[3] Alison Hendry,[4] Florian Manneville,[5] Mary-Carmen Amigo,[6] Zahir Amoura,[7] Danieli Andrade,[8] Laura Andreoli,[9] Bahar Artim-Esen,[10] Tatsuya Atsumi,[11] Tadej Avcin,[12] Michael H Belmont,[13] Maria Laura Bertolaccini,[14] D Ware Branch,[15] Graziela Carvalheiras,[16] Alessandro Casini,[17] Ricard Cervera,[18] Hannah Cohen,[19] Nathalie Costedoat-Chalumeau,[20] Mark Crowther,[21] Guilherme de Jesús,[22] Aurelien Delluc,[23] Sheetal Desai,[24] Maria De Sancho,[25] Katrien M Devreese,[26,27] Reyhan Diz-Kucukkaya,[28] Ali Duarte-Garcia,[29] Camille Frances,[30] David Garcia,[31] Jean-Christophe Gris,[32] Natasha Jordan,[33] Rebecca K Leaf,[34] Nina Kello,[35] Jason S Knight,[36] Carl Laskin,[37] Alfred I Lee,[38] Kimberly Legault,[39] Steve R Levine,[40] Roger A Levy,[41,42] Maarten Limper,[43] Michael D Lockshin,[1] Karoline Mayer-Pickel,[44] Jack Musial,[45] Pier Luigi Meroni,[46] Giovanni Orsolini,[47] Thomas L Ortel,[48] Vittorio Pengo,[49] Michelle Petri,[50] Guillermo Pons-Estel,[51] Jose A Gomez-Puerta,[52] Quentin Raimboug,[53] Robert Roubey,[54] Giovanni Sanna,[55] Surya V Seshan,[56] Savino Sciascia,[57,58] Maria G Tektonidou,[59] Angela Tincani,[6] Denis Wahl,[7] Rohan Willis,[60] Cécile Yelnik,[61] Catherine Zuily,[62] Francis Guillemin,[5] Karen Costenbader,[63] Doruk Erkan,[*] on Behalf of the ACR/EULAR APS Classification Criteria Collaborators

Barbhaiya M, et al. Ann Rheum Dis 2023;82:1258-1270.

Az APS klasszifikációjának menete az ACR/EULAR 2023-as kritériumrendszere alapján

- The 2023 ACR/EULAR APS classification criteria include entry criteria (at least one positive aPL test within 3 years of an aPL associated clinical criterion)
- followed by weighted criteria clustered into six clinical (macrovascular VTE, macrovascular arterial thrombosis, microvascular, obstetric, cardiac valve, and hematological) and two laboratory (LA functional coagulation assay and aCL and/or aβ2GPI IgG/M ELISA) domains.
- Patients accumulating at least three points each from the clinical and laboratory domains are classified as having APS.
- For different aPL-related items included in these domains: a) strict definitions, based on a literature review and steering committee consensus; b) when “equally or more likely” causes exist (except the consideration of VTE and cardiovascular disease risk factors), then the item in question should not be scored; and c) the highest weighted item in each domain should be counted toward the total score.

American College of Rheumatology. Antiphospholipid Syndrome Classification Criteria Calculator. Atlanta, ACR, 2023. Available online at https://rheumatology.org/criteria.

Belépési kritérium:

- 1 dokumentált APS klinikai esemény
- 3 éven belül kimutatott aPL

Besorolás:

Min 3 pont a klinikai

Plusz

Min 3 pont a laboratóriumi doménekből

Additive clinical and laboratory criteria[a]

Do not count a clinical criterion if there is an equally or more likely explanation than APS.
Within each domain, only count the highest weighted criterion towards the total score.

Clinical domains and criteria	Weight
D1. Macrovascular (Venous Thromboembolism [VTE])	
VTE with a high-risk VTE profile[b]	1
VTE without a high-risk VTE profile[c]	3
D2. Macrovascular (Arterial Thrombosis [AT])	
AT with a high-risk CVD profile[c]	2
AT without a high-risk CVD profile[c]	4
D3. Microvascular	
Suspected (one or more of the following)	2
Livedo racemosa (exam)	
Livedoid vasculopathy lesions (exam)	
Acute/chronic aPL-nephropathy (exam or lab)	
Pulmonary hemorrhage (symptoms and imaging)	
Established (one of more of the following)	5
Livedoid vasculopathy (pathology[d])	
Acute/chronic aPL-nephropathy (pathology[d])	
Pulmonary hemorrhage (BAL or pathology[d])	
Myocardial disease (imaging or pathology)	
Adrenal hemorrhage (imaging or pathology)	
D4. Obstetric	
≥3 Consecutive pre-fetal (<10w) and/or early fetal (10w 0d -15w 6d) deaths	1
Fetal death (16w 0d – 33w 6d) in the absence of pre-eclampsia (PEC) with severe features or placental insufficiency (PI) with severe features	1
PEC with severe features (<34w 0d) or PI with severe features (<34w 0d) with/without fetal death	3
PEC with severe features (<34w 0d) and PI with severe features (<34w 0d) with/without fetal death	4
D5. Cardiac Valve	
Thickening	2
Vegetation	4
D6. Hematology	
Thrombocytopenia (lowest 20-130x10^9/L)	2

Új

Újra

Laboratory (aPL) domains and criteria[e]	Weight
D7. aPL test by coagulation-based functional assay (lupus anticoagulant test [LAC])	
Positive LAC (single – one time)	1
Positive LAC (persistent)	5
D8. aPL test by solid phase assay (anti-cardiolipin antibody [aCL] ELISA and/or anti-β_2-glycoprotein-I antibody [aβ_2GPI] ELISA [persistent])	
Moderate or high positive (IgM) (aCL and/or aβ_2GPI)	1
Moderate positive (IgG) (aCL and/or aβ_2GPI)	4
High positive (IgG) (aCL or aβ_2GPI)	5
High positive (IgG) (aCL and aβ_2GPI)	7

Barbhaiya M, et al.
Ann Rheum Dis 2023;82:1258-1270.

American College of Rheumatology. APS Classification Criteria Calculator. Atlanta, ACR, 2023. Available: https://rheumatology.org/criteria.

Rizikó felmérés, stratifikáció

High risk

- LA (12 hét különbséggel 2x, az ISTH javaslata alapján*)
- 2x aPL (LA+aKL vagy ab2GPI)
- 3x aPL (LA+aKL és ab2GPI)
- Magas aPL titer*
- Perzisztáló aPL
- GAPSS score
- Egyéb rizikók
  - SLE,
  - CV rizikók,
  - anamnézisben trombózis vagy terhességi patológia

Low risk

- Izolált aKL vagy ab2GPI
- Alacsony aPL titer
- Tranziens aPL pozitivitás

Medium-high aPL titres.

- Anticardiolipin (aCL) antibody of IgG and/or IgM isotype in serum or plasma present in titres >40 IgG phospholipid (GPL) units or >40 IgM phospholipid (MPL) units, or >the 99th percentile, measured by a standardised ELISA. Antibeta2 glycoprotein I antibody of IgG and/or IgM isotype in serum or plasma in titre >the 99th percentile, measured by a standardised ELISA.[1]

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Rizikó besorolás az ACR/EULAR ajánlása alapján vénás és artériás macrovaszkuláris klinikai doménekben

Barbhaiya M, et al. Ann Rheum Dis 2023;82:1258-1270.

Magas rizikójú VTE profil

Major VTE rizikó faktorok (≥ 1)

- Aktív daganatos betegség
- Major trauma 1 hónapon belül
- Hospitalizáció
- Műtét 3 hónapon belül, 30 percnél hosszabb

Minor VTE rizikó faktorok (≥ 2)

- Aktív autoimmun betegség
- Aktuális fertőzés (pl. sepsis, pneumonia, SARS-CoV2
- HRT
- Centrális katéter
- Hosszú utazás, > 8 óra
- Obesitás (BMI ≥ 30 kg/m2)
- Tartós immobilitás, > 3nap
- Műtét, < 30 perc

Magas rizikójú CVD profil

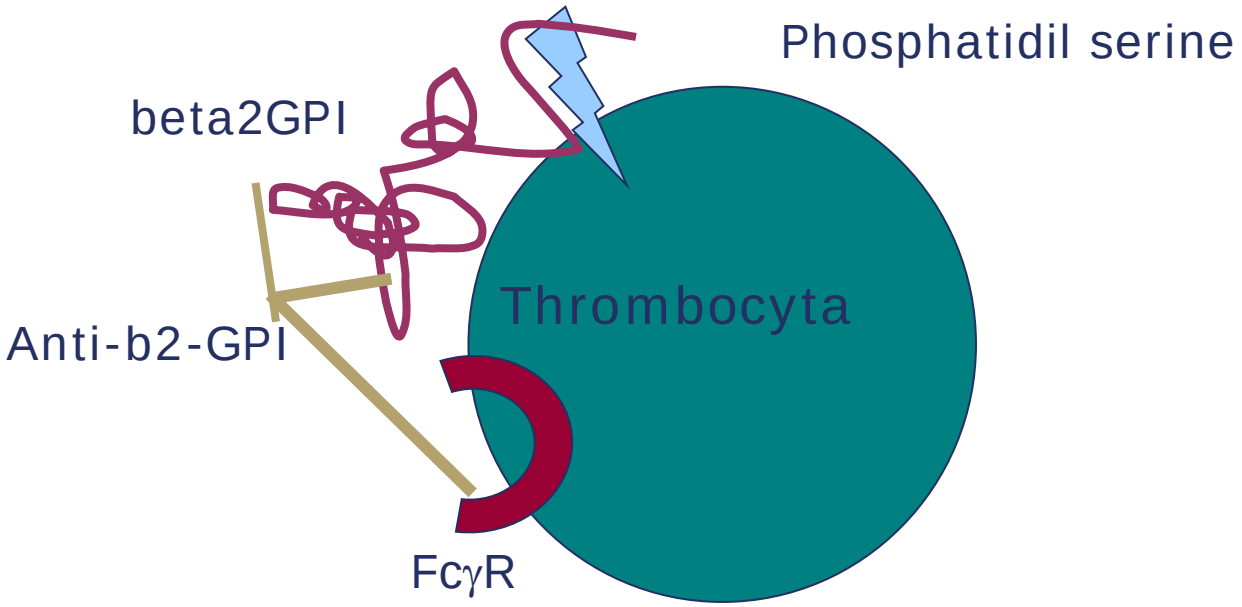
Major CVD rizikó faktorok (≥ 1)

- Hpt ≥ 180/110 Hgmm
- CVE GFR < 60 ml/min
- Diabetes célszerv károsodással
- Hyperlipidemia (súlyos)

Minor rizikó faktorok (≥ 3)

- Artériás Hpt ≥140/90 Hgmm
- Aktuális dohányzás
- Obesitás (BMI ≥ 30 kg/m2)
- Diabetes krónikus célszervkárosodás nélkül
- Hyperlipidemia (mérs.)

Az aPL antitestek hatásmechanizmusa thrombocytopeniában



Asherson R:Autoimm Rev.2006;6:76-80.,
Alegre VA: Br J Dermatol 1989.,
Asherson R et al: Br J Dermatol. 1989

Diff dg: ITP, TTP, DIC, CAPS, HIT

Az APS új 2023-as ACR/EULAR klasszifikációs rendszerének laboratóriumi kritériumai

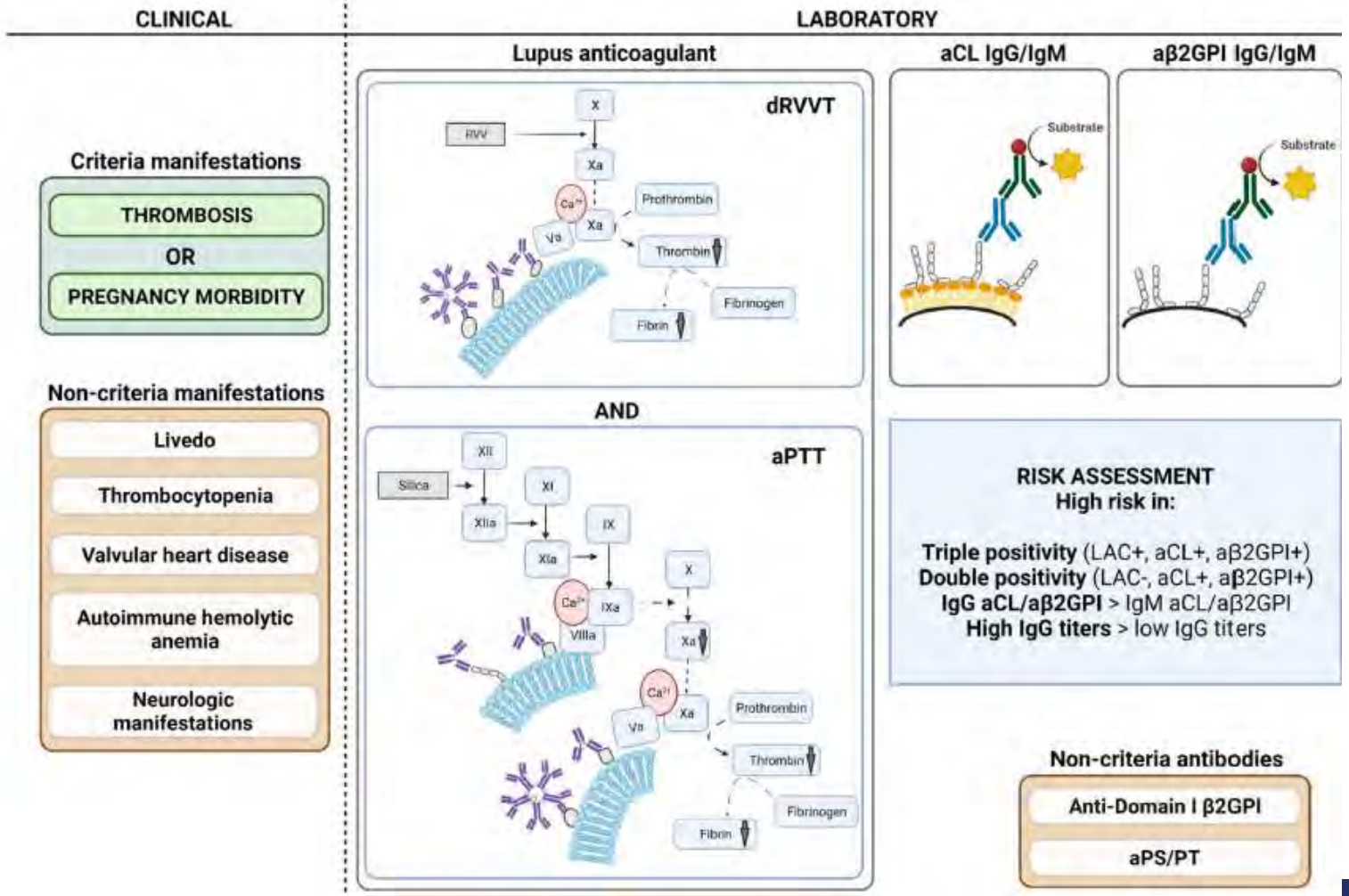
Laboratory (aPL) domains and criteria[e]	Weight
D7. aPL test by coagulation-based functional assay (lupus anticoagulant test [LAC])	
Positive LAC (single – one time)	1
Positive LAC (persistent)	5
D8. aPL test by solid phase assay (anti-cardiolipin antibody [aCL] ELISA and/or anti-β_2-glycoprotein-I antibody [aβ_2GPI] ELISA [persistent])	
Moderate or high positive (IgM) (aCL and/or aβ_2GPI)	1
Moderate positive (IgG) (aCL and/or aβ_2GPI)	4
High positive (IgG) (aCL or aβ_2GPI)	5
High positive (IgG) (aCL and aβ_2GPI)	7

Barbhaiya M, et al. Ann Rheum Dis 2023;82:1258-1270.

Journal of Clinical Medicine
MDPI

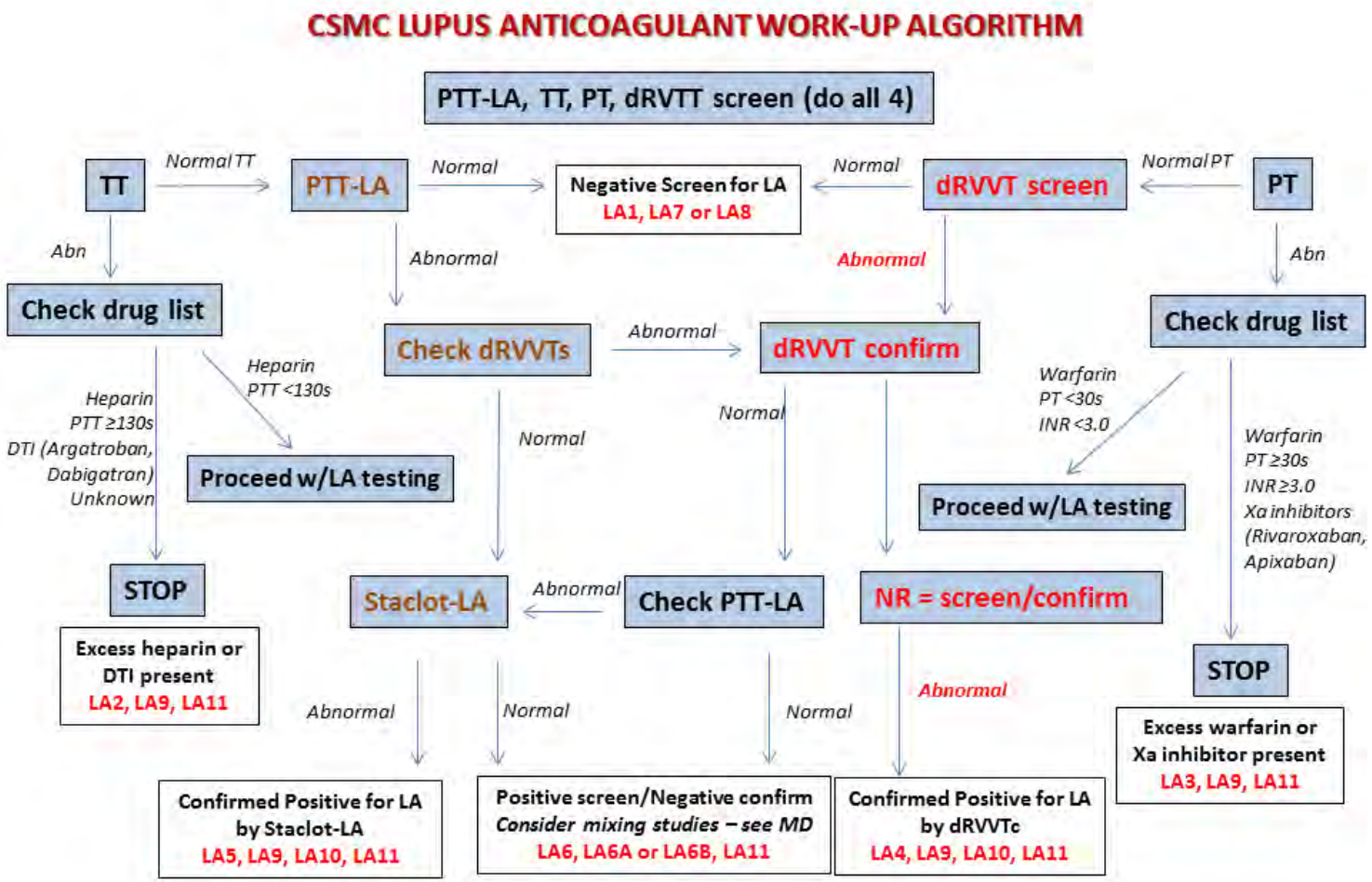
Review

Laboratory Diagnosis of Antiphospholipid Syndrome: Insights and Hindrances



Vandervelde A et al.
J. Clin. Med. 2022, 11, 2164.

Az antifoszfolipid antitestek laboratóriumi diagnosztikája



- Szolid fázisú immunoesszék
- Hemosztázis tesztek

Az LA kimutatása

1. **Screening:** A PL dependens véralvadási idők megnyúlása 2 független vizsgálattal (APTI, dRVVT, higított prothrombin idő ráta)
2. **Mixing:** Az alvadási idő megnyúlása nem korrigálható normál Thr-szegény plazma hozzáadásával.
3. **PL semlegesítés:** Az alvadási idő in vitro megnyúlása korrigálható foszfolipid hozzáadásával
4. **Diff.dg:** Egyéb koagulopátia kizárása.

J Thromb Haemost. 2020;18:2828-39.
Thrombosis Res.2023; 224:30-45.
J Thromb Haemost. 2025;23:731-744.

A LA meghatározása

- ISTH guidance recommends 2 parallel tests, with a dilute Russell's viper venom time (dRVVT) and an LA-sensitive, activated partial thromboplastin time (APTT) as assays of choice. The corresponding testspecific mixing and confirmatory test is performed in response to prolonged screening tests to confirm or refute the presence of a phospholipid-dependent inhibitor.

J Thromb Haemost. 2020;18:2828-39.
Thrombosis Res.2023; 224:30-45.
J Thromb Haemost. 2025;23:731-744.

Received: 4 July 2024 | Revised: 12 September 2024 | Accepted: 17 October 2024

https://doi.org/10.1016/j.jtha.2024.10.022

ISTH GUIDEANCE AND GUIDELINES

J Thromb Haemost. 2025;23:731-744

An update on laboratory detection and interpretation of antiphospholipid antibodies for diagnosis of antiphospholipid syndrome: guidance from the ISTH-SSC Subcommittee on Lupus Anticoagulant/Antiphospholipid Antibodies

Katrien M. J. Devreese[1] | Maria Laura Bertolaccini[2] | D. Ware Branch[3] | Bas de Laat[4] | Doruk Erkan[5] | Emmanuel J. Favaloro[6] | Vittorio Pengo[7] | Thomas L. Ortel[8] | Denis Wahl[9] | Hannah Cohen[10,11]

A klinikai tünetek nem specifikusak APS-re.
Az aPL kimutatásának kulcsszerepe van a klasszifikációban.
A 2023-as klasszifikáiciós kritériumokban csak az ELISA-t fogadják el, egyéb SAP-t nem.
Csak a „klasszikus aPL At-eket fogadják el, az anti-PS/PT, anti-ANX,.. AT-et nem.

PERSPECTIVE IN HEMATOLOGY

DOI: 10.4274/tjh.galenos.2024.2024.0003
Turk J Hematol 2024;41:37-40

Antiphospholipid Syndrome: To Classify or Not to Classify?

Antifosfolipid Sendromu: Sınıflandırmalı mı Yoksa Sınıflandırmamalı mı?

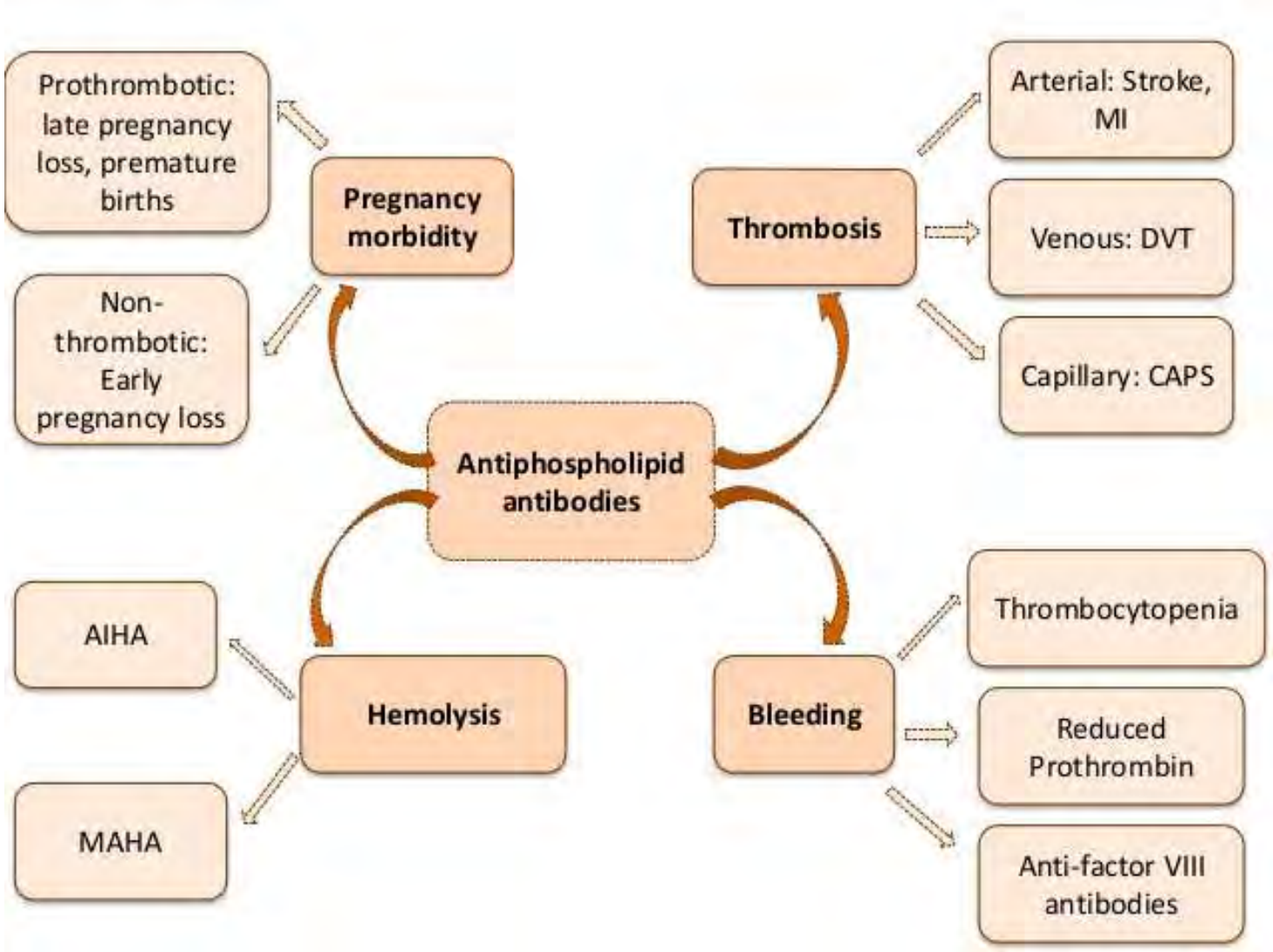
Doruk Erkan

Barbara Volcker Center for Women and Rheumatic Diseases, Hospital for Special Surgery, Weill Cornell Medicine, New York, USA

- The new 2023 ACR/EULAR APS classification criteria **aim to identify homogeneous APS cohorts for research purposes.**
- **Classification criteria are not "diagnostic criteria"** and they should not be used for diagnostic and therapeutic decisions in clinical settings.
- The APS classification for research was established based on the Sapporo criteria, published in 1999 and revised in 2006.
- Given the limitations of the Sapporo criteria, recently **the 2023 ACR/EULAR** APS classification **criteria** were introduced, with significantly **higher specificity (99%)** compared to the revised Sapporo criteria (86%).
- Classification criteria do not necessarily capture patients with rare and unusual manifestations of a disease.

Wilson WA et al. Arthritis Rheum 1999;42:1309-1311. Myiakis S et al. J Thromb Haemost 2006;4:295-306.
Erkan D.: Antiphospholipid Syndrome: To Classify or Not to Classify? Turk J Hematol 2024;41:37-40

Az antifoszfolipid antitestek klinikai manifesztációi



APS terhességi patológia definíciói

Barbhaiya M, et al. Ann Rheum Dis 2023;82:1258-1270.

D4. Obstetric	
≥3 Consecutive pre-fetal (<10w) and/or early fetal (10w 0d -15w 6d) deaths	1
Fetal death (16w 0d – 33w 6d) in the absence of pre-eclampsia (PEC) with severe features or placental insufficiency (PI) with severe features	1
PEC with severe features (<34w 0d) or PI with severe features (<34w 0d) with/without fetal death	3
PEC with severe features (<34w 0d) and PI with severe features (<34w 0d) with/without fetal death	4

Az APS szülészeti manifesztációi

J. Alijotas-Reig et al. J. Clin. Med. 2022, *11*(3), 675
Litvinova E et al. Front Immunol. 2018, 9,2971

A terhesség vagy kezelése befolyásolhatja az aPL kimutathatóságát.

Foszfolipidek	Protein kofaktorok
Foszfatid-sav	Prothrombin
Foszfatidil etanolamin	Annexin A5
Foszfatidil szerin	Vimentin
Foszfatidil inozitol	
Foszfatidil glicerol	
Foszfatidil kolin	

Table 1. Clinical and laboratory descriptions for OAPS and its variants OMAPS and NC-OAPS.

OAPS	**Clinical Criteria**
	1. ≥3 consecutive miscarriages before week 10 of gestation 2. At least one fetal loss after week 10 of gestation 3. At least one premature birth before week 34 of gestation due to PE/eclampsia or placental insufficiency
	Laboratory criteria
	1. Two LA positive tests at least 12 weeks apart 2. Two IgG or IgM aCL positive tests at least 12 weeks apart 3. Two IgG or IgM aβ2GPI positive tests at least 12 weeks apart
OMAPS	**Clinical criteria**
	1. Two consecutive unexplained miscarriages of well-formed embryos 2. Three or more non-consecutive miscarriages of well-formed embryos 3. PE/eclampsia after week 34 of gestation or at puerperium 4. Placental abruption 5. Late premature birth 6. Premature rupture of membranes 7. Unexplained recurrent implantation failure in in vitro fertilization *
	Laboratory criteria
	Fulfil the laboratory criteria described for OAPS
NC-OAPS	**Clinical criteria**
	Fulfil the clinical criteria described for OAPS
	Laboratory criteria
	1. Positivity for LA, aCL or aβ2GPI only detected once 2. Low positive IgG/IgM aCL or aβ2GPI titers 3. Persistent positivity for non-criteria aPL, including IgA-aCL and aβ2GPI 4. Resistance to Annexin A5 anticoagulant activity 5. Thrombocytopenia

* Failure of at least 3 embryo transfer of good-quality embryos. aCL: IgG/IgM anticardiolipin antibodies; aβ2GPI: IgG/IgM antiβ2-glycoprotein I antibodies; aPL: antiphospholipid antibodies; LA: lupus anticoagulant; OAPS: obstetric antiphospholipid syndrome; NC-OAPS: non-criteria OAPS; OMAPS: obstetric morbidity antiphospholipid syndrome; PE: pre-eclampsia.

Korai[1,2]

késői[3]

Klinikum -

Labor +

Klinikum +

Labor -

40%

Az aktuális kezelési ajánlás

Az APS kezelésének lehetőségei

- Antikoaguláns, antiaggregáns Th.
- Immunoduláns Th.
- Antioxidáns Th.

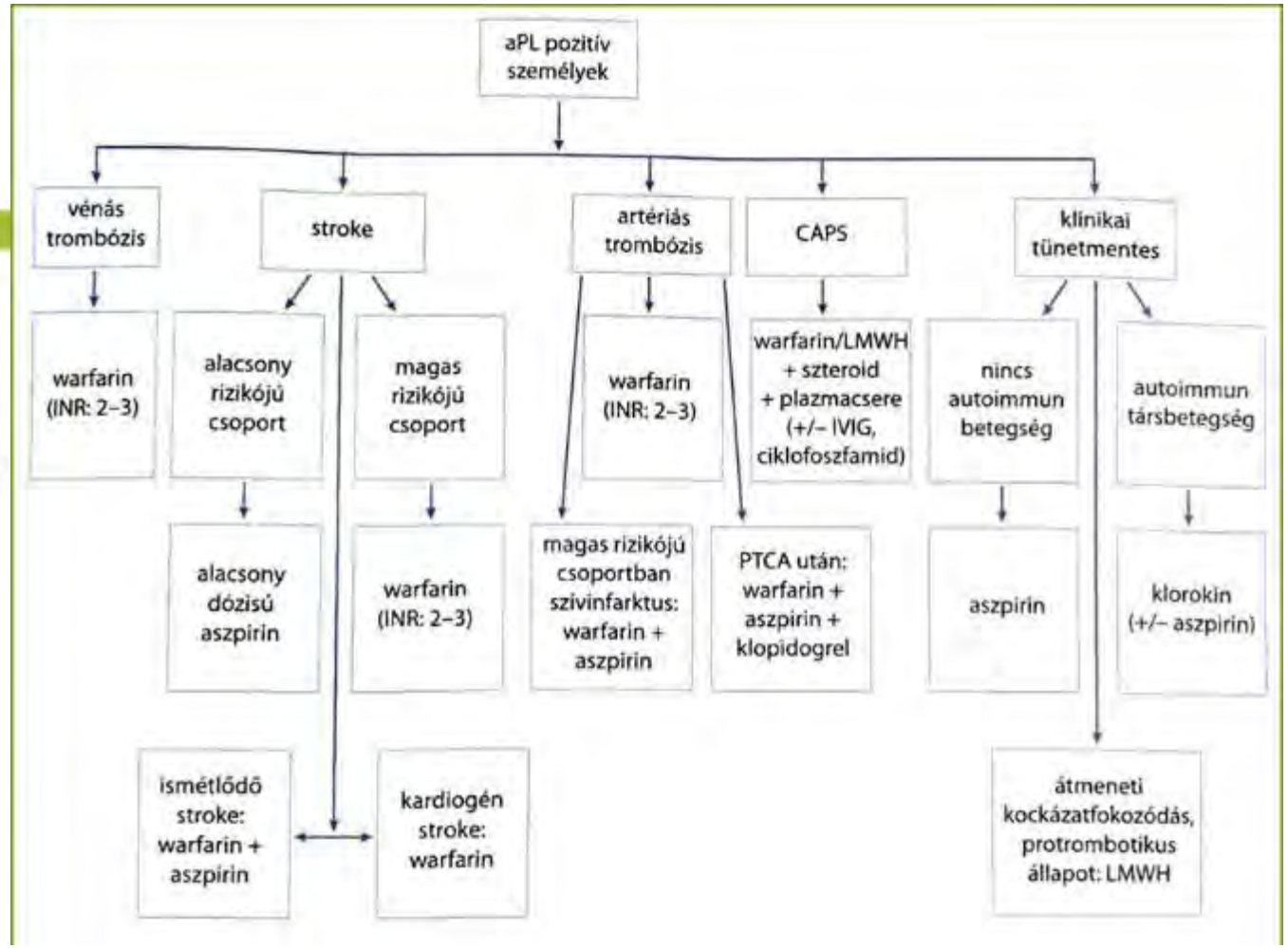
EULAR ajánlás az APS kezelésére

Recommendation

EULAR recommendations for the management of antiphospholipid syndrome in adults

Maria G Tektonidou,[1] Laura Andreoli,[2] Marteen Limper,[3] Zahir Amoura,[4] Ricard Cervera,[5] Nathalie Costedoat-Chalumeau,[6] Maria Jose Cuadrado,[7] Thomas Dörner,[8] Raquel Ferrer-Oliveras,[9] Karen Hambly,[10] Munther A Khamashta,[11] Judith King,[12] Francesca Marchiori,[13] Pier Luigi Meroni,[14] Marta Mosca,[15] Vittorio Pengo,[16] Luigi Raio,[17] Guillermo Ruiz-Irastorza,[18] Yehuda Shoenfeld,[19] Ljudmila Stojanovich,[20] Elisabet Svenungsson,[21] Denis Wahl,[22] Angela Tincani,[2] Michael M Ward[23]

Tektonidou MG, *et al*. *Ann Rheum Dis* 2019;**78**:1296–1304.



Published in final edited form as:
Ann Rheum Dis. 2019 October ; 78(10): 1296–1304. doi:10.1136/annrheumdis-2019-215213.

EULAR recommendations for the management of antiphospholipid syndrome in adults

Maria G Tektonidou[1], Laura Andreoli[2], Marteen Limper[3], Zahir Amoura[4], Ricard Cervera[5], Nathalie Costedoat-Chalumeau[6], Maria Jose Cuadrado[7], Thomas Dörner[8], Raquel Ferrer-Oliveras[9], Karen Hambly[10], Munther A Khamashta[11], Judith King[12], Francesca Marchiori[13], Pier Luigi Meroni[14], Marta Mosca[15], Vittorio Pengo[16], Luigi Raio[17], Guillermo Ruiz-Irastorza[18], Yehuda Shoenfeld[19], Ljudmila Stojanovich[20], Elisabet Svenungsson[21], Denis Wahl[22], Angela Tincani[2], Michael M Ward[23]

Published in final edited form as:
Curr Opin Rheumatol. 2023 May 01; 35(3): 149–160. doi:10.1097/BOR.0000000000000932.

Antiphospholipid syndrome (APS) management: a 2023 update and practical algorithm-based approach

Amala Ambati[1], Jason S. Knight[1], Yu Zuo[1]

1. Primér ASA profilaxis javasolt (EULAR2019) vs. magas rizikójú csoportban megfontolható (2023).

2. Szekunder profilaxisban elsőként VKA választandó, de DOAC megfontolható a nem 3x-os pozitív betegekben, akiknél az INR kontroll nem szervezhető meg, alacsony az adherenciájuk, VKA mellett súlyos mellékhatás lépett fel. (EULAR, ISTH, BSH vsz. ESC, ASH, akik DOAC-ot nem javasolnak)

Alapelvek

Published in final edited form as:
Curr Opin Rheumatol. 2023 May 01; 35(3): 149–160. doi:10.1097/BOR.0000000000000932.

Antiphospholipid syndrome (APS) management: a 2023 update and practical algorithm-based approach

Amala Ambati[1], Jason S. Knight[1], Yu Zuo[1]

Table 1 EULAR recommendations for the prevention and management of APS in adults

Overarching principles

1. Risk stratification in aPL-positive individuals should include determination of the presence of a high-risk aPL profile (defined as any of the following: multiple aPL positivity, lupus anticoagulant or persistently high aPL titres), history of thrombotic and/or obstetric APS, coexistence of other systemic autoimmune diseases such as SLE, and the presence of traditional cardiovascular risk factors.
2. General measures for aPL-positive individuals should include screening for and strict control of cardiovascular risk factors (smoking cessation; management of hypertension, dyslipidaemia and diabetes; and regular physical activity) in all individuals and particularly those with a high-risk aPL profile, screening for and management of venous thrombosis risk factors, and use of LMWH in high-risk situations such as surgery, hospitalisation, prolonged immobilisation and the puerperium.
3. Patient education and counselling on treatment adherence, INR monitoring in patients treated with VKA, use of perioperative bridging therapy with LMWH for patients on oral anticoagulants, oral contraceptive use, pregnancy and postpartum period, postmenopausal hormone therapy, and lifestyle recommendations (diet, exercise) are important in the management of APS.

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Ajánlások: Primér profilaxis (aszpirin)

Primary thromboprophylaxis in aPL-positive subjects

1. In asymptomatic aPL carriers (not fulfilling any vascular or obstetric APS classification criteria) with a high-risk aPL profile with or without traditional risk factors, prophylactic treatment with LDA (75–100 mg daily) is recommended (2a/B).

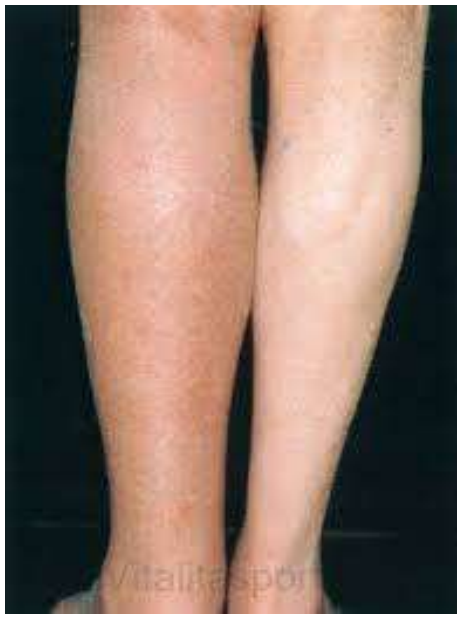
2. In patients with SLE and no history of thrombosis or pregnancy complications:
A. With high-risk aPL profile, prophylactic treatment with LDA is recommended (2a/B).

B. With low-risk aPL profile, prophylactic treatment with LDA may be considered (2b/C).

3. In non-pregnant women with a history of obstetric APS only (with or without SLE), prophylactic treatment with LDA after adequate risk/benefit evaluation is recommended (2b/B).

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Szekunder profilaxis: vénás trombózis (VKA)



4. In patients with definite APS and first venous thrombosis:
A. Treatment with VKA with a target INR 2–3 is recommended (1b/B).

B. Rivaroxaban should not be used in patients with triple aPL positivity due to the high risk of recurrent events (1b/B). DOACs could be considered in patients not able to achieve a target INR despite good adherence to VKA or those with contraindications to VKA (eg, allergy or intolerance to VKA) (5/D).

C. In patients with unprovoked first venous thrombosis, anticoagulation should be continued long term (2b/B).

D. In patients with provoked first venous thrombosis, therapy should be continued for a duration recommended for patients without APS according to international guidelines (5/D). Longer anticoagulation could be considered in patients with high-risk aPL profile in repeated measurements or other risk factors for recurrence (5/D).

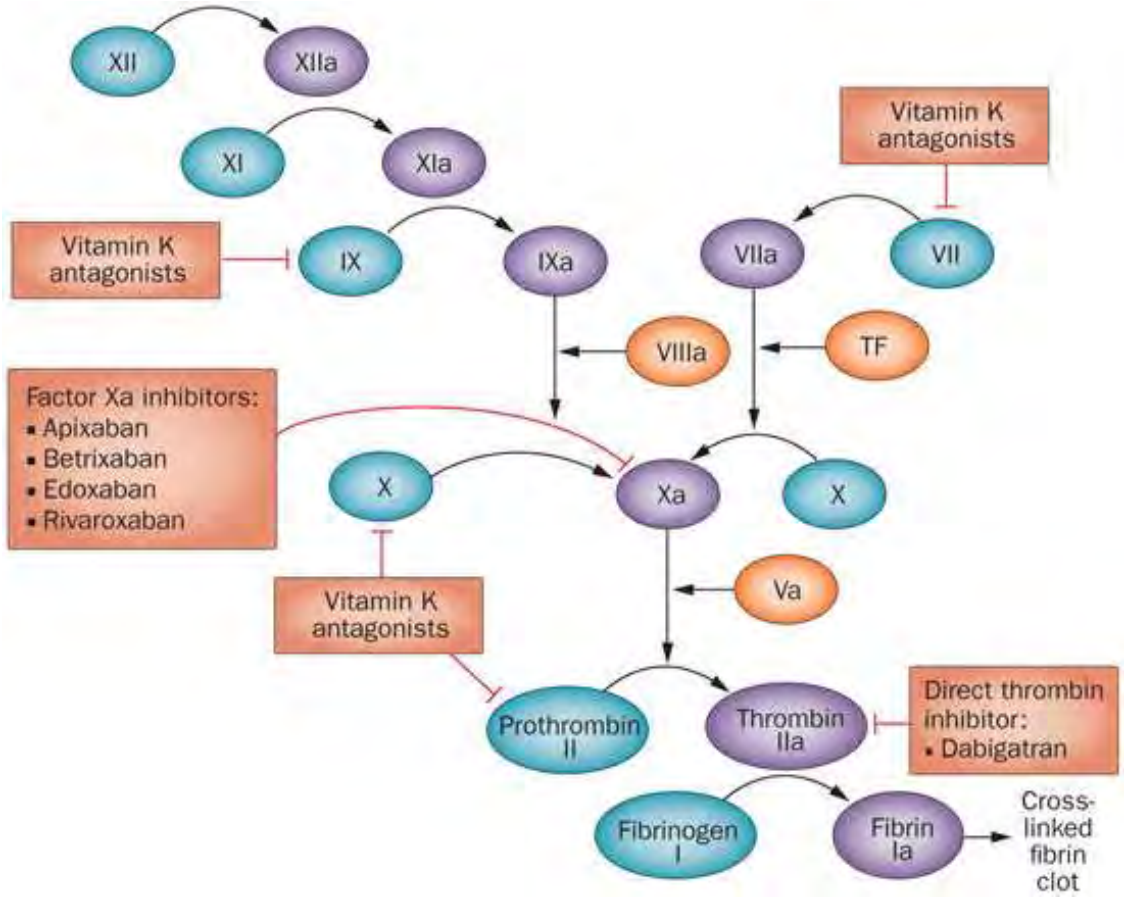
5. In patients with definite APS and recurrent venous thrombosis despite treatment with VKA with target INR of 2–3:
A. Investigation of, and education on, adherence to VKA treatment, along with frequent INR testing, should be considered (5/D).

B. If the target INR of 2–3 had been achieved, addition of LDA, increase of INR target to 3–4 or change to LMWH may be considered (4–5/D).

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Direkt orális inhibitorok

DOI-k:
Dir.trombin inhib:
Dabigatran
Dir.fX gátlók:
Rivaroxaban (RAPS, non-inferiority),
Apixaban,
Endoxaban
Cohen H et al: Lupus 2015;24:1087-94



APS 20%-a van NAOC-on 1/3-ban trombótikus recidiva
J Am Coll Cardiol 2017; 69: 2317-30

APS Munkabiz. 15. Kong. : Nincs elég adat a NOAC alkalmazására ASP-ben
Thromb Res. 2017; 151 (S) 543-47.

Rheumatology (Oxford). 2016 Feb 3. pii: kev445. [Epub ahead of print]

Non-vitamin K antagonist oral anticoagulants and antiphospholipid syndrome.

Sciascia S[1], Lopez-Pedrera C[2], Cecchi I[3], Pecoraro C[3], Roccatello D[4], Cuadrado MJ[5].

DOI-k alkalmazása APS-ben

ORIGINAL RESEARCH | 15 OCTOBER 2019

Rivaroxaban Versus Vitamin K Antagonist in Antiphospholipid Syndrome: A Randomized Noninferiority Trial

Josep Ordi-Ros, MD, PhD; Luis Sáez-Comet, MD, PhD; Mercedes Pérez-Conesa, MD; Xavier Vidal, MD, PhD; Antoni Riera-Mestre, MD, PhD; Antoni Castro-Salomó, MD, PhD; Jordi Cuquet-Pedragosa, MD; Vera Ortiz-Santamaria, MD; Montserrat Mauri-Plana, MD, PhD; Cristina Solé, PhD; Josefina Cortés-Hernández, MD, PhD

- Results: After 3 years of follow-up, **recurrent thrombosis occurred in** 11 patients **(11.6%) in the rivaroxaban group** and 6 **(6.3%) in the VKA group** (RR in the rivaroxaban group, 1.83 [95% CI, 0.71 to 4.76]).
- Conclusion: **Rivaroxaban did not show noninferiority** to dose-adjusted VKAs for thrombotic APS and, in fact, showed a non-statistically significant near doubling of the risk for recurrent thrombosis.

Direkt orális inhibitorokkal végzett vizsgálatok

Study and reference	Type of study	Sample size (DOAC/VKA)	DOAC	VKA	Treatment/follow-up time	Primary endpoint	Thrombosis (DOAC v/s VKA)	Study outcomes
RAPS trial (Cohen et al.) [61]	RCT	116 (57/59)	Rivaroxaban/20 mg OD	Warfarin/2.5	210 days	Changes in ETP	0% vs 0%	ETP is higher in the Rivaroxaban Group. Rivaroxaban does not reach the non-inferiority threshold in APS.
Goldhaber et al. [70]	RCT	151 (71/80)	Dabigatran/150 mg BID	Warfarin/2.5	Up to 36 months	VTE/VTE-related deaths	4.2% vs 5.0%	The efficacy of Dabigatran is not affected by APS or Thrombophilia.
Ordi-Ros et al. [62]	RCT	190 (95/95)	Rivaroxaban/20 mg OD Or 15 mg OD if creatinine clearance is 30-50 mL/min	Warfarin/2.5 (2.0-3.0)	36 months	Thrombosis	11.6% vs 6.3%	Recurrent thrombosis is 11% in rivaroxaban group and 6.3% in VKA group. Rivaroxaban does not show non-inferiority to VKAs in thrombotic APS.
TRAPS (Pengo et al.) [60]	RCT	120 (59/61)	Rivaroxaban/20 mg OD Or 15 mg OD if creatinine clearance is 30-50 mL/ min	Warfarin/2.5	611 days	Incidence of thromboembolic events, major bleeding, vascular deaths	12% vs 0%	The study was stopped due to increased events in the Rivaroxaban group.
ASTRO-APS (Woller et al.) [71]	RCT	30	Apixaban/2.5 mg BID (in 2015), 5 mg BID (since 2016)	Warfarin/2.5	Ongoing trial Follow up: 13 months	Arterial or venous thrombosis	NA	Active trial. The protocol was changed twice to 5 mg BID instead of 2.5 mg BID exclusion of patients with prior arterial thrombosis.

Nem non-inferiority

Dabigatran hatása nem csökkent

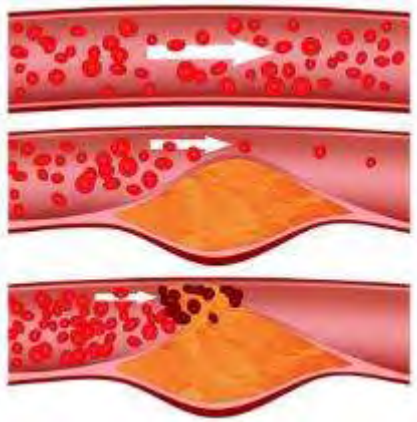
Nem non-inferiority

Le kellett állítani

Dupla dózisú Apixabannal ongoing

Arora S, Nair S, Prabhu R, et al. (October 24, 2021), Cureus 13(10): e19009. DOI 10.7759/cureus.19009
Role of Direct Oral Anticoagulation Agents as Thromboprophylaxis in Antiphospholipid Syndrome.

Szekunder profilaxis: artériás trombózis



6. In patients with definite APS and first arterial thrombosis:
A. Treatment with VKA is recommended over treatment with LDA only (2b/C).

B. Treatment with VKA with INR 2–3 or INR 3–4 is recommended, considering the individual's risk of bleeding and recurrent thrombosis (1b/B). Treatment with VKA with INR 2–3 plus LDA may also be considered (4/C).

C. Rivaroxaban should not be used in patients with triple aPL positivity and arterial events (1b/B). Based on the current evidence, we do not recommend use of DOACs in patients with definite APS and arterial events due to the high risk of recurrent thrombosis (5/D).

7. In patients with recurrent arterial thrombosis despite adequate treatment with VKA, after evaluating for other potential causes, an increase of INR target to 3–4, addition of LDA or switch to LMWH can be considered (4–5/D).

Obstetric APS

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Szekunder profilaxis: terhességi patológia

8. In women with a high-risk aPL profile but no history of thrombosis or pregnancy complications (with or without SLE), treatment with LDA (75–100 mg daily) during pregnancy should be considered (5/D).

9. In women with a history of obstetric APS only (no prior thrombotic events), with or without SLE:
A. With a history of ≥3 recurrent spontaneous miscarriages <10th week of gestation and in those with a history of fetal loss (≥10th week of gestation), combination treatment with LDA and heparin at prophylactic dosage during pregnancy is recommended (2b/B).

B. With a history of delivery <34 weeks of gestation due to eclampsia or severe pre-eclampsia or due to recognised features of placental insufficiency, treatment with LDA or LDA and heparin at prophylactic dosage is recommended considering the individual's risk profile (2b/B).

C. With clinical 'non-criteria' obstetric APS such as a the presence of two recurrent spontaneous miscarriages <10th week of gestation, or delivery ≥34 weeks of gestation due to severe pre-eclampsia or eclampsia, treatment with LDA alone or in combination with heparin might be considered based on the individual's risk profile (4/D).

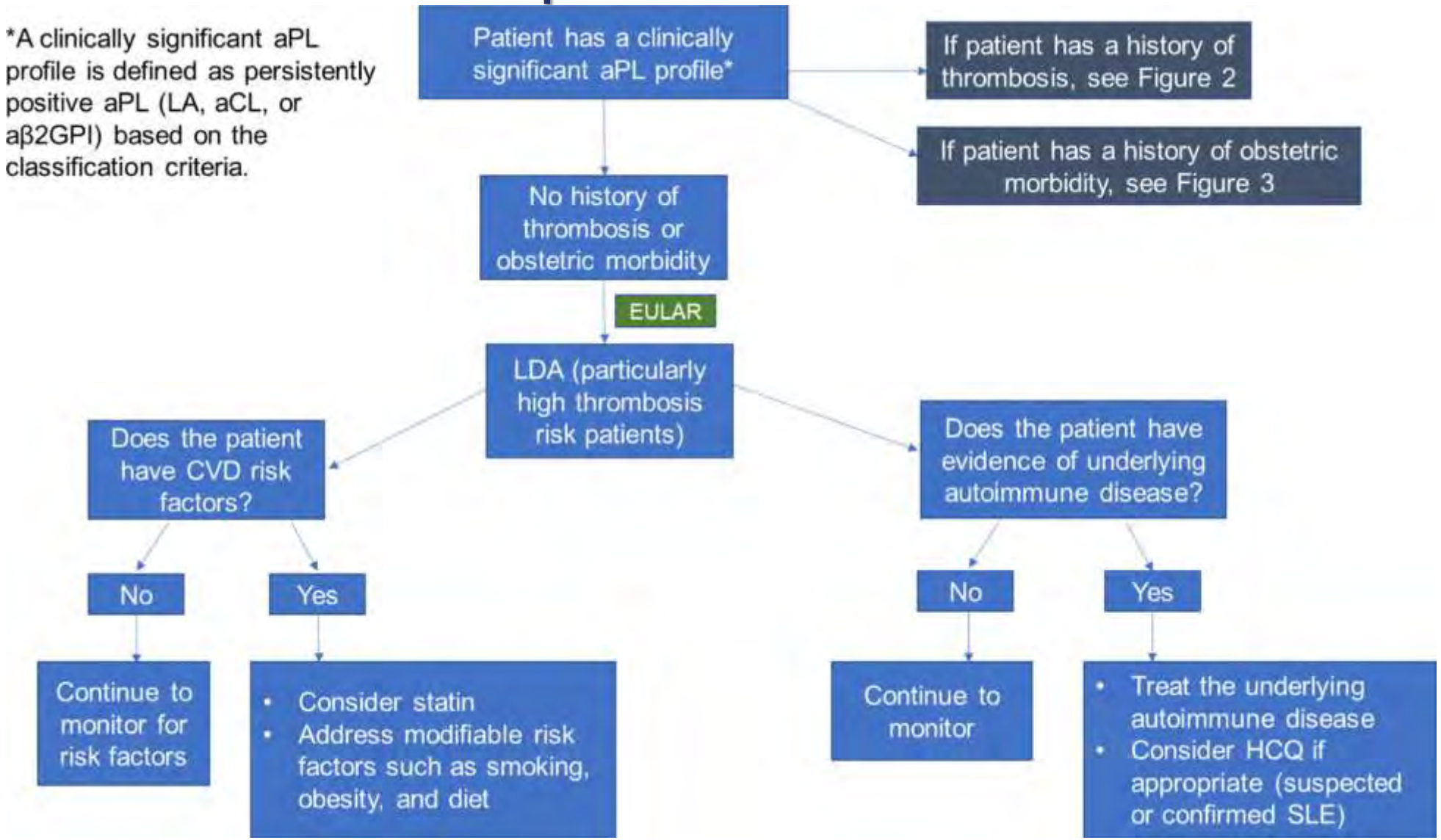
D. With obstetric APS treated with prophylactic dose heparin during pregnancy, continuation of heparin at prophylactic dose for 6 weeks after delivery should be considered to reduce the risk of maternal thrombosis (4/C).

10. In women with 'criteria' obstetric APS with recurrent pregnancy complications despite combination treatment with LDA and heparin at prophylactic dosage, increasing heparin dose to therapeutic dose (5/D) or addition of HCQ (4/D) or low-dose prednisolone in the first trimester (4/D) may be considered. Use of intravenous immunoglobulin might be considered in highly selected cases (5/D).

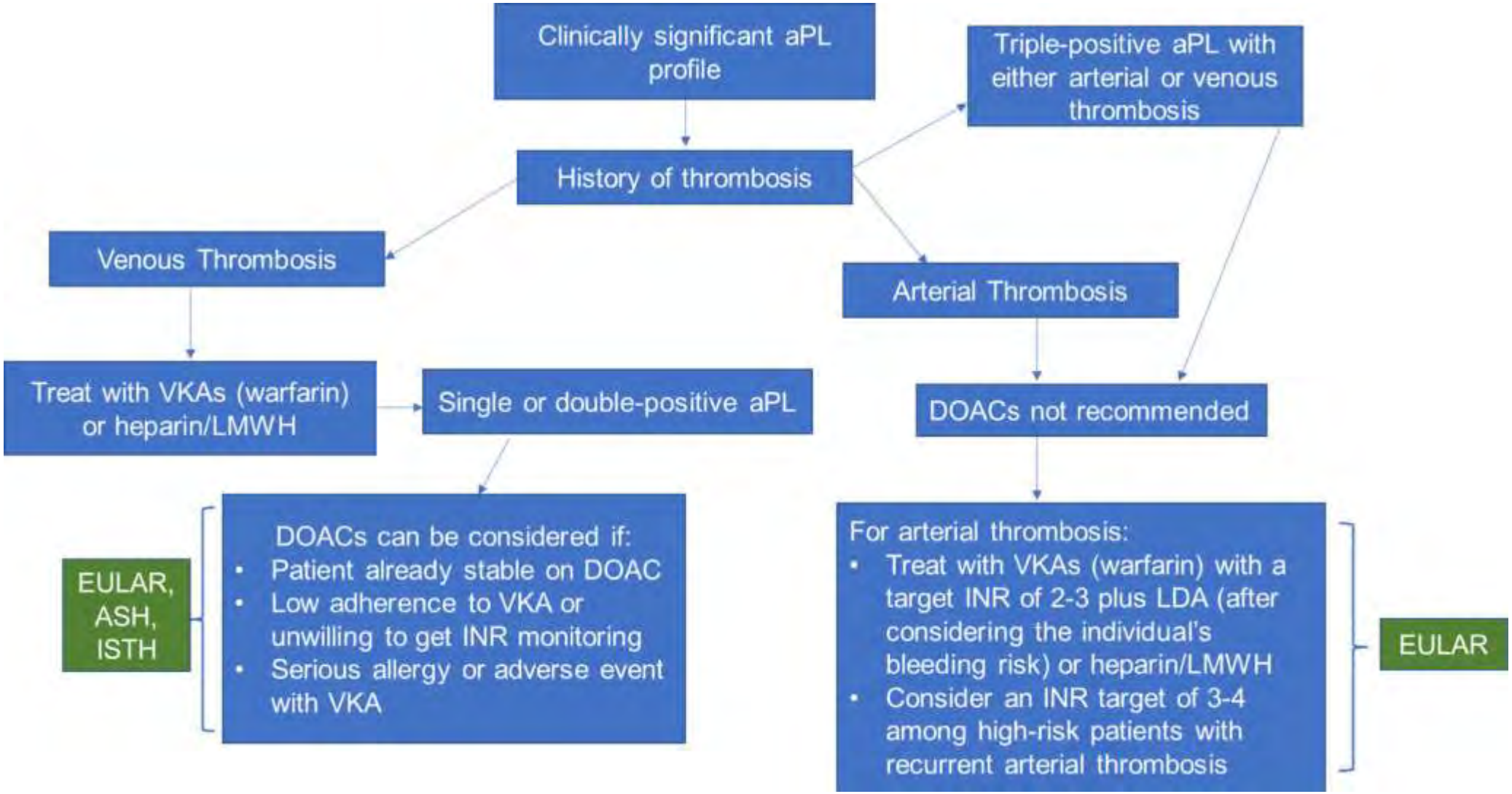
11. In women with a history of thrombotic APS, combination treatment of LDA and heparin at therapeutic dosage during pregnancy is recommended (4/C).

Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Primér profilaxis APS-ben



Szekunder profilaxis APS-ben



APS-s várandós kezelése

Clinically significant aPL profile

Patient is pregnant

History of OB APS

LDA + Prophylactic heparin/LMWH

Remain on heparin/LMWH for 6-12 weeks post-partum

History of Thrombotic APS

LDA + Therapeutic heparin/LMWH

Resume therapeutic anticoagulation post-partum

Asymptomatic aPL Carrier

ACR

LDA

EULAR

High-risk aPL Profile (LA+ or double-positive aPL)

Terápiás ajánlás az OAPS kezelésére

Hab. Ab.

IVF sikertelenség

Thrombosis

Thrombopenia

Veseelégtelenség

Extrém testsúly

Table 5. Suggested therapeutic schedules for OAPS patients.

Gold Standard therapy in spontaneous pregnancy loss: recurrent miscarriage/fetal loss	LMWH 0.4–06 mg/kg/day ("prophylactic" dose) since the positive pregnancy test combined with preconception daily LDA at least one month before starting attempts for a new pregnancy.
Gold Standard Therapy in assisted reproductive techniques (ART)	LMWH 0.4–0.6 mg/kg/day since estrogens are started in the substituted cycle (or 14 days prior to the transfer, if not), combined with preconception LDA, at least one month before starting ART
Women with a previous history of thrombotic APS or thrombosis that appeared during pregnancy	LMWH 1 mg/kg/12 h since the thrombotic event, combined with LDA.
Presence of severe thrombocytopenia (less than 20,000 platelets) or presence of mild-moderate bleeding	Stop LDA LMWH 0.2 mg/kg/day in the case of OAPS LMWH 1 mg/kg/day in thrombotic APS Monitor total platelet count Monitor anti-factor Xa activity
Presence of mild-moderate renal failure (GFR 15–45 mL/min)	Reduce the LMWH dose that was administered and discontinue aspirin. Monitor anti-factor Xa activity monthly
Presence of extreme weights (less than 40 kg or greater than 120 Kg)	LMWH 0.2 to 0.8 mg/kg/day (prophylactic dose adjusted to body weight), since positive pregnancy test combined with preconception LD., Monitoring anti-factor Xa activity monthly.

J. Alijotas-Reig et al. J. Clin. Med. 2022, *11*(3), 675

A refrakter OAPS kezelése

1.
LDA **(4 héttel a gesztáció előtt)**
+ LMWH (profilaxtikus **dózisban az igazolt terhességtől)**

2.
Előzők (LDA+LMWH) + 200-400 mg OHQ

3.
Előzők (LDA + LMWH + OHQ) + 10-15 mg/nap PED **(a terhesség igazolása után mielőbb) vagy az LMWH dózis emelése**

4.
Előzők (LDA + LMWH + OHQ + PED) + IVIG vagy PEX

5.
Előzők (LDA + LMWH + OHQ + PED + IVIG/PEX) + TNFalfa **gátló**

6.
Előzők (LDA + LMWH + OHQ + PED + IVIG/PEX + TNFi) + hidrofil sztatin (20-40 mg/nap pravastatin)

J. Alijotas-Reig et al. J. Clin. Med. 2022, *11*(3), 675 közleménye alapján

OAPS-re utaló hisztopatológiai eltérések és okai

aPL

Thromboticus

aPL

Anti-angiogén

aPL

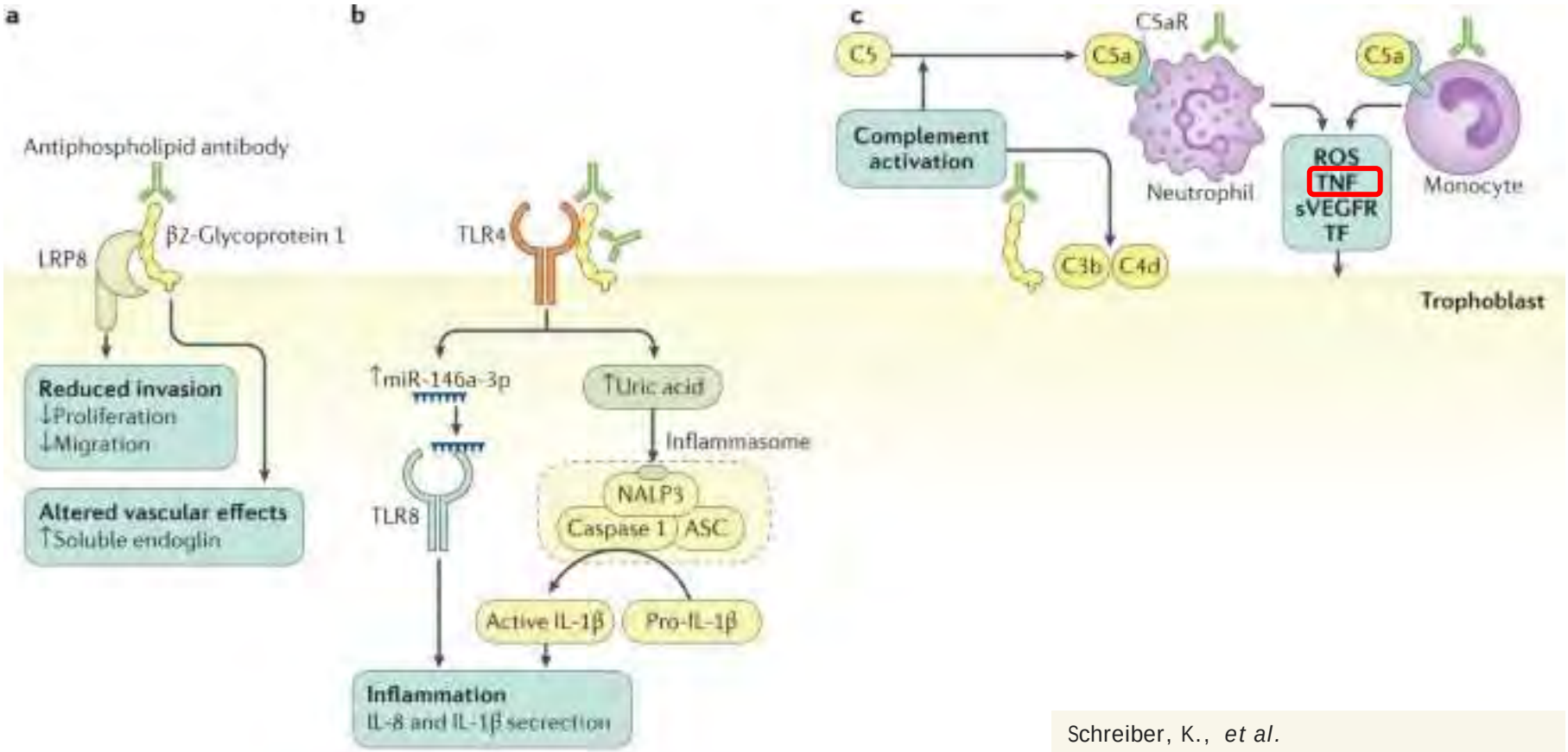
Inflammatoricus

Tissue Affectation	Histologic Features aPL-Related
Decidua	Necrosis Acute Inflammation Chronic Inflammation Partial Remodeling spiral arteries Vessel thrombus
Placenta	Villous infarcts Hydropic villi Stromal fibrosis Syncytial knots Complement deposition C4d Intervillous thrombus

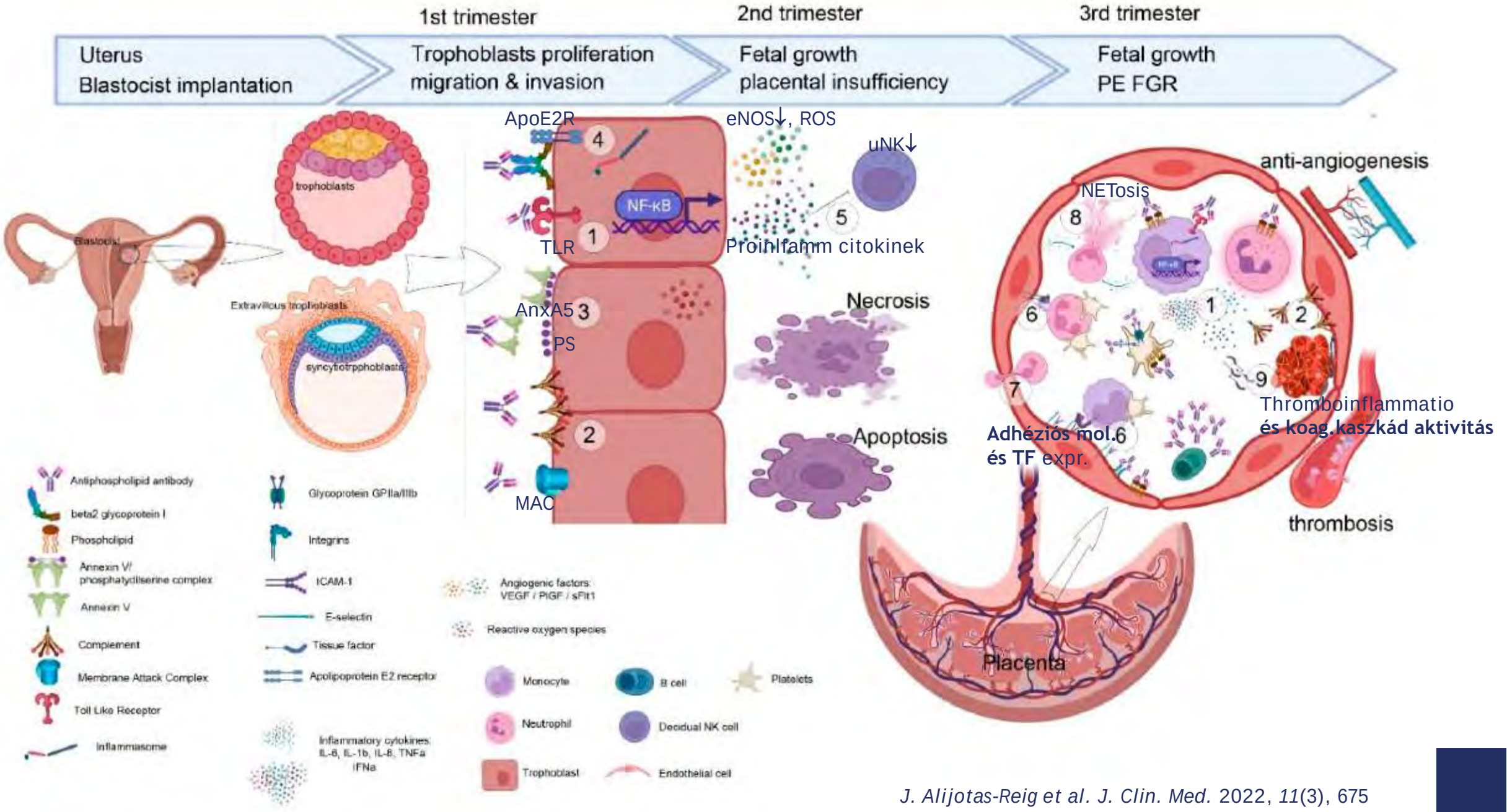
1. Innate immunsejtek:
a. neutrophylek,
b. monocyták,
c. thrombocyták
2. Endothelsejtek
3. Throphoblast

J. Alijotas-Reig et al. J. Clin. Med. 2022, *11*(3), 675

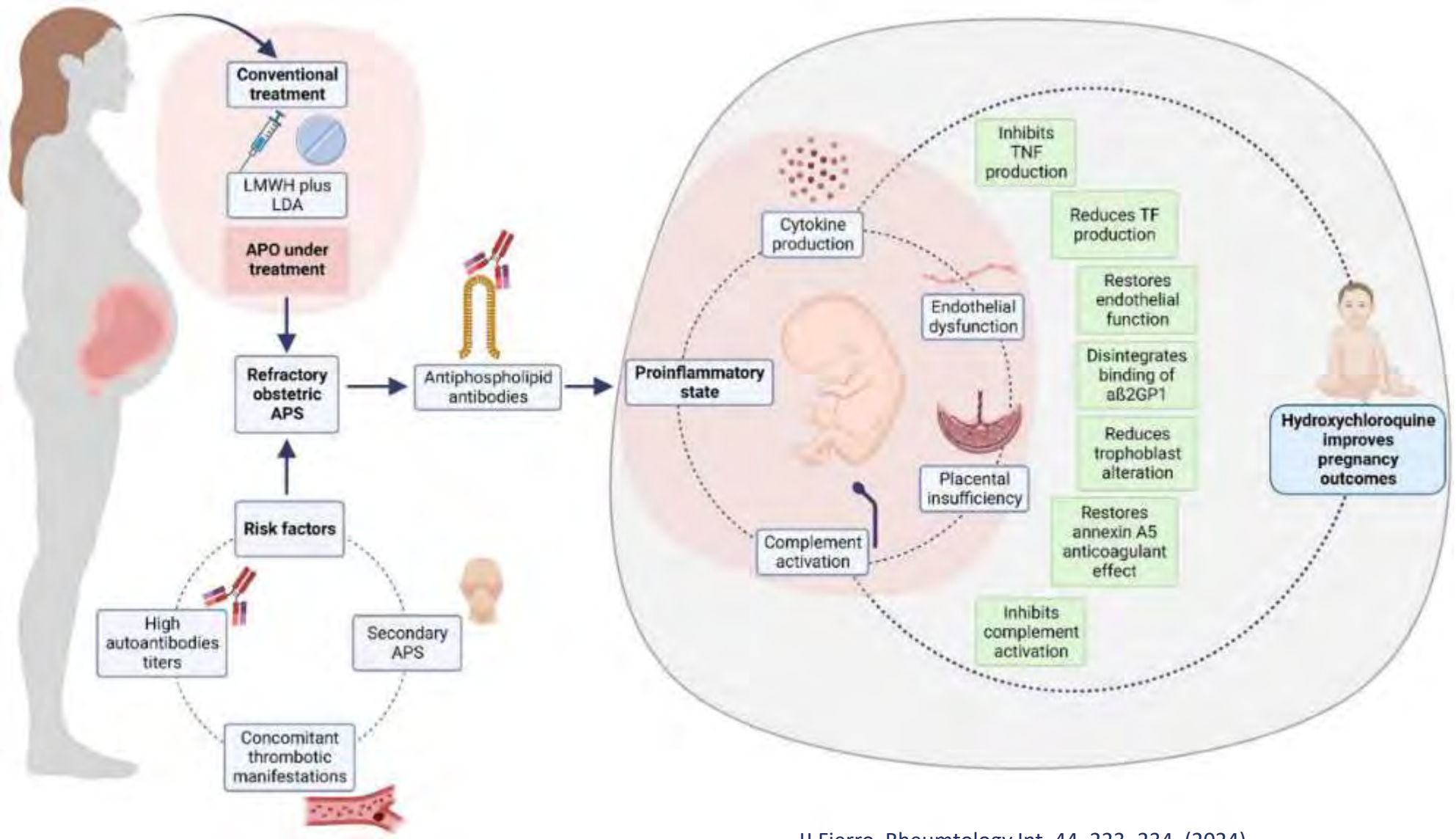
Az OAPS patomechanizmusa



Schreiber, K., *et al.*
Nat Rev Dis Primers 4, 17103 (2018).



J. Alijotas-Reig et al. J. Clin. Med. 2022, *11*(3), 675



JJ Fierro, Rheumtology Int. 44, 223–234, (2024)

Katasztrófa antifoszfolipid szindróma (CAPS)

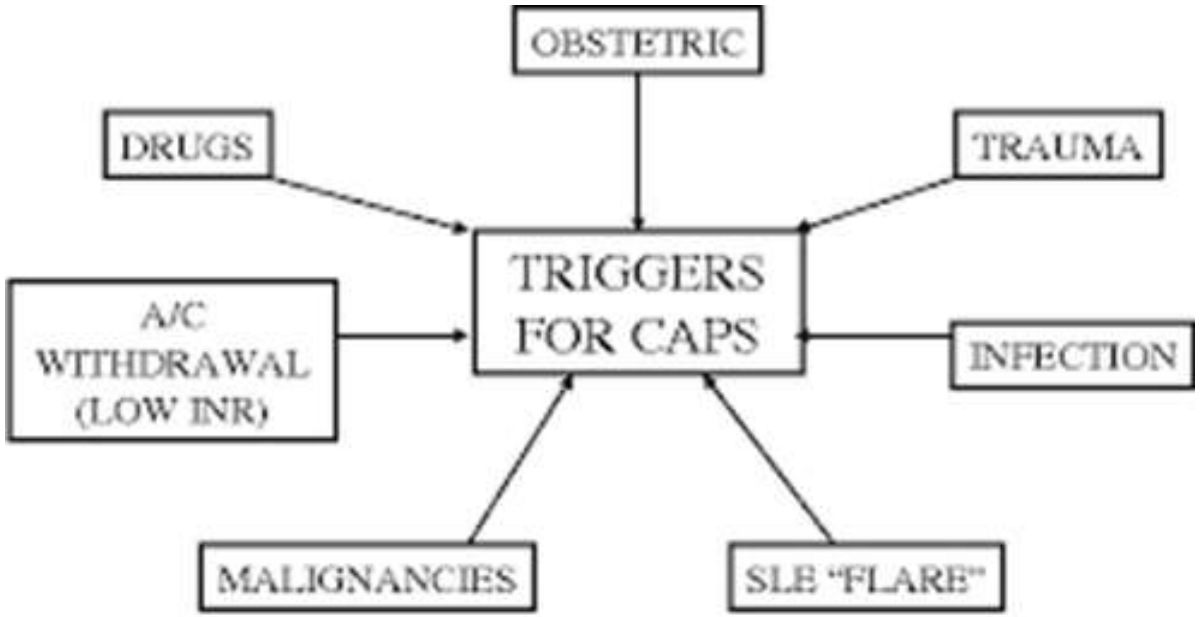
Ronald Asherson

- Klasszifikációs kritériumok:
  - Vaszkuláris trombózis legalább 3 szerv vagy szervrendszer területén.
  - A tünetek rövid időn (<1 héten belül) alakulnak ki.
  - Kisér okklúzió kimutatás szövettanilag ≥1 szervben/szövetben
  - aPL antitestek kimutatása magas titerben.

Criteria
1. Evidence of involvement of three or more organs, systems, and/or tissues
2. Development of manifestations simultaneously or in less than a week
3. Histopathological confirmation of small vessel occlusion in ≥1 organ/tissue
4. Laboratory confirmation of the presence of antiphospholipid antibodies ≥12 weeks

Jacobs L et al. Antibodies 2024, 13, 21

Katasztrófa antifoszfolipid szindróma (CAPS)



Precipitáló faktorok (50%):

- Fertőzés (22%)
- Műtét (10%)
- Antikoaguláns elhagyása vagy szuboptimális INR (8%)
- Egyéb gyógyszer, szülészeti komplikáció (7-7%)
- Daganat (5%)
- Lupus flare (3%)

1. Asherson R et al.: Lupus 2003;12:530-4.,
2. Cevera R et al.: J Autoimmun 2009; 32:240-5

A CAPS klinikai manifesztációi

Retinal – Arterial and venous thrombosis

Lung – Acute respiratory distress syndrome, pulmonary embolism, alveolar hemorrhage, pulmonary edema

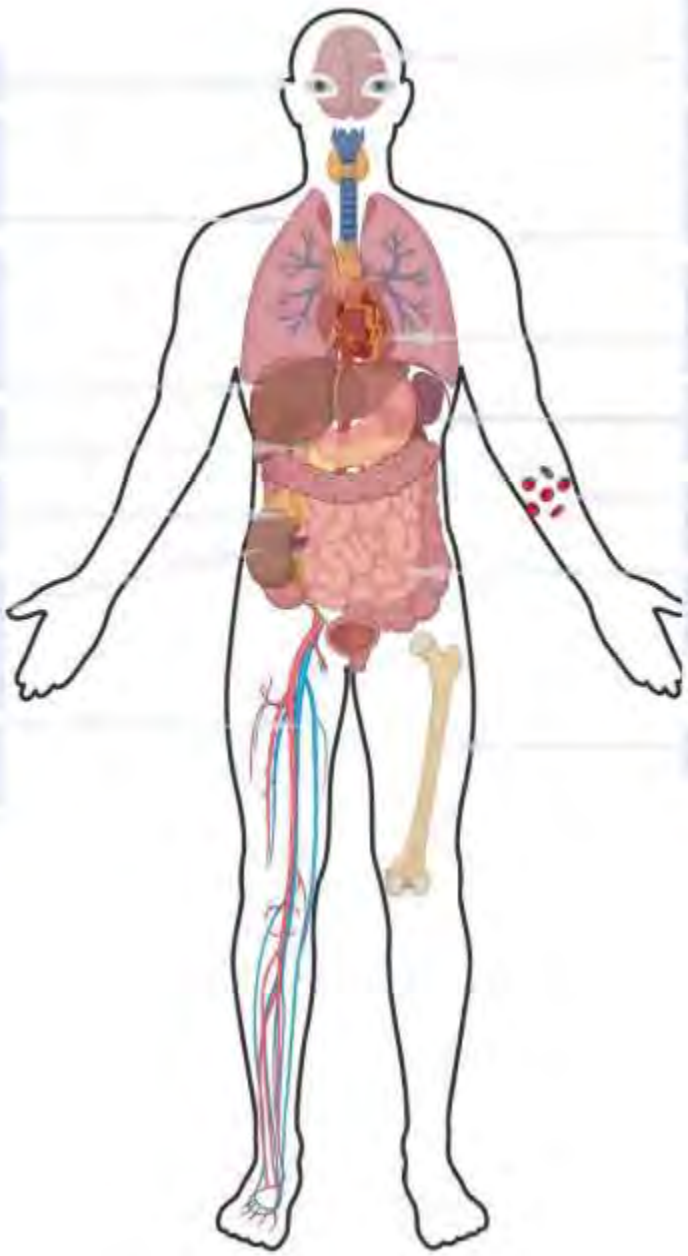
Liver – Micro-thrombosis, Budd-Chiari, hepatic vein or portal vein thrombosis, liver failure, elevated liver enzymes, jaundice, hepatomegaly

Gall bladder – Micro-thrombosis, cholecystitis

Adrenal gland – Hemorrhage, infarcts, venous thrombosis, Addison's disease

Kidney – Arterial and venous thrombosis, infarcts, ischemia, glomerulonephritis, interstitial nephritis, renal failure, arterial hypertension, proteinuria, hematuria

Peripheral vessel – Peripheral venous or arterial thrombosis



Braine – Stroke, transient ischemic attack, infarcts, micro and macro-thrombosis, venous sinus thrombosis, hemorrhage, encephalopathy, seizure, headache

Skin – Livedo racemosa, ulcer, necrosis, ischemia, thrombosis, purpura, cyanosis, Raynaud's phenomenon, ecchymosis, erythema nodosum, epidermolysis bullosa, subungual splinter hemorrhage

Heart – Myocardial infarction, micro-infarcts, atrial or right ventricle thrombosis, heart failure, valvulopathy, Libman-Sacks endocarditis, cardiomegaly

Spleen – Arterial and venous thrombosis, infarcts, splenomegaly

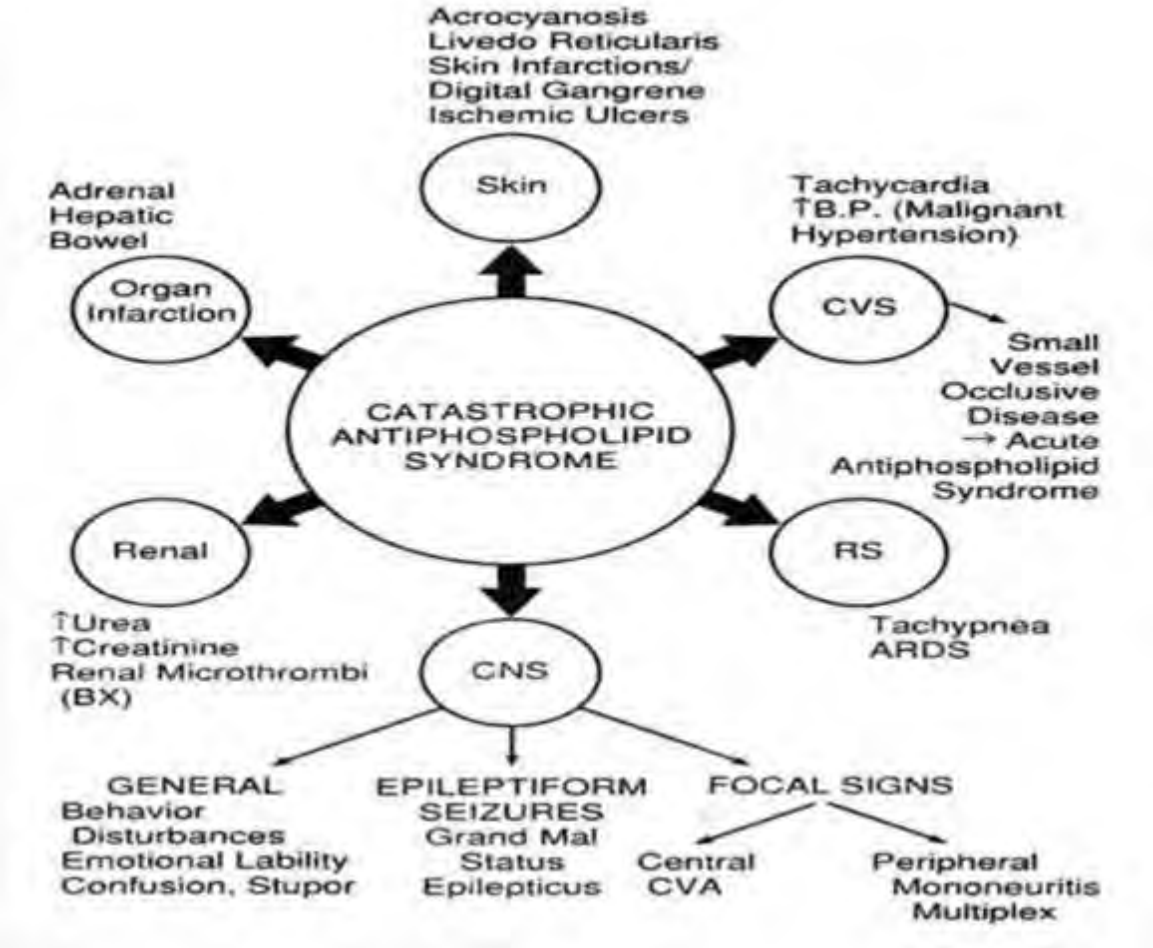
Hematological – Thrombotic microangiopathic hemolytic anemia, disseminated intravascular coagulation

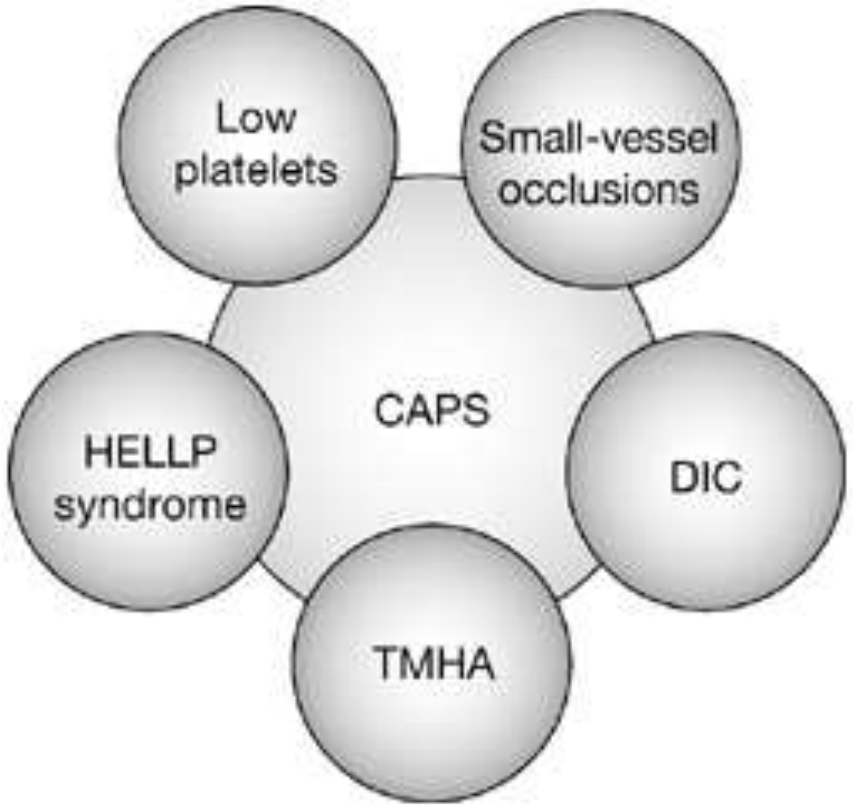
Gastrointestinal – Micro-thrombosis, ischemia, hemorrhage, perforation, ileus

Bone marrow – Infarcts, pancytopenia

Jacobs L et al. Antibodies 2024, 13, 21

A CAPS klinikai fenotípusai

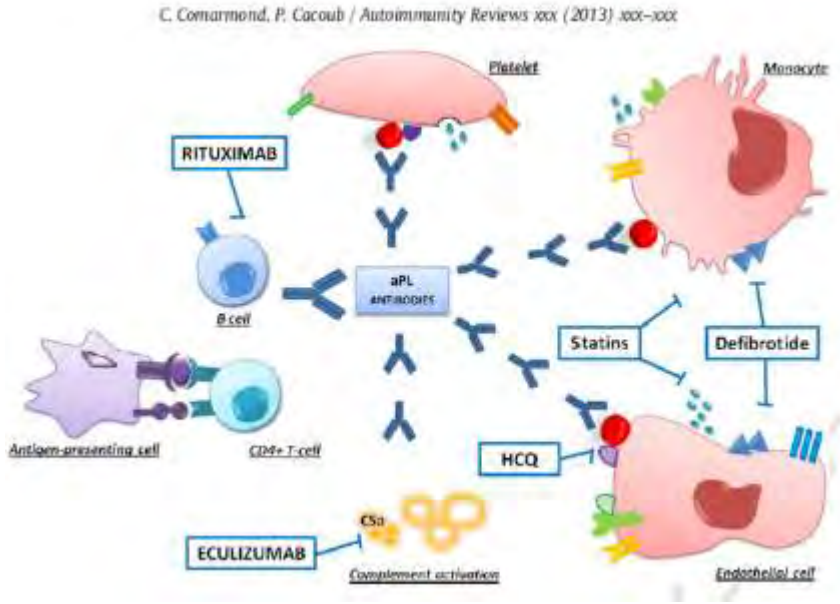




Cervera R, https://slideplayer.com/slide/8339194/

Nature Clinical Practice Rheumatology **volume 2**, pages81–89 (2006)

CAPS terápiája



12. A. Prompt treatment of infections by early use of anti-infective medications in all aPL-positive individuals and minimisation of interruptions in anticoagulation or low INR level in patients with thrombotic APS are recommended to help prevent the development of CAPS (4/D).

B. For first-line treatment of patients with CAPS, combination therapy with glucocorticoids, heparin and plasma exchange or intravenous immunoglobulins is recommended over single agents or other combinations of therapies. Additionally, any triggering factor (eg, infections, gangrene or malignancy) should be treated accordingly (5/D).

In patients with refractory CAPS, B cell depletion (eg, rituximab) or complement inhibition (eg, eculizumab) therapies may be considered (4/D).

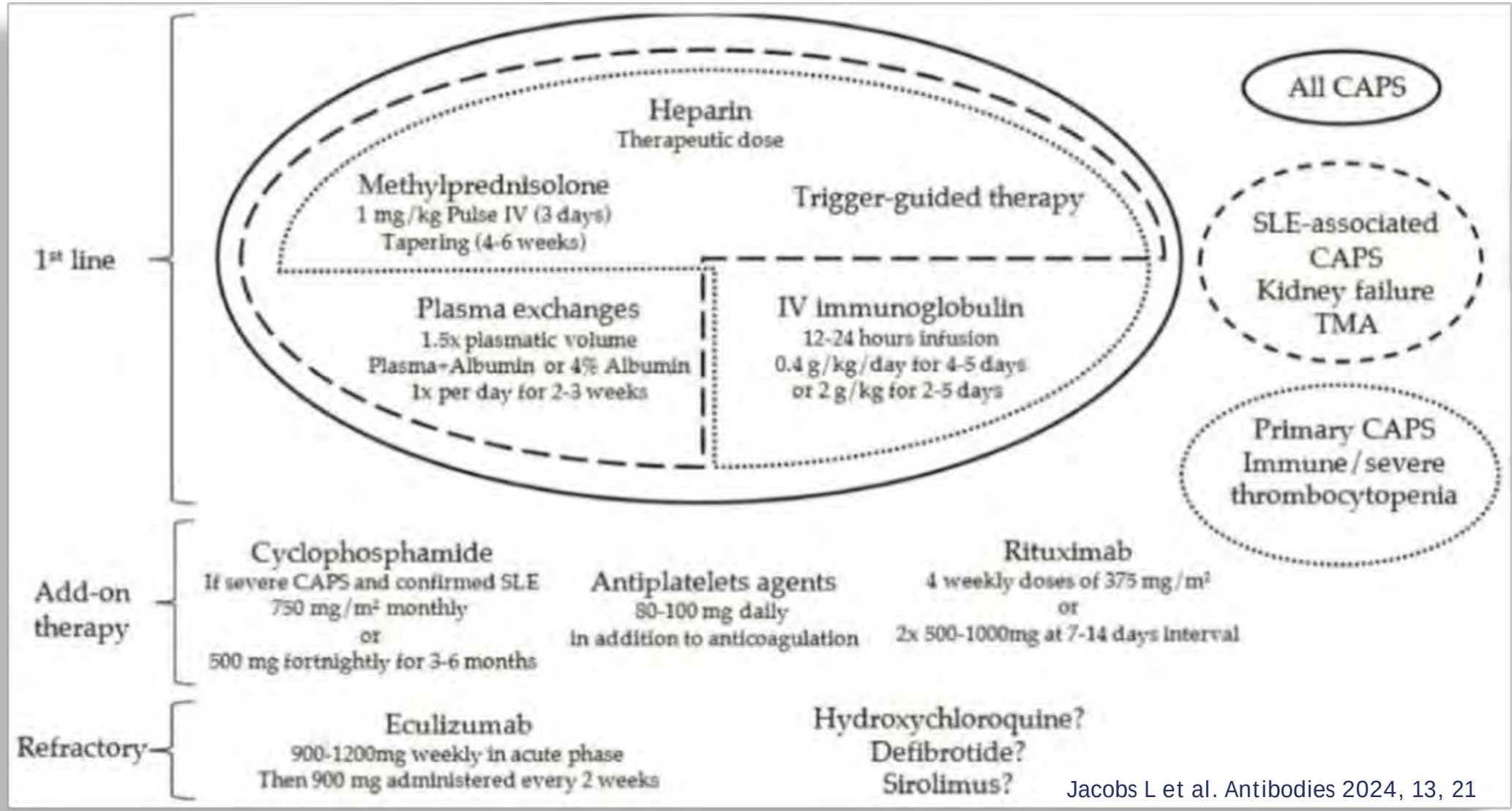
Tektonidou MG, et al. Ann Rheum Dis 2019;78:1296-1304.

Terápiás lépcsők a CAPS kezelésében

Túlélési arány:

- CAPS: antikoaguláns, szteroid, PEX - 72%.
- SLE-asszociált CAPS: antikoguláns, szteroid, PEX - 65%.
- Primer CAPS: antikoaguláns, szteroid, IVIG - 82%.

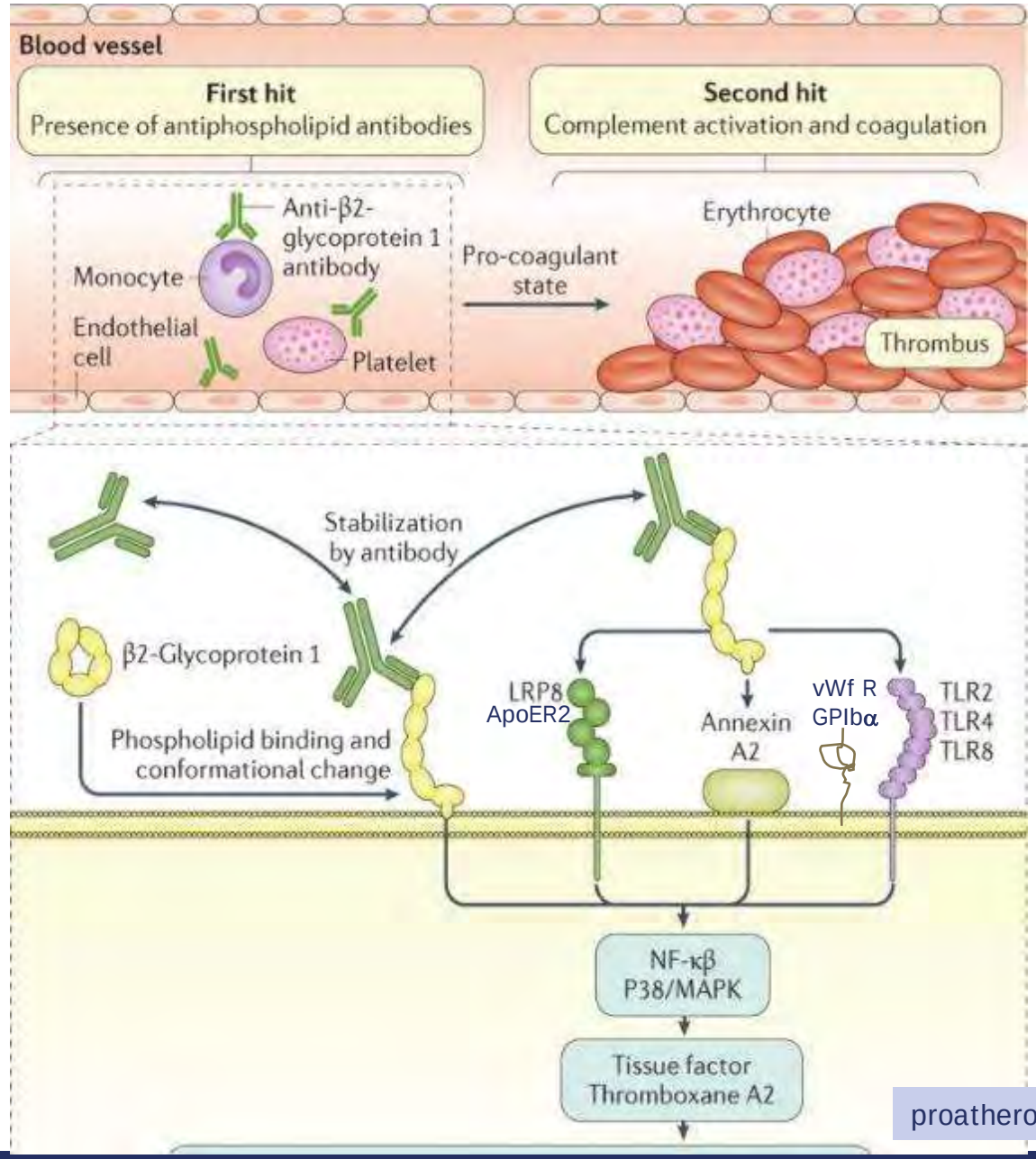
- Korábban a mortalitás 50%-os volt.



Jacobs L et al. Antibodies 2024, 13, 21

Új terápiás célpontok és lehetőségek a patogenetikai útvonalak mentén

APS **patofiziológia**
Thrombosis
Kétlépcsős modell



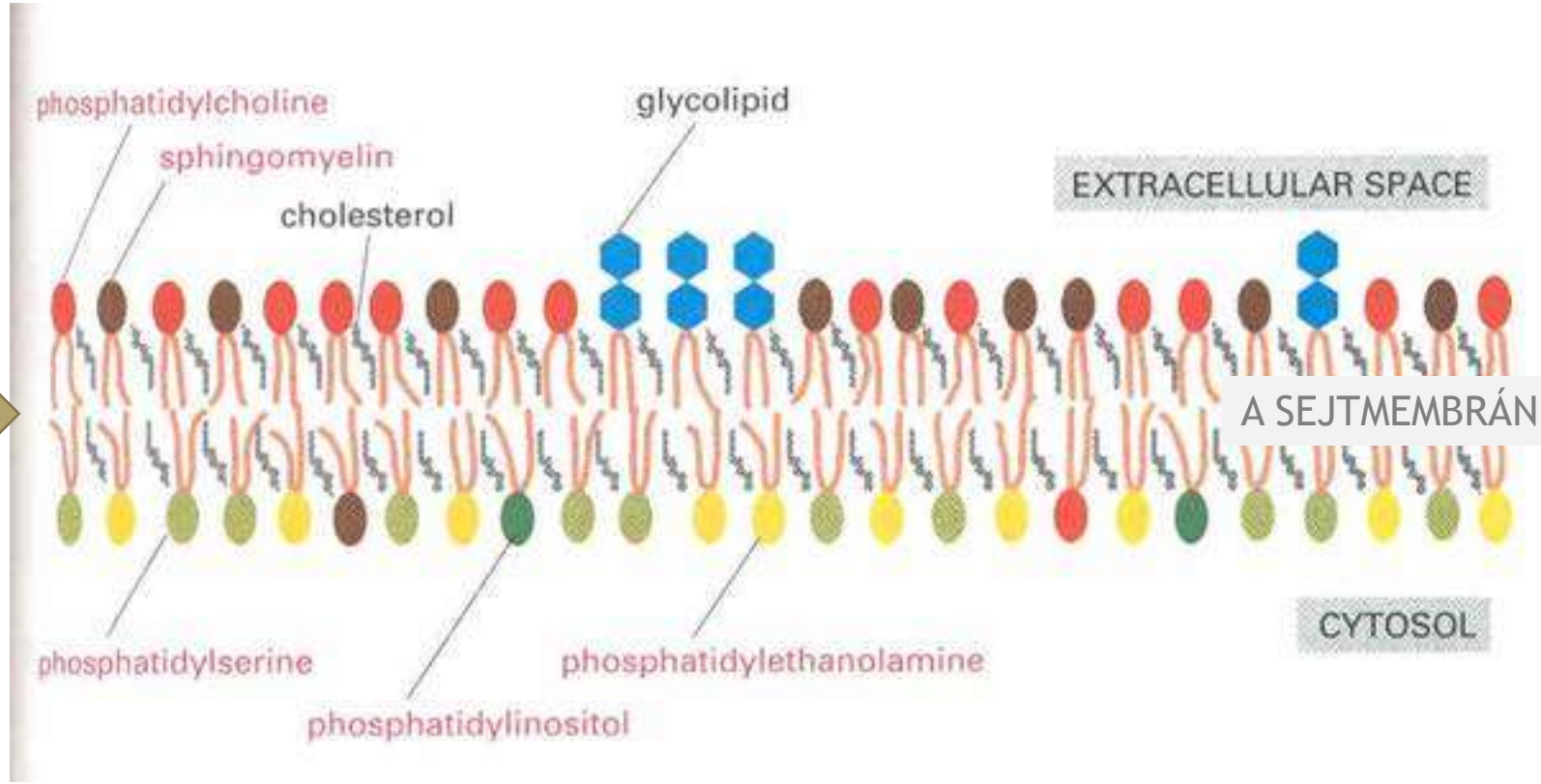
LRP8: Low-density lipoprotein receptor-related protein 8,
ApoER2: apolipoprotein E receptor 2
vWf R: von Willebrand faktor recptor
GPIbalfa: glicoprotein Ib alfa
TLR: toll like receptor

Schreiber, K., *et al. Nat Rev Dis Primers* 4, 17103 (2018).

Kétlépcsős modell

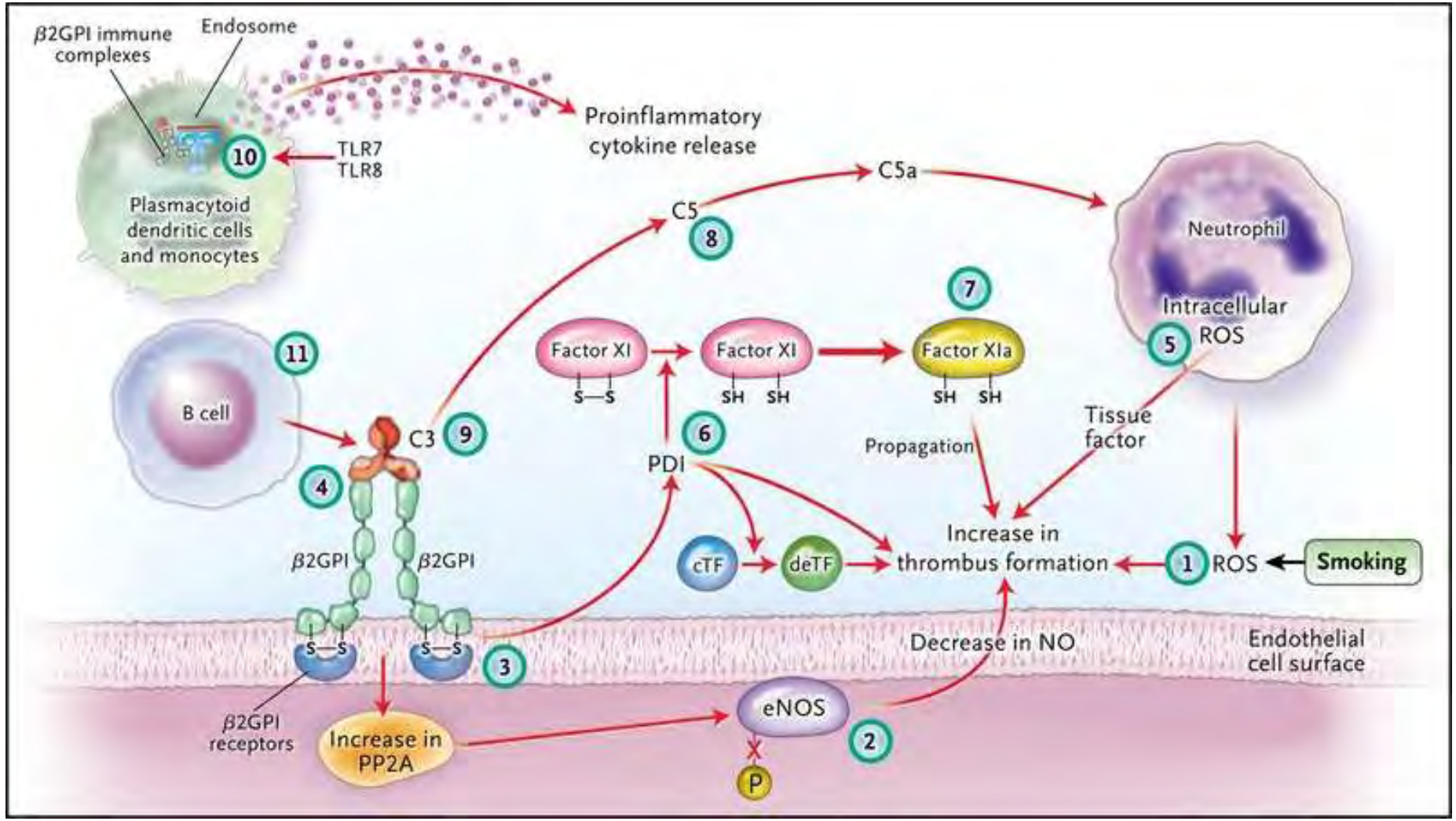
„Second hit”

Tumor
Infekció
Gyulladás
Terhesség
Trauma
Műtét
Gyógyszer



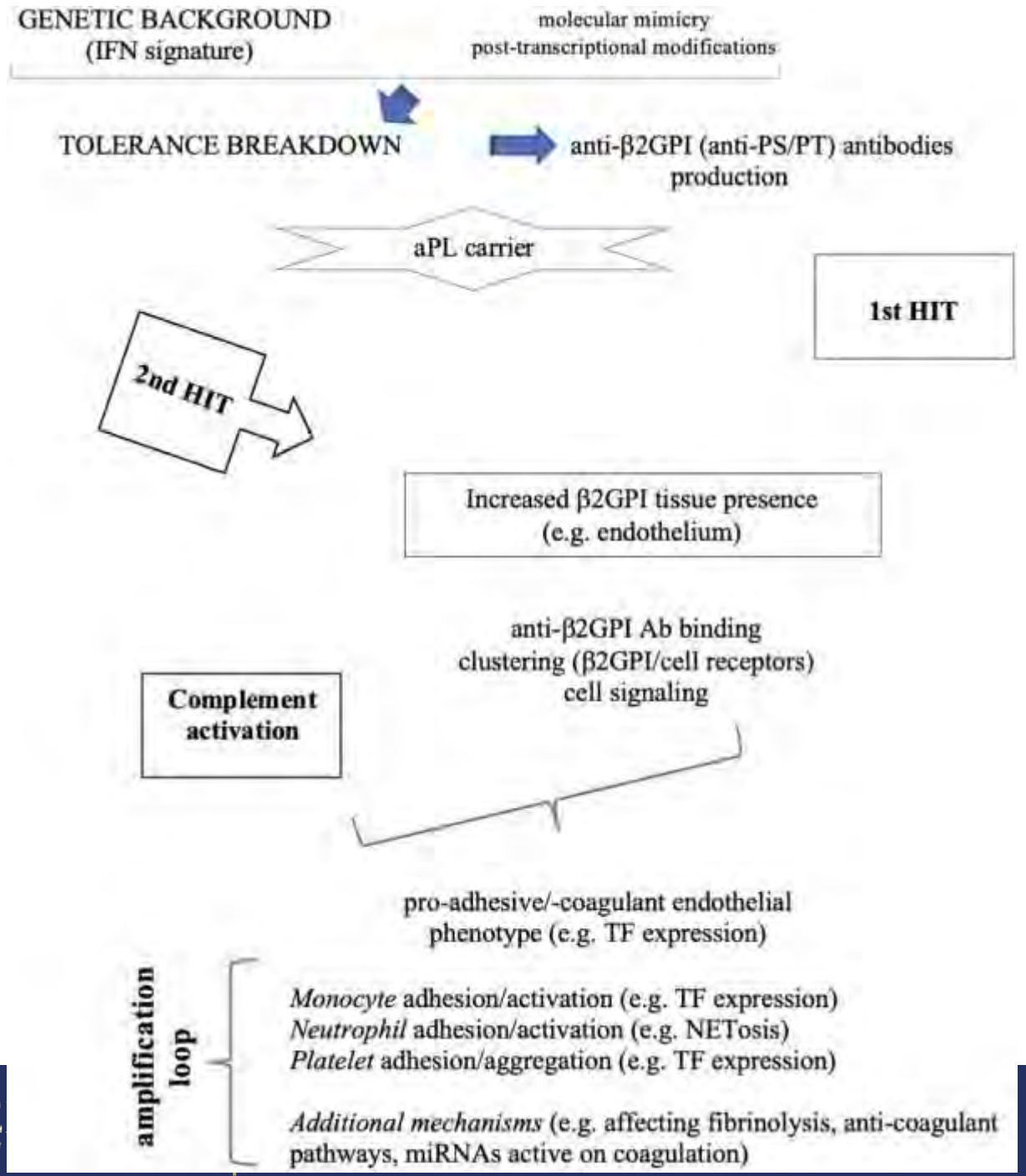
https://datagrid.hu/boda/Transzport/Beadando/Kripli.htm

APS: **Patofiziológiája**- thrombosis



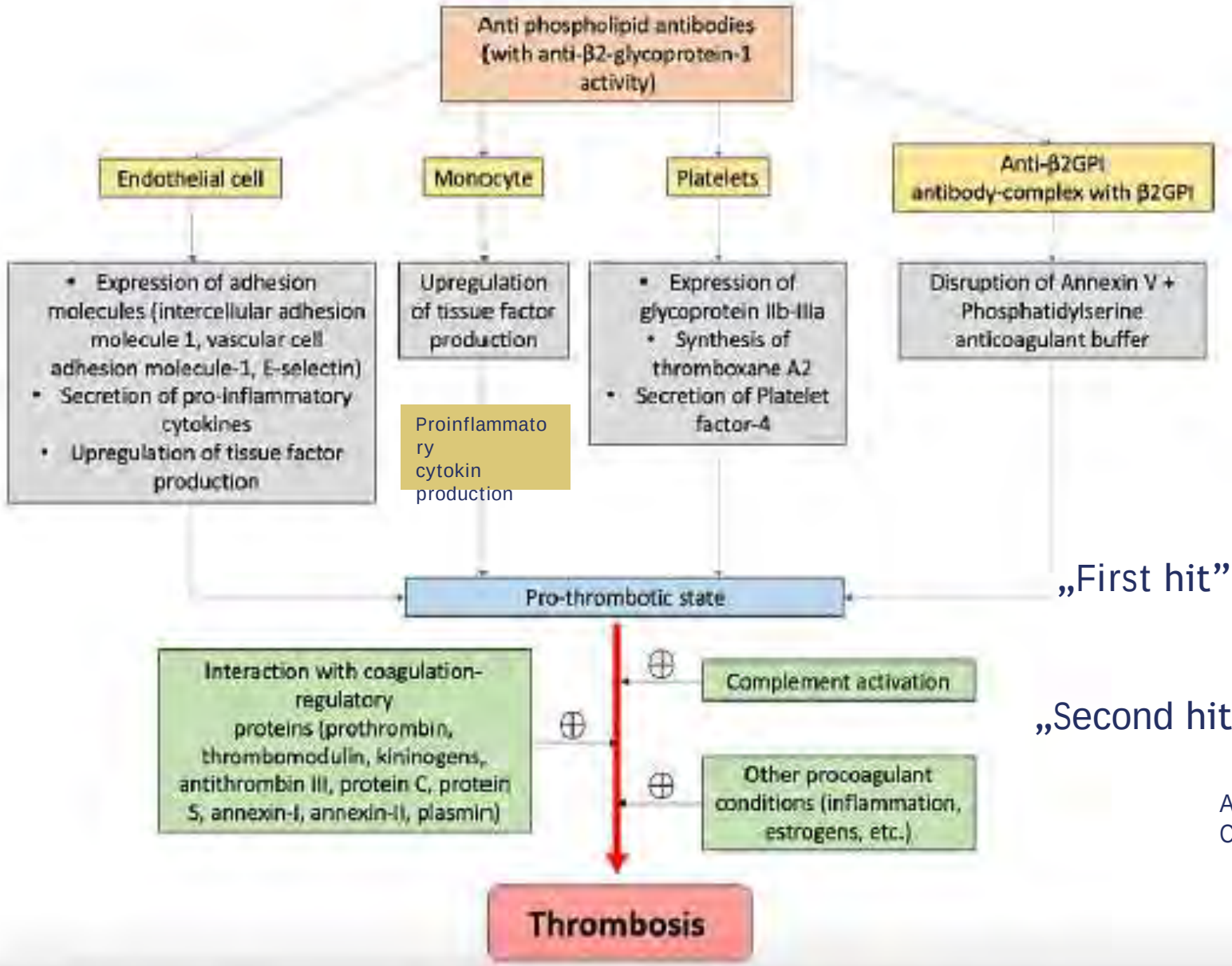
N Engl J Med 2013; 368:1033-1044

Az APS patogenezise



E Raschi et al. Rheumatology, 2024, 63, SI4-SI13

APS: Patofiziológia-immunológiai hatások

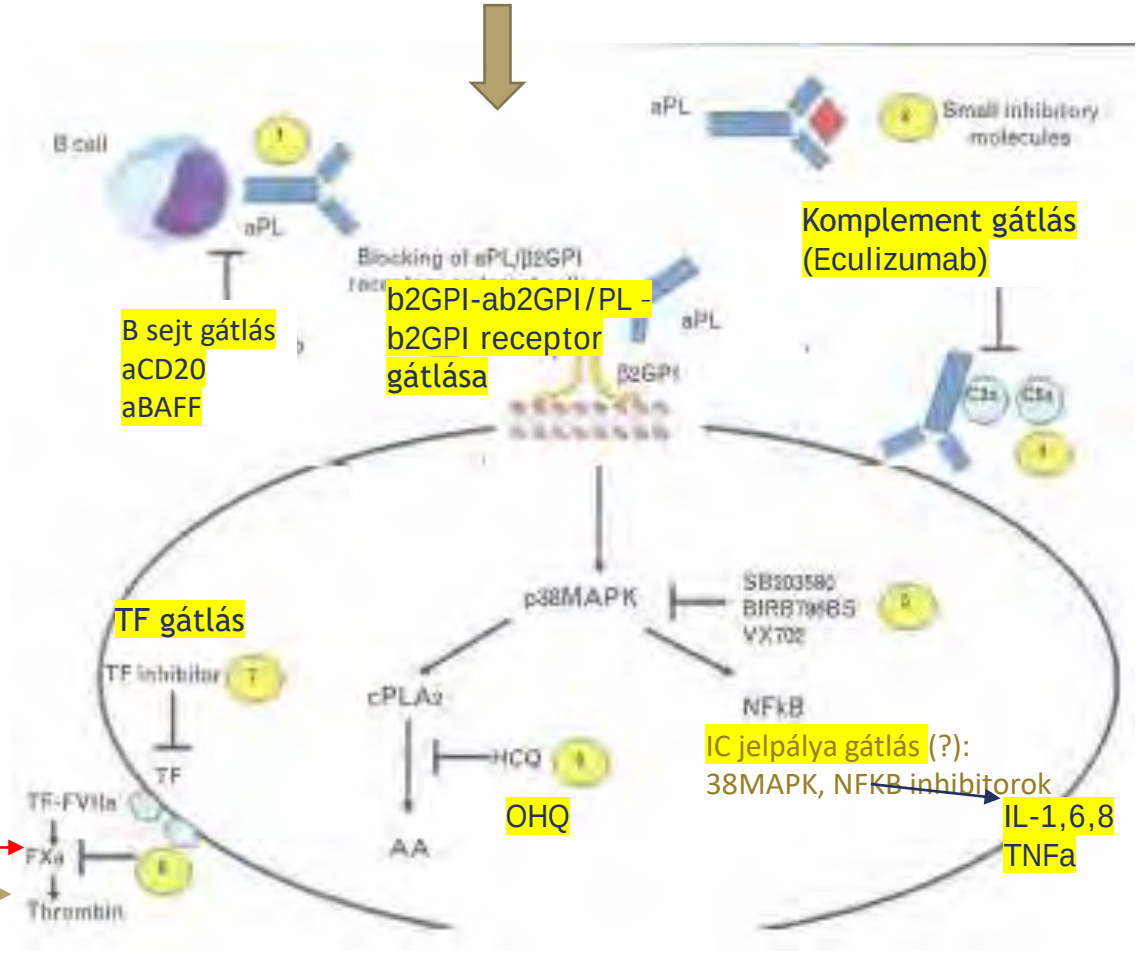


„First hit”

„Second hit”

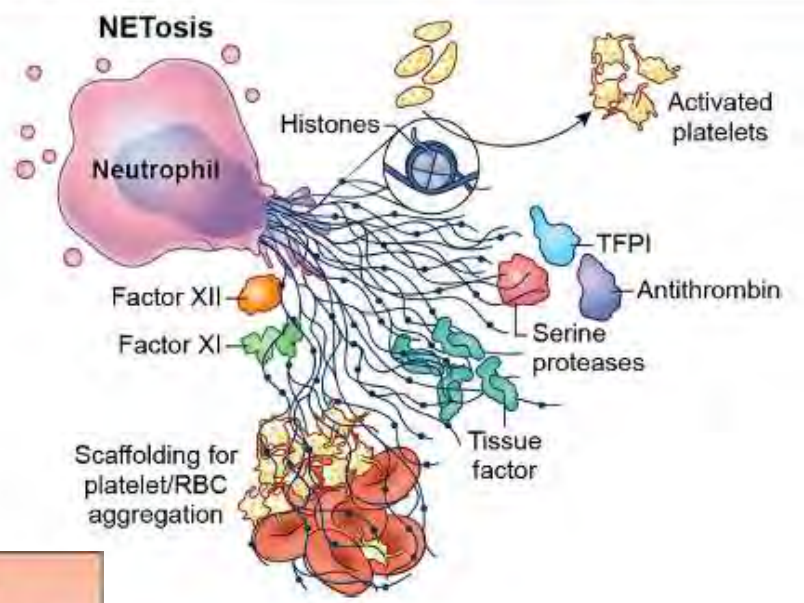
Arora S, et al. (2021)
Cureus 13(10): e19009. DOI 10.7759/cureus.19009

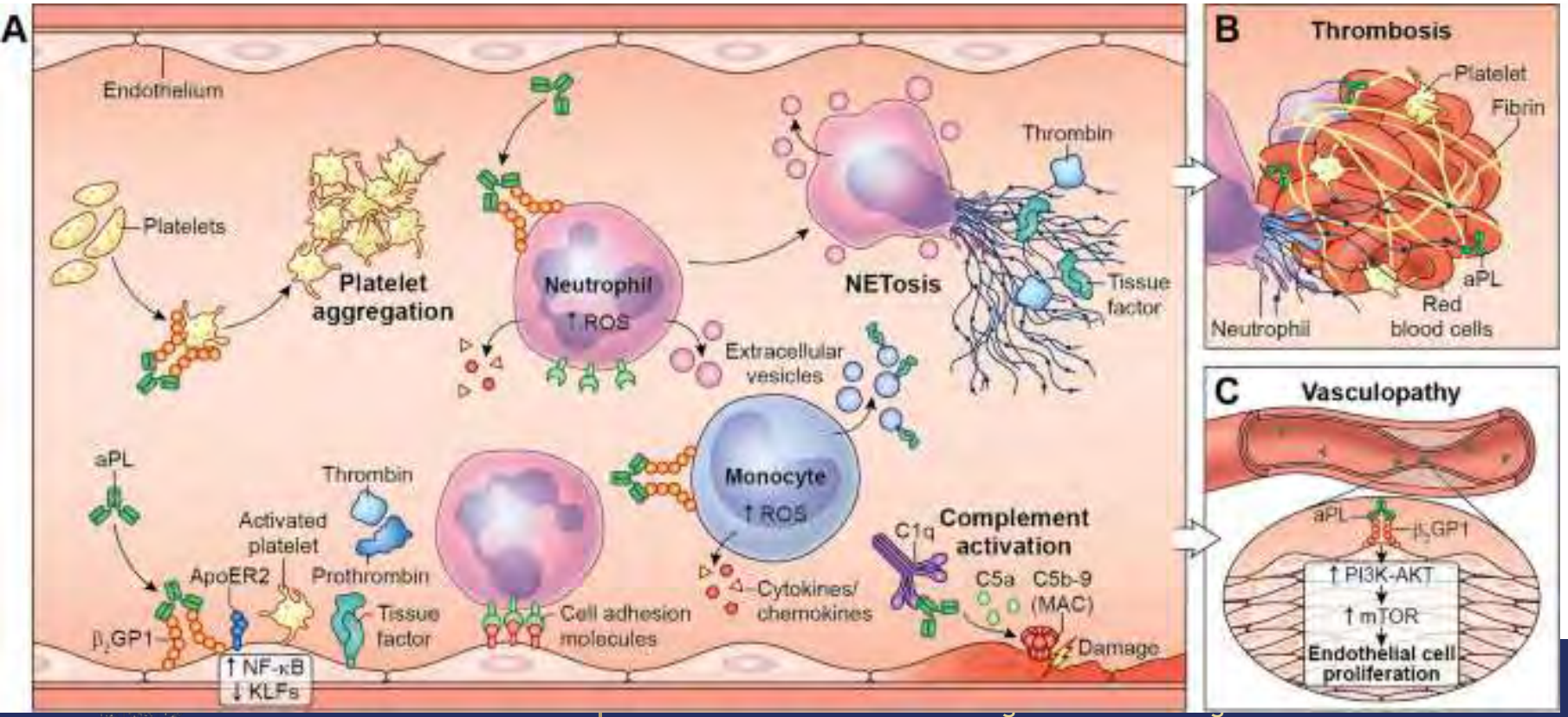
Innovatív, célzott terápiás lehetőségek az APS kezelésére



Lopez-Pedrera Ch. Et al: Int. Immunopharmacol 2015;27:200-8.
Galli M.: Autoimm Highlights 2014; 5: 1-7.

APS - **patofiziológia**: **Obliteratív** vasculopathia
Immun thrombosis - **thromboinflammáció**

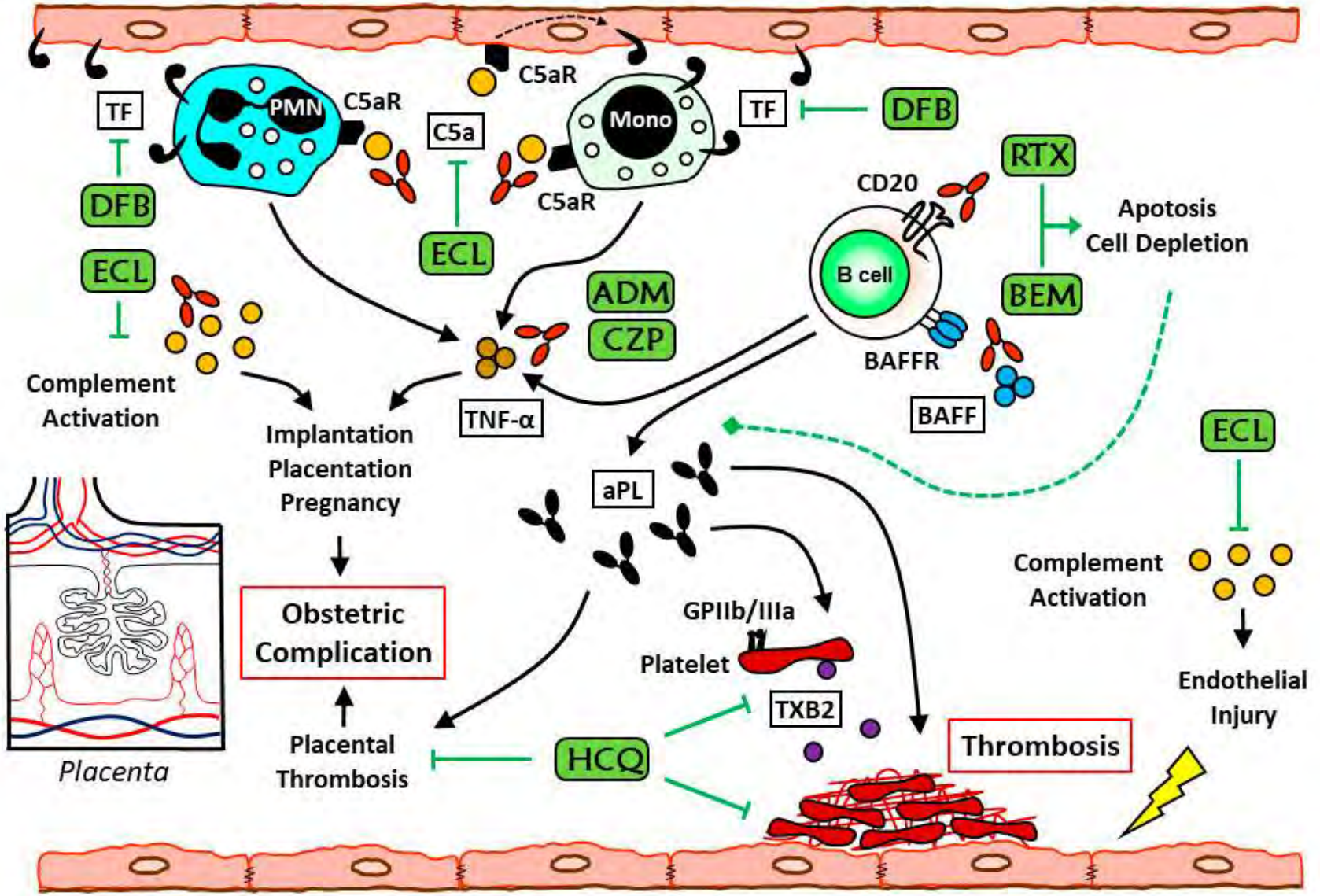




Thrombocyták aktiválják
az alvadási kaszkádot,
a komplementrendszert,
az endothel sejteket és
a neutrophyl leukocytákat

J.S. Knight, Y. Kanthi.
Seminars in Immunopathology (2022) 44:347–362

Immunológiai terápiás célpontok az APS patogenezisében



ADM: Adalimumab; BEM: belimumab;
CZP: certolizumab; ECL: eculizumab;
DFB: defibrotide; GPIIb/IIa: Glycoprotein IIb/IIIa;
HCQ: hydroxychloroquine; RTX: rituximab;
TF: tissue factor; TXB2: Thromboxane B2.

Mormile I et al.
Biomedicines 2021, 9, 132.

antioxidants

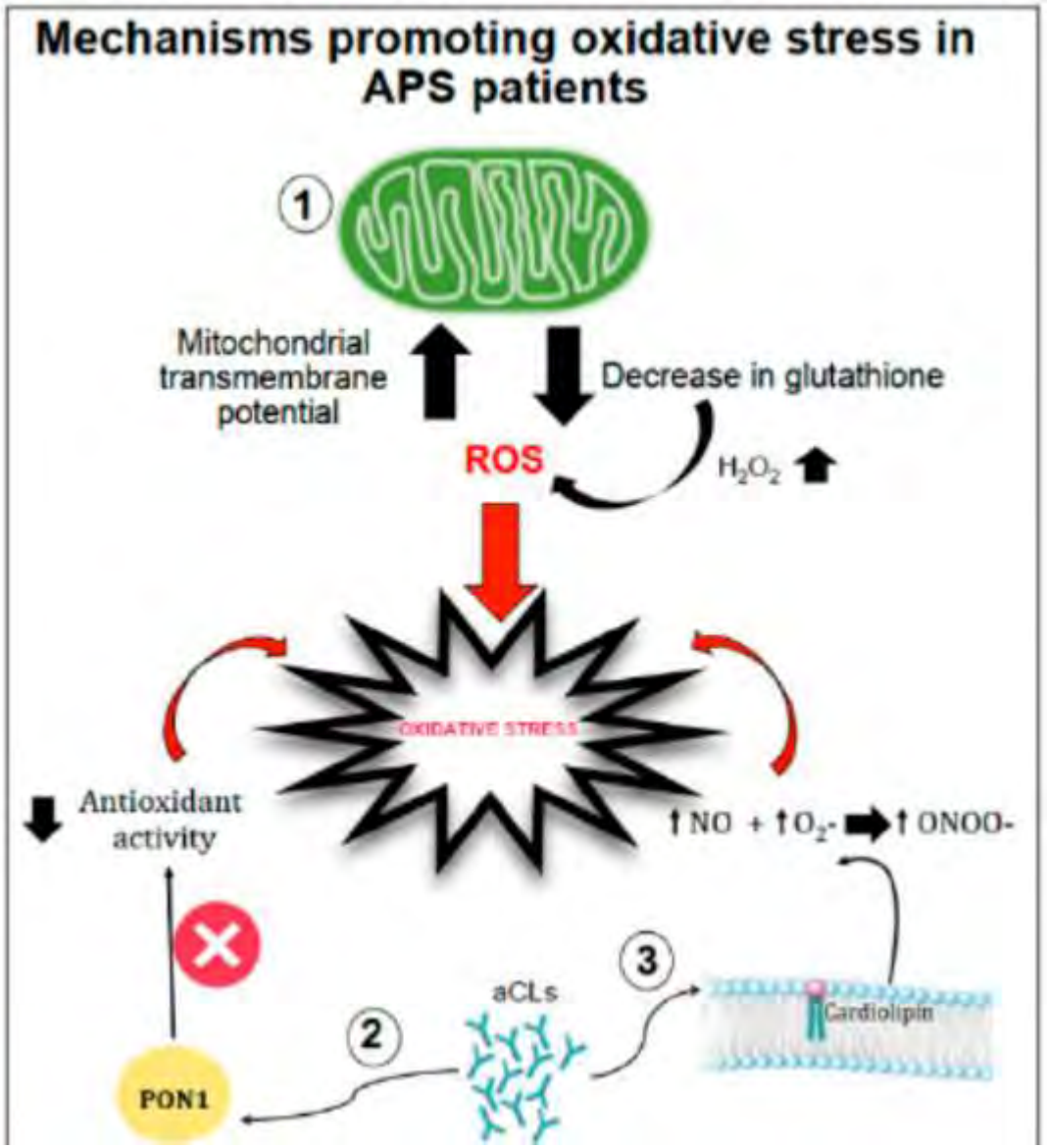
MDPI

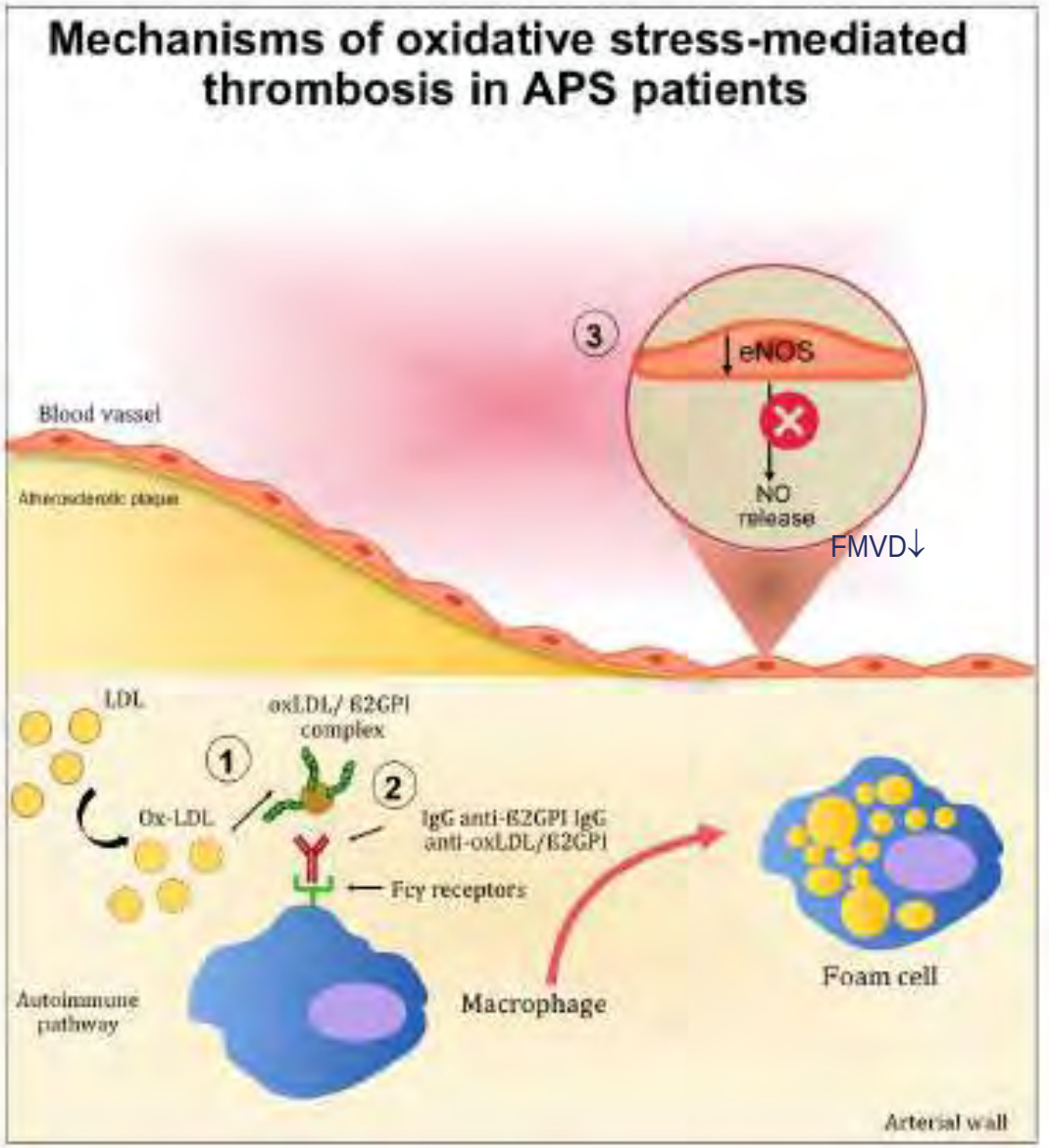
Review

Oxidative Stress in the Pathogenesis of Antiphospholipid Syndrome: Implications for the Atherothrombotic Process

Cristina Nocella [1], Simona Bartimoccia [2], Vittoria Cammisotto [3], Alessandra D'Amico [4], Daniele Pastori [1], Giacomo Frati [2,5], Sebastiano Sciarretta [2,5], Paolo Rosa [2], Chiara Felici [2], Oliviero Riggio [6,7], Antonella Calogero [2], Roberto Carnevale [2,8,*] and SMiLe Group [7,†]

Nocella C. et al. Antioxidants 2021, 10, 1790. https://doi.org/10.3390/antiox10111790





Nocella C. et al. Antioxidants 2021, 10, 1790. https://doi.org/10.3390/antiox10111790

Új irányvonalak az APS kezelésében

4. Antioxidant Treatment in APS Patients: The State of the Art

Common treatments for APS are long-term anticoagulation with vitamin K antagonists and antiplatelet drugs. To reinforce the effects of these therapies and to fight the effects of oxidative stress in APS, several potential new therapeutic approaches are under investigation. Strategies to inhibit oxidative stress involve drugs such as dabigatran and statins that, with different molecular mechanisms, can reduce vascular oxidative stress and inflammation and improve endothelial function.

A potential new therapeutic strategy should be represented by natural molecules such as vitamins, CoQ10, and omega-3 polyunsaturated fatty acid (n-3 PUFA) (Table 2).

Nocella C. et al. Antioxidants 2021, 10, 1790. https://doi.org/10.3390/antiox10111790

Protektív aPL antitestek?

Medium/high titre of aPL with serological characteristics comparable to those found in APS patients and may persistently present for a long time in asymptomatic carriers.

Recent data suggest that the epitope specificity of these anti-b2GPI-dependent aPL is mainly directed against D5 rather than D1 as in symptomatic patients. It has been speculated that antibodies against D5 are not pathogenic.

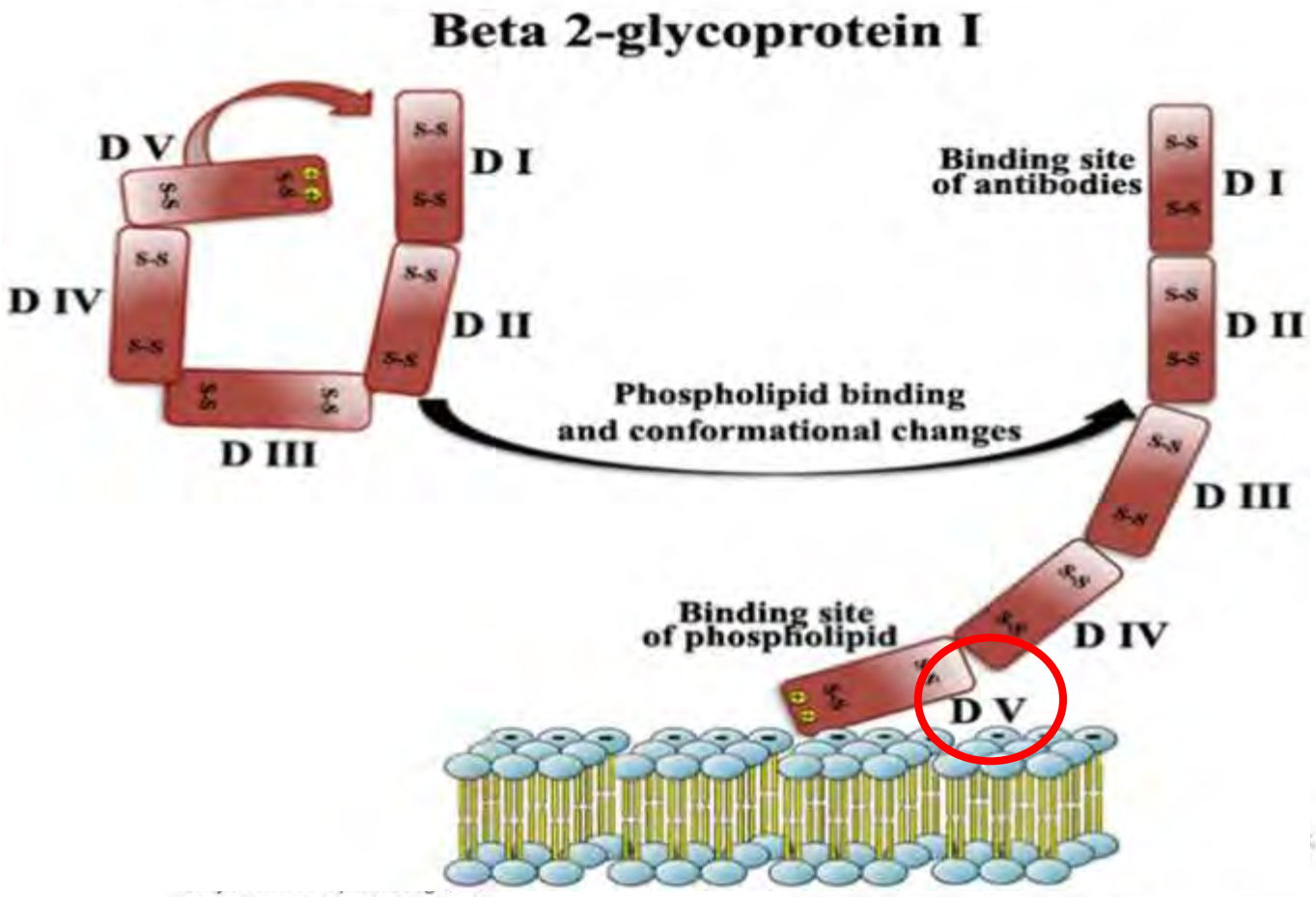
The results obtained from the APS rat model revealed that IgG from monospecific anti-D5 positive sera fail to trigger complement activation and to promote blood clotting, suggesting that they are not pathogenic.

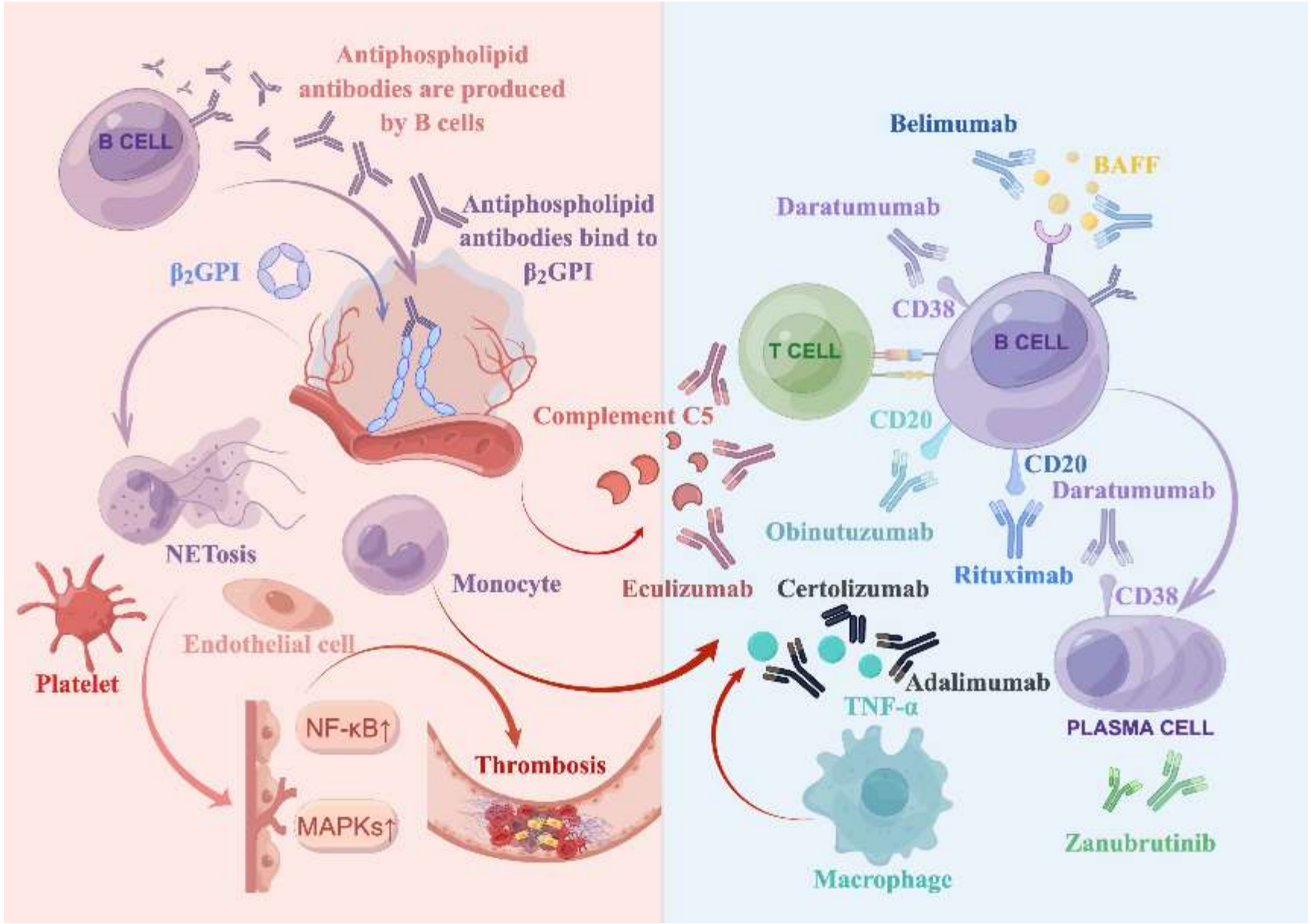
These antibodies react with an epitope close to the PL-binding site of the molecule and inhibit the binding of b2GPI to anionic structures/ cell receptors behaving as a sort of 'protective' antibodies. These findings were confirmed by in vitro experiments.

The prevalence of these 'protective' aPL would explain why the carriers do not display any clinical manifestation.

The inhibition of b2GPI binding and the pathogenic effect of b2GPI-dependent aPL by a synthetic peptide mimicking the PL-binding site of D5 (TIFI) further supports the relevance of D5 in b2GPI binding and allowing the exposure of the immunodominant epitope in D1 [66, 106].

E Raschi et al. Rheumatology, 2024, 63, SI4-SI13





Yun et al. 10.3389/fimmu.2023.1145145

Medication	Mechanism	Perspective
Eculizumab	Complement 5 inhibitor	For CAPS refractory to standard treatment, CAPS receiving kidney transplantation, acute TMA in patients with aPL-related nephropathy, APS during pregnancy, or pediatric CAPS (2, 33, 34)
Rituximab	Type I anti-CD20 monoclonal antibody	For thrombocytopenia, hemolytic anemia, or other aPL-mediated hematological and microthrombotic manifestations or noncriteria manifestations; an alternative option for CAPS which is refractory to standard treatment, refractory obstetric APS, and pediatric CAPS (2, 33, 35)
Obinutuzumab	Type II anti-CD20 monoclonal antibody (B-cell depletion mainly *via* DCD)	Alternative option for rituximab in APS (36)
Belimumab	BAFF/Blys inhibitor	Potential treatment for aPL-positive patients, or primary APS with high thrombotic risk (37–39)
Daratumumab	Anti-CD38 monoclonal antibody	Potential treatment for refractory APS (40, 41)
Zanubrutinib	BTK inhibitor	Unclear, evidence still being collected
Anti-TNF-α therapy	Anti-TNF-α monoclonal antibody: adalimumab, certolizumab	In refractory obstetric APS (42)

CAPS, catastrophic antiphospholipid syndrome; TMA, thrombotic microangiopathy; APS, Antiphospholipid syndrome; DCD, direct cell death; BAFF/Blys, B cell activating factor/B-lymphocyte stimulator; BTK, bruton tyrosine kinase.

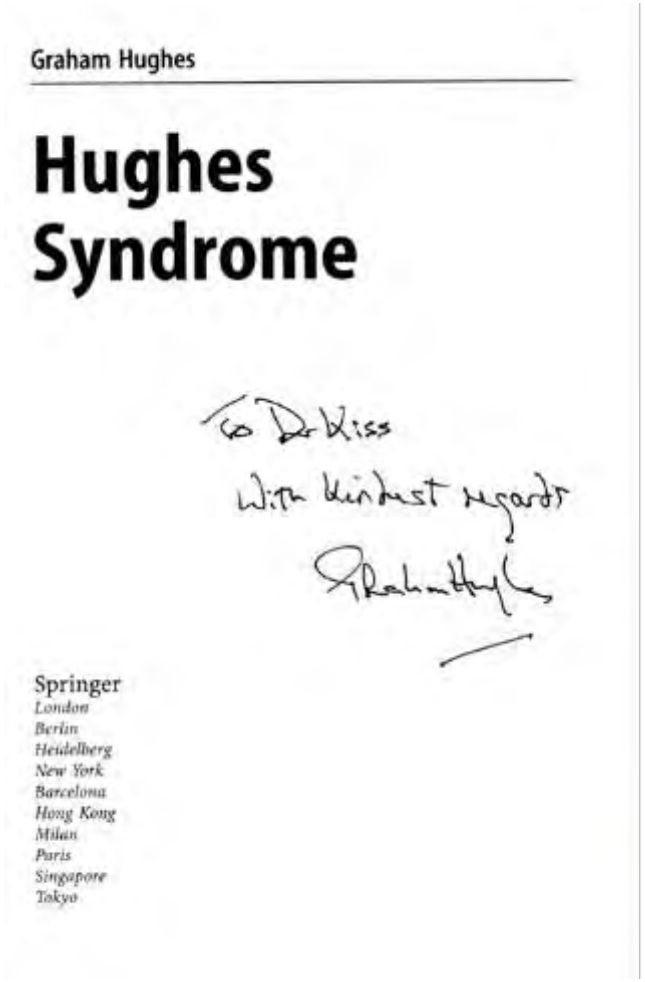
Yun et al. 10.3389/fimmu.2023.1145145

Összefoglalás

- Az APS magas morbiditású és mortalitású szisztémás autoimmun betegség, ami hemosztázis zavart, thromboemboliás, atherothromboticus, microcirculatios eltéréseket és pathológiás kimenetelű terhességet okoz.
- Az aPL antitestek egyértelmű kóroki szerepe igazolt. Kimutatásuk alapvető a klasszifikációban. (LA-t sokszor nem néznek, vagy nem korrekt módon)
- Az EULAR kidolgozta a besorolás kritériumait, ami nem azonos egyértelműen a diagnózis felállításával.
- Több nemzetközi szakmai társaság mellett az EULAR is megfogalmazta a terápiás ajánlást, ill. algoritmust.
- Fontos szerepe és terápiás konzekvenciája van a rizikóbesorolásnak.
- Antitrhomboticus és immunmoduláns kezeléseket is vegyük számításba!
- Figyeljünk a CAPS rizikófaktoraira!

Köszönöm a figyelmet!

Kérdések


Graham Hughes
Hughes Syndrome
To Dr Kiss
With kindest regards
Springer
London
Berlin
Heidelberg
New York
Barcelona
Hong Kong
Milan
Paris
Singapore
Tokyo

Hirdetés

- **Immunológiai alapfolyamatok molekuláris mechanizmusai és egyéb érdekességek az immunológia területén c. tanfolyam**
- Időpont: november 13-14
- Helyszín: RIK Kulturális és Konferencia Központ
- PhD Tanfolyam; a kurzus kódja: 7511, kredit: 1, tájékozódni lehet: https://phd.semmelweis.hu/public/kurzusok/6487 linken.
- Pót jelentkezés díja: 1 000 Ft
- **Szabadon választható** szakmai továbbképzés. Jelentkezni az oftexen.
- SE-SZTOK/2025.II/00308. Kredit: 32. Képzési díj: 24 000 Ft.

Program:

CIME: IMMUNOLÓGAI ALAPFOLYAMATOK MOLEKULÁRIS MECHANIZUSAI ÉS EGYÉB ÉRDEKESSÉGEK AZ IMMUNOLÓGIA TERÜLETÉN						
Dátum	**kezdés**	**befejezés**	**előadás címe**	**Előadó**	**titulus**	**tudományos fokozat**
2025.11.13	**8:15**	**8:30**	**Megnyitó**	**Kiss Emese**	**Prof. Dr.**	**egyetemi tanár**
	8:30	9:15	Patológiás autoimmunitás	Prohászka Zoltán	Prof. Dr.	egyetemi tanár
	9:15	10:00	Autoinflammáció	Szamosi Szilvia	Dr.	e.docens, PhD, med Habil
	10:00	10:15	Szünet			
	10:15	11:00	Autoinflammatórikus folyamatok experimentális modellezése.	Mócsai Attila	Prof. Dr.	egyetemi tanár
	11:00	11:45	Allergiás betegségek mechanizmusai	Müller Veronika	Prof. Dr.	e.tanár, MTA doktora
	11:45	12:10	Ebédszünet			
	12:10	12:55	A fibrózis patofiziológiája	Szűcs Gabriella	Prof. Dr.	e.tanár, oktató orvos
	12:55	13:40	Immundefektusok molekuláris alapjai	Kriván Gergely	Dr.	egyetemi docens, PhD., oktatóorvos
	13:40	13:55	Szünet			
	13:55	14:40	Genetikai vizsgálatok	Balogh István	Prof. Dr.	egyetemi tanár
	14:40	15:25	Hiperinflammációs szindrómák (MAS, citokinvihar, szepszis, CAPS)	Szekanecz Zoltán	Prof. Dr.	e.tanár, MTA doktora
2025.11.14	8:30	9:15	Eozinofil sejtek fiziológiás és patológiás szerepköre	Bácsi Attila	Prof. Dr.	e.tanár, MTA doktora
	9:15	10:00	Vérlemezkék szerepe az immunválasz szabályozásában	Kappelmayer János	Prof. Dr.	e.tanár, MTA doktora
	10:00	10:15	Szünet			
	10:15	11:00	Ritka betegségek a gyulladásos és hemosztázis patomechanizmusok határmesgyéjéről	Bodó Imre	Dr.	e.docens, PhD
	11:00	11:45	A thrombotikus és gyulladásos események modulátorai: neutrophil granulocyták és thrombocyták hálózata	Szederjesi Attila	Dr.	PhD
	11:45	12:10	Ebédszünet			
	12:10	12:55	Nyirokszöveti stromasejtek	Balogh Péter	Prof. Dr.	egyetemi tanár, MTA doktora
	12:55	13:40	A veleszületett limfoid sejtek (ILC) típusai, jellemzőik és szerepeik	Balogh Péter	Prof. Dr.	egyetemi tanár, MTA doktora
	13:40	13:55	Szünet			
	13:55	14:40	Citokinek és receptoraik	Boldizsár Ferenc	Dr.	e.docens, PhD
	14:40	15:25	Immunmediált inflammatórikus betegségek	Balog Attila	Prof. Dr.	e.tanár, PhD