Sindrome Antifosfolipido: Cuestiones a debate

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Definition

- **Clinical Features**
  - **-Thrombosis**
    - **Venous/arterial**
  - **-Pregnancy morbidity**
    - **Early loss (<12w)**
    - **Foetal death (>12w)**
    - **Prematurity**
    - **Pre-eclampsia**
- **Antibodies**
  - **-anti-β2 GP1**
  - **-aCL**
- **LA: Not an Ab**

Other clinical features

Mycroangiopathy

- **Renal**
- **Heart**
- **Skin: Legs ulcers**
  Skin necrosis
  Livedo Reticularis

Other clinical features

- Trombocytopenia
- Hemolytic Anemia
- Hypertension
- Cardiac Valve
- Chronic headache
- Epilepsy
- Corea
- TransverseMyelitis

No thrombotic mechanism proven

How to interpret aPL results?

- **Anti-cardiolipin alone**
- **Anti-β2-glycoprotein 1 alone**
- **Usually, together**
- **Lupus anticoagulant alone**

  Coagulation times prolonged (DRVVT and/orAPTT)

Treatment

- **Primary Prophylaxis:**

  aPL positives without thrombosis
- **Secondary Prophylaxis:**

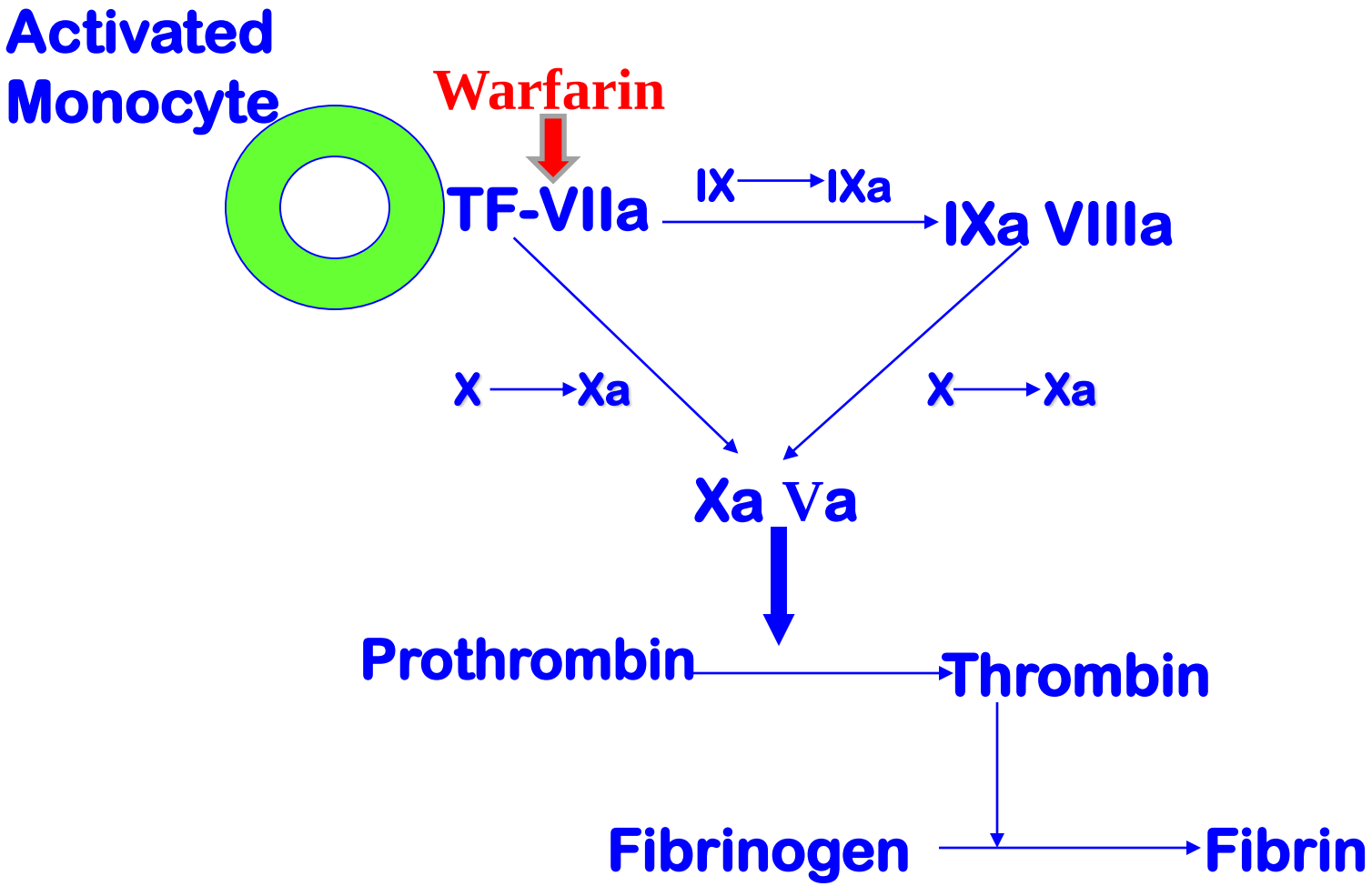
  1st thrombosis

  Recurrent Thrombosis
- **Obstetric APS**

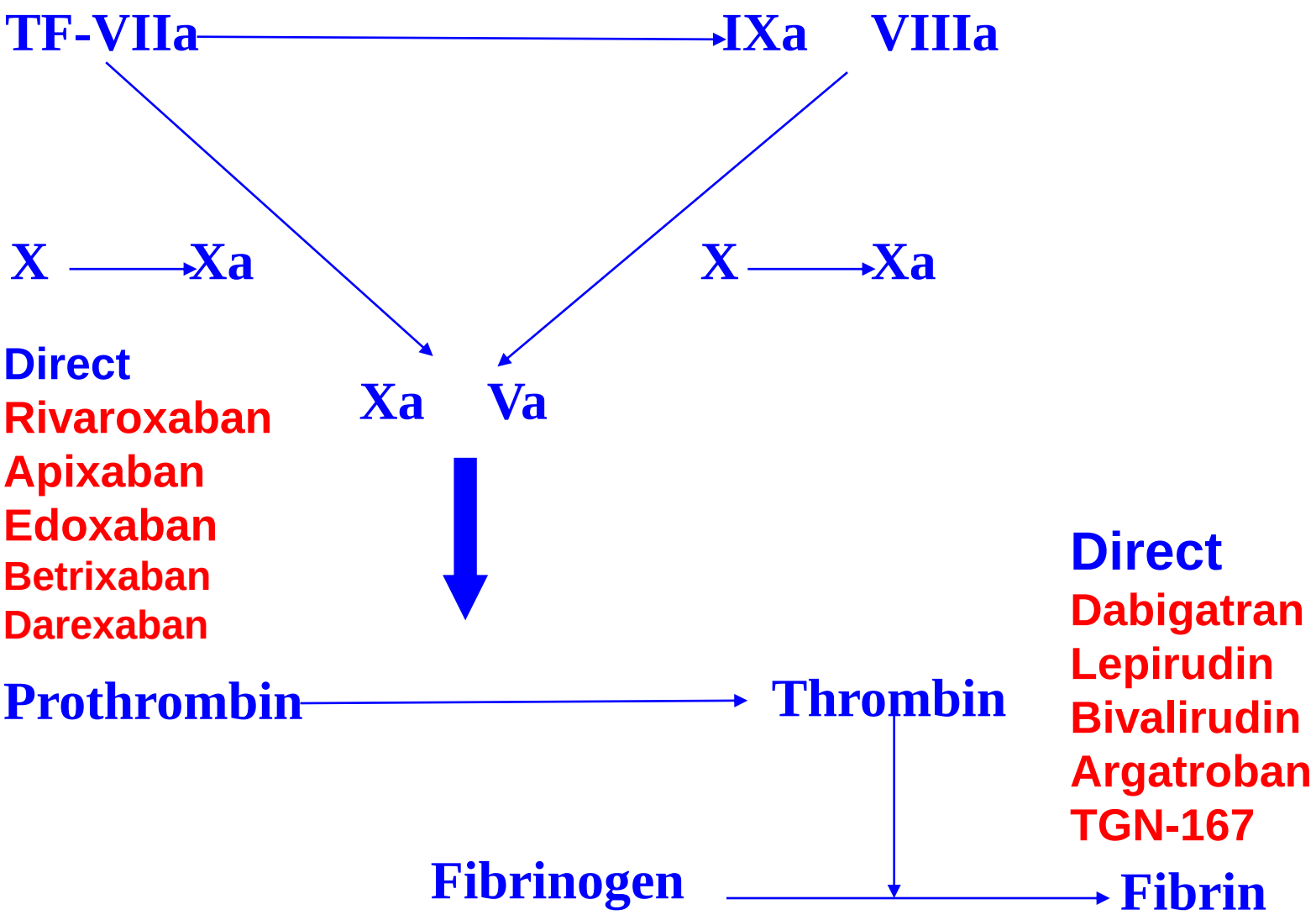
Treatment of thrombosis

- **No criteria: low risk of reccurrences, similar to general population**
- **Defined APS 1st venous thrombosis: INR 2.0-3.0**
- **Defined APS arterial thrombosis:**
  - **Warfarin INR 3.0-4.0**
  - **Warfarin INR 2.0-3.0 + Low dose Aspirin**

Tissue Factor

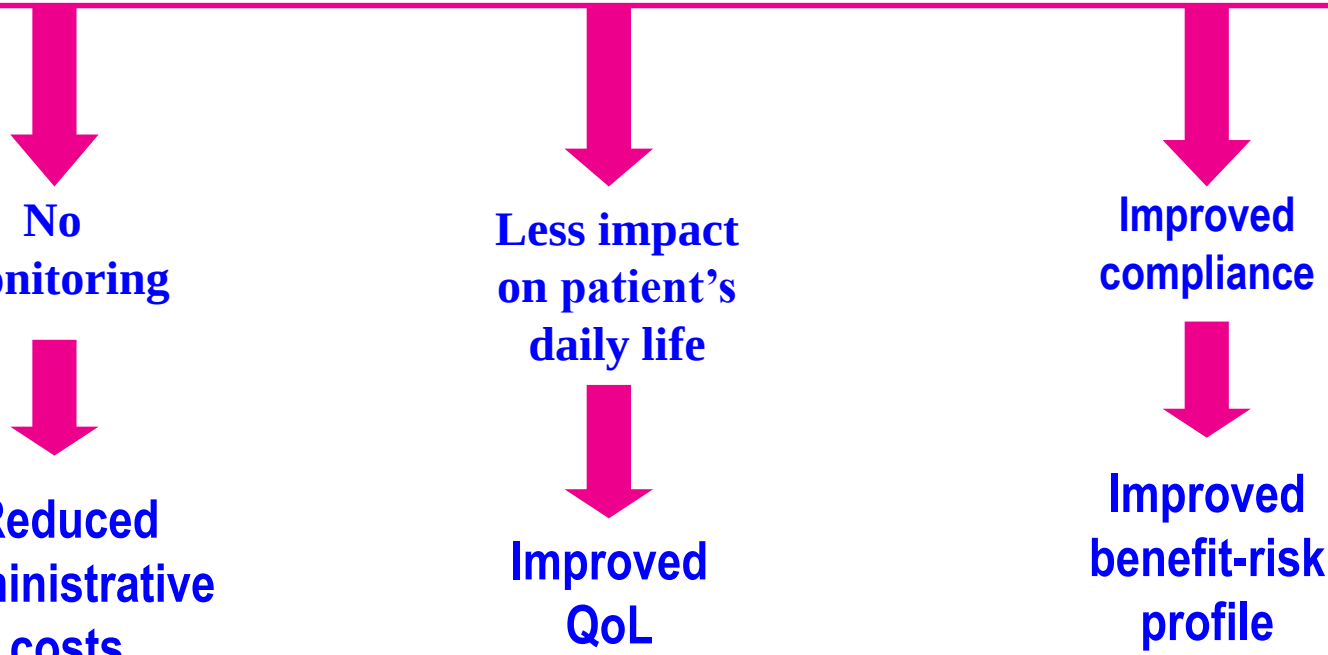


Can we use DOAC in APS?



Which are the DOAC advantages?

- Simplified dosing regimen
- Predictable anticoagulation and no need for routine coagulation monitoring
- Can be given at fixed doses
- Few drug interactions
- No dietary restrictions



Mavrakanas T *et al. Pharmacol Ther* 2011;130:46–58

Clinical Trials Data

- **Patients: APS with previous VT taking warfarin (INR 2.5)**
- **Intervention: Randomized to continue with warfarin or receive Rivaroxaban.**
- **The primary outcome was percentage change in endogenous thrombin generation (ETG) to day 42**
- **Secondary end points: Other thrombin generation parameters, thrombosis, and bleeding**
- **Treatment effect was measured as the ratio of rivaroxaban to warfarin for thrombin generation.**

Cohen H et al. Lancet Haematol 2016

Endogenous thrombin generation

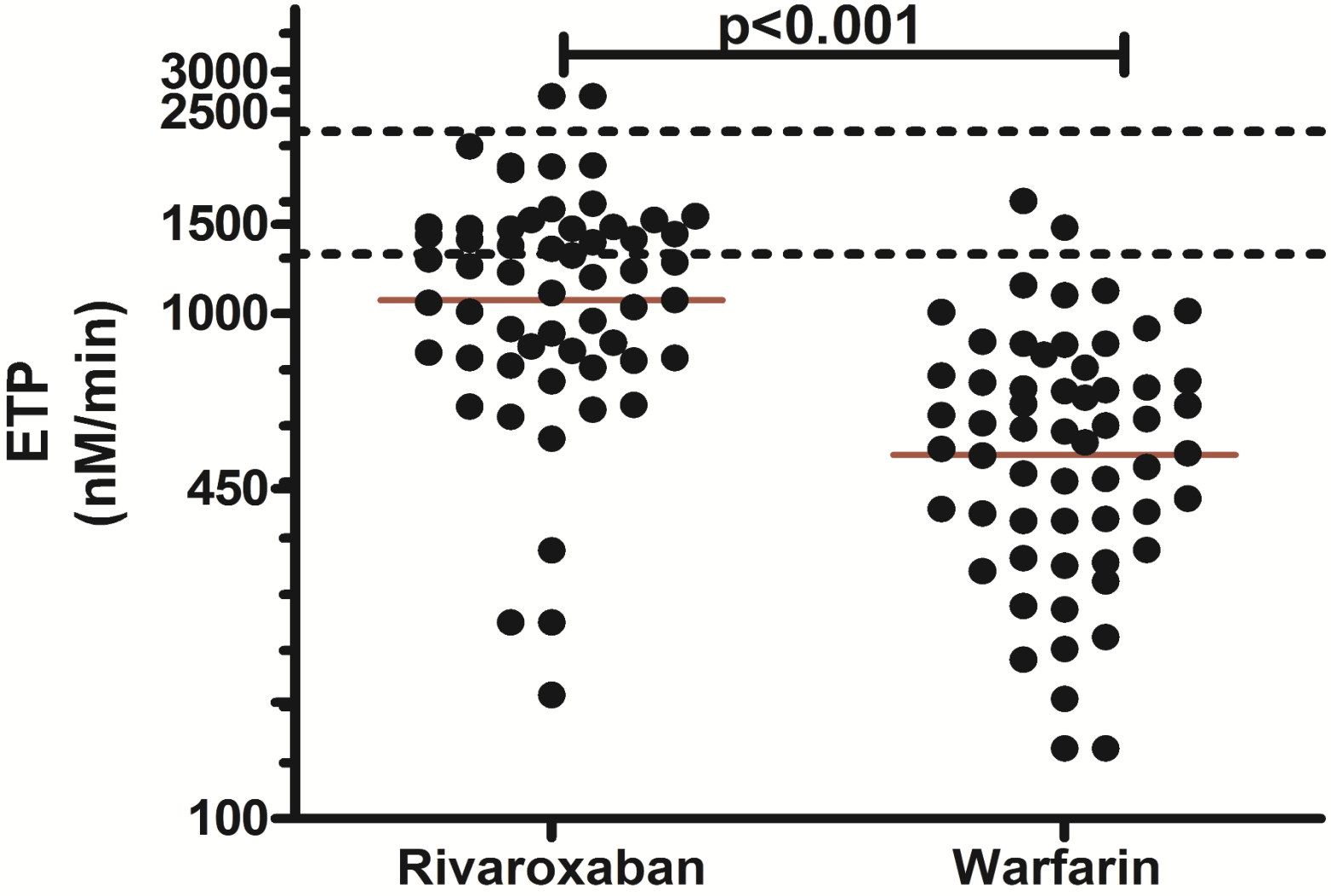
- **It is a parameter that decreases upon hypocoagulation and increases in hypercoagulability, in proportion to the thrombin forming capacity of a plasma sample**

Schattauer F Thromb Haemost 1995

Clinical Trials Data

- **ETG was higher in the rivaroxaban than in the warfarin group ($p<0{\cdot}0001$).**
- **Peak thrombin generation was lower in the rivaroxaban group ($p=0{\cdot}0006$).**
- **No thrombosis or major bleeding**

ETG parameters Day 42



Clinical Trials Data

- **Aim: To compare efficacy and safety of Rivaroxaban vs Warfarin to prevent secondary thrombosis**
- **Patients: Triple positivity (LA, aCL and anti- β2 GPI) and previous thrombosis. 120 patiens (59 randomized to rivaroxaban and 61 to warfarin)**
- **Intervention: Rivaroxaban 20 mg/day vs warfarin (INR target 2.5)**
- **Outcome: thrombotic events prevention, haemorrhage and death due to vascular events**

Pengo V et al. Blood 2018

Clinical Trials Data

- **Premature trial interruption because of an excess of events in the rivaroxaban arm.**
- **Mean follow-up was 569 days.**
- **7 (12%) thrombosis in rivaroxaban arm (4 CVA, 3 MI). No event in warfarin arm.**
- **Major bleeding: 6 patients: 4 (7%) in the rivaroxaban group, 2 (3%) in the warfarin group.**
- **No death was reported.**
- **Rivaroxaban in high-risk patients with APS was associated with an increased rate of events vs warfarin**

What to do when aPL become negative?

- **aPL negativization ocur in about 9% of patients**
- **More frequent in patients positive for only one antibody**

Radin M et al. Thromb Haemost 2019

- **Systematic review of papers reporting negativization and outcome: No conclusions**

What to do when aPL become negative?

- **Profound dysregulation that aPL produce at molecular level (increase expression of tissue factor, endothelial dysfunction and up-regulation of proteins etc)**
- **We do not know if this dysregulation is reversible when aPL become negative**
- **Not to stop anticoagulation when seroconversion**

Sciascia S et al. Autoimm Rev 2017