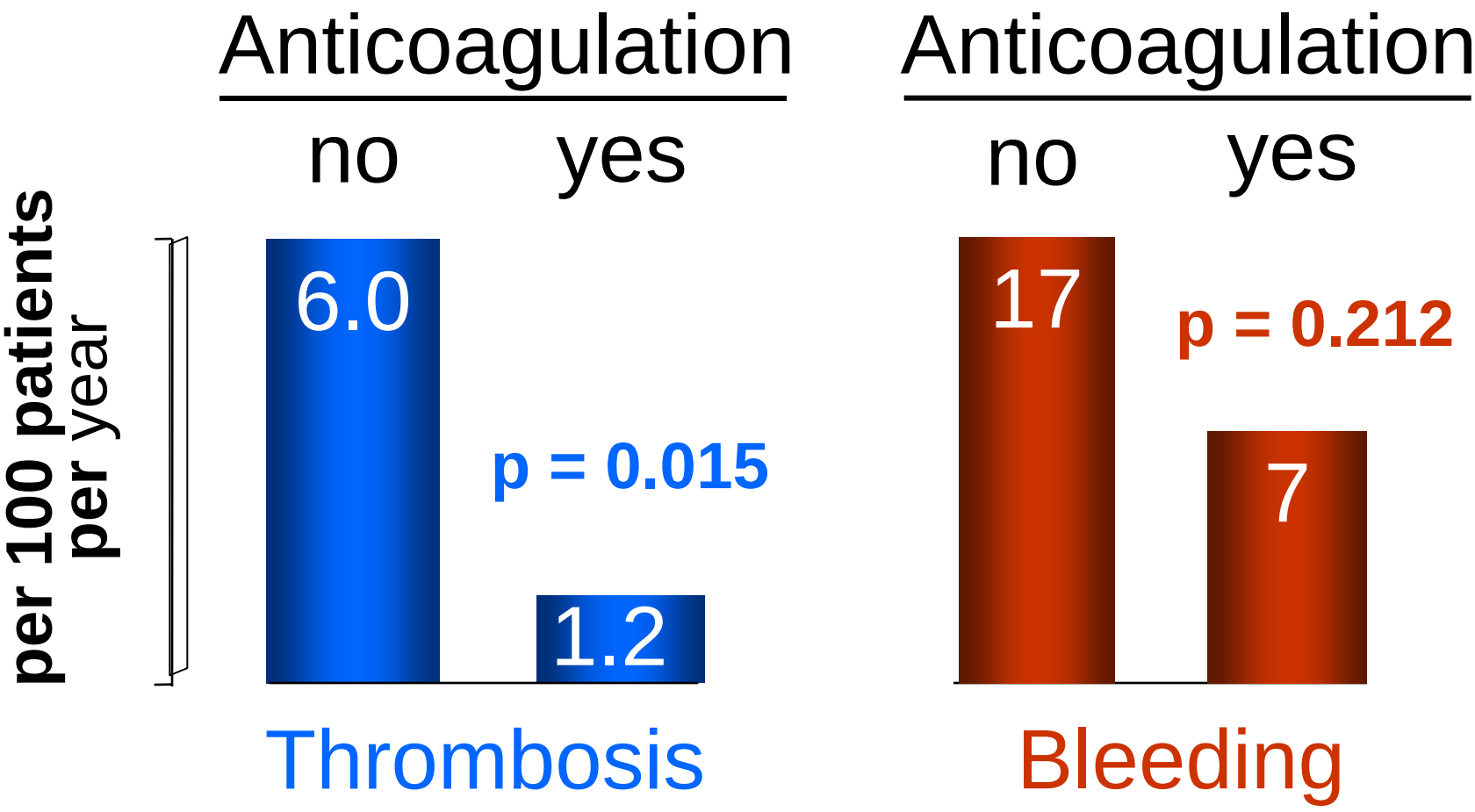
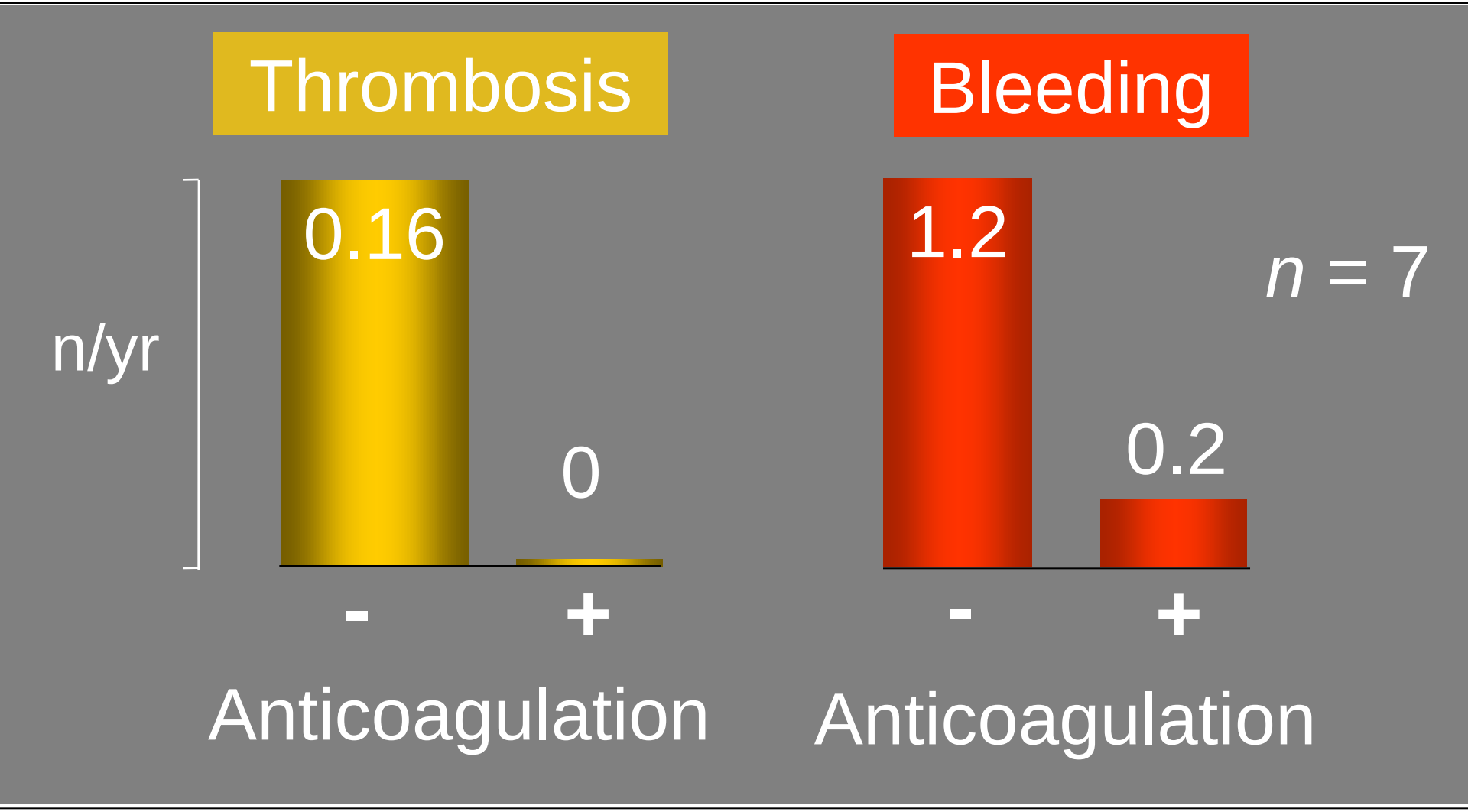
PHRC

Chronic Portal Vein Thrombosis



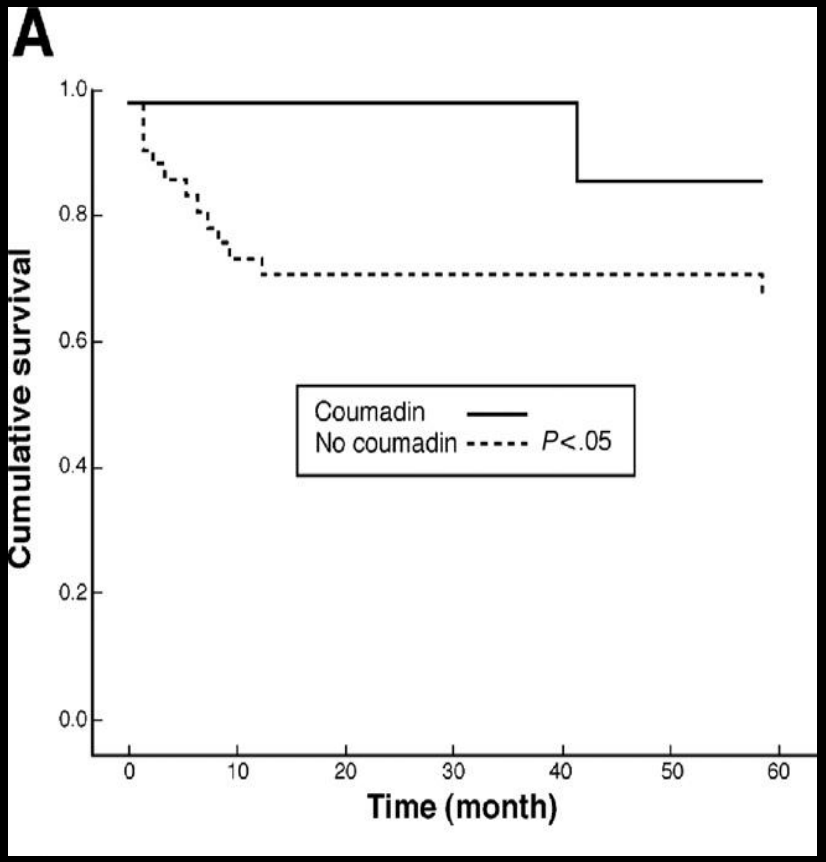
Condat et al. Gastroenterology 2001; 120:490

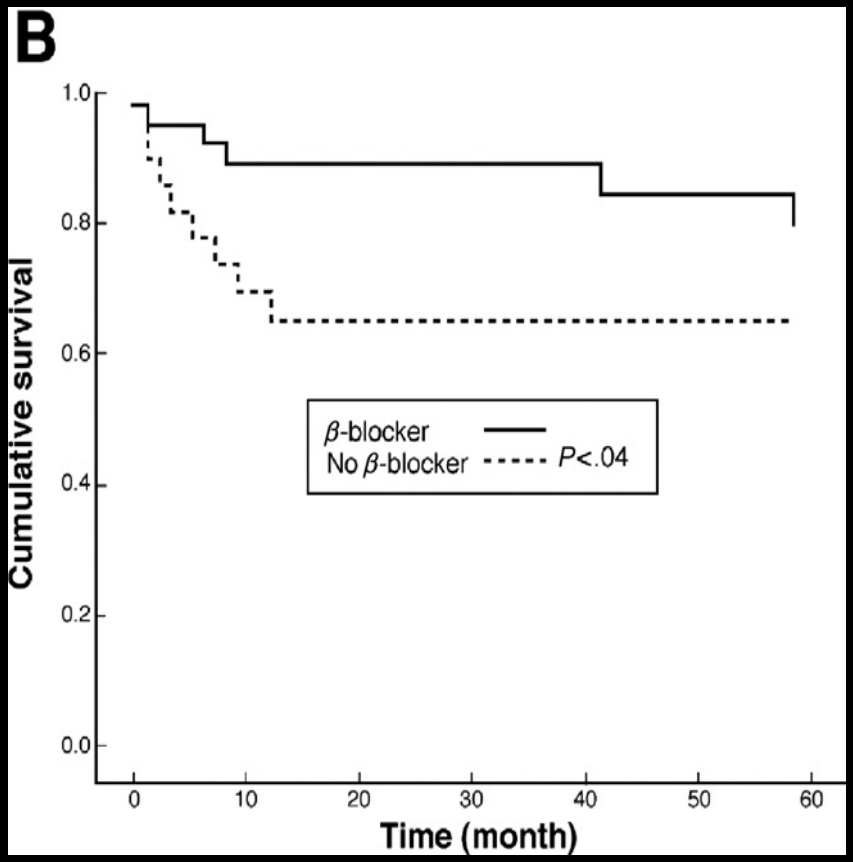
Portal vein thrombosis - Warfarin



Kitchens, J Thromb Thrombolysis 2007

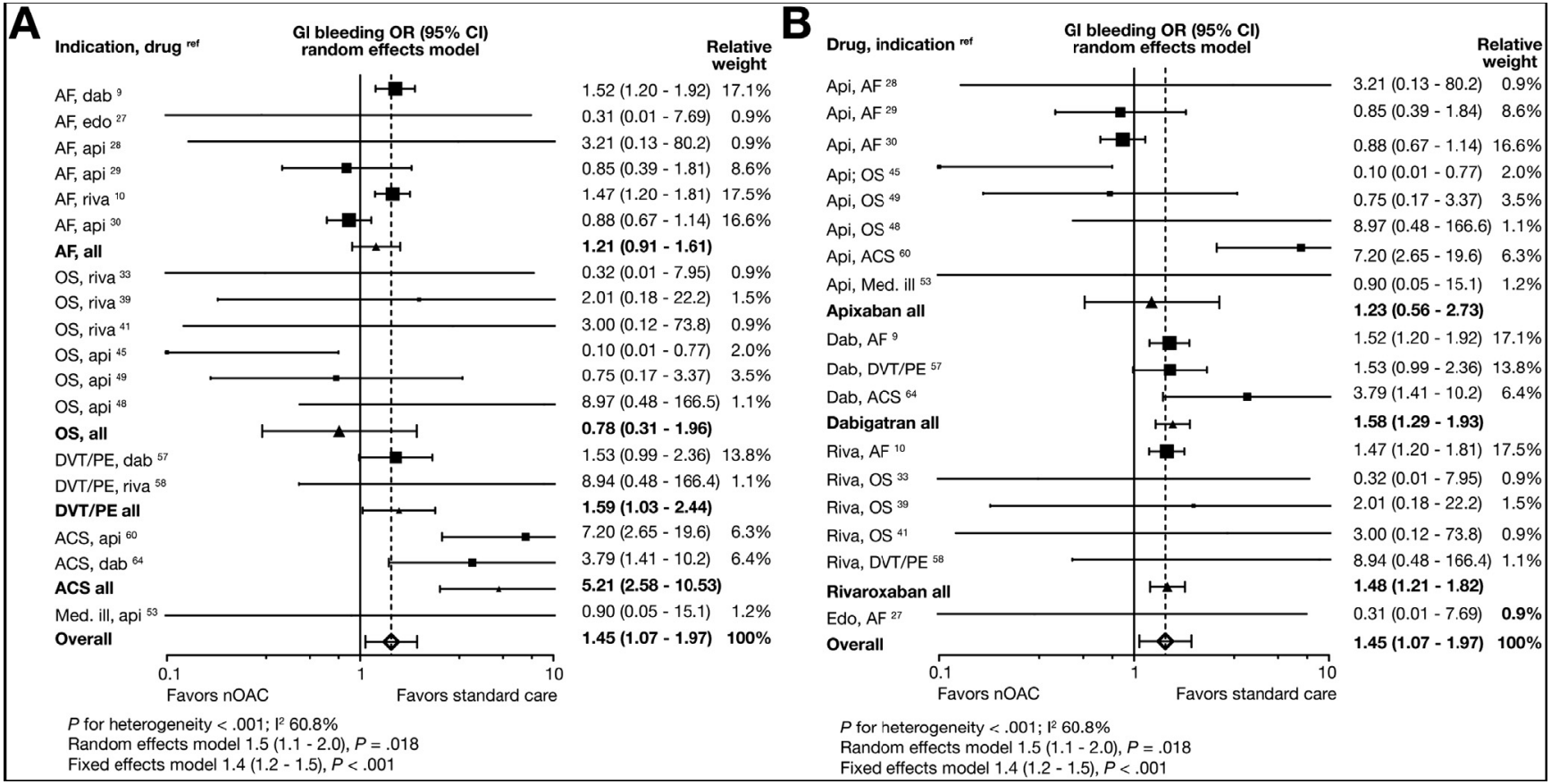
Anticoagulation and non-selective B-blockers appears to improve outcome of patients with chronic portomesenteric venous thrombosis





Orr DW et al. Clin Gastroenterol Hepatol 2007

Risk of NOAC s GI bleeding



OR for GIB 1.45 (95% confidence interval [CI],1.071.97)

Clinically relevant(OR, 0.98; 95% CI, 0.88–1.10; I2, 65%)

Bleeding risk known for NOAC in DVT(0.7 % major bleeding/7%non relevant bleeding)

Chronic Portal Vein Thrombosis
Current international guidelines

No clear recommendation for anticoagulation

American Association for the Study of the Liver (Hepatology 2009)

Baveno consensus conference (J Hepatol 2010)

Study context

- 22 related competence centers (regional academic hospitals) and 16 collaborating hospitals,
- **obtained a selective national grant of 481 818 euros** (national PHRC)
- Xarelto (Rivaroxaban=antiX) vs abstention
- No support from laboratories

Working Hypothesis

- In patients with chronic portal vein thrombosis, without strong prothrombotic condition*
- Xarelto reduces the risk of thromboembolic event,
- while the risk of death, the risk of gastrointestinal haemorrhage related to portal hypertension, and the risk of other types of haemorrhage are not significantly increased.

* i.e. without myekloproliferative disease, paroxysmal nocturnal hemoglobinuria, antiphospholipid syndrome, homozygous FII or homozygous FV Leiden, or composite heterozygotes FII/FV Leiden

End points

Primary end point:

Efficacy :Incidence of thromboembolic event in any territory (arterial or venous, splanchnic or extra splanchnic

Secondary end point

Safety:

- Major and clinically relevant bleedings
- Gastrointestinal non major bleedings related to portal hypertension
- Other gastrointestinal non major bleedings
- Other adverse events
- Survival
- Coagulation activation in each group

Study design

- Multicentric, interventional study.
- Recruitment period: 2 years
- Treatment period: 2 to 4 years (Based on the recruitment date)
- Sample size: 300

Treatment

Anti-Xa Rivaroxaban (Xarelto) 15 mg/jr

2-4 years

Inclusion criteria

- > 18 yrs old
- Portal vein cavernoma or >6 months PVT
- No MPD or APLS or homozygous factor V leiden/factor 2 mutations
- No past history of spontaneous thrombosis
- PHT prophylaxy

Schedule

Month	Screen	0	1	3	6	12	18	24	Q 6
In/exclusion	X								
Informed consent	X								
Past history	X								
Thrombophilia screen	X								
Visit	X	X	X	X	X	X	X	X	X
Clinical signs	X	X	X	X	X	X	X	X	X
Treatment data	X	X	X	X	X	X	X	X	X
Intervention data	X	X	X	X	X	X	X	X	X
Lab A	X	X	X	X	X	X	X	X	X
Thrombin generation	X				X				
Circulating drug level	X				X			X	
Doppler ultrasound	X				X	X	X	X	X
MRI	X				X	X		X	
Endoscopy	X							X	

Feasibility

Beaujon screening : 84 patients

Centres de compétence :50

Eviter biais

Critères robustes

Évènements thrombotiques

Imagerie centralisée relue en aveugle

TDM ou echo-doppler si douleur >6h permanente ou SIRS

Eviter biais

Évènements hémorragiques aigus:

>2 CG

<2 points d hgb

Syndrome du compartiment

Site critique (cerebral)

Décès

Experts indépendants

Chaque EI sera évalué par un groupe d experts indépendants d'un autre centre.

Critics from Ecrin

- Also exclude cancers
- Methodology:
  - events calculated on retrospective high thrombotic risk, better to calculate on bleeding risk known for NOAC (0.7 % major bleeding/7%non relevant bleeding)
  - 2 judgement factors bleeding and thrombosis

Choice of anticoagulation ?

Anticoagulant	Positive	Negative
Heparins: IV or subcutaneous	Standard dose Cheap	HIT Inacceptable for patients already on oral therapy
VKA	Cheap	Blood monitoring
Noac	More conveniant Attractive	No antidote Expensive Gastric toxicity

Quel nouveau projet avec même montant?

- Diminuer nombre de centres : Ecrin
- Recenser les patients

Conclusion

- Difficulté mise en place de l'étude
- Nombre malades et financement
- Ecrin solution en partie pour augmenter le nombre d'inclusion mais très incertain
- Rester motivés malgré difficultés
- Recenser les patients +++