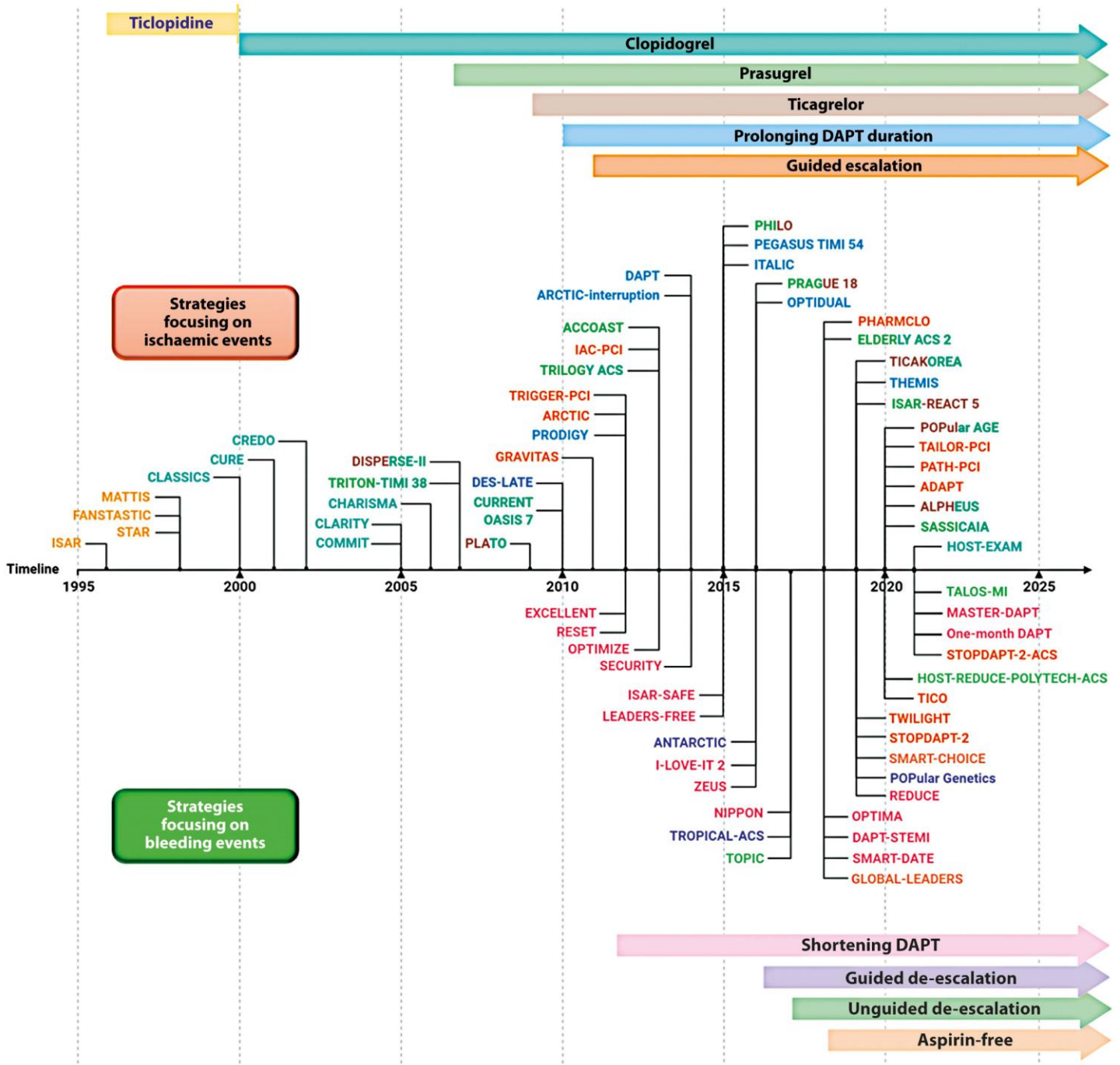
OPT – BIRISK TRIAL (CLOPIDOGREL VERSUS DAPT)

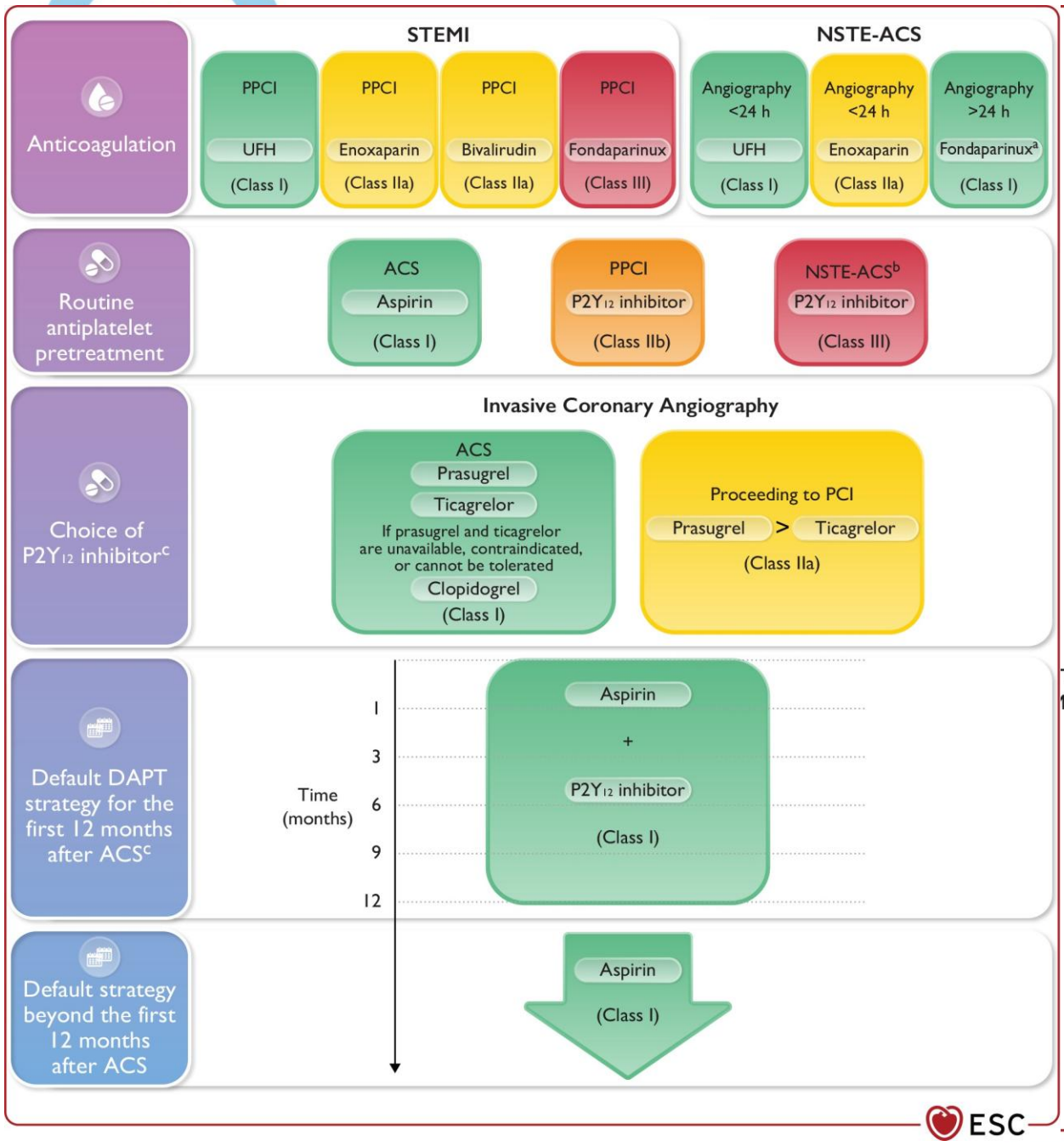
Daniel Rob

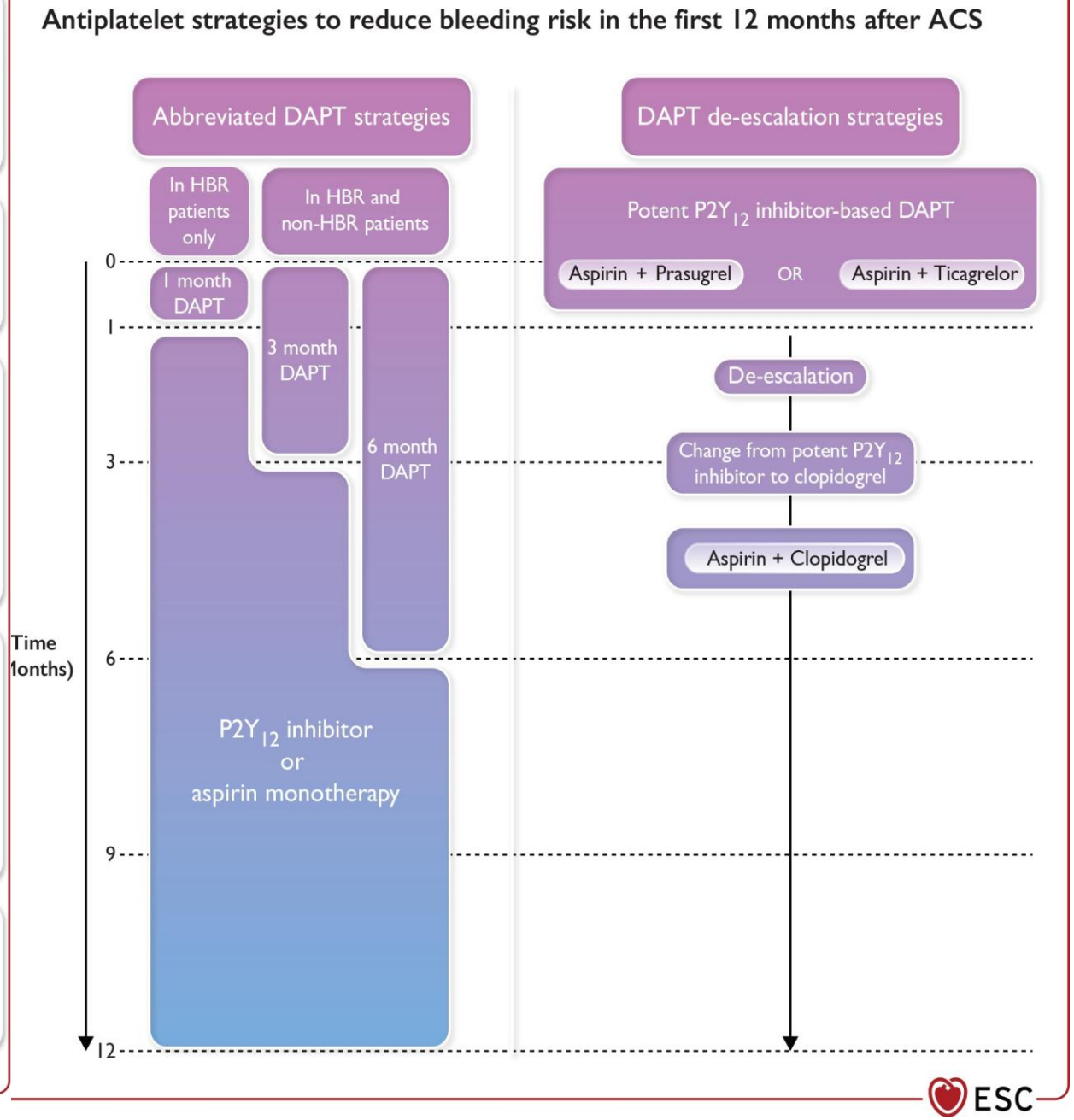
II. interní klinika kardiologie a angiologie,
Všeobecné fakultní nemocnice v Praze
1. lékařské fakulty Univerzity Karlovy

Antiagregace a studie…



EuroIntervention 2022;17:e1371-e1396. DOI: 10.4244/EIJ-D-21-00904





Byrne, R. A., et al. (2023). European heart journal, 44(38), 3720-3826.

Proč tedy další studie?

- Definování optimální protidestičkové terapie po AKS s PCI u pacientů s vysokým ischemickým i krvácivým rizikem (bi-risk) zůstává otázkou.
- Extenze DAPT nad 12m redukuje ischemické příhody za cenu zvýšení rizika krvácivých příhod
- **P2Y12 inhibitor monoterapie má potenciál zachovat stejnou/lepší redukci ischemického rizika a snížit riziko krvácení (GIT) vs ASA**

Li Y, et al. Rationale and design of the OPT-BIRISK double-blinded, placebo-controlled randomized trial. Am Heart J. (2020) 228:1–7. 10.1016/j.ahj.2020.07.005

Optimal antiPlatelet Therapy for high Bleeding and Ischemic RISK patients

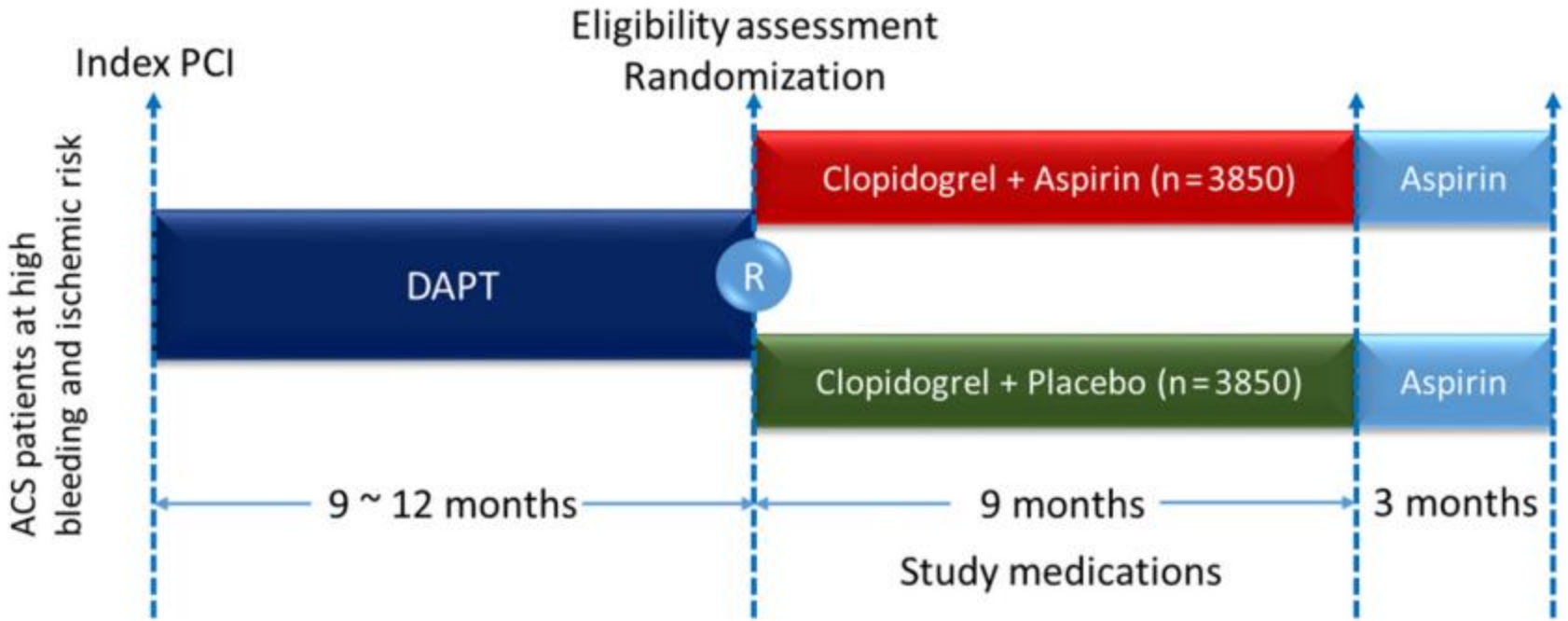
OPT-BIRISK

Study Design

OPT-BIRISK

Optimal antiPlatelet Therapy for high Bleeding and Ischemic RISK patients

Investigator-initiated, multicenter, double-blind, placebo-controlled, randomized trial



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Klíčová inclusion a exclusion kritéria

Inclusion criteria

- ACS patients at both high ischemic and bleeding risk treated with DES
- Completed 9-12 months of DAPT (aspirin plus either clopidogrel or ticagrelor)
- Free from major adverse clinical events during 6-months prior to randomization

Exclusion criteria

- Any interruption, abruption, or discontinuation on DAPT during the recent 6 months
- Planned coronary revascularization or non-cardiac surgery within 90 days
- Moderate to severe liver function dysfunction
- Platelet count $<100*10^9/L$
- Life expectancy <1 year

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Criteria for "*bi-risk*"

- Patients <65 yrs: high bleeding risk *AND* high ischemic risk
- Patients 65-75 yrs: high bleeding risk *OR* high ischemic risk
- Patients ≥75 yrs

High bleeding risk	High ischemic risk
Female gender	Troponin-positive ACS
Iron deficiency anemia	Previous stent thrombosis
Stroke (hemorrhagic or ischemic) history	Previous CV events (iStroke, MI, PAD, PCI)
Diabetes mellitus need medications	Diabetes mellitus need medications
Chronic kidney disease (eGFR<60ml/min/1.73m^2)	Chronic kidney disease (CCr<60ml/min)
	Multivessel disease Left main of proximal LAD disease Long-lesion with total stent length >30mm Thrombotic target lesion True bifurcations (0,1,1 or 1,1,1) need 2 stents Calcified lesion requiring atherectomy

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Study endpoints

Primary endpoint

- **BARC types 2,3,5 bleeding 9 mo after randomization**

Key secondary endpoint

- **Major adverse cardiac and cerebral events (MACCE) 9 mo after randomization**
  (all-cause mortality, MI, stroke or clinically-driven revascularization)

Other endpoints

- **Individual components of MACCE, any bleeding, and stent thrombosis**

Sample size

- **Assuming 25% relative reduction of primary events (clopidogrel monoRx vs. DAPT; 4.5% and 6.0%); 10% lost to f/u; 2-sided alpha 0.05; 80% power; n=7700**

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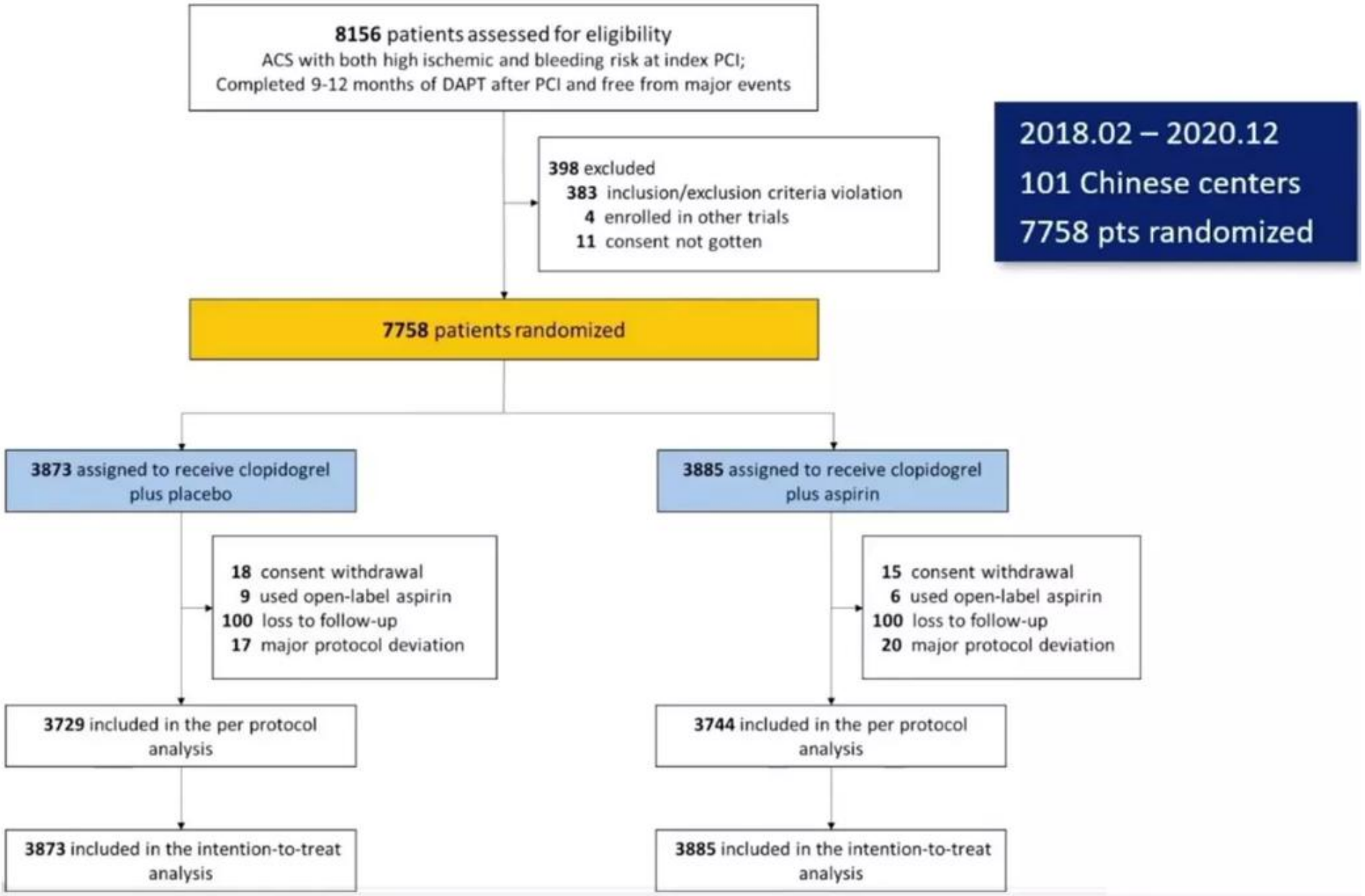

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	Clopidogrel plus Aspirin (N=3885)	Clopidogrel plus Placebo (N=3873)
Age, years	64.7 ± 9.1	64.9 ±8.9
Female sex	41.2%	40.9%
Diabetes mellitus	52.4%	52.5%
Previous myocardial infarction	18.4%	18.1%
Previous PCI	24.2%	24.0%
Previous ischemic stroke	15.2%	15.0%
Peripheral artery disease	5.5%	6.0%
Previous bleeding events	4.9%	4.6%
ACS presentation		
Unstable angina	62.1%	61.5%
NSTEMI	16.9%	18.0%
STEMI	21.0%	20.5%
Anemia	6.3%	6.5%
eGFR<60 ml/min/1.73m^2	6.8%	6.4%

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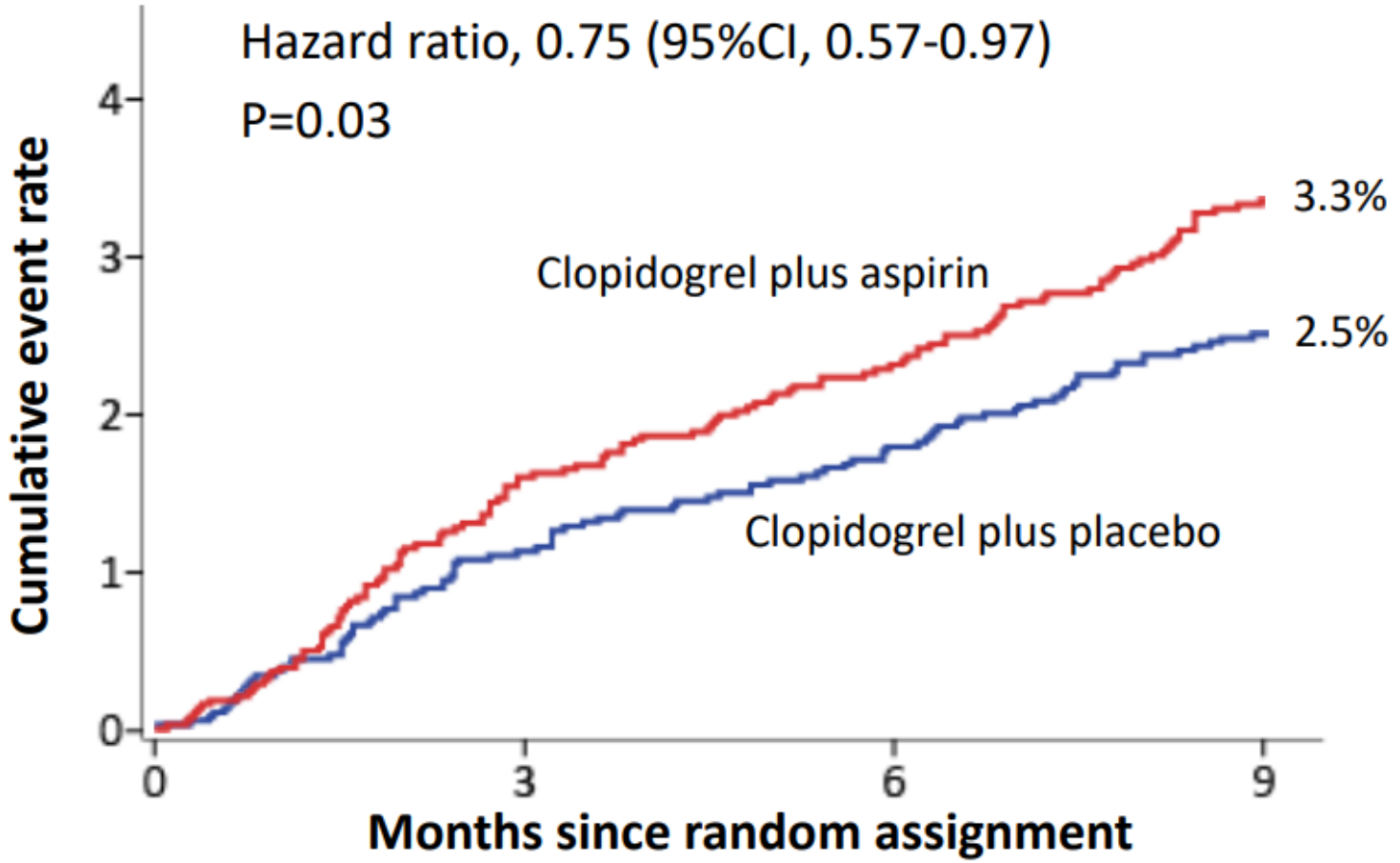
Primary Endpoint- BARC types 2,3,5 bleeding



No. at risk				
Clop. + Aspirin	3885	3819	3786	3741
Clop. + Placebo	3873	3826	3797	3768

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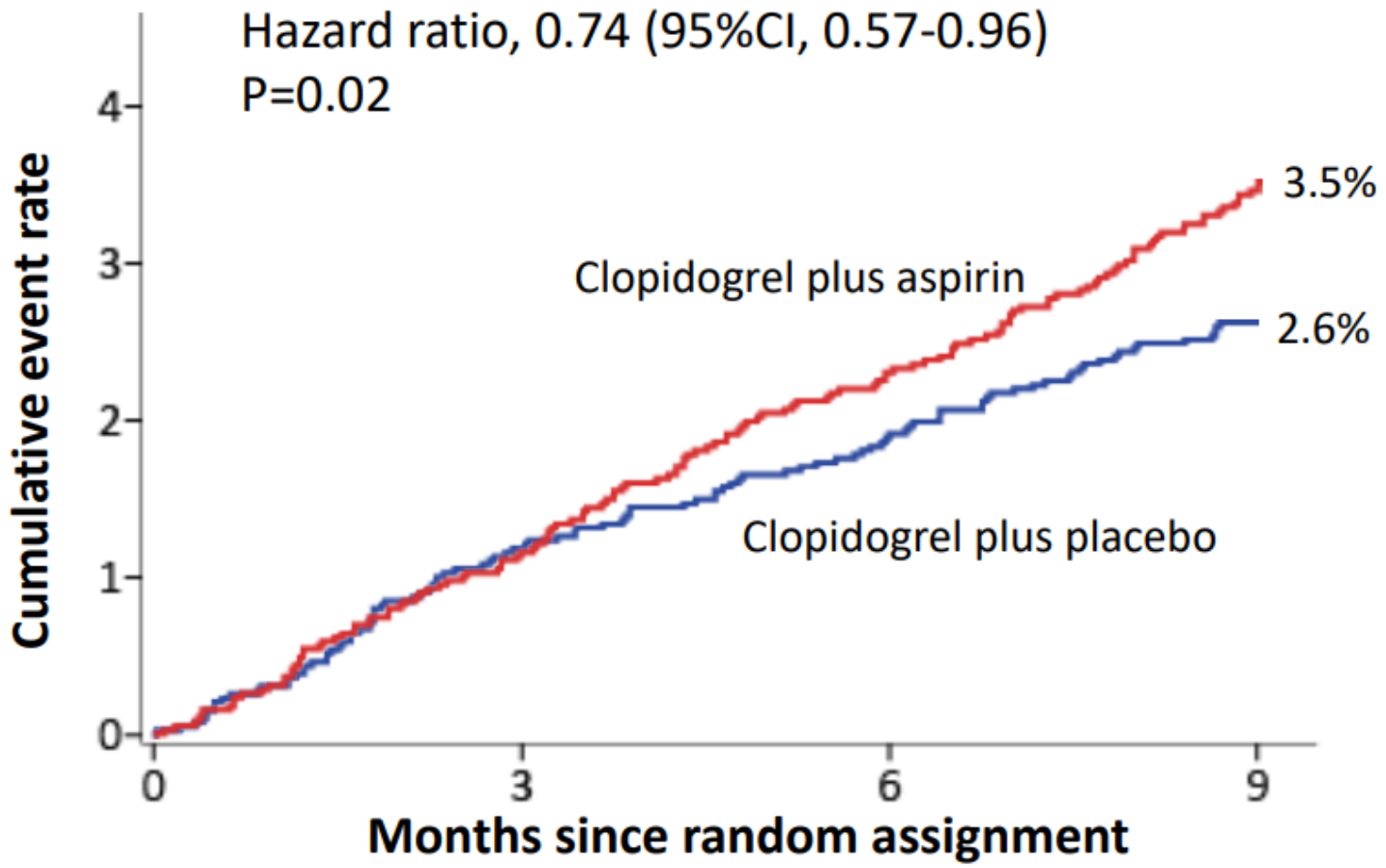
Key Secondary Endpoint- MACCE



No. at risk				
Clop. + Aspirin	3885	3839	3795	3749
Clop. + Placebo	3873	3827	3800	3772

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Secondary Endpoints- Other

	Clopidogrel plus Aspirin (N=3885)	Clopidogrel plus Placebo (N=3873)	Hazard ratio (95%CI)	P value
BARC types 1, 2, 3 or 5 bleeding	704 (18.1%)	560 (14.5%)	0.78 (0.70-0.88)	<0.0001
BARC types 3 or 5 bleeding	26 (0. 7%)	22 (0.6%)	0.85 (0.48-1.50)	0.57
Death from any cause	18 (0.5%)	13 (0.3%)	0.72 (0.35-1.48)	0.38
From cardiovascular causes	9 (0.2%)	11 (0.3%)	1.23 (0.51-2.96)	0.65
Myocardial infarction	27 (0.7%)	16 (0.4%)	0.59 (0.32-1.10)	0.10
Stroke	33 (0.8%)	26 (0.7%)	0.79 (0.47-1.32)	0.37
Clinically-driven revascularization	71 (1.8%)	53 (1.4%)	0.75 (0.52-1.07)	0.11
Stent thrombosis, definite or probable	1 (0.03%)	2 (0.05%)	2.01 (0.18-22.11)	0.57

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Limitations

- The incidence of the primary bleeding endpoint was lower than that estimated. However, it was similar to that observed in recent RCTs involving East Asian patients.
- The trial was not powered to demonstrate the superiority of clopidogrel monotherapy versus DAPT for the ischemic MACCE endpoint. The positive outcomes should thus be considered hypothesis generation.
- All patients were “bi-risk” at the time of index PCI. However, enrolled patients were event-free after 9-12 months of DAPT, indicating a relatively stable status. Nonetheless, these patients represent a large cohort seen in clinical practice in whom the question of continuing DAPT vs. de-escalation to clopidogrel monotherapy at this time has not previously been addressed.
- Whether the results can be generalized to Western populations needs to be verified.

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Závěr, dopady do praxe?

- Extenze clopidogrelem po 12 měsících DAPT u AKS s PCI má nižší výskyt krvácivých i ischemických příhod v porovnání s extenzí DAPT nad 12m.
- Jak dlouhá extenze clopidogrelem – jen 9 měsíců (lifelong?).
- Série studií ukazuje, že P2Y12 inhibitors jsou lepší variantou v porovnání s aspirinem jako léčba po DAPT (například Twilight study).