REDUCE: A Randomized Trial of 3-Month vs 12-Month DAPT After Implantation of a Bioabsorbable Polymer-Based Metallic DES With a Luminal CD34+ Antibody Coating in Patients With ACS

12-Month Clinical Outcomes

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on behalf of the REDUCE trial investigators

ClinicalTrials.gov NCT02118870

Background

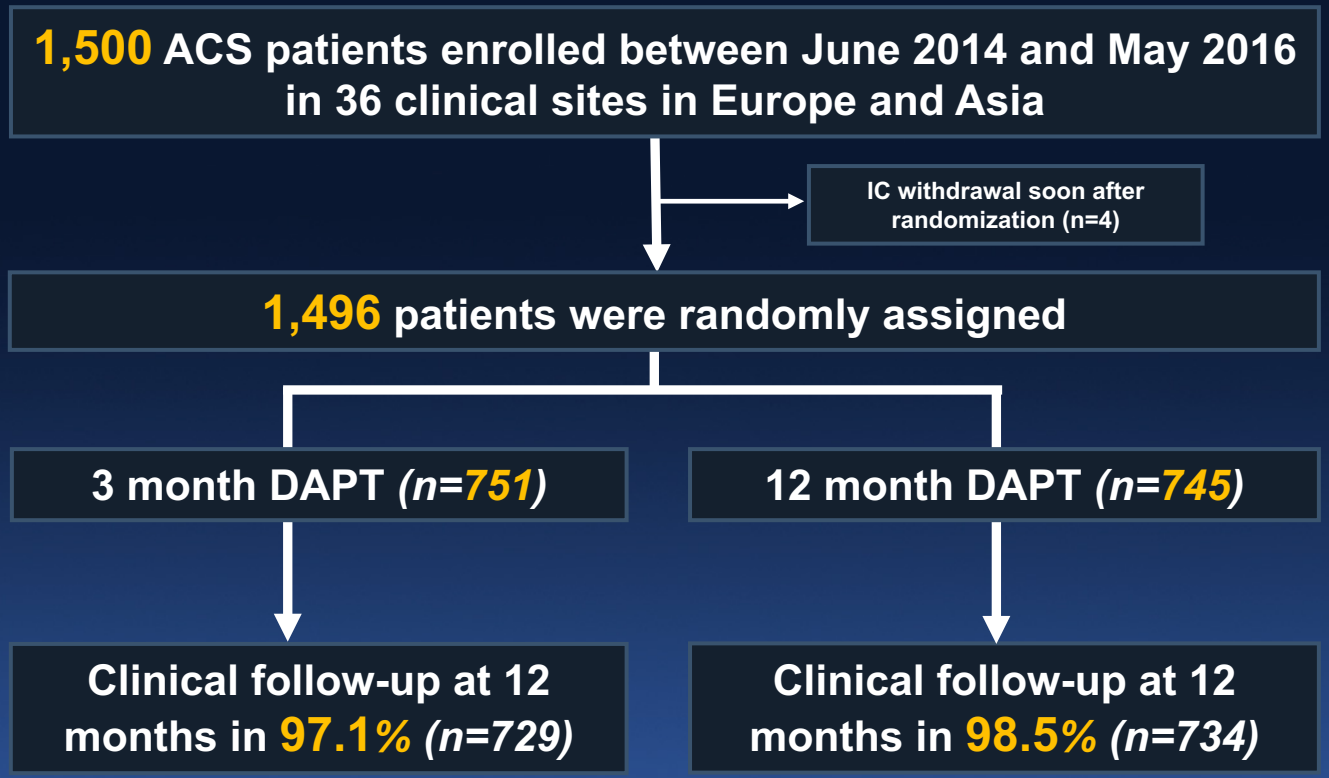
- Short-term DAPT reduces bleeding rates, without increasing thrombotic complications [1-2]. Therefore, recent guidelines recommend 6-12 months DAPT for patients with stable angina treated with new generation DES [3]
- The optimal duration of DAPT in ACS patients treated with DES is still unclear, especially in the era of new anticoagulants/antiplatelet agents
- The COMBO Dual Therapy Stent, which combines abluminal release of sirolimus *(to prevent neointima formation)* and capture of endothelial progenitor cells *(to enhance stent re-endothelialization)* [4] may be attractive in the context of ACS

1. Navarese et al. *BMJ 2015;350:h1618*
2. Palmerini et al. *Lancet 2015; 385: 2371-82*
3. Windecker et.al. *Eurintervention 2015;10:1024-9*
4. Granada et al. *Circ Cardiovasc Interv 2010;3:257-266*

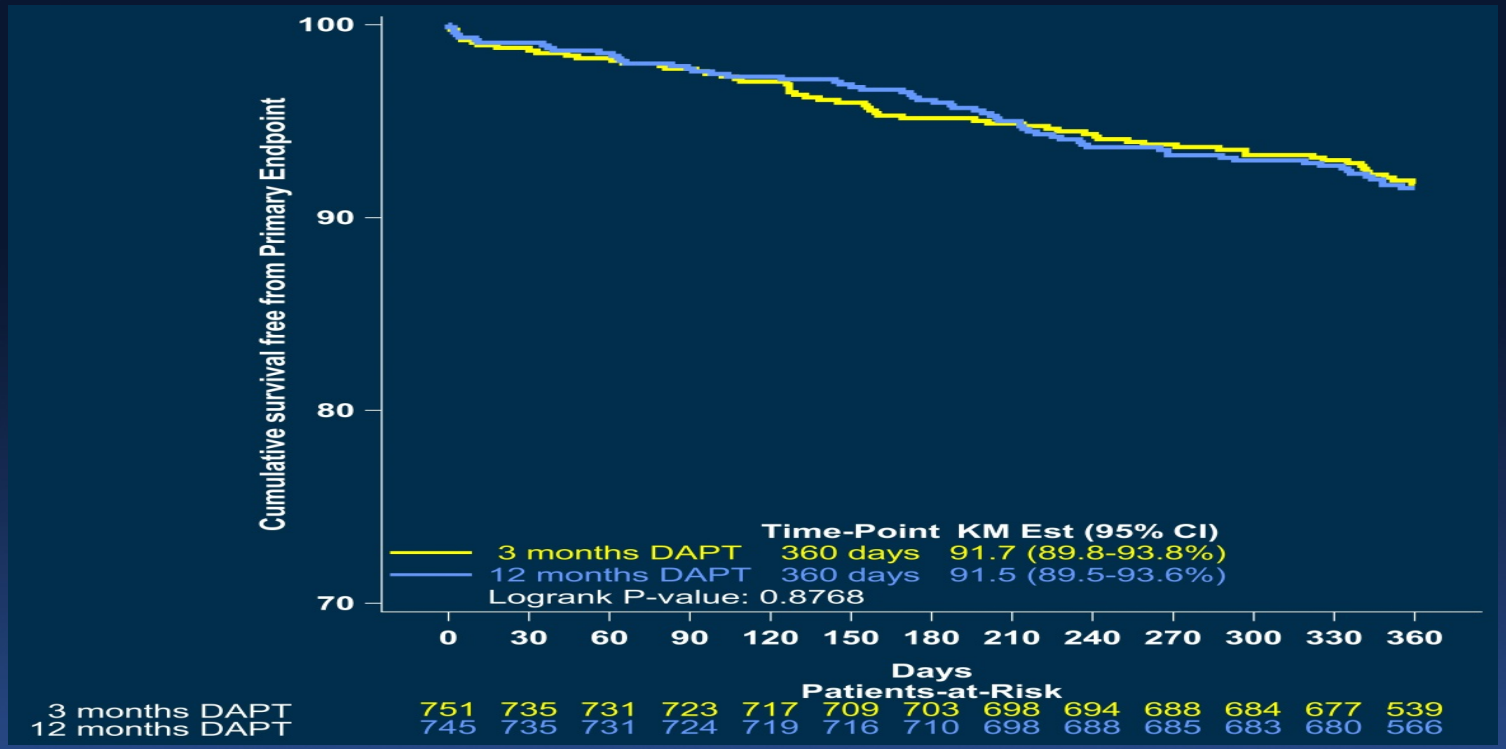
Methods

- **Design:** Investigator-initiated prospective, multicenter, randomized study with two randomization groups (3 *versus* 12 months DAPT) *(NCT02118870)*
- **Objective:** To evaluate the non-inferiority of a combined safety and efficacy endpoint of a short-term 3 months DAPT, compared to standard 12-month DAPT strategy, in ACS patients treated with the COMBO stent
- **Primary Endpoint:**
  Composite of all cause death, MI, ST, stroke, TVR or bleeding *(BARC II, III, V)*
- **Secondary Endpoints:**
  - Pre-specified Landmark analysis of Primary Endpoint from 3 to 12 month
  - Individual components of the composite endpoint

Results: Flow Chart



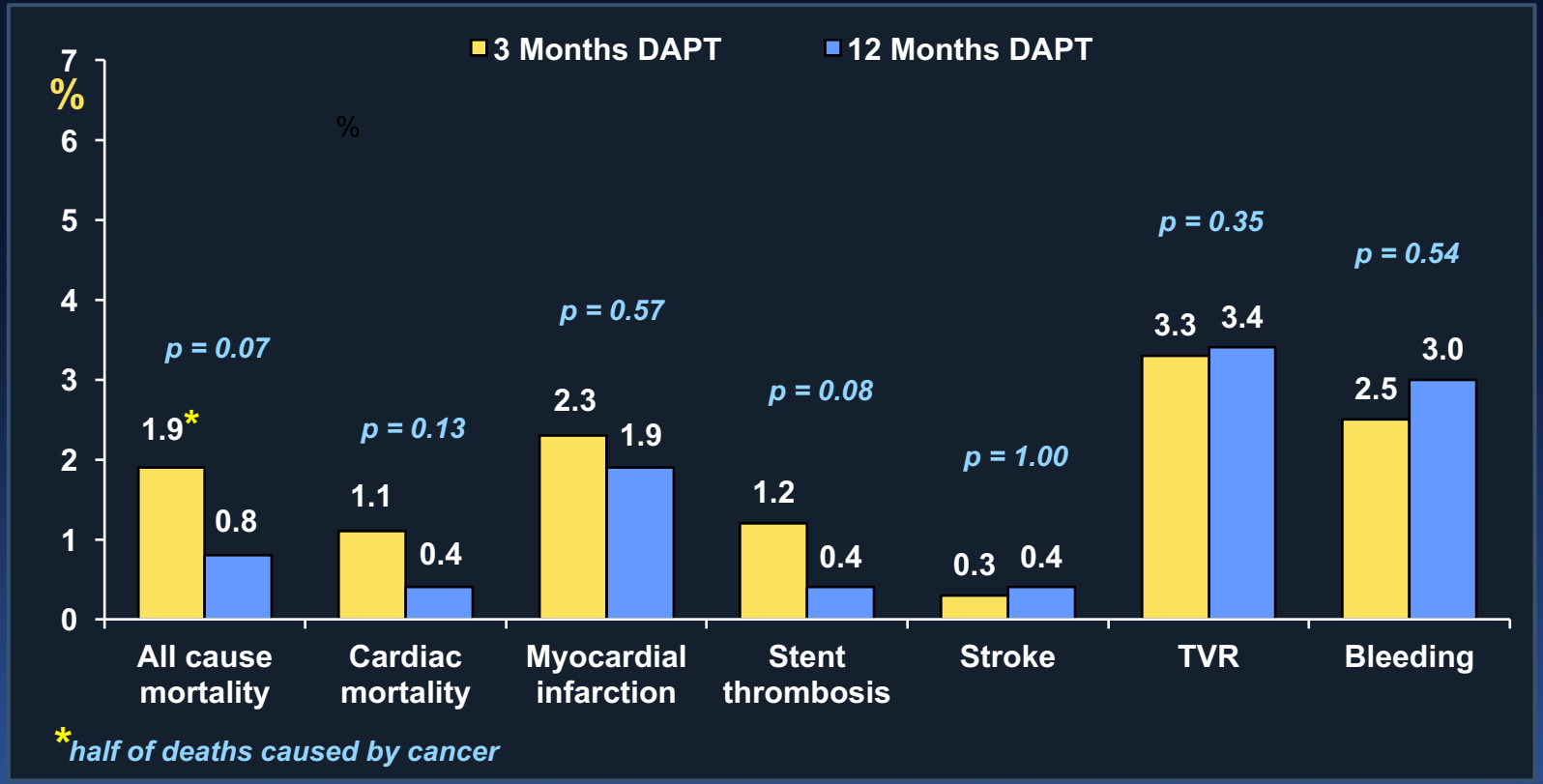
Results: Primary Study Endpoint



Analysis set	3 month DAPT n = 729	12 month DAPT n = 734	Risk difference	Upper bound of 1 sided 97.5% CI	OR (95% CI)	P non-inferiority
Intention to treat	8.2	8.4	-0.002	0.027	0.97 (0.67-1.41)	<0.001

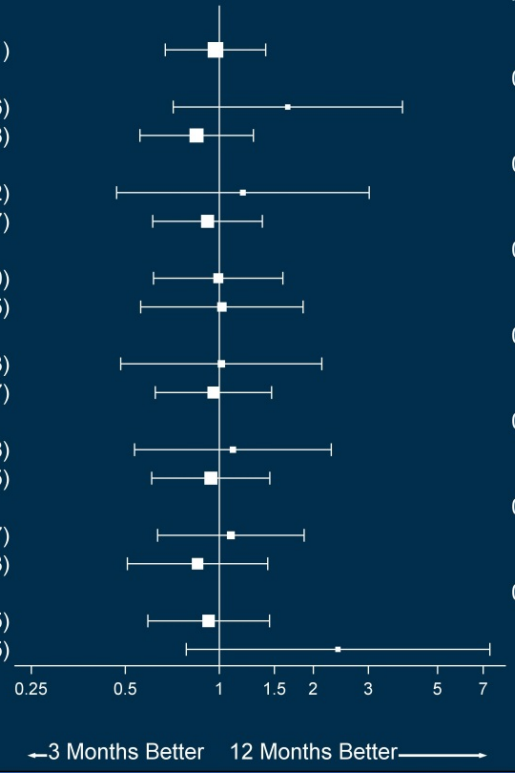
Results confirmed by PP and AT analysis, and after adjustment for gender (adjusted OR (95% CI) = 0.95 (0.66–1.38), p=0.81)

Results: Secondary Study Endpoints



Results: Subgroup Analysis

Subgroup	3 Months DAPT Events/N (%)	12 Months DAPT Events/N (%)	OR (95% CI)	P Value*
All	60/ 729 (8.2)	62/ 734 (8.4)	0.97 (0.67 - 1.41)	
Age				0.16
≥ 75 (yrs)	16/ 100 (16.0)	10/ 97 (10.3)	1.66 (0.71 - 3.86)	
< 75 (yrs)	44/ 629 (7.0)	52/ 637 (8.2)	0.85 (0.56 - 1.28)	
Gender				0.61
Female	9/ 127 (7.1)	10/ 166 (6.0)	1.19 (0.47 - 3.02)	
Male	51/ 602 (8.5)	52/ 567 (9.2)	0.92 (0.61 - 1.37)	
Diagnosis				0.95
Non-STEMI	36/ 372 (9.7)	39/ 400 (9.8)	0.99 (0.62 - 1.60)	
STEMI	24/ 357 (6.7)	22/ 333 (6.6)	1.02 (0.56 - 1.85)	
Geographic region				0.89
Asian site	15/ 222 (6.8)	15/ 225 (6.7)	1.01 (0.48 - 2.13)	
European site	45/ 507 (8.9)	47/ 509 (9.2)	0.96 (0.62 - 1.47)	
Diabetes				0.70
Yes	18/ 158 (11.4)	15/ 144 (10.4)	1.11 (0.54 - 2.28)	
No	42/ 570 (7.4)	46/ 589 (7.8)	0.94 (0.61 - 1.45)	
Vessel Disease				0.52
Multi	32/ 264 (12.1)	28/ 249 (11.2)	1.09 (0.63 - 1.87)	
Single	28/ 464 (6.0)	34/ 485 (7.0)	0.85 (0.51 - 1.43)	
Zwolle Risk Score				0.12
≤ 3	40/ 527 (7.6)	43/ 527 (8.2)	0.92 (0.59 - 1.45)	
> 3	10/ 80 (12.5)	5/ 89 (5.6)	2.40 (0.78 - 7.35)	



* P-Value is the test of interaction between treatment and each subgroup unadjusted for multiplicity.

Consistent results across all subgroups, without any significant statistical interaction

Conclusion

- The REDUCE trial is the first study restricted to ACS patients, comparing a short 3-month *vs* a standard 12-month DAPT
- The main finding of the present study is that, among ACS patients treated with the COMBO stent, 3-month DAPT is not inferior to 12-month DAPT
- This finding is consistent for all pre-specified subgroups
- Therefore, a shorter DAPT strategy could be considered, if necessary, even in ACS population
- Future large trials are needed to further investigate and confirm the safety of short-term DAPT regimen in ACS patients in the era of new ADP antagonists and new generation DES