



Anatomical Location and Bleeding Risk as Potential Drivers of DAPT duration

Insights from the (Prolonging Dual Antiplatelet Treatment After Grading Stent-Induced Intimal Hyperplasia) PRODIGY trial.

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On behalf of the PRODIGY investigators

Speaker's name: Francesco Costa

- I do not have any potential conflict of interest**

- PRODIGY was an independent and investigator-driven study which did not receive funding by any pharmaceutical or device company**

Background and aim of the study

- Optimal duration of Dual antiplatelet therapy after stent implantation is still debated.
- International guidelines suggest tailoring DAPT duration according to patient ischaemic and bleeding risk. However, a reproducible method of weighing these risks has not yet been proposed.

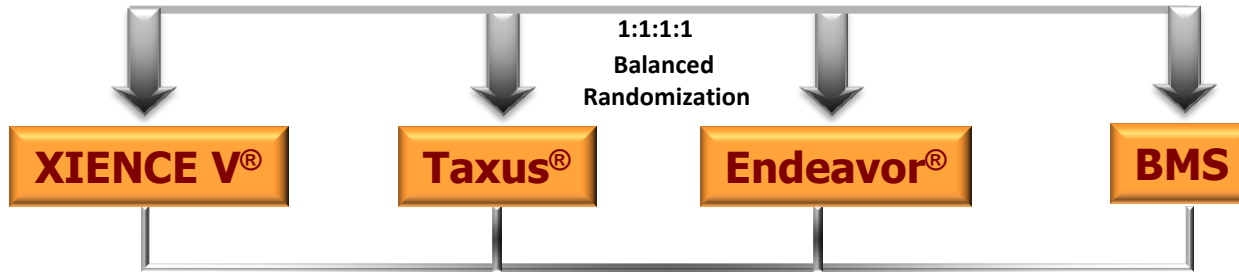
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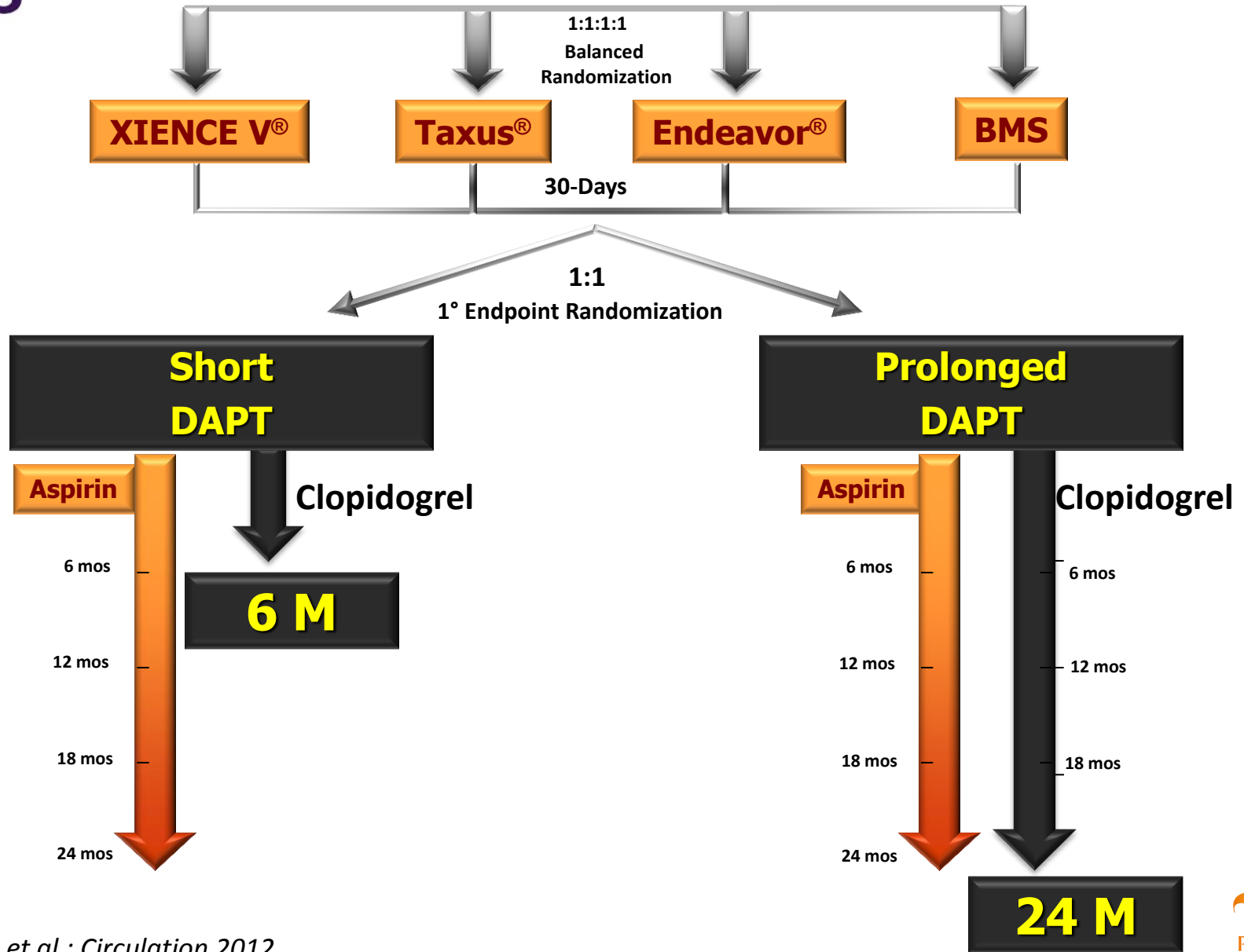
Two study hypotheses

- **Bleeding risk status** is a treatment modifier for DAPT duration with respect to bleeding endpoints
- **Lumen narrowing of the left main and/or proximal LAD** is a treatment modifier for DAPT duration regarding ischemic endpoints

PRODIGY Study Flow Chart (N= 1970)*



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*Valgimigli et al.; Circulation 2012

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Bleeding Risk Score: Background

- We compared three bleeding risk scores in the PRODIGY trial and found CRUSADE to be slightly superior for prediction of major bleeding.
- Bleeding risk scores were not available in 24 patients, that have been excluded from the analysis accordingly.
- We used a CRUSADE score cut-off of 40 to define patients at high bleeding risk, as previously reported*.

Bleeding Risk Score: Study Profile

PRODIGY patient population

Patients with High CRUSADE score (>40)

Patients without High CRUSADE score (≤ 40)

307 (15.8%)

1639 (84.2%)

144

Treated with
24-month DAPT

163

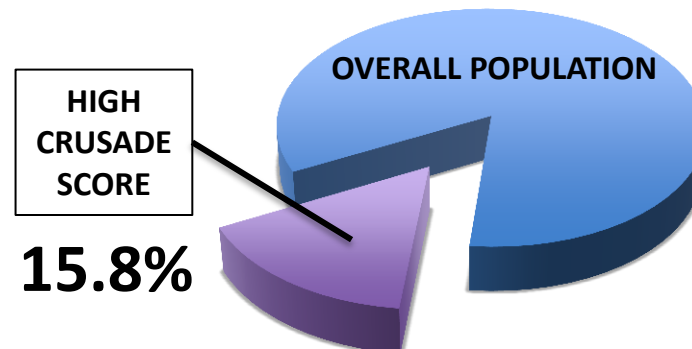
Treated with
6-month DAPT

831

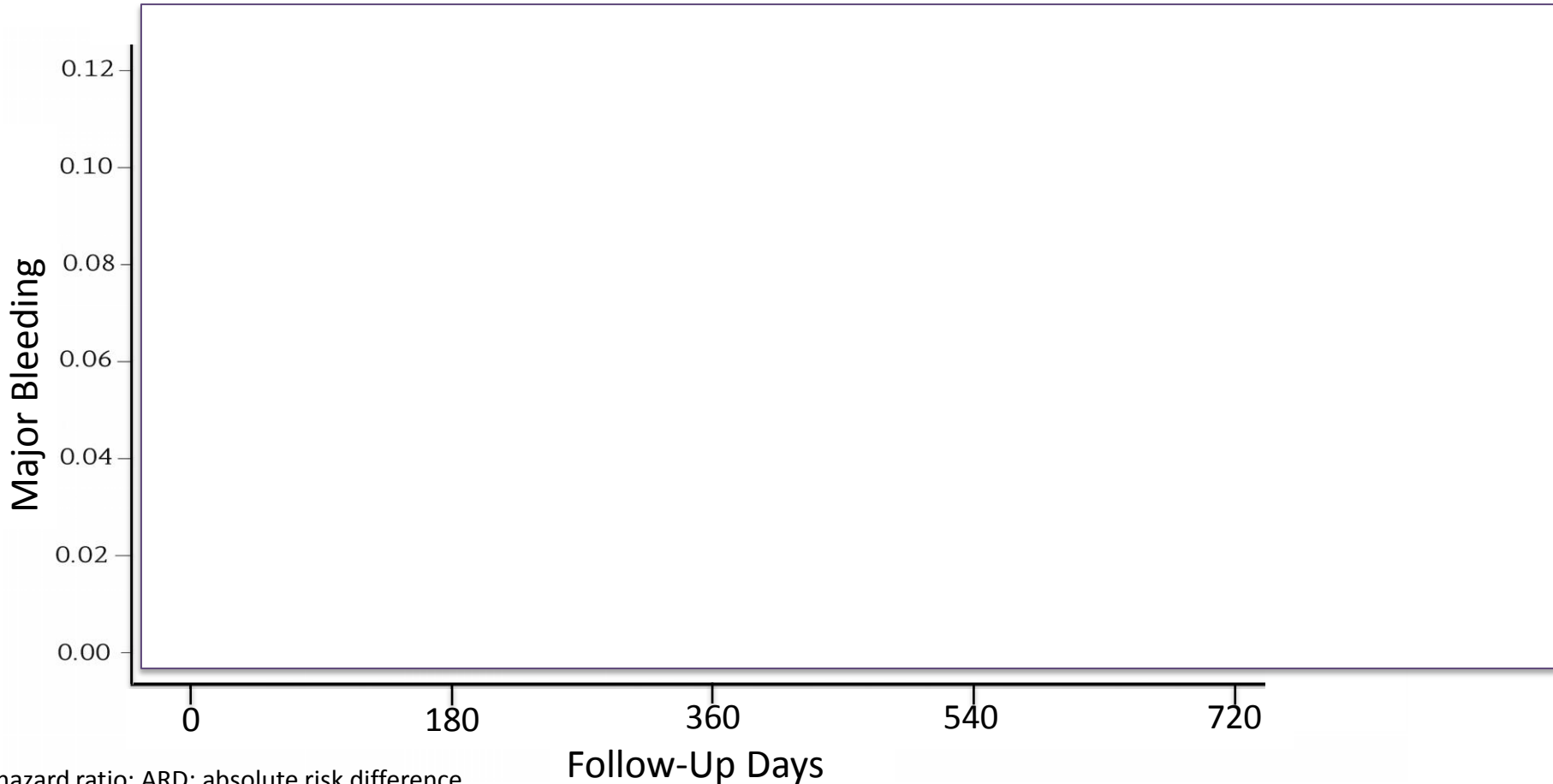
Treated with
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808

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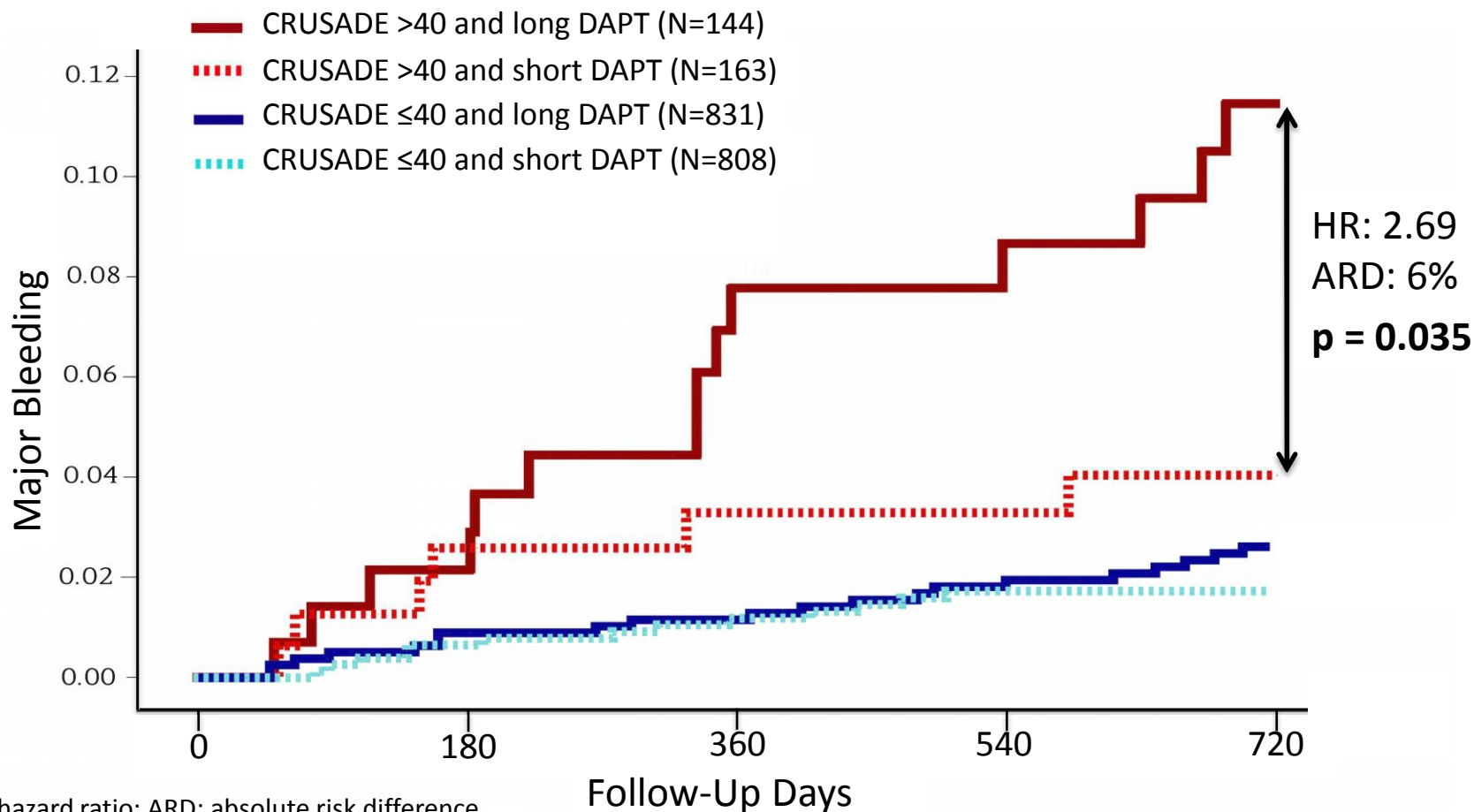
Major Bleeding (BARC 3/5) by DAPT duration



HR: hazard ratio; ARD: absolute risk difference

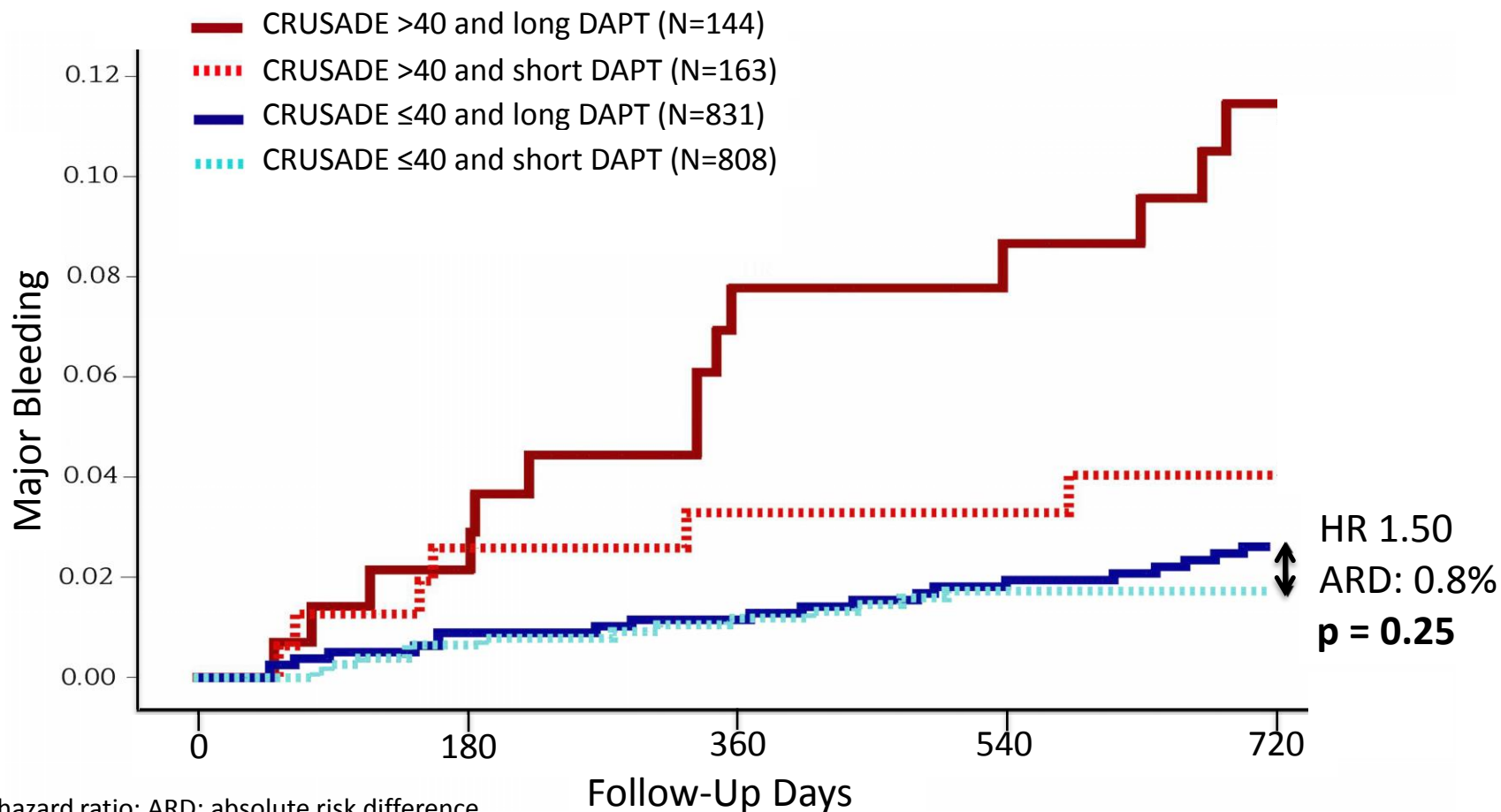
Major Bleeding (BARC 3/5) by DAPT duration

Pts at high bleeding risk had almost three-fold increase in major bleeding if treated with Long DAPT regimen, with a NNTH of 17 (as compared to 67 in the unselected population),
 No significant increase of major bleeding was noted after a long DAPT in patient not at high bleeding risk according to CRUSADE.



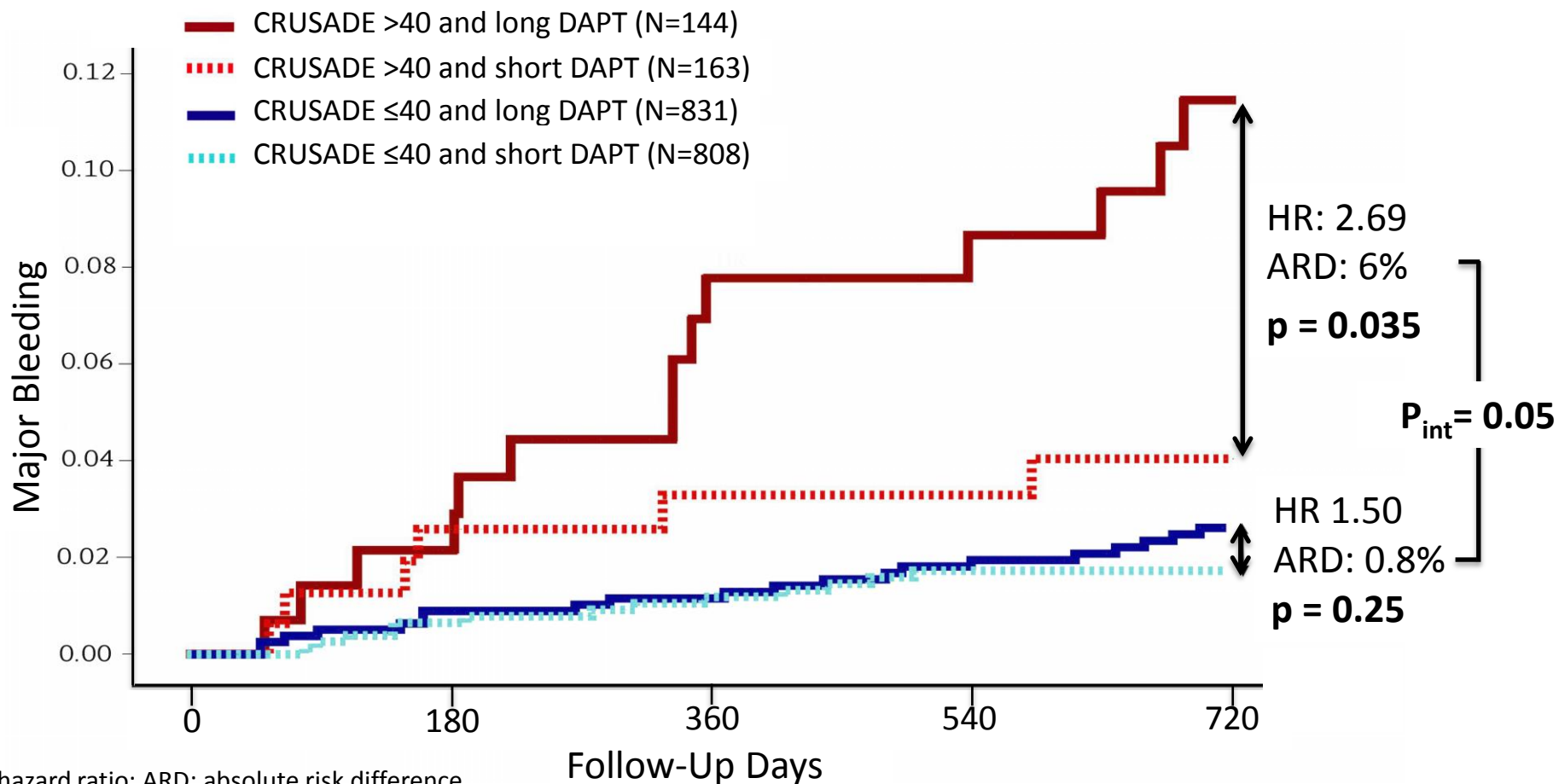
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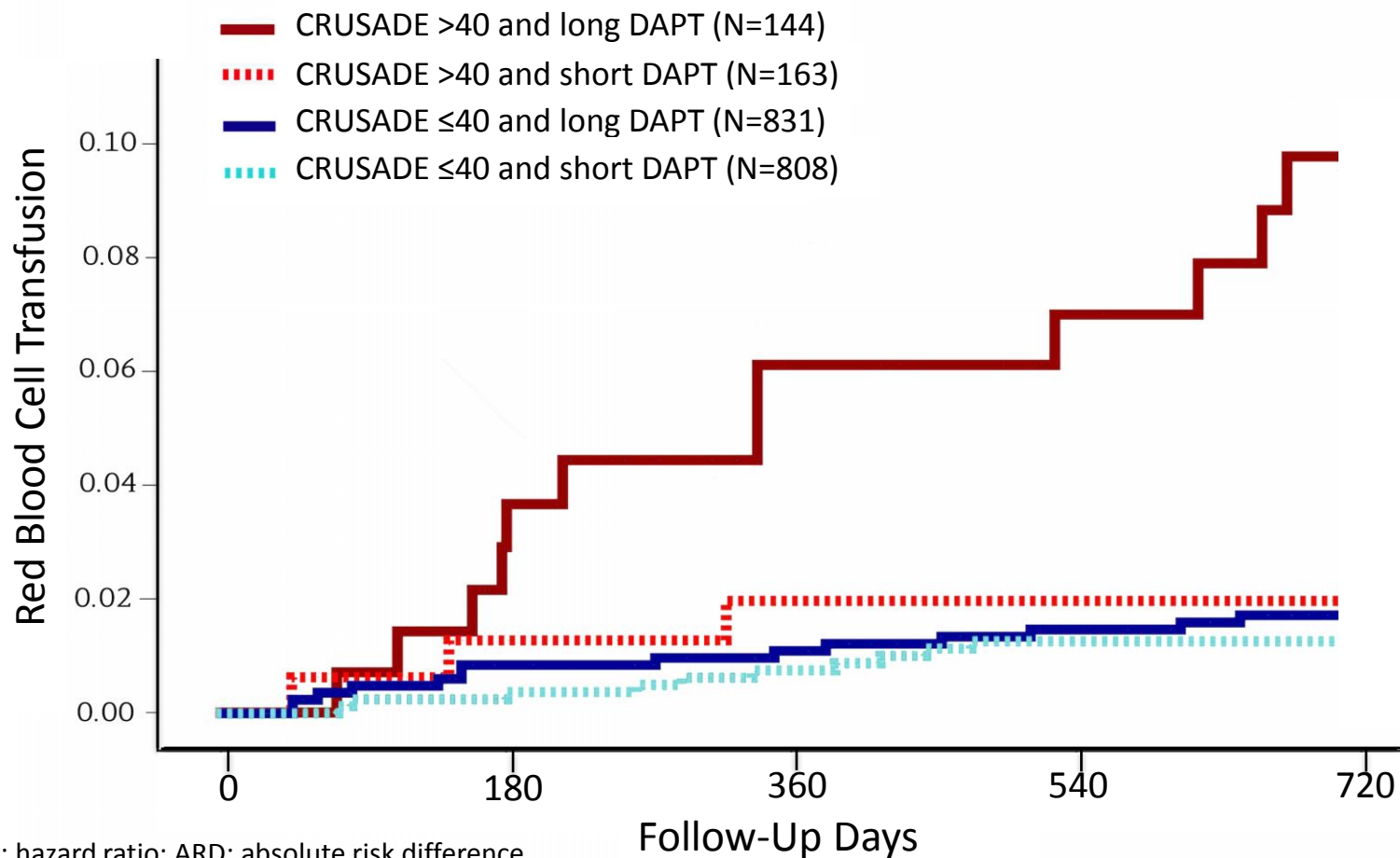
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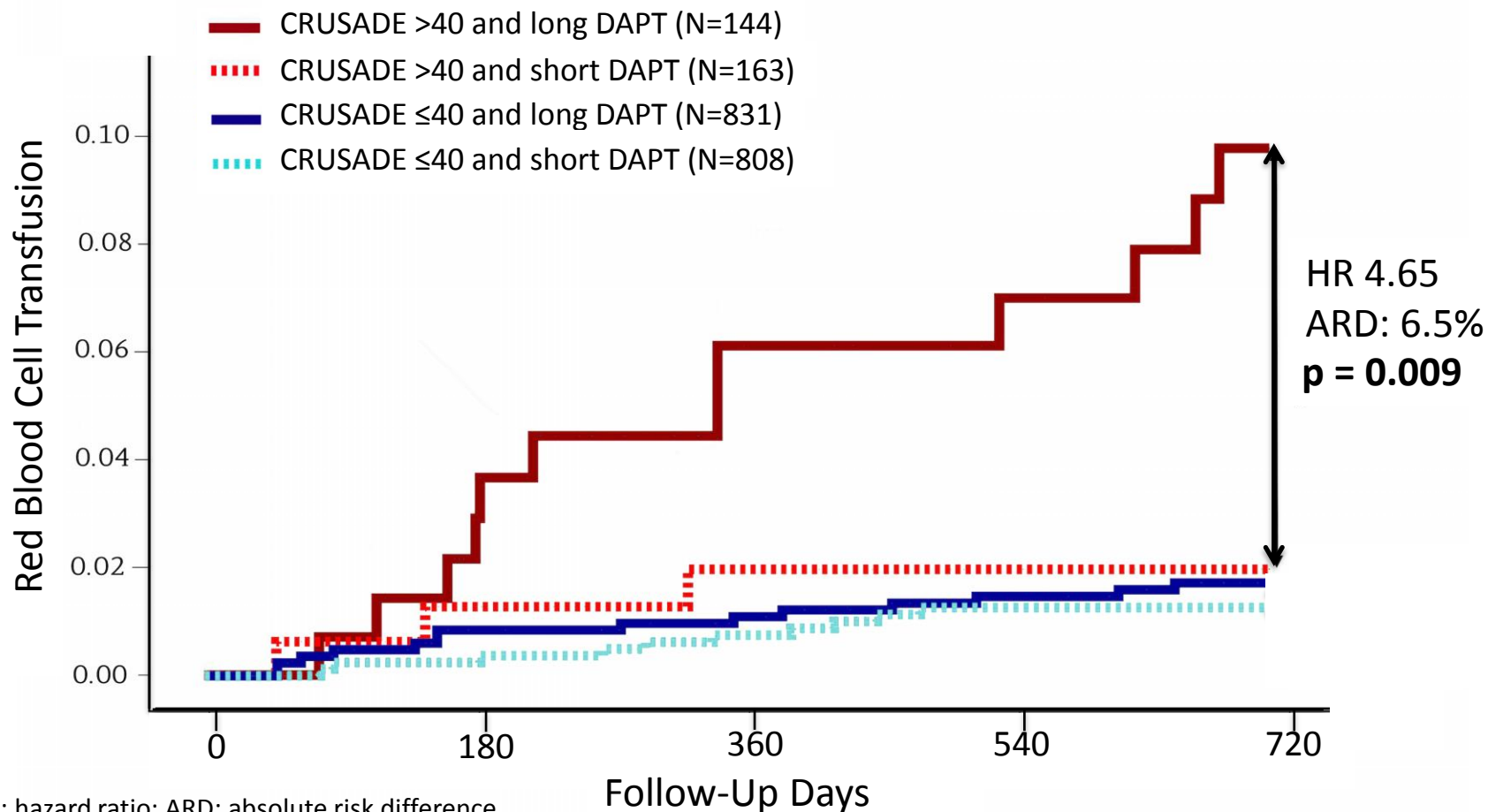
Red blood cell transfusion by DAPT duration

Pts at high bleeding risk had almost five-fold increase in transfusion if treated with Long DAPT, with a NNTH of 15 (as compared to 71 in the unselected population), whereas no increase of need for transfusion was noted in the 24 vs. 6 month DAPT group in the group not at high bleeding risk according to CRUSADE.



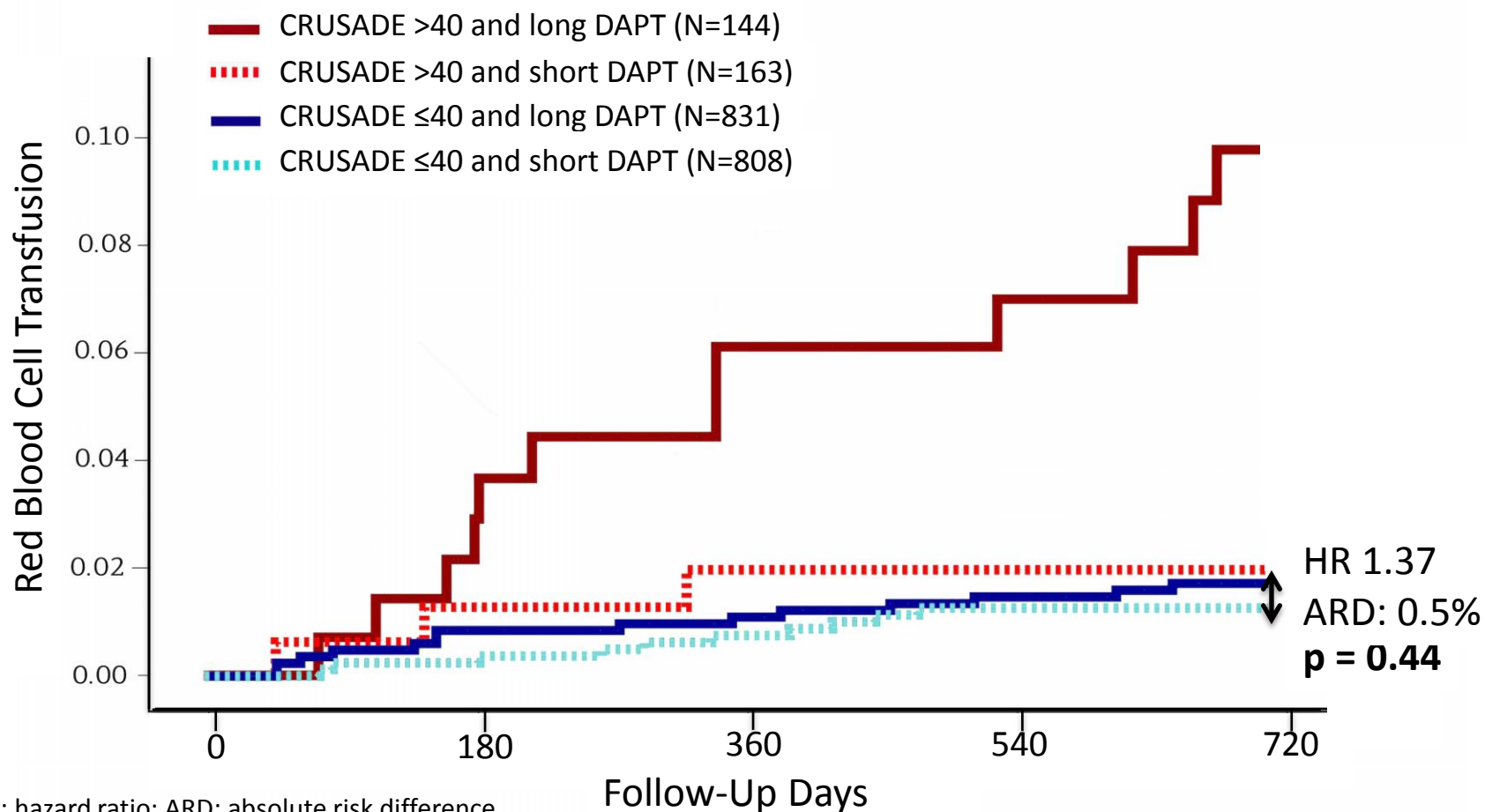
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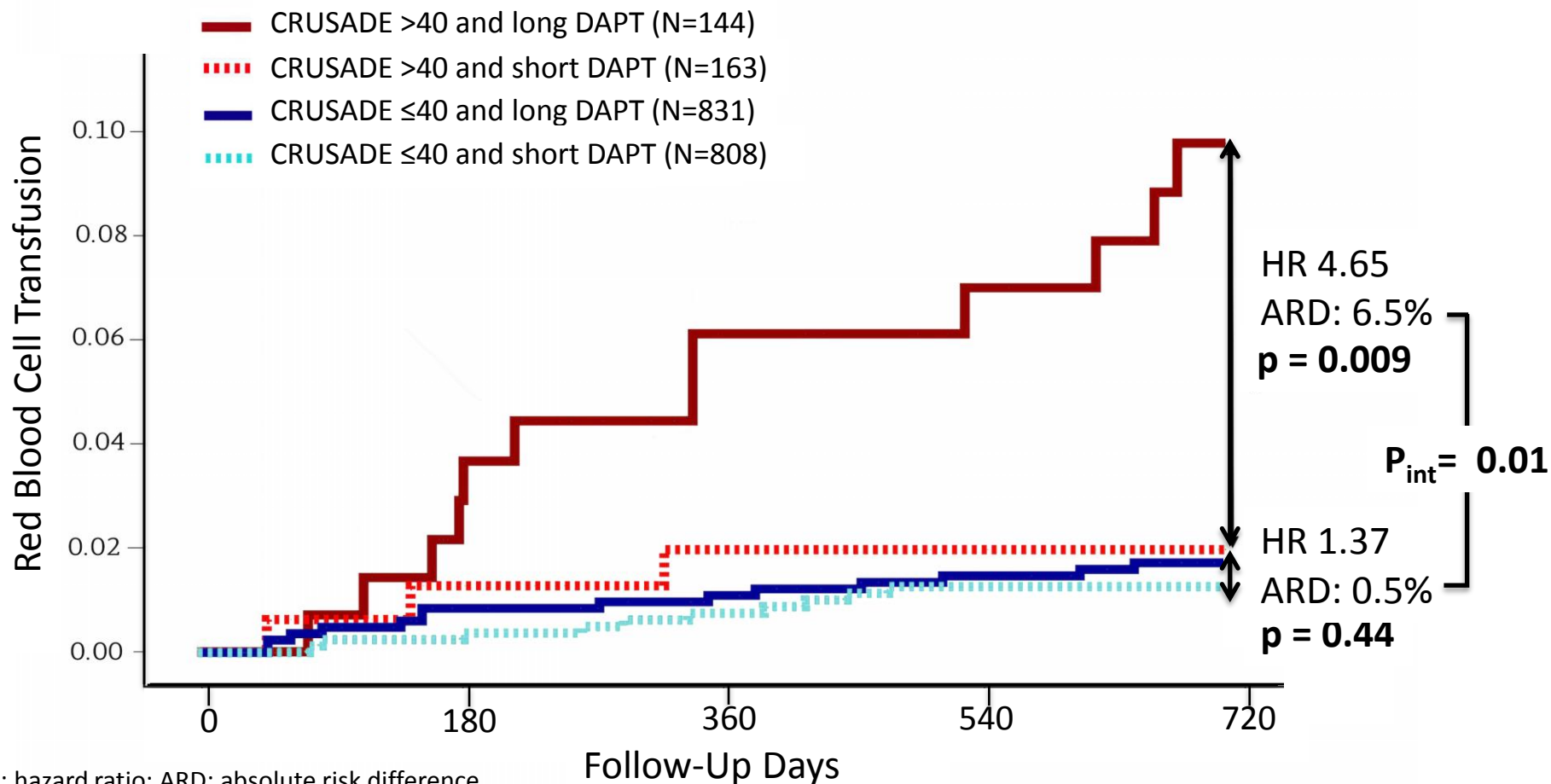
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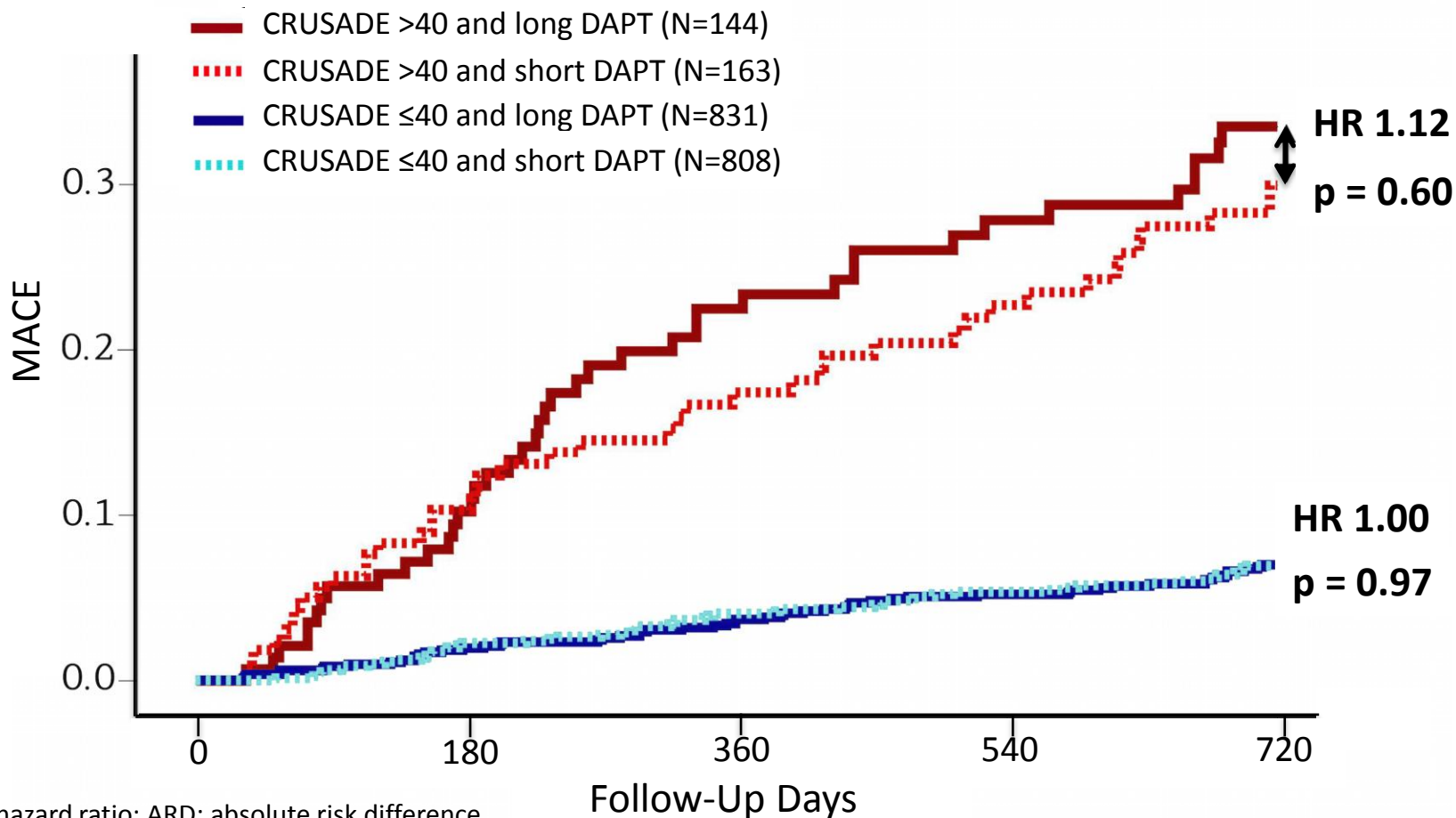
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All cause Death, all MI, CVA (MACE) by DAPT duration

No significant benefit in terms of MACE was noted in patients treated with 24 vs. 6 month DAPT irrespective of the bleeding risk profile.



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Lumen Narrowing LM/pLAD: Study Profile

PRODIGY patient population

**Patients with Lumen narrowing (>30%)
on the Left main or Proximal Left anterior
descending artery**

**Patients without Lumen narrowing
on the Left main or Proximal Left anterior
descending artery**

953 (54.3%)

801 (45.7%)

471

Treated with
24-month DAPT

482

Treated with
6-month DAPT

405

Treated with
24-month DAPT

396

Treated with
6-month DAPT

35 Stent LM
143 Stent pLAD
109 LN LM
362 LN pLAD

35 Stent LM
137 Stent pLAD
91 LN LM
368 LN pLAD

Patients Characteristics

	LM/pLAD Lumen Narrowing (N=953)	No LM/pLAD Lumen Narrowing (N=801)	p Value
Age (yr.)	68.2±11.6	66.6±11.1	0.03
Diabetes (%)	23.0	23.8	0.68
Creatinine Clearance (ml/min)	77.4±31.1	82.5±43.6	0.005
Left Ventricle Ejection Fraction	50.9±11.2	51.2±9.7	0.53
Multivessel Disease (%)	71.4	61.3	<0.0001
Number of Treated Lesions	1.62±0.96	1.47±0.86	0.001
Number of Stent Implanted	1.98±1.3	1.76±1.2	<0.0001
Total Stent Length (mm)	41.9±30.5	37.4±29.3	0.002
Total ACC/AHA score	4.11±2.49	3.47±2.00	<0.0001

Patients with LM/pLAD Lumen narrowing had **higher risk profile**. Within subgroups, baseline and angiographic characteristics were well matched between the 6 month and 24 month DAPT arms.

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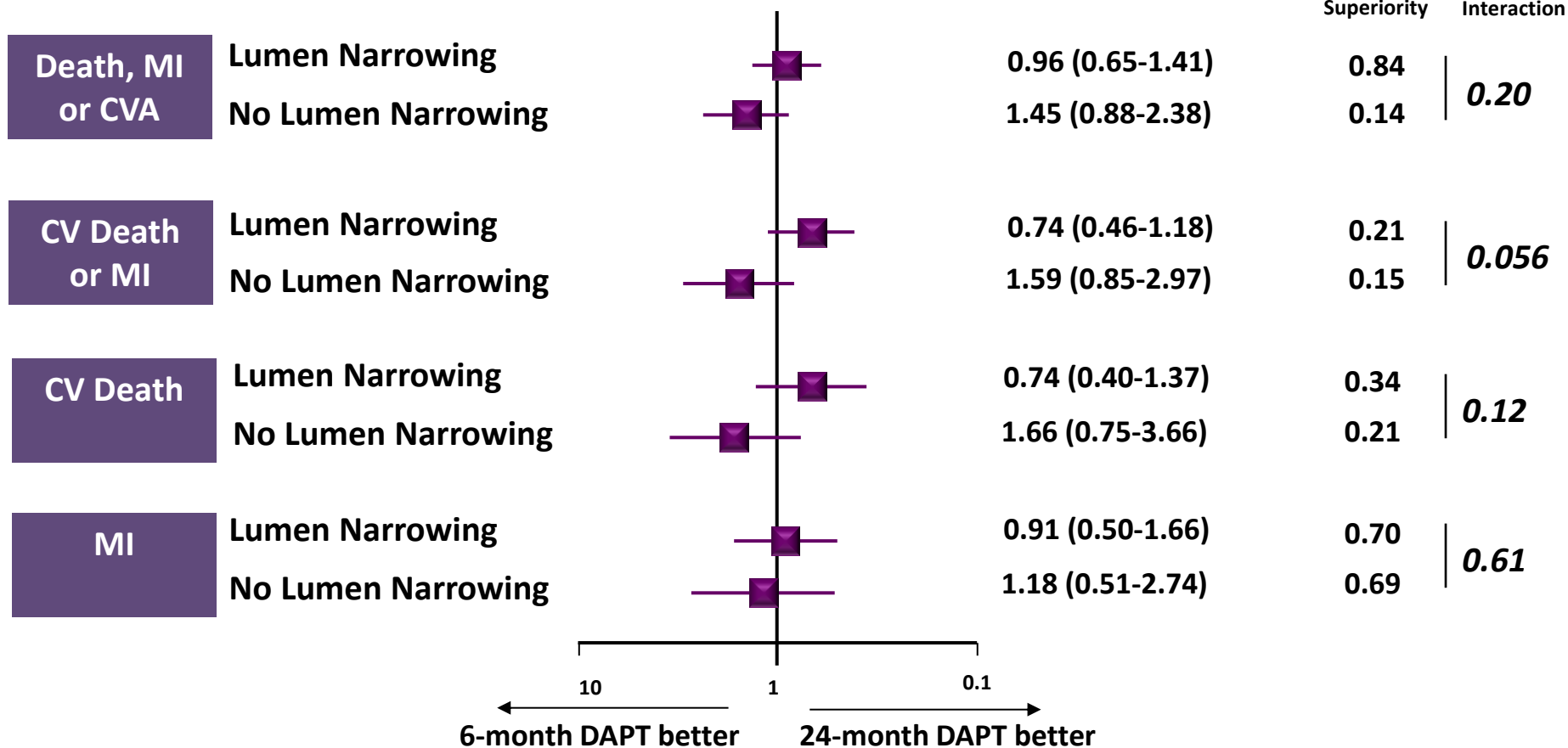
Results

Patient Oriented Endpoints

LM/pLAD Lumen Narrowing

HAZARD RATIO (95% CI)

P-VALUES



Results

Stent Oriented Endpoints

LM/pLAD Lumen Narrowing

HAZARD RATIO (95% CI)

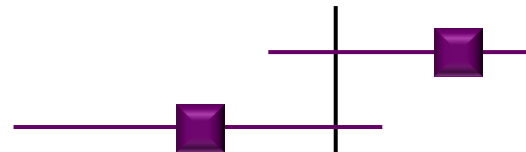
P-VALUES

Superiority | Interaction

**Definite
ST**

Lumen Narrowing

No Lumen Narrowing



0.24 (0.03-2.13)

4.93 (0.57-42.3)

0.20

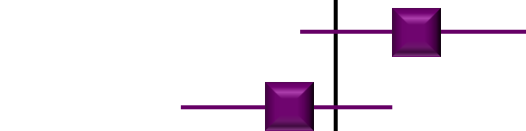
0.15

0.054

**Def, Prob
ST**

Lumen Narrowing

No Lumen Narrowing



0.39 (0.10-1.52)

1.75 (0.51-5.99)

0.17

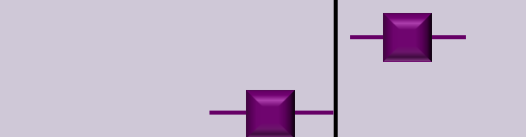
0.37

0.11

**Def, Prob,
Poss. ST**

Lumen Narrowing

No Lumen Narrowing



0.45 (0.23-0.89)

2.15 (1.01-4.58)

0.02

0.046

0.002

100 10 1 0.1

← 6-month DAPT better

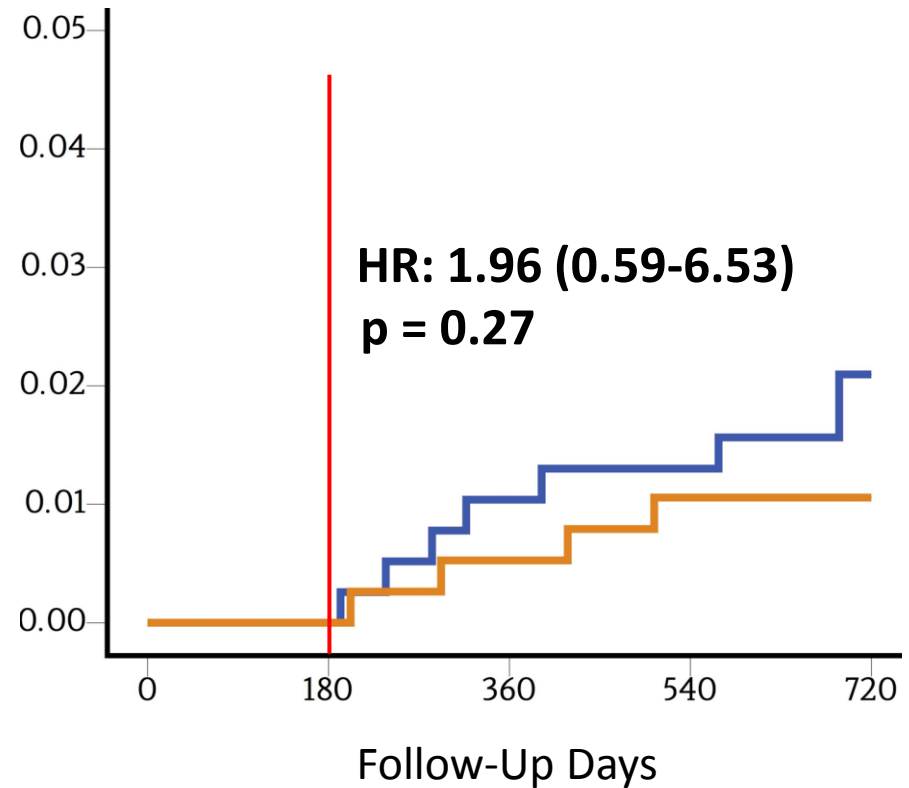
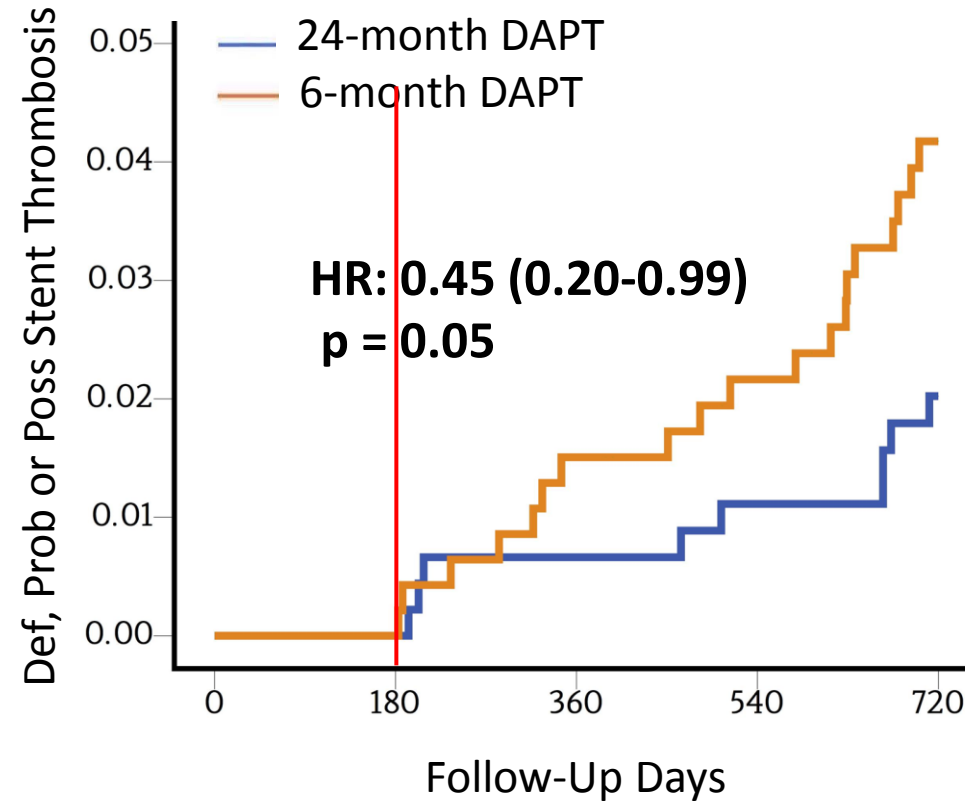
→ 24-month DAPT better

Results: Stent Related Endpoints

Def, Prob or Poss Stent Thrombosis (Landmark Analysis)

LM/pLAD Lumen Narrowing

No LM/pLAD Lumen Narrowing



$p_{\text{int}} = 0.044$

Limitations

- As a post-hoc analysis these results should be interpreted as hypothesis generating and should be confirmed in properly designed prospective studies.
- The CRUSADE score was designed to predict early in hospital bleeding. Dedicated scores designed to predict long term bleeding could better describe bleeding hazard in patients treated with different DAPT regimens.
- The definition of Lumen Narrowing was based on visual estimation and could suffer inter and intra-individual variability.

Summary

- Twenty-four month DAPT was associated with a higher risk of major bleeding and transfusion in patients with high CRUSADE (15.8% of the all-comer population), but not in those with low or intermediate score (84.2% of the all-comer population).
- Twenty-four as compared to 6 month DAPT significantly reduced the rate of definite, probable or possible stent thrombosis in patients with Left Main and/or proximal LAD lumen narrowing.
- The CRUSADE score and the presence of lumen narrowing of the left main/proximal LAD might be useful in guiding the selection of DAPT duration, based on the individual bleeding and ischemic risk.

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Acknowledgements

Special thanks goes to all the PRODIGY investigators and to the study steering committee.



PRODIGY

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