Duration of Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation

A Pooled Analysis of the REAL-LATE and the ZEST-LATE Trial

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Correlation of Clopidogrel Therapy Discontinuation in *REAL*-world Patients Treated with Drug-Eluting Stent Implantation and *L*ate Coronary *A*rterial *T*hrombotic *E*vents:

REAL-LATE Trial

Patients on current dual antiplatelet therapy without MACCE or major bleeding for at least the first 12 months after DES implantation (Total N=2,000)

1:1 randomization Stratified by
(1) centers
(2) Initial DES types

Aspirin + clopidogrel Dual-therapy (N=1,000)

Aspirin Mono-therapy (N=1,000)

Regular Clinical assessment after randomization

Primary end points: The composite of cardiac death or MI

Evaluation of the Long-term Safety After Zotarolimus-Eluting Stent, Sirolimus-Eluting Stent, or Paclitaxel-Eluting Stent Implantation for Coronary Lesions - Late Coronary Arterial Thrombotic Events

ZEST-LATE Trial

Patients without MACCE or major bleeding within the first 12 months, who enrolled in the ZEST Trial (N=2,000)

1:1 randomization stratified by
(1) initial DES type
(2) Enrolling sites

Aspirin + clopidogrel Dual-therapy (N=1,000)

Aspirin Mono-therapy (N=1,000)

Regular clinical assessment after randomization

Primary end points: The composite of cardiac death or MI

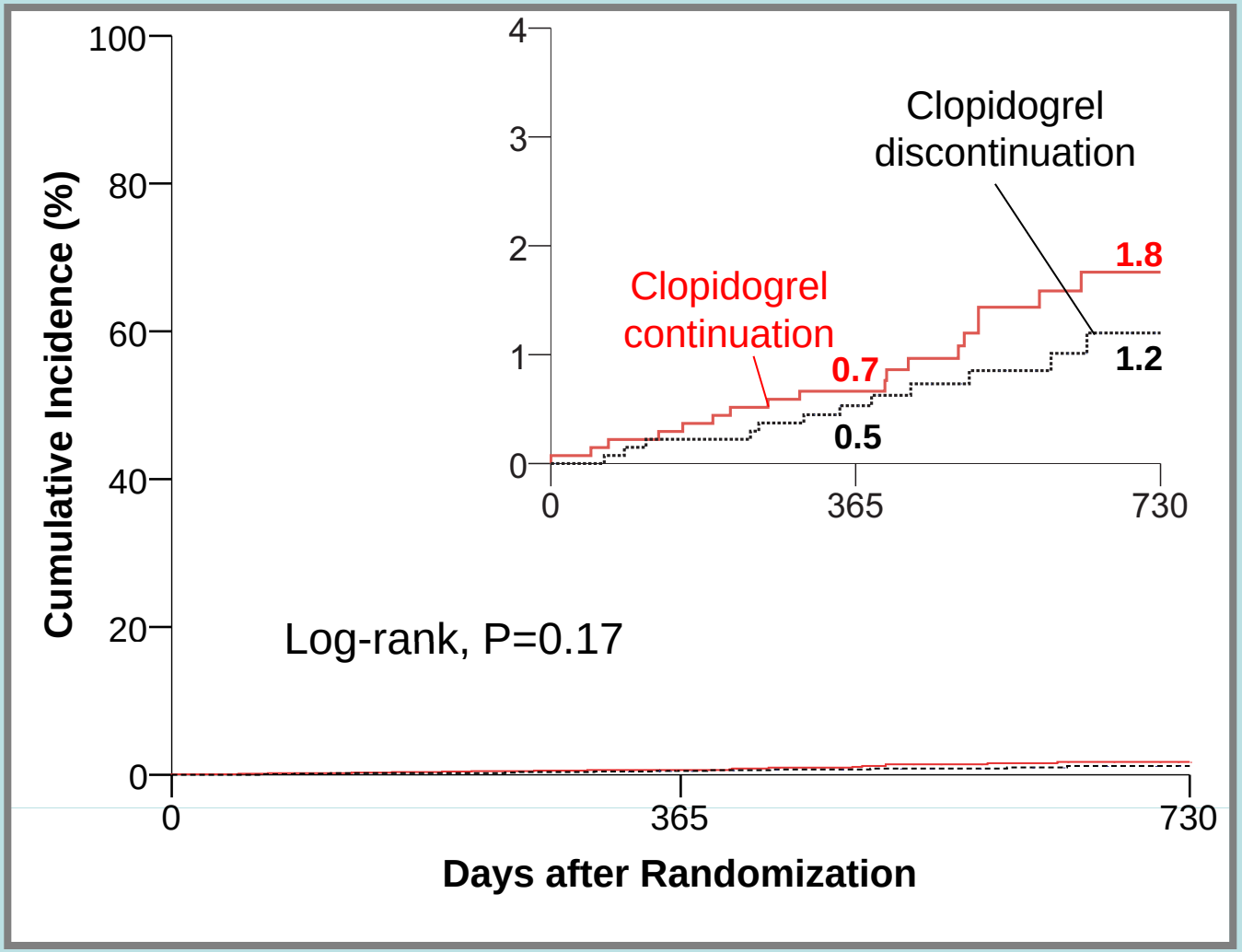
Trial Procedures and Follow-Up

- Patients in both trials were randomly assigned either to clopidogrel (75 mg per day) plus low-dose aspirin (100 to 200 mg per day) or low-dose aspirin alone.
- The treatment allocation was performed using a preestablished, computer-generated randomization scheme, stratified according to site and type of DES.
- Both were open-label trials without blinding of either the study subjects or the investigators.
- Follow-up evaluations were performed every six months. at these visits, data pertaining to patients' clinical status, all interventions, outcome events, adverse events, and drug compliance were recorded.

Status of Dual Antiplatelet Therapy during Follow-up

Characteristic	Clopidogrel Continuation (n=1357)	Clopidogrel Discontinuation (n=1344)	P Value
Aspirin			
At randomization	1348/1357 (99.3)	1338/1344 (99.6)	0.45
6 Mo after randomization	1338/1349 (99.2)	1328/1333 (99.6)	0.14
12 Mo after randomization	1129/1143 (98.8)	1103/1117 (98.7)	0.95
18 Mo after randomization	752/759 (99.1)	722/730 (98.9)	0.37
24 Mo after randomization	327/333 (98.2)	313/318 (98.4)	0.82
Clopidogrel			
At randomization	1335/1357 (98.4)	59/1344 (4.4)	<0.001
6 Mo after randomization	1297/1349 (96.1)	78/1332 (5.9)	<0.001
12 Mo after randomization	1011/1143 (88.5)	72/1117 (6.4)	<0.001
18 Mo after randomization	654/758 (86.3)	46/730 (6.3)	<0.001
24 Mo after randomization	276/333 (82.9)	14/318 (4.4)	<0.001

Primary End Point: cardiac death or myocardial infarction

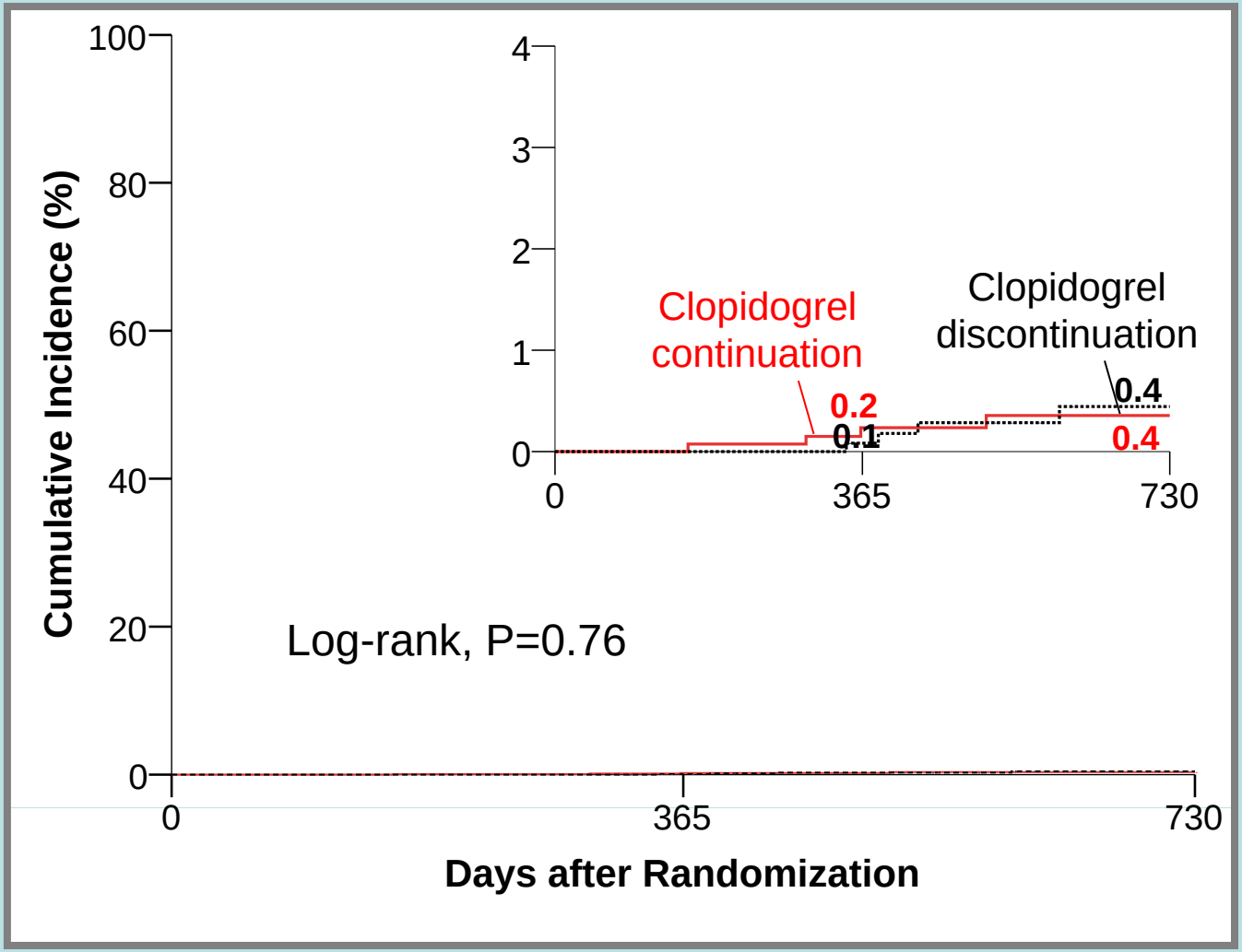


No. at Risk

Continuation group	1357	1122	299
Discontinuation group	1344	1100	301

Outcome	Total Events		Cumulative Event Rate At 12 Months		Cumulative Event Rate At 24 Months		Hazard Ratio (95% CI)	P Value
	Dual Therapy	Aspirin Only	Dual Therapy	Aspirin Only	Dual Therapy	Aspirin Only		
Primary End Point								
Cardiac death or MI	20	12	0.7	0.5	1.8	1.2	1.65 (0.80-3.36)	0.17
Secondary End Points								
Death	20	13	0.5	0.5	1.6	1.4	1.52 (0.75-3.5)	0.24
MI	10	7	0.4	0.3	0.8	0.7	1.41 (0.54-3.71)	0.49
Stroke	9	4	0.3	0.3	1.0	0.3	2.22 (0.68-7.20)	0.19
Stent thrombosis, definite	5	4	0.2	0.1	0.4	0.4	1.23 (0.33-4.58)	0.76
Repeat revascularization	36	26	1.7	1.1	3.1	2.4	1.37 (0.83-2.27)	0.22
Death or MI	27	17	0.8	0.8	2.3	1.7	1.57 (0.85-2.88)	0.15
Death, MI, or stroke	35	20	1.1	1.1	3.2	1.8	1.73 (0.99-3.0)	0.051
Cardiac death, MI, or stroke	28	15	1.0	0.8	2.7	1.3	1.84 (0.99-3.45)	0.06
Major bleeding, TIMI criteria‡	3	1	0.2	0.1	0.2	0.1	2.96 (0.31-28.46)	0.35

Definite Stent Thrombosis



No. at Risk

Continuation group	1357	1124	301
Discontinuation group	1344	1102	303

Conclusion

- In this combined analysis of two randomized multi-center trials, we found no significant benefit associated with clopidogrel continuation as compared with clopidogrel discontinuation after 12 months in reducing the incidence of cardiac death or myocardial infarction for patients who had received drug-eluting coronary stents.

- The rate of composite outcomes (all-cause or cardiac death, myocardial infarction, or stroke) was greater with clopidogrel continuation than with clopidogrel discontinuation, but this difference was not statistically significant.