European Society of Cardiology Congress 2026 – Annual Scientific Session
Hot Line 3 (August 29, 2026)

Clopidogrel vs. Extended DAPT after High-Risk PCI: The A-CLOSE randomized Clinical Trial

Clopidogrel monotherapy vs. Extended DAPT in high-ischaemic-risk patients 12 months after DES implantation

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On the behalf of the A-CLOSE investigators

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Background

- Current guidelines recommend 6 to 12 months of dual antiplatelet therapy (DAPT) after DES implantation, with growing evidence supporting **long-term P2Y12 inhibitor monotherapy**—particularly **clopidogrel monotherapy**—as a preferred maintenance strategy.

*Eur Heart J **2023**;44:3720-3826 / **2024**;45:3415-3537*
*J Am Coll Cardiol **2023**;82:833-955 / **2025**;85:2135-2237*
*Lancet **2021**;397:2487-96 / Lancet **2025**;405:1252-63*

- For patients at **high ischaemic risk, extended DAPT beyond 12 months** after DES implantation **reduced ST and MACE vs. aspirin monotherapy** in the DAPT trial, **but increased bleeding**.

*New Engl J Med **2014**;371:2155-66 / JAMA 2016;315:1735-49*

- However, the comparative impact of **clopidogrel monotherapy vs. extended DAPT in high-ischaemic-risk patients remains uncertain.**

Objective

- To investigate whether **clopidogrel monotherapy** is **non-inferior** to **extended DAPT with clopidogrel plus aspirin** for 24 months with respect to net adverse clinical events in **patients at high ischaemic risk 12 months after DES implantation.**

If non-inferiority for the primary endpoint is met,
***key secondary ischaemic and bleeding endpoints** will be tested for superiority in a prespecified sequence.*

Trial design and population

- **Investigator-initiated, multicentre, randomised, open-label, non-inferiority trial**
  (ClinicalTrials.gov number, NCT03947229)
- **Enrolment period: August 2019 through August 2023**
- **Conducted at 19 sites in South Korea;** Investigators (Participating site)

1. Byeong-Keuk Kim (Yonsei University Severance Hospital)
2. Kyounghoon Lee (Gachon University Gil Medical Center)
3. Deok-Kyu Cho (Yonsei University Yongin Severance Hospital)
4. Yun-Hyeong Cho (Hanyang University Myongji Hospital)
5. Sung Gyun Ahn (Yonsei University Wonju Severance Hospital)
6. Kyeong Ho Yun (Wonkwang University Hospital)
7. Ji-Yong Jang (National Health Insurance Service Ilsan Hospital)
8. Seunghwan Kim (Inje University Haeundae Paik Hospital)
9. Yong Hoon Kim (Kangwon National University Hospital)
10. Yong-Hwan Park (Sungkyunkwan Univ Samsung Changwon Hospital)
11. Sung Uk Kwon (Inje University Ilsan Paik Hospital)
12. Seung-Ho Hur (Keimyung University Dongsan Medical Center)
13. Tae Soo Kang (Dankook University Hospital)
14. Eun-Seok Shin (Ulsan University Hospital)
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16. Ki-Hyun Jeon (Seoul National University Bundang Hospital)
17. Ung Kim (Yeungnam University Medical Center)
18. Won-Ho Kim (Eulji University Hospital)
19. Bum-Kee Hong (Yonsei University Gangnam Severance Hospital)

Principal Investigators: Byeong-Keuk Kim

Study Criteria

Inclusion criteria

(1) **Age >19 years**
(2) **DES implantation 12 months** (−1 to +5 months) **prior to randomization**
(3) **High-risk characteristics for ischemic events** (at least one features)

*High-risk patients; **clinical criteria***

1. **Acute coronary syndrome**
2. **History of cerebrovascular accidents**
3. **Peripheral artery revascularization**
4. **Diabetes Mellitus**
5. **Chronic kidney disease** / 6. **Heart failure** (LVEF ≤40%)

*High-risk lesions; **angiographic or procedural criteria***

1. **Left main diseases** / 2. **Bifurcation lesions**
3. **Chronic total occlusion**
4. **In-stent restenotic lesions** / 5. **Graft lesions**
6. **Diffuse long lesions** (total stent length ≥28 mm)
7. **Calcified lesions** (requiring rotational atherectomy)
8. **Multivessel disease with multiple stents**
9. **Small vessel disease** (stent diameter of ≤2.5 mm)

Exclusion criteria

(1) **Age >80 years**
(2) **Major bleeding within 3 months** before randomisation
(3) **Need for chronic oral anticoagulation**
(4) Pregnancy or potential childbearing
(5) Life expectancy <1 year
(6) Refusal or inability to provide informed consent

Randomization and follow-up

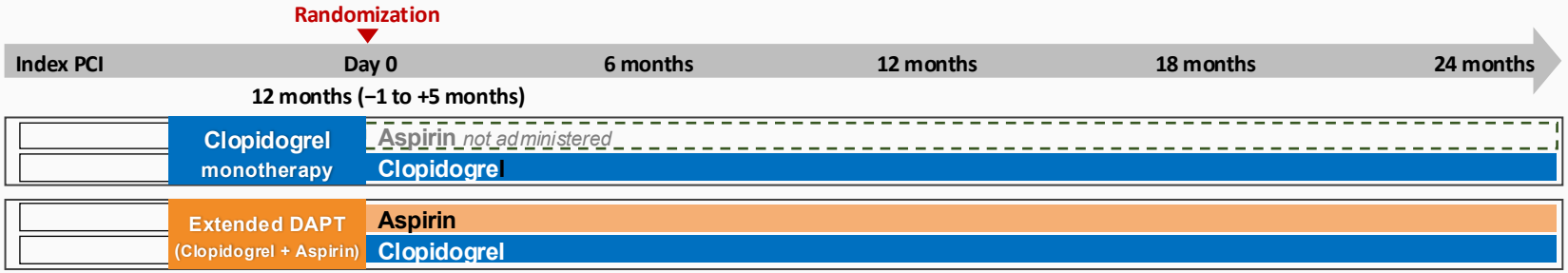
Patients with high-ischemic risk
12 months after DES implantation (N=3200)

1:1 Randomization

Stratified by acute coronary syndrome at index PCI and age (≥75 years)

Clopidogrel monotherapy (n = 1600)	Extended DAPT (n = 1600)

Primary Endpoint: Net Adverse Clinical Events at 24 months after randomization
Composite of all-cause death, MI, stent thrombosis, stroke, or BARC type 2, 3, or 5 bleeding



Trial end points

- Primary end point

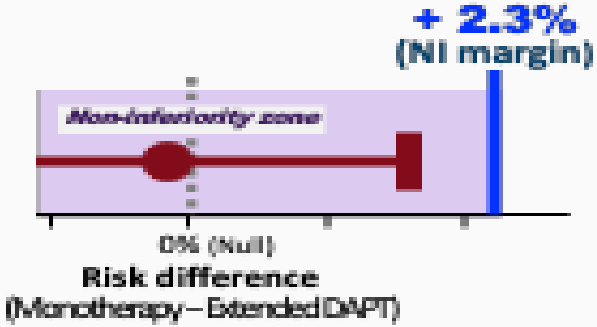
  Net adverse clinical events; Composite of **all-cause death, MI, stent thrombosis, stroke,** or **BARC type 2, 3, or 5 bleeding** at 24 months

- Key secondary end points ; Tested in a prespecified hierarchical order.
  - **Composite ischaemic end point;**
    All-cause death, MI, stent thrombosis, or stroke
  - **Bleeding end point;**
    BARC type 2, 3, or 5 bleeding

- Other secondary end points
  . Individual components of the primary end point
  . Prespecified composite end points

Statistical considerations

- **Sample size estimation**
  - The trial was designed to test **whether** clopidogrel monotherapy would be **non-inferior** to extended DAPT with respect to the primary endpoint at 24 months.
  - Assuming a 24-month primary end point incidence of **7.0%** in each group and 5% attrition rate, a sample size of **3200 patients** provided 80% power at a one-sided alpha level of 0.05.
  - **Non-inferiority** was established if the upper boundary of the two-sided 90% CI, estimated from Kaplan–Meier curves, fell below the **margin of 2.3 percentage points**.



- **Statistical analysis**
  - Primary intention-to-treat analysis
  - Cumulative incidences; Kaplan–Meier method and compared with log-rank test
  - Key secondary endpoints; Prespecified **hierarchical sequence at a two-sided alpha level of 0.05**

Baseline characteristics (1)

	Clopidogrel Monotherapy (n=1,601)	Extended DAPT (n=1,602)
Age — yr	**62.6** ± 9.5	**62.6** ± 9.8
Male sex	1,295 (80.9%)	1,319 (82.3)
High-risk clinical factors		
• **Acute coronary syndrome**	**1,271 (79.4%)**	**1,270 (79.3%)**
ST-segment elevation MI	354 (22.1%)	342 (21.3%)
Non–ST-segment MI	461 (28.8%)	476 (29.7%)
Unstable angina	456 (28.5%)	452 (28.2%)
• **Diabetes mellitus**	**644 (40.2%)**	**647 (40.4%)**
• **Heart failure** (LVEF ≤40%)	60 (3.7%)	73 (4.6%)
• **Chronic kidney disease**	**160 (10.0%)**	**166 (10.4%)**
• **Previous CVA**	97 (6.1%)	111 (6.9%)
• **Previous peripheral artery revascularization**	20 (1.2%)	24 (1.5%)

*The baseline characteristics did not differ between the two groups.

Baseline characteristics (2)

	Clopidogrel Monotherapy (n=1,601)	Extended DAPT (n=1,602)
High-risk lesion factors		
• **Unprotected left main artery disease**	**170 (10.6%)**	**177 (11.0%)**
• **Bifurcation lesion**	**422 (26.4%)**	**441 (27.5%)**
• **Chronic total occlusion**	**176 (11.0%)**	**181 (11.3%)**
• **In-stent restenosis**	158 (9.9%)	159 (9.9%)
• **Bypass graft lesion**	22 (1.4%)	22 (1.4%)
• **Diffuse long lesion**	**1,094 (68.3%)**	**1,103 (68.9%)**
• **Severe calcification requiring atherectomy**	57 (3.6%)	53 (3.3%)
• **Multivessel disease with multiple stents**	**560 (35.0%)**	**563 (35.1%)**
• **Small vessel disease**	309 (19.3%)	332 (20.7%)
Procedural Characteristics		
No. of treated vessels	1.2 ± 0.5	1.2 ± 0.5
No. of stents implanted	1.6 ± 0.8	1.6 ± 0.8
Total stent length — mm	**43.4 ± 26.0**	**43.8 ± 26.5**
Mean stent diameter — mm	3.16 ± 0.41	3.15 ± 0.42

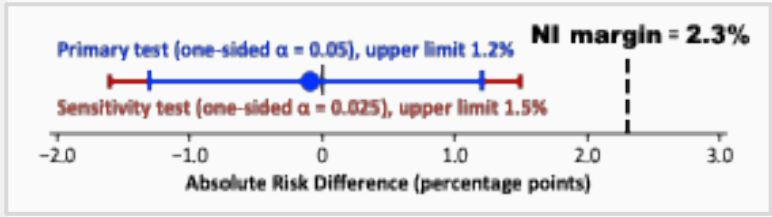
*The baseline characteristics did not differ between the two groups.

Primary Endpoint

Composite of all-cause death, MI, stent thrombosis, stroke, or BARC type 2, 3, or 5 bleeding at 24 months

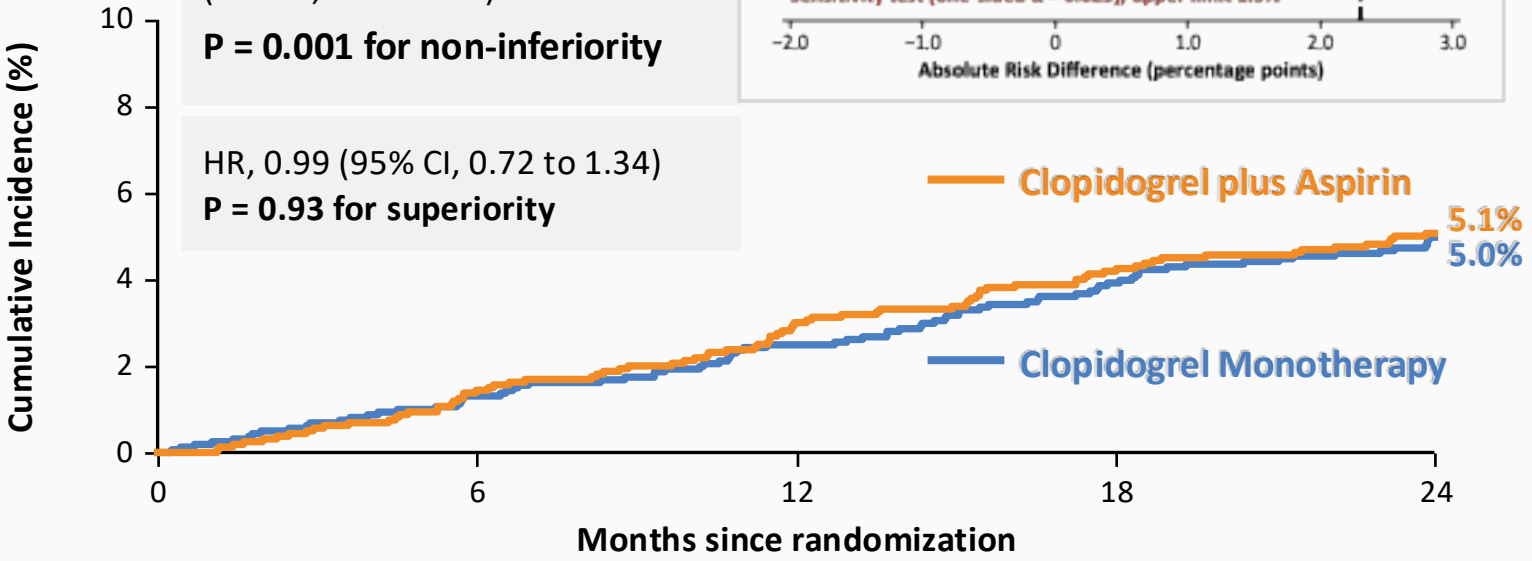
Difference, − 0.1 percentage points
(90% CI, −1.3 to 1.2)

P = 0.001 for non-inferiority



HR, 0.99 (95% CI, 0.72 to 1.34)

P = 0.93 for superiority



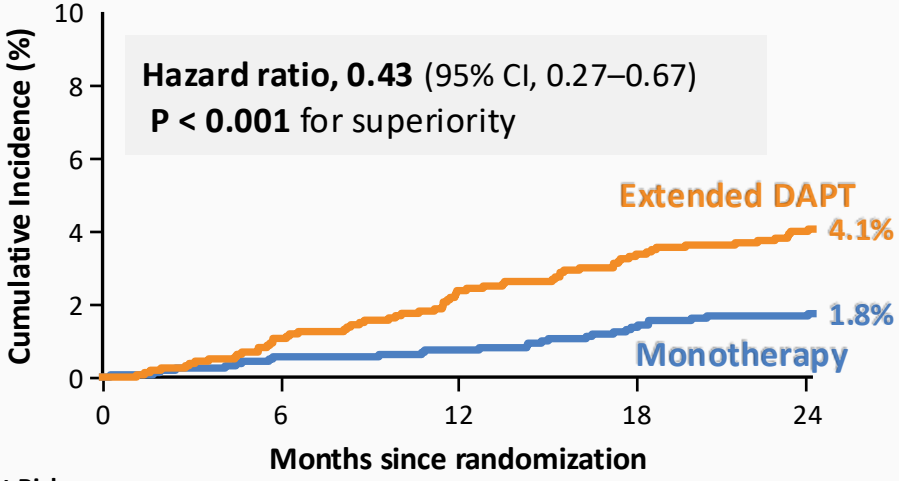
No. at Risk

Clopidogrel Monotherapy	1601	1580	1561	1538	1521
Clopidogrel plus Aspirin	1602	1579	1554	1535	1521

Key Secondary End Points

Key Bleeding End Point

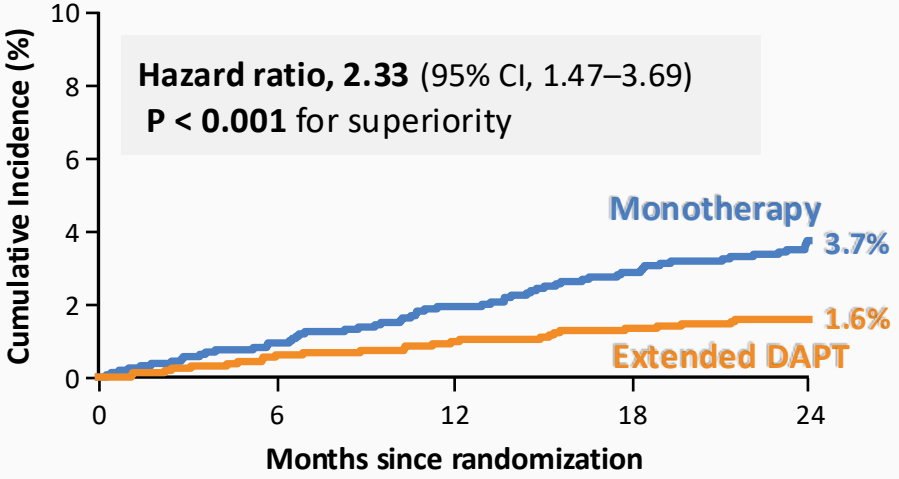
BARC type 2, 3, or 5 bleeding at 24 months



No. at Risk					
Clopidogrel monotherapy	1601	1588	1580	1565	1553
Clopidogrel plus aspirin	1602	1580	1559	1543	1529

Key Ischaemic End Point

All-cause death, MI, stent thrombosis, or stroke at 24 months



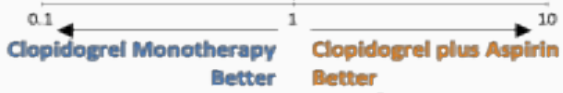
No. at Risk					
Clopidogrel monotherapy	1601	1586	1570	1555	1541
Clopidogrel plus aspirin	1602	1592	1586	1580	1576

Other Secondary Endpoints

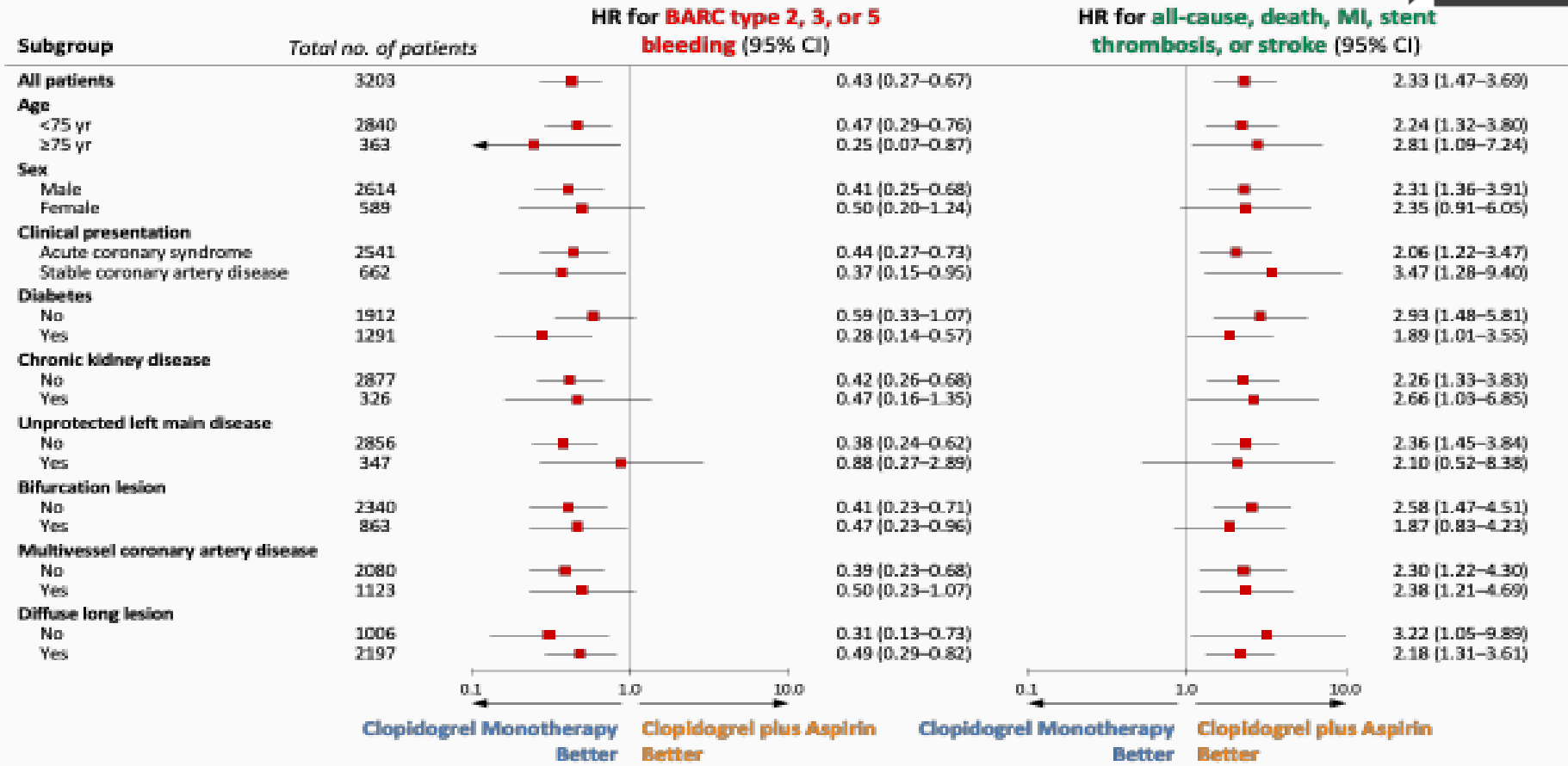
	Clopidogrel Monotherapy (N=1601)	Clopidogrel plus Aspirin (N=1602)	Hazard ratio (95% CI)	P value
Individual events				
All-cause death	**21 (1.3%)**↑	**7 (0.4%)**↓	**3.01** (1.28 to 7.09)	**0.008**
Cardiovascular death	**14 (0.9%)**↑	**3 (0.2%)**↓	**4.68** (1.35 to 16.30)	**0.007**
Myocardial infarction	**23 (1.4%)**↑	**6 (0.4%)**↓	**3.86** (1.57 to 9.49)	**0.001**
Stent thrombosis (definite or probable)	**12 (0.8%)**↑	**3 (0.2%)**↓	**4.02** (1.13 to 14.24)	**0.020**
Stroke	19 (1.2%)	15 (0.9%)	1.27 (0.65 to 2.51)	0.484
Ischemic stroke	14 (0.9%)	6 (0.4%)	2.34 (0.90 to 6.10)	0.072
Hemorrhagic stroke	5 (0.3%)	9 (0.6%)	0.56 (0.19 to 1.67)	0.290
BARC type 3 or 5 bleeding	**15 (0.9%)**↓	**35 (2.2%)**↑	**0.42** (0.23 to 0.78)	**0.004**
BARC type 2 bleeding	**13 (0.8%)**↓	**30 (1.9%)**↑	**0.43** (0.22 to 0.82)	**0.009**
Composite events				
All-cause death, MI, stent thrombosis, or TVR	**57 (3.6%)**↑	**24 (1.5%)**↓	**2.40** (1.49 to 3.86)	**<0.001**
All-cause death, MI, stent thrombosis, stroke, or TVR	**74 (4.6%)**↑	**37 (2.3%)**↓	**2.02** (1.36 to 3.00)	**<0.001**

Primary Endpoint by subgroup

Subgroup	No. of patients with event / total no. of patients (Kaplan-Meier estimate, %) Clopidogrel Monotherapy	Clopidogrel plus Aspirin	Hazard Ratio (95% CI)
All patients	80/1601 (5.0%)	81/1602 (5.1%)	0.99 (0.72–1.34)
Age			
<75 yr	63/1428 (4.4%)	63/1412 (4.5%)	0.99 (0.70–1.40)
≥75 yr	17/173 (9.8%)	18/190 (9.5%)	1.04 (0.54–2.02)
Sex			
Male	61/1295 (4.7%)	64/1319 (4.9%)	0.97 (0.68–1.38)
Female	19/306 (6.2%)	17/283 (6.0%)	1.04 (0.54–1.99)
Clinical presentation			
Acute coronary syndrome	58/1271 (4.6%)	62/1270 (4.9%)	0.93 (0.65–1.33)
Stable coronary artery disease	22/330 (6.7%)	19/332 (5.7%)	1.17 (0.63–2.16)
Diabetes			
No	46/957 (4.8%)	38/955 (4.0%)	1.21 (0.79–1.86)
Yes	34/644 (5.3%)	43/647 (6.6%)	0.79 (0.50–1.24)
Chronic kidney disease			
No	62/1441 (4.3%)	68/1436 (4.7%)	0.91 (0.64–1.28)
Yes	18/160 (11.2%)	13/166 (7.8%)	1.45 (0.71–2.95)
Unprotected left main disease			
No	69/1431 (4.8%)	73/1425 (5.1%)	0.94 (0.67–1.30)
Yes	11/170 (6.5%)	8/177 (4.5%)	1.45 (0.58–3.61)
Bifurcation lesion			
No	55/1179 (4.7%)	52/1161 (4.5%)	1.04 (0.71–1.52)
Yes	25/422 (5.9%)	29/441 (6.6%)	0.90 (0.52–1.53)
Multivessel coronary artery disease			
No	44/1041 (4.2%)	55/1039 (5.3%)	0.79 (0.53–1.18)
Yes	36/560 (6.4%)	26/563 (4.6%)	1.41 (0.85–2.33)
Diffuse long lesion			
No	19/507 (3.7%)	24/499 (4.8%)	0.78 (0.42–1.42)
Yes	61/1094 (5.6%)	57/1103 (5.2%)	1.08 (0.75–1.55)



Key Secondary Endpoints by subgroup



Summary of the A-CLOSE trial

Among patients with high risk for ischaemic events 12 months after DES implantation,

- **Clopidogrel Monotherapy** was **noninferior to Extended DAPT** of aspirin plus clopidogrel for net adverse clinical events.

- However, as compared with **Extended DAPT**, **Clopidogrel monotherapy** was associated with a **higher risk of the key ischemic end point**, with **higher rates of all-cause and cardiovascular death**, despite a **lower risk of the bleeding** end point.

Conclusion & Clinical Implications

- The **divergent ischaemic & bleeding effects** in A-CLOSE highlight the **inherent trade-off** between **Extended DAPT** and **Monotherapy**, **cautioning against routine de-escalation in high-ischemic-risk patients.**

→ These findings broaden the evidence for antiplatelet therapy beyond 12 months post-DES and support an individualized strategy guided by ischaemic & bleeding risks rather than a uniform approach.