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RESEARCH CORRESPONDENCE

1-Year Clinical Performance of COMBO Stent Versus Xience Stent in All-Comers Patients With Coronary Artery Disease

The novel COMBO dual-therapy stainless-steel coronary stent (DTS) (OrbusNeich Medical BV, Hoevelaken, the Netherlands) is a device that combines a sirolimus-eluting layer with a prohealing layer with anti-CD34^{+} antibodies, which attracts circulating endothelial progenitor cells. These endothelial progenitor cells can differentiate into endothelial cells, promoting rapid endothelialization. This device has not yet been compared with the well-established cobalt-chromium Xience everolimus-eluting stent (Abbott Vascular, Santa Clara, California) in an all-comers population. Our aim is to evaluate clinical outcomes after the use of COMBO DTS or Xience in a balanced all-comers patient population.

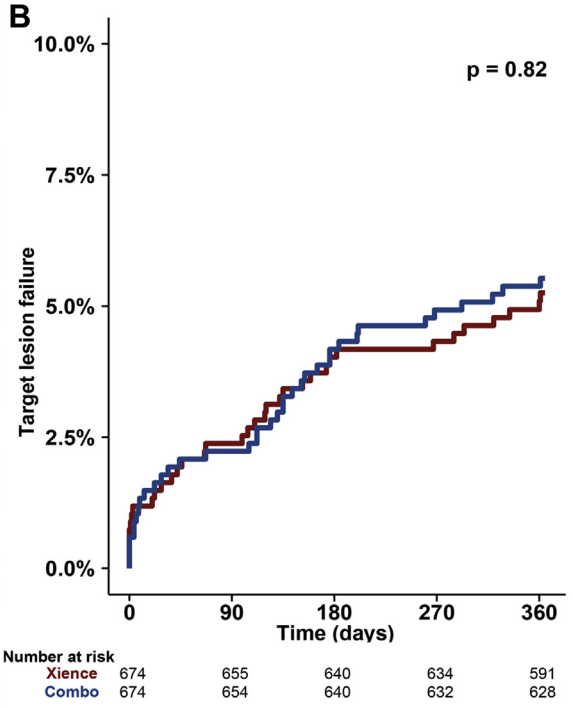
The REMEDEE Registry enrolled 1,000 patients treated with COMBO stent (1). The randomized AIDA trial compared patients treated with Xience versus Absorb bioresorbable vascular scaffold (Abbott Vascular) (2). Both trials are investigator-initiated, prospective, multicenter all-comers studies, and used the same endpoint definitions. A propensity-matched analysis was performed for COMBO DTS versus Xience, using 13 baseline variables: age, sex, insulin-treated diabetes mellitus, hypertension, previous myocardial infarction (MI), previous percutaneous coronary intervention, previous bypass surgery, acute coronary syndrome, number of treated lesions, target vessel location, stent length and diameter, and American College of Cardiology/American Heart Association classification. The method of matching has been described previously (3). In short, patients were 1-to-1 greedy matched

FIGURE 1 Baseline Characteristics of the Matched Cohort and Kaplan-Meier Estimate of the Primary Endpoint Target Lesion Failure at 1-Year Follow-Up

A

	Xience	COMBO	p-value
N=	674	674	
Female (%)	170 (25)	158 (23)	0.49
Age, years (mean (sd))	64.2 (10.5)	64.6 (11.3)	0.46
Diabetes Mellitus (%)	113 (17)	129 (19)	0.29
Insulin treated DM (%)	35 (5)	44 (7)	0.35
Hypertension (%)	365 (54)	382 (57)	0.38
Previous CABG (%)	23 (3)	32 (5)	0.27
Previous PCI (%)	163 (24)	190 (28)	0.11
Previous MI (%)	147 (22)	161 (24)	0.40
Acute coronary syndrome (%)	350 (52)	348 (52)	0.96
RCA treated (%)	197 (29)	206 (30)	0.63
Stent diameter (mean (sd))	3.1 (0.4)	3.15 (0.4)	0.82
Total stent length (mean (sd))	24.0 (12.6)	23.0 (11.6)	0.12

B



(A) Baseline characteristics of the matched cohort. **(B)** Target lesion failure at 1-year follow-up in a balanced all-comers cohort comparing patients treated with Xience and COMBO stent. Target lesion failure in COMBO is 5.5% and Xience is 5.3% (hazard ratio: 1.05; 95% confidence interval: 0.66 to 1.76; p = 0.82). CABG = coronary artery bypass graft; DM = diabetes mellitus; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery.

using the nearest-neighbor method. The caliper was set at 0.2. Cox regression analyses were used to compare clinical outcomes between both stent types. Values of $p < 0.05$ were considered statistically significant. Target lesion failure, a composite of cardiac death, target vessel MI (using the Third Universal Definition of MI [4]), and any target lesion revascularization was the primary endpoint of this analysis. Also, the separate endpoints of target lesion failure were analyzed. Definite and probable stent thrombosis were evaluated with the Academic Research Consortium criteria for stent thrombosis (5).

The analysis yielded 674 patients-pairs. All baseline characteristics were well balanced between both groups, as presented in **Figure 1A**. Number of treated lesions did not differ between both groups ($p = 0.68$) and American Heart Association/American College of Cardiology lesion classification distribution was the same ($p = 0.42$). Target lesion failure occurred in 5.5% of patients treated with COMBO DTS and in 5.3% of patients with Xience (hazard ratio [HR]: 1.05; 95% confidence interval [CI]: 0.66 to 1.76; $p = 0.82$) (**Figure 1B**). Rates of cardiac death were 1.3% in both COMBO DTS and Xience patients (HR: 1.68; 95% CI: 0.4 to 2.51; $p = 1.00$). Target vessel MI occurred in 0.8% patients ($n = 6$) with COMBO DTS and 2.2% patients with Xience ($n = 15$) (HR: 0.4; 95% CI: 0.15 to 1.02; $p = 0.06$). Target lesion revascularization was numerically higher in patients with COMBO 4.5% ($n = 30$) versus 2.7% ($n = 18$) in patients with Xience (HR: 1.68; 95% CI: 0.93 to 3.00; $p = 0.08$). Definite or probable stent thrombosis occurred in 0.7% of both groups ($n = 5$ in COMBO DTS; $n = 5$ in Xience) (HR: 1.00; 95% CI: 0.29 to 3.46; $p = 1.00$).

Xience is currently widely used as a workhorse stent. This analysis shows that COMBO DTS shows similar results in clinical outcomes compared with Xience in a complex all-comers patient population. The added value of the prohealing layer is currently being investigated in the REDUCE trial (NCT02118870), which evaluates 3 versus 12 months of dual-antiplatelet therapy after acute coronary syndrome in patients treated with COMBO DTS. The HARMONEE trial (NCT02073565) is a prospective study in patients with ischemic coronary disease and non-ST-segment elevated MI, randomizing patients to Xience or COMBO stent. Although results are currently awaited, the HARMONEE patient population is not an all-comers population. This analysis is the first to compare clinical performance between COMBO DTS and Xience stent in all-comers patients. No significant differences between the 2 devices were found.

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