MARKETING BULLETIN

Biostable polymer vs Biodegradable polymer

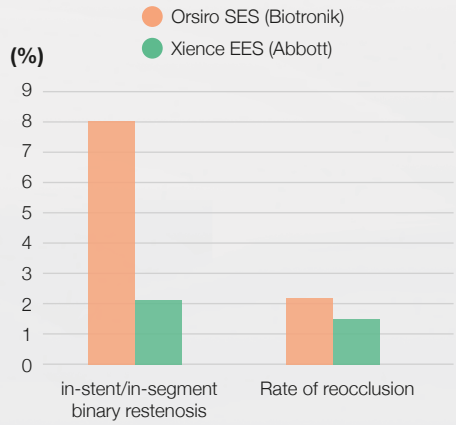
It is considered that biodegradable polymer DES have potential advantages over durable polymer DES. Nevertheless, the evidence from randomized clinical trials suggests that they are comparable in terms of efficacy and safety. Biodegradable polymer drug eluting stents are superior to first generation durable polymer drug eluting stents but not to newer generation durable polymer stents in reducing target vessel revascularization. **Second generation durable polymer stents, and especially stents with cobalt chromium platform, have the best combination of efficacy and safety**. The superiority of biodegradable polymer stents in the context of excellent clinical outcomes with newer generation durable polymer stents needs to be proven.

In order to support the above statement, we would like to share with you a broad list of studies and their outcomes.

The first one is **PRISON IV**, a prospective, randomized, single-blinded, multicenter trial of 330 consecutive patients with successfully recanalized native total or chronic total coronary occlusions. The trial was designed to compare Biotronik's hybrid, ultra-thin strut Orsiro sirolimus-eluting stent (SES) with a **biodegradable polymer** versus Abbott Vascular's thin-strut Xience everolimus-eluting stent (EES) with a **durable polymer**.

Results from **PRISON IV** trial **failed to show non-inferiority** of hybrid, ultra-thin strut sirolimus-eluting stents (Orsiro SES) with a biodegradable polymer compared to thin-strut everolimus-eluting stents (Xience EES) with a durable polymer **in terms of in-segment late lumen loss** in successfully treated chronic total occlusions.

	Orsiro SES (Biotronik)	Xience EES (Abbott)	p
in-segment late lumen loss	0.12±0.59	0.07±0.46 mm	0.52
in-stent/in-segment **binary restenosis**	8.0 %	2.1 %	0.028
Rate of reocclusion	2.2 %	1.4 %	0.68



In addition, although the rate of binary restenosis was low overall in this complex lesion subset, it was higher with the Orsiro SES compared with the Xience EES.
Target vessel failure and major adverse cardiac events were comparable between both groups.

The second one is **TWENTE III**, a large, prospective, randomized, multicenter trial with three arms, comparing two DES with biodegradable coatings (Orsiro SES and Synergy EES) versus DES with a durable coating (Resolute Integrity) in 3540 all-comers.

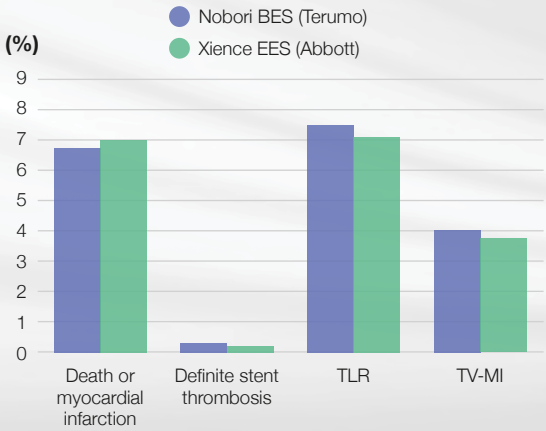
In the conclusion EES Synergy and SES Orsiro stents, which both have dissimilar biodegradable polymer coatings, were **non-inferior** to the thin strut durable polymer zotarolimus-eluting Resolute Integrity stent.

The following two trials - **the NEXT trial and the COMPARE** trial were comparing the Nobori (Terumo) biodegradable biolimus-eluting stent (BES) versus Xience (Abbott Vascular) permanent polymer-based cobalt-chromium everolimus-eluting stent (CoCr-EES)

Both trials were characterized by low event rates which were almost half those expected, resulting in their being underpowered for their primary endpoint, and justifying the present analysis. In this pooled analysis, three-year rates were similar between the two groups.

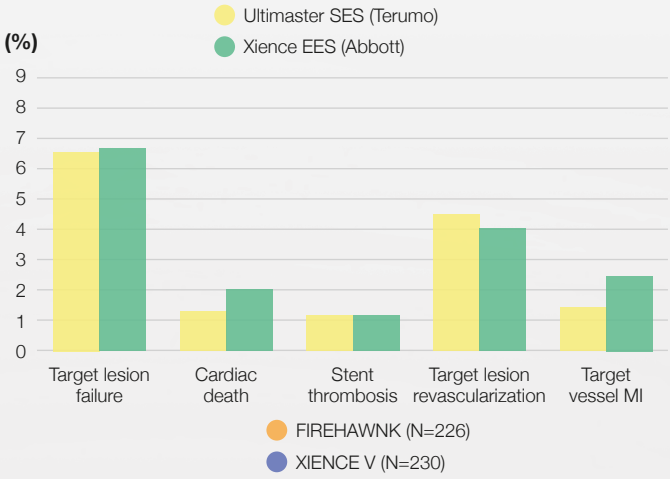
At 3 years	Nobori BES (Terumo)	Xience EES (Abbott)	p
Death or myocardial infarction	6.8%	7.0%	0.85
Definite stent thrombosis	0.31%	0.26%	0.74
Target lesion revascularization	7.4%	7.1%	0.8
Target vessel myocardial infarction	4.0%	3.7%	0.72

As we can see, Nobori BES has showed similar rates of TV-MI compared to Xience EES.



One more trial **CENTURY II** showed no significant difference between Xience (DP-EES) and Ultimaster (BP-SES) - included 525 patients with lesions of reference diameter ≤2.5 mm. Treatment was randomly assigned: 277 patients received BP-SES (399 lesions) and 248 patients received DP-EES (377 lesions). See the primary outcome below.

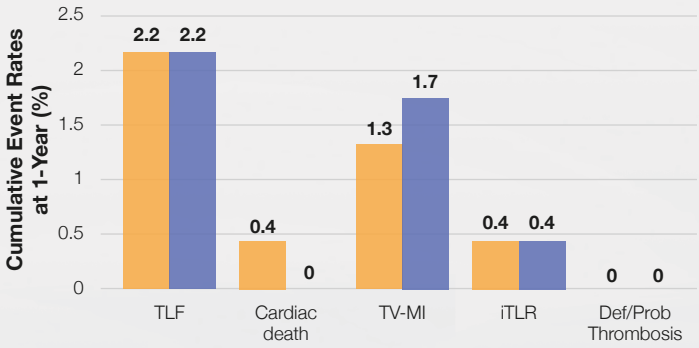
At 12 months	Ultimaster SES (Terumo)	Xience EES (Abbott)	p
Target lesion failure	6.5%	6.6%	0.66
Cardiac death	1.3%	2.0%	0.34
Stent thrombosis	1.1%	1.1%	0.99
Target lesion revascularization	4.5%	4.0%	0.89
Target vessel MI	1.3%	2.4%	0.17



Target market - Asia

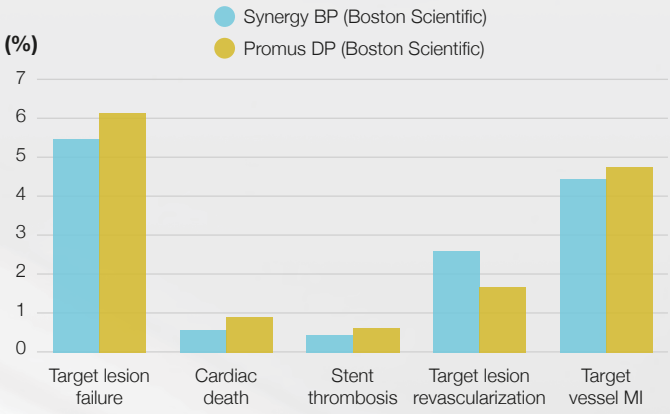
Following existing comparative trials, it wouldn´t be correct to leave behind the **TARGET I trial** with Xience (Abbott) vs Firehawk (Microport). Although Microport is not a very well-known company in Europe, it´s the biggest Chinese company with a full range of cardiovascular devices including two DES with durable and biodegradable polymers.

For the primary endpoint of in-stent late lumen loss at 9-month follow-up Firehawk BP-SES stent was noninferior to Xience V DP-EES (Abbott) stent and had a comparable clinical outcome at 3 years. In addition, the 3-year patient follow-up results showed that there were still no significant differences between the two groups up to 3 years, and no definite/probable stent thrombosis occurred in both groups.



There is one more clinical trial program which was design by Boston Scientific to support approval of the first biodegradable polymer DES in the U.S. The EVOLVE Trial enrolled 1,684 patients with native coronary artery lesions and randomized patients to receive either the Synergy (BP-EES) or Promus (DP-EES) stent.

At 12 months	Synergy BP (Boston Scientific)	Promus DP (Boston Scientific)	p
Target lesion failure	5.5%	6.1%	0.85
Cardiac death	0.5%	0.9%	0.34
Stent thrombosis	0.4%	0.6%	0.50
Target lesion revascularization	2.6%	1.7%	0.21
Target vessel MI	4.3%	4.7%	0.71



At 2 years, target lesion failure was 9.4% for Synergy and 8.5% for Promus, respectively. Adverse events including death and revascularization were not significantly different between the 2 treatment groups, according to the study.

Key message

The last but not least is **Angiolite Trial** a randomized, prospective and multicenter trial to evaluate the clinical performance of **Angiolite DES** versus the second-generation DES Xience in 223 patients with PCI indication.

Preliminary QCA data Angiolite shows non-inferiority vs Xience Alpine®. Even though not all the patients' data was analyzed yet, **Angiolite already shows similar safety as Xience**.

At 6 months	Angiolite SES (iVascular)	Xience EES (Abbott)
In-stent late lumen loss	0.07 mm	0.09 mm
In-stent binary restenosis	0%	0 %

Take home message:

As a conclusion, on the basis of current evidence, it therefore remains undetermined whether there are significant differences in safety and efficacy between drug eluting stents with biodegradable polymer versus drug eluting stents with durable polymer.