BIOFLOW-V

Bayesian Analysis

of prospective, multi-center, randomized controlled trial (BIOFLOW-V) combined with prospectively collected data from two historical randomized trials (BIOFLOW-II and BIOFLOW-IV)

Conclusions

- Orsiro demonstrated unequivocal non-inferiority to Xience[1] for the outcome of Target Lesion Failure (TLF) at 12 months (Bayesian posterior probability 100%)
- There is a strong trend towards superiority of Orsiro in TLF at 12 months (Bayesian posterior probability 96.9%)
- The expected TLF rate is reduced by absolute 2.6% with Orsiro compared to Xience
- The present study represents the first large, randomized trial to demonstrate improved outcomes of any DES over Xience, establishing a new benchmark for DES

Study design

Pooled analysis including patients level outcome of BIOFLOW-II, BIOFLOW-IV and BIOFLOW-V.

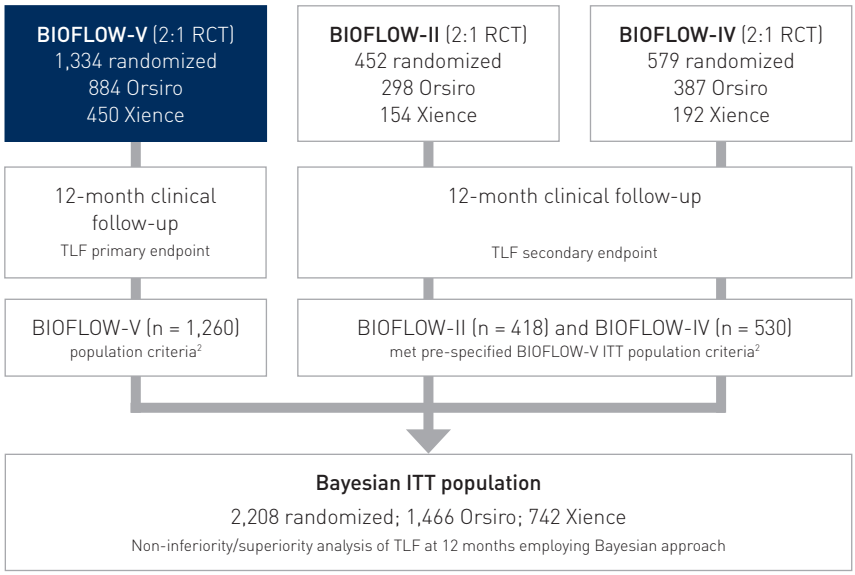
Endpoints

Primary endpoint

- TLF at 12 months defined as a composite of cardiac death, target-vessel myocardial infarction or any clinically-driven target lesion revascularization

Statistical methods

- Bayesian Analysis
- A Bayesian probability of >97.5% results in proven non-inferiority



Bayesian Analysis

The study design and benefits of a Bayesian approach are published by the American Heart Journal[3]:

"While the traditional frequentist framework for clinical trials emphasizes separate results from individual studies, Bayesian methods provide a formal method to synthesize prior data with new data. When appropriate data are available, this methodology may facilitate a more efficient study, by permitting potentially smaller sample sizes in the prospectively conducted study, potentially greater safety due to knowledge of historical outcomes, and potentially greater precision with primary endpoints."

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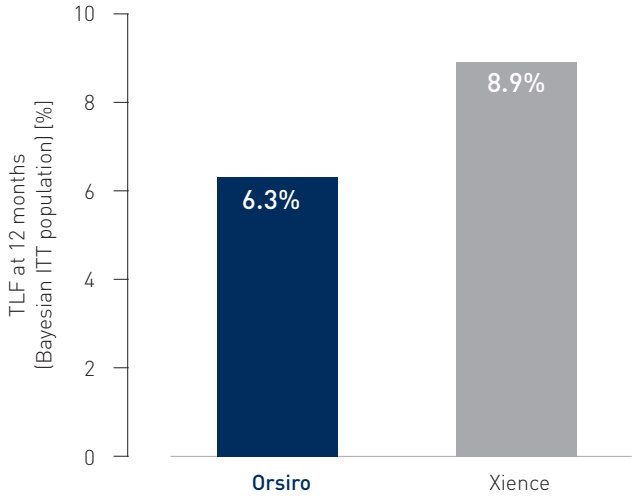
Primary endpoint at 12 months (Bayesian ITT population)

	Orsiro n = 1,466	Xience n = 742
TLF, posterior mean	6.3 ± 0.8	8.9 ± 1.2

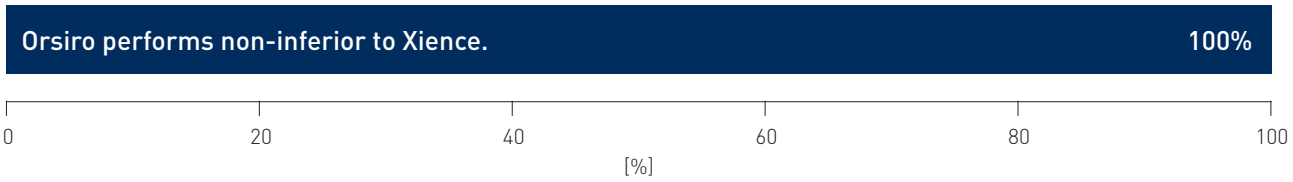
Estimated effect size at 12 months

-2.6% TLF



Bayesian posterior probability on TLF at 12 months

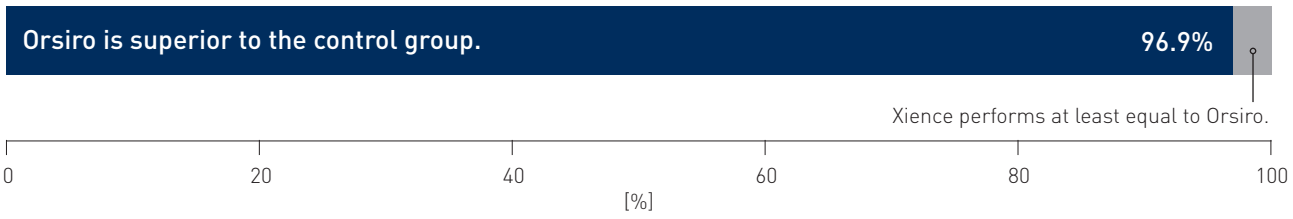
- **Non-inferiority**



Interpretation

There is 100% confidence that the difference in TLF at 12 months is smaller than 3.85% (pre-defined non-inferiority margin) demonstrating unequivocal non-inferiority. The estimated treatment effect of Orsiro is a reduction of TLF by absolute 2.6%.

- **Superiority (post-hoc)**



Interpretation

A post-hoc superiority analysis showed a 96.9% probability of Orsiro being superior to the control group, meaning that the TLF rate of Orsiro is smaller than the one of the control group.

1 Xience is a registered trademark of Abbott Cardiovascular Systems Inc.; 2 BIOFLOW-V ITT population criteria: BIOFLOW-V enrolment criteria, at least 330 days of follow-up experienced an endpoint event prior to 330 days; 3 Doros G et al. Rationale of a Novel Study Design for the BIOFLOW V Study, a Prospective, Randomized Multi-Center Study to Assess the Safety and Efficacy of the Orsiro Sirolimus-Eluting Coronary Stent System Utilizing a Bayesian Approach. American Heart Journal. 2017.
Source: Kandzari D et al. Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents versus Thin Durable Polymer Everolimus-Eluting Stents in Patients Undergoing Coronary Revascularization (BIOFLOW-V): a randomised trial. The Lancet. 2017.

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