AsiaIntervention 2015;1:91-92

Biodegradable or durable polymer: more data required

Andrew T. L. Ong*, MBBS, PhD, FRACP

Department of Cardiology, Westmead Hospital, Westmead, NSW 2145, Australia

In this issue of AsiaIntervention, Wan Azman Wan Ahmad reports on the final five-year results of the BEACON II clinical registry, a 497-patient real-world, all-comers registry conducted at 12 Asia Pacific sites[1]. This single-arm study followed up patients in whom BioMatrix (Biosensors Europe SA, Morges, Switzerland) Biolimus A9-eluting stent(s) were implanted. Biolimus A9 is an analogue to sirolimus, and is released from a biodegradable polymer, polylactic acid (PLA), applied to the abluminal surface of the stent.

Article, see page 102

This trial was predominantly conducted in Asia with nine sites, with the remaining three sites located in the Pacific. Historically, most drug-eluting stent trials were US-centric and/or Eurocentric, mirroring the headquarters of the drug-eluting stent companies. Companies, for regulatory purposes or otherwise, have recognised that Asian patients may be different from Caucasian patients: therefore, information regarding their response to drug-eluting stents may provide new insights[2]. To date, company-sponsored stent trials in Asia have generally been registries. This is the second contemporary report to be published in AsiaIntervention, after the RESOLUTE ASIA Registry[2]. As the specialist interventional cardiology journal of the region, it is a privilege for both the authors and the journal to be able to publish trials pertinent to the audience and the patients in this region.

Remarkably for a registry, clinical follow-up was available for 94% of the population at five years. The most striking finding in this registry is the low definite stent thrombosis rate of 0.8% at one year, and a cumulative incidence of 1.2% at five years, with an incidence of 0.4% from years one to five[1].

The authors emphasise the biodegradable polymeric system as being the principal reason for the low observed rate of very late stent thrombosis. As we move into the second decade of drug-eluting stents, the use of biodegradable polymers in drug-eluting stent systems has become a popular choice over durable polymers **(Table 1)**. This move was an industry response to the clinical and pathological findings of the first generation of drug-eluting stents, in which a significant inflammatory response was associated with the use of durable polymers[3]. It is worth noting that human post-mortem studies of second-generation systems utilising durable polymers demonstrate a lack of the inflammatory response seen with earlier stents[4].

The largest trial utilising the BioMatrix stent was the LEADERS trial. The five-year results demonstrated a lower incidence of definite stent thrombosis when compared to the durable polymer-coated sirolimus-eluting stent (2.6% vs. 4.5%, respectively, p=0.06)[5]. When a landmark analysis was performed at one year, there was a significant reduction in late stent thrombosis (0.66% vs. 2.5%, respectively, p=0.003). A meta-analysis of biodegradable versus durable polymers also suggested that there was a benefit of the former in the reduction of late stent thrombosis[6].

One must interpret the results with the utmost caution, as the devices compared were completely different. It is well understood that the efficacy of a particular device is a triangular synergy among the platform (the stent), a carrier (usually a polymer), and an agent (a drug)[7]. As such, any valid comparison would have to differ in only

**Corresponding author: Department of Cardiology, Westmead Hospital, Westmead, NSW, 2145, Australia. E-mail: AndrewTLOng@gmail.com*

DOI: 10.4244/AsiaIntery_V1I2A16

Table 1. List of drug-eluting stents from the major manufacturers.

Biodegradable polymer	Durable polymer
BioMatrix (Biolimus A9™**)	Promus PREMIER™¶/Element™¶ (everolimus)
SYNERGY™¶ (everolimus)	Resolute Onyx™§/Integrity™§ (zotarolimus)
Orsiro¶¶ (sirolimus)	XIENCE Xpedition®* (everolimus)
Nobori®§§ (Biolimus A9)	
Ultimaster®§§ (sirolimus)	
Absorb*/Absorb GT1* (everolimus)	

*Abbott Vascular, Santa Clara, CA, USA; **Biosensors Europe SA, Morges, Switzerland; ¶Boston Scientific Corp., Marlborough, MA, USA; ¶¶Biotronik, Bülach, Switzerland; §Medtronic, Minneapolis, MN, USA; §§Terumo Corp., Tokyo, Japan

the carrier. To date, the largest randomised trial to compare the efficacy of a biodegradable versus durable polymer utilising the same drug (everolimus) has been the EVOLVE II trial, in which 1,648 patients were randomised to receive either the SYNERGY everolimus-eluting biodegradable polymer stent or the PROMUS Element Plus everolimus-eluting durable polymer stent (both Boston Scientific Corporation, Marlborough, MA, USA). This study is scheduled to report results up to five years. However, to date, only 12-month results have been reported. These demonstrated no difference in outcomes: in particular, the incidence of definite stent thrombosis at one year was 0.4% vs. 0.6%, respectively, p=0.5[8].

The interventional community awaits the long-term results of this trial, with the same company providing both stents, as it will provide the scientific validity to demonstrate the benefit, if any, of biodegradable polymers over second-generation durable polymers. Until then, in the absence of any other trials where the difference is only the polymer, one should only comment on the safety and efficacy of the entire device (drug, polymer and stent) over another, and not of its individual components.

Conflict of interest statement

The author has no conflicts of interest to declare.

References

1. Ahmad WA, Koh TH, Santoso T, Tresukosol D, Soerianata S, Wilkins GT, Nair D, Walters DL, Jayasinghe R, Ong TK, Low AF, Ghapar AK, Abidin IZ. Long-term outcomes with Biolimus A9-eluting stents in real-world, all-comers Asia Pacific patients. Final 5-year report of the BEACON (Biolimus Eluting A9 Coronary Stent Obviating Luminal Narrowing) II Clinical Registry. *AsiaIntervention.* 2015;1:102-8.

2. Zambahari R, Lee MK, Hiremath S. Resolute zotarolimus-eluting coronary stent implantation in Asian patients with multivessel disease and long lesions: clinical outcomes in RESOLUTE Asia. *AsiaIntervention.* 2015;1:18-25.

3. Virmani R, Guagliumi G, Farb A, Musumeci G, Grieco N, Motta T, Mihalcsik L, Tespili M, Valsecchi O, Kolodgie FD. Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious? *Circulation.* 2004;109:701-5.

4. Otsuka F, Vorpahl M, Nakano M, Foerst J, Newell JB, Sakakura K, Kutys R, Ladich E, Finn AV, Kolodgie FD, Virmani R. Pathology of second-generation everolimus-eluting stents versus first-generation sirolimus- and paclitaxel-eluting stents in humans. *Circulation.* 2014;129:211-23.

5. Serruys PW, Farooq V, Kalesan B, de Vries T, Buszman P, Linke A, Ischinger T, Klauss V, Eberli F, Wijns W, Morice MC, Di Mario C, Corti R, Antoni D, Sohn HY, Eerdmans P, Rademaker-Havinga T, van Es GA, Meier B, Jüni P, Windecker S. Improved safety and reduction in stent thrombosis associated with biodegradable polymer-based biolimus-eluting stents versus durable polymer-based sirolimus-eluting stents in patients with coronary artery disease: final 5-year report of the LEADERS (Limus Eluted From A Durable Versus ERodable Stent Coating) randomized, noninferiority trial. *JACC Cardiovasc Interv.* 2013;6:777-89.

6. Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S, Jüni P, Schömig A, Windecker S, Kastrati A. Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials. *Eur Heart J.* 2012;33:1214-22.

7. Serruys PW, Kutryk MJ, Ong AT. Coronary-artery stents. *N Engl J Med.* 2006;354:483-95.

8. Kereiakes DJ, Meredith IT, Windecker S, Lee Jobe R, Mehta SR, Sarembock IJ, Feldman RL, Stein B, Dubois C, Grady T, Saito S, Kimura T, Christen T, Allocco DJ, Dawkins KD. Efficacy and safety of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent: the EVOLVE II Randomized Trial. *Circ Cardiovasc Interv.* 2015 April 8. [Epub ahead of print].