

Evaluation of the XIENCE™ V Everolimus-Eluting Coronary Stent System in the Female Latin American Population of the SPIRIT Women Single-Arm Study: One-year Clinical Follow-up Data

Liliana Grinfeld¹, Carla R. Agatiello², Alexandre Abizaid³, Jorge Belardi⁴, Pedro Lemos⁵, Marcos Marino⁶, José M. Torres Viera⁷, Marianne Stuteville⁸, Florencia Rolandi⁹, Cécile Dorange¹⁰, Marie Claude Morice¹¹

ABSTRACT

Background: Drug-eluting stent trials have predominantly examined male populations of European descent. The SPIRIT Women single-arm study evaluates the XIENCE™ V everolimus-eluting stent in complex *de novo* lesions in a real world female population, including Latin American patients. This analysis provides insight into how this population responds to stenting when compared to non-Latin American patients. **Methods:** Of the 1,572 patients enrolled from 73 sites outside the United States, 138 (9%) were recruited from Argentina, Brazil, and Venezuela. **Results:** Target lesions had vessel reference diameter ranging between 2.25 mm and 4 mm and a lesion length \leq 28 mm. The baseline characteristics were similar between the groups, with the exception of higher prevalence of hypertension, anterior myocardial infarction (MI), and a family history of coronary artery disease in the Latin American cohort. Lesions tended to be more complex in Latin American women, with a smaller vessel reference diameter, longer lesion length, increased eccentricity and angulation, and more type B2/C lesions. Events were adjudicated according to the guidelines of the Academic Research Consortium. At one year, the composite endpoint of death, MI, and target vessel revascularisation (TVR) was 12.1% in the non-Latin American population and 10.1% in the Latin American population ($P = 0.58$). **Conclusions:** At one year, the low rates of adverse cardiac events, including stent thrombosis, target lesion failure, cardiac death, MI, and TVR in Latin

RESUMO

Avaliação do Stent Coronário Eluidor de Everolimus XIENCE™ V na População Feminina Latino-Americana do Estudo de Braço Único SPIRIT Women: Acompanhamento Clínico de Um Ano

Introdução: Os estudos com stents farmacológicos têm avaliado predominantemente populações masculinas de descendência europeia. O estudo de braço único SPIRIT Women avalia o stent eluidor de everolimus XIENCE™ V em lesões *de novo* complexas em uma população feminina do mundo real, incluindo pacientes latino-americanas. Esta análise permite compreender como essa população responde ao implante de stent, comparativamente a pacientes não latino-americanas. **Métodos:** Das 1.572 pacientes matriculadas em 73 locais fora dos Estados Unidos, 138 (9%) foram recrutadas na Argentina, no Brasil e na Venezuela. **Resultados:** As lesões-alvo tinham diâmetro de referência do vaso entre 2,25 mm e 4 mm e extensão da lesão \leq 28 mm. As características basais foram semelhantes entre os grupos, com exceção de maior prevalência de hipertensão arterial, infarto do miocárdio (IM) de parede anterior e história familiar de doença arterial coronária na coorte latino-americana. As lesões tendiam a ser mais complexas em mulheres latino-americanas, com menor diâmetro de referência do vaso-alvo, maior extensão da lesão, maior excentricidade e angulação e mais lesões tipo B2/C. Os eventos foram adjudicados de acordo com as definições do *Academic Research Consortium*. Em um ano, o desfecho combinado de

¹ MD PhD. Head of the Hemodynamics and Interventional Cardiology Service, Invasive Cardiology Unit, Hospital Italiano de Buenos Aires. Buenos Aires, Argentina.

² MD. Interventional cardiologist, Invasive Cardiology Unit, Hospital Italiano de Buenos Aires. Buenos Aires, Argentina.

³ Associate Professor. Director, Invasive Cardiology Service, Instituto Dante Pazzanese de Cardiologia. São Paulo, SP, Brazil.

⁴ MD. Director, Cardiology Division, Instituto Cardiovascular de Buenos Aires. Buenos Aires, Argentina.

⁵ Associate Professor. Director, Haemodynamics and Interventional Cardiology Service, Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. São Paulo, SP, Brazil.

⁶ MD. Interventional cardiologist, Hospital Madre Teresa. Belo Horizonte, MG, Brazil.

⁷ MD. Clinical and interventional cardiologist, Clinica Santa Sofia. Caracas, Venezuela.

⁸ Clinical scientist, Abbott Vascular. Diegem, Belgium.

⁹ MD. Cardiologist, Clinical Cardiology Unit, Hospital Italiano de Buenos Aires. Buenos Aires, Argentina.

¹⁰ Master in sciences, Abbott Vascular. Diegem, Belgium.

¹¹ MD. Head of Institut Cardiovasculaire Paris Sud. Paris, France.

Correspondence to: Liliana Grinfeld. Hospital Italiano de Buenos Aires – Gascón 450 – PB 1181 – Buenos Aires, Argentina.
E-mail: liliana.grinfeld@gmail.com

Received on: 5/1/2012 • Accepted on: 7/4/2012

American women were comparable to those of non-Latin American women, despite the higher complexity of lesions. These results demonstrate the safety and efficacy of the XIENCETM V stent in this small cohort of Latin American patients, and are in line with what is observed in larger and more varied populations.

DESCRIPTORS: Coronary artery disease. Drug-eluting stents. Women. Latin America.

Environmental and genetic risk factors, such as abdominal obesity, diabetes, dyslipidemia, smoking, and hypertension have been identified as predisposing factors to a significantly increased risk of cardiovascular events in the female Latin American population. Drug-eluting stents are now widely accepted as safe and effective therapies for patients with coronary artery disease. Drug-eluting stents inhibit neo-intimal proliferation by locally delivering an anti-proliferative drug, reducing the restenosis rate and the need for repeat revascularization procedures.¹

The XIENCETM V (everolimus-eluting stent system Abbott Vascular – Santa Clara, USA) was extensively evaluated in the SPIRIT clinical trials, SPIRIT FIRST² and SPIRIT II,³ where XIENCETM V was evaluated, respectively, against the bare metal MULTI-LINK VISIONTM RX stent (Guidant Vascular Intervention – Santa Clara, USA) and the paclitaxel-eluting stent TAXUSTM (Boston Scientific – Natick, USA), demonstrated superiority when compared to the latter in terms of in-stent late loss at six months. Subsequently, this improvement in clinical outcomes was demonstrated in up to five years of follow up in SPIRIT FIRST.⁴ SPIRIT III demonstrated the superiority of XIENCETM V when compared to TAXUSTM in terms of in-segment late loss at 8 months and non-inferiority for the secondary endpoint of target vessel failure at nine months.⁵ In addition, the patients treated with the everolimus-eluting stent in this study had a significantly improved event-free survival at two years when compared to patients receiving the TAXUSTM stent.⁶

The aforementioned SPIRIT trials were primarily conducted in male populations of European descent with a relatively low-risk profile and simple lesions. When compared to the rest of the world, the Latin America population has shown a higher prevalence of diabetes and hypertension⁷ and a higher proportion of smokers, especially in larger cities.⁸

The present study reports the clinical follow-up data at one year in the Latin American population compared to the non-Latin American population of the SPIRIT Women single-arm study. This study evaluated

morte por todas as causas, IM e revascularização do vaso-alvo (RVA) foi de 12,1% na população não latino-americana e de 10,1% na população latino-americana (P = 0,58). **Conclusões:** Em um ano, os baixos índices de eventos cardíacos adversos, incluindo trombose do stent, falha da lesão-alvo, morte cardíaca, IM e RVA nas mulheres latino-americanas foram comparáveis aos das mulheres não-latino-americanas, apesar da maior complexidade das lesões. Esses resultados demonstram a segurança e a eficácia do stent XIENCETM V nessa pequena coorte de pacientes latino-americanas, à semelhança do que é observado com populações maiores e mais variadas.

DESCRITORES: Doença da artéria coronariana. Stents farmacológicos. Mulheres. América Latina.

the performance of XIENCETM V in complex *de novo* lesions in a real-world female population (n = 1,572). A significant proportion of the study population (138 patients; 9%) was recruited from Latin American sites in Argentina, Brazil, and Venezuela, thereby providing insight into how this population responds to the implantation of everolimus-eluting stents when compared to the non-Latin American patient population.

METHODS

Study design and patient selection

SPIRIT Women is a prospective, single arm, multi-centre study aimed at evaluating the performance of XIENCETM V in the real world, according to its instructions for use, in the treatment of female patients with *de novo* coronary artery lesions. The study protocol was approved by the medical ethics committee of each participating institution, and all patients gave written informed consent.

Between July of 2007 and March of 2009, 1,572 patients were enrolled at 73 clinical sites outside the United States, of whom 9% (n = 138) were recruited from sites in Argentina (36), Brazil (82), and Venezuela (20).

Patients (aged > 18 years) were recruited for the study from the general interventional cardiology population who had been admitted for a PCI procedure. Inclusion criteria included: evidence of myocardial ischemia, stable or unstable angina, silent ischemia or a positive functional study, or a reversible change in the ECG consistent with ischaemia. Patients were required to be suitable candidates for myocardial revascularisation and had to agree to undergo clinical follow-up as required per protocol. Patients with child-bearing potential had to have a negative pregnancy test within seven days before treatment. In addition, coronary anatomy had to allow for an optimal treatment with a maximum of four stents planned for *de novo* target lesions with target vessel reference diameter between 2.25 mm and 4.0 mm and target lesion length ≤ 28 mm by visual estimation. Patients were excluded

if they had participated in another device or drug study or had completed the follow-up phase of another study within 30 days prior to enrolment or if they had undergone previous stenting in the target vessel, whether bare-metal or drug-eluting stent.

The XIENCE™ V everolimus-eluting stent

A detailed description of the device has been published elsewhere.⁹ In brief, XIENCE™ V everolimus-eluting stent system includes a MULTI-LINK VISION™ metal platform on a delivery system with drug-eluting coating. The drug-eluting coating is composed of fluorinated acrylic polymers and the anti-proliferative drug everolimus (Certican®, Novartis Pharmaceuticals Corporation – Basel, Switzerland). Stents are available in diameters of 2.25, 2.5, 2.75, 3.0, 3.5, and 4.0 mm and lengths of 8, 12, 15, 18, 23, and 28 mm.

Study procedure

After confirmation of the angiographic inclusion criteria and before implantation of the first stent, patients were entered via an interactive voice response system (ICON Clinical Research – Eastleigh, UK). All registered patients were considered enrolled in the study and were required to remain in the study until the conclusion of the follow-up period. Periprocedural drug therapy was administered according to standard hospital practice. Unfractionated heparin or bivalirudin was used for procedural anticoagulation. The use of glycoprotein IIb/IIIa inhibitors was left to the discretion of the surgeon. All patients enrolled in the study were recommended to receive a loading dose ≥ 300 mg of clopidogrel. After the procedure, the protocol recommended that patients receive a daily dose of 75 mg of clopidogrel for a minimum of six months and ≥ 75 mg of aspirin daily indefinitely.

Clinical follow-up

Clinical follow up was scheduled at 30 days, one year, and two years after the procedure and included assessment of angina, adverse event data collection, details of subsequent coronary intervention, protocol required medications and use and changes of concomitant medications.

Study outcomes

The primary outcome was the composite incidence of all death, myocardial infarction (MI), and target vessel revascularisation (TVR) at one year. Secondary outcomes included, but were not limited to acute success (clinical device and procedure) and stent thrombosis rates.

Source document verification

Source document verification was routinely performed in 20% of random cases and in 100% of all reported adverse events during the study, resulting in an

overall rate of 30%. For sites with low rates of adverse event reporting, additional monitoring visits and source document verification were performed. All outcome-related events were adjudicated by the independent Clinical Events Committee (CEC) that had access to source documentation.

Definitions

All study outcome events were adjudicated by the independent CEC in accordance with the Academic Research Consortium (ARC) definitions.¹⁰

All adverse events were reported bimonthly to the independent Data and Safety Monitoring Board (DSMB), which reviewed data to identify safety issues related to the conduct of the study.

– Death: All deaths were considered cardiac unless an unequivocal non-cardiac cause could be established. Specifically, any unexpected death, even in patients with coexisting potentially fatal non-cardiac disease (e.g., cancer, infection), was classified as cardiac.

– Cardiac death: Any death due to an immediate cardiac cause (e.g., MI, low cardiac output syndrome, fatal arrhythmia) was considered cardiac death. Unwitnessed death and death of unknown cause were classified as cardiac death. Cardiac death included all procedure-related deaths, such as those related to concomitant treatment.

– Myocardial infarction: MI classification and criteria for diagnosis were defined in accordance with the ARC criteria as follows: for non-procedural/spontaneous MI, troponin or CK-MB levels had to be $>$ two times the upper normal range; for peripercutaneous coronary intervention, troponin or CK-MB levels had to be \geq three times the upper normal range; for peri-myocardial revascularisation, troponin or CK-MB levels had to be \geq five times the upper normal range. The peri-procedural period included the first 48 h and 72 h after percutaneous coronary intervention and myocardial revascularisation, respectively. All late events that were not associated with a revascularisation procedure were considered spontaneous. One blood sample was taken from each patient within the post-procedure hospitalisation period of CKMB or troponin levels analysis.

– Target lesion revascularisation: TLR is defined as any repeat percutaneous intervention or coronary artery bypass graft (CABG) surgery to treat any segment of the target vessel. The target lesion is defined as a segment 5 mm proximal and 5 mm distal to the stent.

– Target vessel revascularisation: TVR is defined as any repeat percutaneous intervention or CABG surgery of any segment of the target vessel. It is defined as the major coronary vessel, which includes the target lesion and its proximal and distal branches.

– Target lesion failure: TLF is defined as cardiac death, target vessel MI, or ischaemia-induced TLR (percutaneous coronary intervention or coronary artery bypass graft surgery).

– Stent thrombosis: Characterised as acute (< one day), subacute (one to 30 days) and late (> 30 days) and defined in accordance with the ARC guidelines as definitive (acute coronary syndrome with angiographic or pathologic confirmation of stent thrombosis), probable (unexplained death \leq 30 days or target vessel-MI without angiographic confirmation), and possible (unexplained death > 30 days after stent placement).

– Clinical device success: Successful delivery and deployment of the study stent (in case of stent overlapping, a successful delivery and deployment of the first and second stents) at target lesion and successful withdrawal of the stent delivery system with final residual stenosis < 50% of the target lesion by quantitative coronary angiography (QCA) (or by visual estimation if QCA unavailable), without using a device outside the assigned treatment strategy. Bailout patients were included as a clinical device success only if the above criteria were met.

– Clinical procedure success: successful delivery and deployment of the study stent or stents at the intended target lesion and successful withdrawal of the stent delivery system, with final residual stenosis < 50% of the target lesion by QCA (or by visual estimation if QCA was unavailable) and/or the use of any adjunctive device without the occurrence of death, MI not clearly attributed to a non-target vessel, and/or TLR during hospitalisation within a maximum of seven days of the index procedure. In multiple-lesion settings, each lesion must have met clinical procedure success criteria.

Statistical analysis

All analyses were performed based on the intent to treat population. The study sample size was based on the primary endpoint of the composite rate of all death, MI, and TVR at one year. A sample size of 1,550 patients produces a narrow two-sided 95% confidence interval for the clinical outcomes estimates. The half-width of the two-sided confidence interval for the primary outcome ranged between 1.5% and 1.7%, assuming a true rate between 10% and 14%. Continuous variables were summarised as mean and standard deviation and compared with a *t*-test. Binary variables are presented as percentages and were compared with the Fisher's exact test. P-values are not based on formal hypothesis testing and are provided for descriptive purposes only.

RESULTS

9% (138/1572) of the SPIRIT Women population was recruited from sites within Latin America, including 59% (82/138) from sites in Brazil, 26% (36/138) from sites in Argentina, and 14% (20/138) from sites in

Venezuela. At one year, clinical follow up was obtained in 100% of the Latin American patients and in 98.0% of the patients at non-Latin American sites.

There was no significant difference in the overall mean age between patients recruited from Latin American sites when compared to those from non-Latin American sites (Table 1). However, there was a trend for the Latin American patients to be younger: 46.4% of patients had ages ranging between 18 and 65 years vs. 38.5% of patients from non-Latin American sites ($P = 0.08$). When compared to non-Latin American patients, Latin American patients had a higher prevalence of hypertension requiring medication (85% vs. 77%; $P = 0.03$), prior myocardial infarction (33% vs. 25%; $P = 0.03$), and family history of coronary artery disease (51% vs. 35%; $P \leq 0.001$). Latin American patients had an increased body mass index (28.5 kg/m² vs. 27.5 kg/m²; $P = 0.03$), which was primarily driven by a lower mean height, as there was no difference in mean weight between the two patient populations. Resting diastolic blood pressure was also higher in the Latin American population (77 mmHg vs. 74 mmHg; $P = 0.004$), whereas resting systolic blood pressure was higher in the non-Latin American population (136 mmHg vs. 132 mmHg; $P = 0.03$). There was a trend toward more frequent diabetes in the Latin American population when compared with the non-Latin American population (40.9% vs. 33.5%; $P = 0.09$), and the non-Latin American population was more likely to be treated with oral hypoglycemic medication (25% vs. 19%; $P = 0.09$) or exercise and diet (6.6% vs. 2.9%; $P = 0.04$). There was a significantly higher number of non-Latin American patients who were diagnosed with renal failure (11% vs. 3%, respectively; $P = 0.002$).

The administration of GIIb/IIIa medication prior to the index procedure was much less frequent in the Latin American population (2.9% in Latin American patients vs. 14.3% in non-Latin American patients; $P < 0.0001$).

A total of 2,246 lesions were treated (Table 2). There was no difference in the number of target lesions between the two populations. The vessel reference diameter was significantly smaller in the Latin American population (2.75 mm vs. 2.90 mm; $P < 0.001$); however, the stenosis diameter was greater in the non-Latin American population (83.2% vs. 80.6%; $P < 0.001$). Type B2/C lesions (American College of Cardiology/American Heart Association) were higher in the Latin American patients when compared to the non-Latin American patients (82.2% vs. 70.8%; $P = 0.001$). The prevalence of bifurcation lesions was comparable between the two populations; however, eccentricity and angulation were more prevalent in the Latin American population. Target lesions were on average 2 mm longer in the Latin American population (17.0 mm vs 15.1 mm), of whom 36.9% had lesions > 20 mm, as compared to 27.8% in the non-Latin American population.

As shown in Table 3, at one year, the primary composite endpoint of all death, MI, and TVR was comparable between the Latin American and non-Latin American populations. In addition, target vessel failure (cardiac death, TV-MR, and TLR) was not significantly different between the two populations within one year of the follow up. No

difference was observed in non-hierarchical event rates within one year of follow-up between the two populations. Stent thrombosis rates (definite and probable) were low in the two study populations, with a one-year cumulative stent thrombosis rate of 0 in Latin American patients and 0.65% in non-Latin American patients.

TABLE 1
Baseline patient characteristics

	Latin American (n = 138)	Non-Latin American (n = 1,434)	P
Age, years	65 ± 10	67 ± 10.8	0.11
Current smoker, %	15.9	14.3	0.61
Hypertension*, %	85.4	77.1	0.03
Hypercholesterolemia*, %	64.6	63.5	0.85
Diabetes, %	40.9	33.5	0.09
Insulin-dependent diabetes, %	8.8	10.9	0.56
Family history of CAD, %	51.1	34.7	< 0.001
Prior cardiac intervention, %	15.2	17.4	0.56
Prior MI, %	33.3	24.8	0.03
Patients with > 1 target lesion, %	34.8	31.4	0.44
Number of target lesions	1.4 ± 0.7	1.4 ± 0.7	0.92

* Requiring medication.
CAD = coronary artery disease; MI = myocardial infarction; n= number of patients.

TABLE 2
Baseline lesion characteristics*

	Latin American (n = 138)	Non-Latin American (n = 1,434)	P
Type B2/C lesion, %	82.2	70.8	< 0.001
Type C, D, F, G bifurcation†, %	100	84.8	0.60
Left main coronary artery, %	0.5	1.1	0.71
Longer lesions ≥ 20 mm, %	36.9	27.8	0.008
Calcification – moderate or severe, %	24.7	30.4	0.10
Thrombus, %	4	6.3	0.27
Eccentric lesion, %	79.8	41	< 0.001
Lesion angulation > 45°, %	31.3	21.7	< 0.001
Stenosis diameter, %	80.6 ± 11.7	83.2 ± 11.3	< 0.001
Vessel reference diameter, mm	2.75 ± 0.37	2.90 ± 0.43	< 0.001
Lesion length, mm	17 ± 6.6	15.1 ± 6.4	< 0.001

* Visual assessment by the investigator.
† Medina classification 1,1,0; 1,1,1; 1,0,1; 0,1,1.
n = number of patients.

TABLE 3
Hierarchical adverse events at 1 year

	Latin American (n = 138)	Non-Latin American (n = 1,434)	P
Primary endpoint*, %	10.1	12.1	0.58
Target lesion failure†, %	9.4	10.7	0.77
Death, %	0.7	1.6	0.72
Myocardial infarction, %	9.4	8.9	0.88
Target vessel revascularisation, %	0	0.4	> 0.99

* Death, myocardial infarction, or target vessel revascularisation.
† Cardiac death, myocardial infarction related to the target vessel, or ischaemia-induced target lesion revascularisation.
n = number of patients.

DISCUSSION

The importance of observational research, particularly post-approval registries with drug-eluting stents, has increased in recent years as they provide real-world safety data in larger and more representative patient populations than controlled clinical trials. The SPIRIT Women single-arm study, as a multinational trial, not only provides a large database with a sufficient number of outcomes to be analysed but also allows for the comparison of geographical variations among female patients with complex *de novo* lesions treated with the XIENCE™ V stent.

Latin America is the fourth-largest geographic area in the world, with an estimated population close to 380 million inhabitants distributed in its 12 countries. Latin American citizens represent a conglomerate of different cultures, and the socioeconomic status of the population is quite heterogeneous. The use of drug-eluting stents has increased significantly in this region, from 2% in 2002 to more than 25% in 2007.¹¹ Different international clinical trials and observational registries, primarily in patients with heart failure and acute coronary syndromes, have documented that geographic location may affect baseline characteristics, the care process and patient outcomes.¹²⁻¹⁶ However, little information is available in the context of drug-eluting stents. The E-Five Registry, a large prospective, nonrandomised, multicentre, international registry, assessed the safety and effectiveness of the Endeavor™ zotarolimus-eluting stent (Medtronic – Minneapolis, USA) in real-world patients with symptomatic coronary artery disease undergoing percutaneous coronary intervention. Latin American patients, when compared with Europeans, had a higher rate of hypertension and prior myocardial infarction, a finding that coincides with the data gathered in this study.¹⁷ A higher prevalence of family history of cardiovascular disease and body mass index and a trend toward higher diabetes (40.9% vs. 33.5%) was

also found. Lesion characteristics were also different. The lesions were more complex and eccentric, with longer lesion length and smaller diameter vessels among Latin American females when compared to non-Latin American females. However, the rate of use of GPIIb/IIIa was significantly lower in Latin America, a finding that is frequently observed in this region, most likely as a result of economic factors.

Despite the above-mentioned differences, clinical outcomes were comparable between Latin American and non-Latin American patients, as evidenced also by the E-five registry. Prior reports had shown that the inclusion of Latin American patients was an independent predictor of death. This result was observed in the PURSUIT study, where Latin American patients with unstable angina were twice as likely to die within six months than their North American counterparts, a difference not explained by the difference in baseline risk.¹⁵

One possible hypothesis explaining these contradictory results may be the greater variability in the realworld standard of care provided to patients with acute coronary syndromes, including the rate of revascularization, when compared to drug-eluting stent registries in which all patients were treated invasively. It should also be considered that most of the patients in SPIRIT Women had a stable clinical condition, representing a less at-risk population.

In both the Latin American and non-Latin American populations, a lower incidence of major adverse cardiac events was observed when compared to the 15.7% reported by the NHLBI Dynamic Registry, in unselected women treated with drug-eluting stents, even when the lesion characteristics were similar. Also of note, stent thrombosis rates were 50% lower than in the female population of that registry (1.3%).¹⁸

Two complications are of special interest for the female population because of their prevalence and prognostic impact. In-hospital bleeding was low and comparable in both regions. Vascular complications were significantly higher in hospitalised Latin American patients and even higher at one year, probably because closure devices are not a standard of care.

Limitations of the study

This study was limited by the single-arm design and the inherent lack of a control arm for direct comparison. Lesion characteristics were assessed and reported by the investigator at the time of the procedure without the evaluation of a central laboratory. All efforts were made to collect all adverse events; 100% of source documents were examined for reported adverse events, and additional monitoring visits and source document verification were performed for sites with low rates of adverse event reporting.

CONCLUSIONS

At one year, the low rates of adverse cardiac events, including stent thrombosis, target vessel failure, cardiac death, ARC defined MI and revascularisation in the Latin American cohort were comparable to those of the non-Latin American cohort despite the higher complexity of lesions. These results provide a strong demonstration of the safety and efficacy of XIENCE™ V in this small cohort of Latin American patients and are in line with those of larger and more varied populations. This analysis highlights the need for further regional studies and reports.

CONFLICT OF INTEREST

Jorge Belardi is a consultant for Medtronic, Inc. (Minneapolis, USA). Marianne Stuteville and Cécile Dorange work for Abbott Vascular (Diegem, Belgium). The other authors declare no conflicts of interest.

REFERENCES

1. Doostzadeh J, Clark LN, Bezenek S, Pierson W, Sood PR, Sudhir K. Recent progress in percutaneous coronary intervention: evolution of the drug-eluting stents, focus on the XIENCE V drug-eluting stent. *Coron Artery Dis.* 2010;21(1):46-56.
2. Serruys P, Ong AT, Piek JJ, Neumann FJ, van der Giessen WJ, Wiemer M, et al. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: the SPIRIT first trial. *EuroIntervention.* 2005;1(1):58-65.
3. Serruys P, Ruygrok P, Neuzner J, Piek JJ, Seth A, Schofer JJ, et al. A randomized comparison of an everolimus-eluting coronary stent with a paclitaxel-eluting coronary stent: the SPIRIT II trial. *EuroIntervention.* 2006;2(3):286-94.
4. Wiemer M, Serruys PW, Miquel-Hebert K, Neumann FJ, Piek JJ, Grube E, et al. Five-year long-term clinical follow-up of the XIENCE V everolimus eluting coronary stent system in the treatment of patients with de novo coronary artery lesions: the SPIRIT FIRST trial. *Catheter Cardiovasc Interv.* 2010;75(7):997-1003.

5. Stone GW, Midei M, Newman W, Sanz M, Hermiller JB, Williams J, et al. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: a randomized trial. *JAMA.* 2008;299(16):1903-13.
6. Stone GW, Midei M, Newman W, Sanz M, Hermiller JB, Williams J, et al. Randomized comparison of everolimus-eluting and paclitaxel-eluting stents: two-year clinical follow-up from the Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with *de novo* Native Coronary Artery Lesions (SPIRIT) III trial. *Circulation.* 2009;119(5):680-6.
7. Lanas F, Avezum A, Bautista LE, Diaz R, Luna M, Islam S, et al. Risk factors for acute myocardial infarction in Latin America: the INTERHEART Latin America Study. *Circulation.* 2007;115(9):1067-74.
8. Schargrodsky H, Hernández-Hernández R, Champagne BM, Silva H, Vinuesa R, Silva Ayçaguer LC, et al. CARMELA: assessment of cardiovascular risk in seven Latin American cities. *Am J Med.* 2008;121(1):58-65.
9. Ding NI, Pacetti SD, Tang FW, Gada M, Roorda W. XIENCE V: stent design and rationale. *J Interv Cardiol.* 2009;22 Suppl. 1: S18-S27.
10. Cutlip D, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation.* 2007;115(17):2344-51.
11. The Heart Organization. Slides and resources [Internet]. Montreal, Canada; 2012 [cited 2012 July 23]. Available from: <http://www.theheart.org/resource-center/782307.do>
12. Van de Werf F, Topol EJ, Lee KL, Woodlief LH, Granger CB, Armstrong PW, et al. Variations in patient management and outcomes for acute myocardial infarction in the United States and other countries: results from the GUSTO trial. Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries. *JAMA.* 1995;273(20):1586-91.
13. Budaj A, Brieger D, Steg PG, Goodman SG, Dabbous OH, Fox KA, et al. Global patterns of use of antithrombotic and antiplatelet therapies in patients with acute coronary syndromes: insights from the Global Registry of Acute Coronary Events (GRACE). *Am Heart J.* 2003;146(6):999-1006.
14. Chang WC, Midodzi WK, Westerhout CM, Boersma E, Cooper J, Barnathan ES, et al. Are international differences in the outcomes of acute coronary syndromes apparent or real? A multilevel analysis. *J Epidemiol Community Health.* 2005;59(5):427-33.
15. Cohen MG, Pacchiana CM, Corbalán R, Perez JE, Ponte CI, Oropeza ES, et al. Variation in patient management and outcomes for acute coronary syndromes in Latin America and North America: results from the Platelet IIb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy (PUR-SUIT) trial. *Am Heart J.* 2001;141(3):391-401.
16. Blair JE, Zannad F, Konstam MA, Cook T, Traver B, Burnett JC Jr, et al. Continental differences in clinical characteristics, management, and outcomes in patients hospitalized with worsening heart failure results from the EVEREST (Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan) program. *J Am Coll Cardiol.* 2008;52(20):1640-8.
17. Lotan C, Meredith IT, Jain A, Feres F, Firszt A, Garcia AF, et al. Clinical outcomes by geographic region for patients implanted with the Zotarolimus-eluting stent. *Arq Bras Cardiol.* 2011;96(5):352-62.
18. Abbott JD, Vlachos HA, Selzer F, Sharaf BL, Holper E, Glaser R, et al. Gender-based outcomes in percutaneous coronary intervention with drug-eluting stents (from the National Heart, Lung, and Blood Institute Dynamic Registry). *Am J Cardiol.* 2007;99(5):626-31.

APPENDIX

Sponsor: Abbott Cardiovascular Systems, Inc., a subsidiary of Abbott Vascular (Santa Clara, CA, USA)

Principal investigator: Marie-Claude Morice (Paris, France)

Co-principal investigator: Stephan Windecker (Bern, Switzerland)

Steering Committee: Maria Grazia Modena (Italy), Ghada Mikhail (United Kingdom), Fina Mauri i Ferré (Spain), Ruth Strasser (Argentina), Liliana Grinfeld (Argentina)

Clinical Events Committee (CEC): K. Koch (Amsterdam, the Netherlands), B. Rensing (Utrecht, The Netherlands), G. Sianos (Thessaloniki, Greece), R. Tölg (Bad Segeberg, Germany), M. Wiemer (Bad Oeynhausen, Germany), E. McFadden (Cork, Ireland), A. Hoye (Hull, United Kingdom)

Data Safety Monitoring Board (DSMB): J. Tijssen (Amsterdam, the Netherlands), T. Lefèvre (Massy, France), P. Urban (Geneva, Switzerland), K. Fox (Edinburgh, United Kingdom)

The following Latin American investigators and institutions participated in the SPIRIT Women Trial and are listed with the respective number of patients enrolled: Alexandre Abizaid/Instituto Dante Pazzanese de Cardiologia (São Paulo, SP, Brazil) – 46 patients; Pedro Lemos/Instituto do Coração do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (São Paulo, SP, Brazil) – 24 patients; José M. Torres Viera/Clinica Santa Sofia (Caracas, Venezuela) – 20 patients; Liliana Grinfeld/Hospital Italiano de Buenos Aires (Buenos Aires, Argentina) – 19 patients; Jorge Belardi/Instituto Cardiovascular de Buenos Aires (Buenos Aires, Argentina) – 17 patients; Marcos Marino/Hospital Madre Teresa (Belo Horizonte, MG, Brazil) – 12 patients
