

## **Amendment 1**

Meta-analysis of Two Year Data from the SPIRIT II and SPIRIT III RCT

## Introduction

The purpose of this ad-hoc meta-analysis is to present a review of all available two year data from the SPIRIT II and SPIRIT III randomized controlled trials (RCT). The SPIRIT II clinical trial was a multi-center randomized controlled trial conducted in Europe, India, and New Zealand to continue assessing the safety and performance of the XIENCE™ V Everolimus Eluting Coronary Stent System (XIENCE V) in the treatment of subjects with a maximum of two *de novo* native coronary artery lesions each in a different epicardial vessel, compared to TAXUS® Paclitaxel Eluting Coronary Stent System (TAXUS). The SPIRIT III clinical study was a multi-center randomized controlled trial designed to demonstrate the non-inferiority of XIENCE V to TAXUS with regards to the primary endpoint of in-segment late loss at 240 days among subjects with up to two *de novo* native coronary artery lesions each in a different epicardial vessel. Poolability of these two trials for a meta-analysis is justified because these two studies have subjects with similar baseline and angiographic characteristics and the key elements of study design including inclusion and exclusion criteria and endpoint definitions are comparable.

Within the following discussion, the subject types are defined as:

- Eligible Subjects – A range of subjects eligible for 2-year follow-up whether or not they completed their follow-up visits
- Completers – Subjects who completed their 2-year follow-up on or before October 30, 2007 and the associated data were monitored and adjudicated
- Early Terminators – Subjects who withdrew from the study, were lost to follow-up, or died and the associated data were monitored and adjudicated. These patients may or may not be part of the eligible subjects depending on their procedure date (e.g. a subject who withdrew on day 30 and as of October 30, 2007 he/she would have not have reached the early 2-year window).

As of October 30, 2007, the pool of eligible subjects ranged from 392 – 747 depending on whether the early (702 days) or late (758 days) follow-up window was used as the 2 year cut-off date. Of the subjects who were enrolled in the SPIRIT II and SPIRIT III trials, 529 subjects had completed their two year follow-up and 74 subjects were early terminators for a total of 603 subjects (referred to as the 2 year follow-up subset) that are used in the following analyses. The data for these 603 subjects who were completers or who were early terminators were monitored and events were adjudicated by independent clinical events committees (CECs). Of the 603 subjects who were completers or who were early terminators, 422 subjects received XIENCE V and 181 subjects received TAXUS.

## Results

Table 1 presents the baseline demographics for the pooled SPIRIT II and SPIRIT III 2 year follow-up subset. This subset is similar to all subjects that participated in the trials. Ethnicity and race were not collected in the SPIRIT II trial; therefore, the denominators reflect SPIRIT III subjects for those baseline characteristics.

**Table 1 Baseline Demographics – Per-Subject Analysis  
(Intent-to-Treat Population) (Pooled SII + SIII RCT)**

Subject Characteristics	XIENCE V 2-Y FU Subset (N=422)	TAXUS 2-Y FU Subset (N=181)	XIENCE V All Subjects (N=892)	TAXUS All Subjects (N=410)
Age (year) Mean ± SD (n) [95% Confidence Interval] <sup>1</sup>	62.75 ± 10.54 (422) [61.74, 63.76]	62.84 ± 10.72 (181) [61.27, 64.42]	62.91 ± 10.48 (892) [62.22, 63.60]	62.63 ± 10.09 (409) [61.65, 63.61]
Male Subjects [95% Confidence Interval] <sup>2</sup>	70.4% (297/422) [65.77%, 74.70%]	68.5% (124/181) [61.20%, 75.20%]	70.3% (627/892) [67.17%, 73.28%]	68.2% (279/409) [63.46%, 72.70%]
Ethnicity - Hispanic or Latino [95% Confidence Interval] <sup>2</sup>	1.7% (4/236) [0.46%, 4.28%]	3.4% (4/116) [0.95%, 8.59%]	3.0% (20/669) [1.84%, 4.58%]	3.6% (12/332) [1.88%, 6.23%]
Race <sup>3</sup>				
American Indian or Alaskan Native [95% Confidence Interval] <sup>2</sup>	1.3% (3/236) [0.26%, 3.67%]	0.0% (0/116) [0.00%, 3.13%]	0.4% (3/669) [0.09%, 1.30%]	0.6% (2/332) [0.07%, 2.16%]
Asian [95% Confidence Interval] <sup>2</sup>	0.4% (1/236) [0.01%, 2.34%]	1.7% (2/116) [0.21%, 6.09%]	0.4% (3/669) [0.09%, 1.30%]	0.9% (3/332) [0.19%, 2.62%]
Black or African Heritage [95% Confidence Interval] <sup>2</sup>	7.6% (18/236) [4.58%, 11.79%]	11.2% (13/116) [6.10%, 18.40%]	6.6% (44/669) [4.82%, 8.73%]	9.0% (30/332) [6.18%, 12.65%]
Native Hawaiian or Pacific Islanders [95% Confidence Interval] <sup>2</sup>	0.8% (2/236) [0.10%, 3.03%]	0.0% (0/116) [0.00%, 3.13%]	0.4% (3/669) [0.09%, 1.30%]	0.3% (1/332) [0.01%, 1.67%]
White [95% Confidence Interval] <sup>2</sup>	89.8% (212/236) [85.25%, 93.37%]	87.9% (102/116) [80.58%, 93.24%]	92.1% (616/669) [89.77%, 94.01%]	89.5% (297/332) [85.64%, 92.55%]

<sup>1</sup> By normal approximation.

<sup>2</sup> By Clopper-Pearson exact confidence interval.

<sup>3</sup> Subject can be counted in more than one race category.

Note: Ethnicity and race information were not collected in Spirit II study.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Table 2 presents the baseline risk factors for the pooled SPIRIT II and SPIRIT III 2 year follow-up subset. This subset is similar to all subjects that participated in the trials. Possible exceptions include unstable angina which was less frequent in the XIENCE V all subjects group, prior MI and MI within two months were more frequent in the XIENCE V groups.

**Table 2 Baseline Risk Factors – Per-Subject Analysis  
(Intent-to-Treat Population) (Pooled SII + SIII RCT)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>XIENCE V All Subjects (N=892)</b>	<b>TAXUS All Subjects (N=410)</b>
All Diabetes [95% Confidence Interval] <sup>1</sup>	26.1% (110/422) [21.94%, 30.53%]	25.7% (46/179) [19.47%, 32.75%]	27.9% (249/892) [24.99%, 30.98%]	27.1% (110/406) [22.83%, 31.70%]
Current Tobacco Use [95% Confidence Interval] <sup>1</sup>	25.1% (102/407) [20.92%, 29.57%]	27.4% (46/168) [20.80%, 34.78%]	25.3% (220/869) [22.46%, 28.35%]	23.8% (93/391) [19.65%, 28.32%]
Hypertension Requiring Medication [95% Confidence Interval] <sup>1</sup>	69.9% (295/422) [65.28%, 74.25%]	68.9% (124/180) [61.58%, 75.57%]	74.0% (660/892) [70.98%, 76.84%]	72.3% (295/408) [67.69%, 76.59%]
Hypercholesterolemia Requiring Medication [95% Confidence Interval] <sup>1</sup>	70.0% (287/410) [65.31%, 74.40%]	70.1% (124/177) [62.73%, 76.70%]	72.8% (638/876) [69.75%, 75.75%]	72.1% (290/402) [67.48%, 76.47%]
All Prior Cardiac Interventions [95% Confidence Interval] <sup>1</sup>	27.5% (116/422) [23.28%, 32.01%]	24.3% (44/181) [18.25%, 31.23%]	30.0% (267/889) [27.03%, 33.17%]	28.1% (115/409) [23.81%, 32.74%]
Prior Cardiac Intervention on Target Vessel (s) [95% Confidence Interval] <sup>1</sup>	8.2% (34/413) [5.77%, 11.31%]	7.3% (13/177) [3.97%, 12.23%]	9.1% (80/876) [7.31%, 11.24%]	9.2% (37/401) [6.58%, 12.49%]
Stable Angina [95% Confidence Interval] <sup>1</sup>	54.3% (228/420) [49.39%, 59.12%]	52.8% (95/180) [45.21%, 60.25%]	55.5% (488/880) [52.10%, 58.77%]	50.5% (204/404) [45.51%, 55.48%]
Stable Angina CCS III or IV [95% Confidence Interval] <sup>1</sup>	18.1% (76/420) [14.53%, 22.12%]	20.0% (36/180) [14.42%, 26.60%]	20.2% (178/880) [17.62%, 23.04%]	17.3% (70/404) [13.76%, 21.38%]
Unstable Angina [95% Confidence Interval] <sup>1</sup>	24.8% (104/420) [20.71%, 29.18%]	26.7% (48/180) [20.36%, 33.76%]	20.8% (183/880) [18.16%, 23.63%]	26.5% (107/404) [22.24%, 31.07%]
Unstable Angina Braunwald Class III [95% Confidence Interval] <sup>1</sup>	8.3% (35/420) [5.87%, 11.40%]	10.6% (19/180) [6.48%, 15.99%]	7.3% (64/880) [5.65%, 9.19%]	9.9% (40/404) [7.17%, 13.24%]
Prior MI [95% Confidence Interval] <sup>1</sup>	27.1% (112/413) [22.89%, 31.68%]	22.1% (40/181) [16.28%, 28.85%]	23.7% (207/873) [20.93%, 26.68%]	19.3% (78/404) [15.57%, 23.50%]
MI Within 2 Months [95% Confidence Interval] <sup>1</sup>	9.0% (37/409) [6.45%, 12.25%]	5.5% (10/181) [2.68%, 9.93%]	6.7% (58/869) [5.11%, 8.54%]	3.5% (14/404) [1.91%, 5.75%]
<b>% of Diseased, Native, Major Epicardial Coronary Arteries</b>				
Single [95% Confidence Interval] <sup>1</sup>	64.2% (271/422) [59.44%, 68.80%]	68.5% (124/181) [61.20%, 75.20%]	65.7% (586/892) [62.48%, 68.81%]	67.6% (277/410) [62.79%, 72.07%]
Double [95% Confidence Interval] <sup>1</sup>	27.5% (116/422) [23.28%, 32.01%]	24.9% (45/181) [18.75%, 31.82%]	26.0% (232/892) [23.16%, 29.02%]	24.1% (99/410) [20.08%, 28.59%]
Triple or More [95% Confidence Interval] <sup>1</sup>	8.3% (35/422) [5.84%, 11.35%]	6.1% (11/181) [3.07%, 10.61%]	8.3% (74/892) [6.57%, 10.30%]	7.8% (32/410) [5.40%, 10.84%]

<sup>1</sup> By Clopper-Pearson exact confidence interval.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Table 3 presents the baseline lesion characteristics determined by the angiographic core laboratory for the pooled SPIRIT II and SPIRIT III 2 year follow-up subset. This subset is similar to all subjects that participated in the trials. Possible exceptions include eccentricity and the B2 lesion class suggesting that subjects who completed their two year follow-up had more complex lesions than the general population.

**Table 3 Baseline Lesion Characteristics by Angiographic Core Laboratory – All-Lesion Analysis (Intent-to-Treat Population) (Pooled SII + SIII RCT)**

	<b>XIENCE V 2-Y FU Subset (N=422) (M=494)</b>	<b>TAXUS 2-Y FU Subset (N=181) (M=211)</b>	<b>XIENCE V All Subjects (N=892) (M=1032)</b>	<b>TAXUS All Subjects (N=410) (M=474)</b>
<b>Target Vessel</b>				
LAD [95% Confidence Interval] <sup>1</sup>	40.5% (200/494) [36.12%, 44.96%]	44.1% (93/211) [37.27%, 51.05%]	41.1% (423/1028) [38.12%, 44.23%]	43.8% (207/473) [39.24%, 48.37%]
Circumflex or Ramus [95% Confidence Interval] <sup>1</sup>	28.3% (140/494) [24.40%, 32.54%]	25.1% (53/211) [19.42%, 31.53%]	28.0% (288/1028) [25.29%, 30.87%]	26.4% (125/473) [22.51%, 30.65%]
RCA [95% Confidence Interval] <sup>1</sup>	31.2% (154/494) [27.11%, 35.46%]	30.3% (64/211) [24.21%, 37.02%]	30.7% (316/1028) [27.93%, 33.66%]	29.6% (140/473) [25.52%, 33.94%]
LMCA [95% Confidence Interval] <sup>1</sup>	0.0% (0/494) [0.00%, 0.74%]	0.5% (1/211) [0.01%, 2.61%]	0.1% (1/1028) [0.00%, 0.54%]	0.2% (1/473) [0.01%, 1.17%]
<b>Aneurysm</b> [95% Confidence Interval] <sup>1</sup>	0.0% (0/487) [0.00%, 0.75%]	0.0% (0/209) [0.00%, 1.75%]	0.3% (3/1017) [0.06%, 0.86%]	0.0% (0/471) [0.00%, 0.78%]
<b>Calcification (Moderate or Severe)</b> [95% Confidence Interval] <sup>1</sup>	30.6% (149/487) [26.53%, 34.90%]	27.3% (57/209) [21.36%, 33.85%]	27.4% (278/1016) [24.64%, 30.22%]	24.2% (114/471) [20.40%, 28.33%]
<b>Eccentric</b> [95% Confidence Interval] <sup>1</sup>	58.9% (287/487) [54.42%, 63.34%]	54.1% (113/209) [47.06%, 60.96%]	39.2% (399/1017) [36.22%, 42.31%]	38.2% (180/471) [33.81%, 42.77%]
<b>Thrombus</b> [95% Confidence Interval] <sup>1</sup>	1.4% (7/487) [0.58%, 2.94%]	1.9% (4/209) [0.52%, 4.83%]	1.8% (18/1017) [1.05%, 2.78%]	1.3% (6/471) [0.47%, 2.75%]
<b>American College of Cardiology/ American Heart Association (ACC/AHA) Lesion Class</b>				
A [95% Confidence Interval] <sup>1</sup>	4.3% (21/485) [2.70%, 6.54%]	2.4% (5/208) [0.79%, 5.52%]	5.6% (57/1013) [4.29%, 7.23%]	5.1% (24/467) [3.32%, 7.55%]
B1 [95% Confidence Interval] <sup>1</sup>	24.5% (119/485) [20.77%, 28.62%]	26.4% (55/208) [20.58%, 32.99%]	32.6% (330/1013) [29.70%, 35.56%]	32.3% (151/467) [28.11%, 36.79%]
B2 [95% Confidence Interval] <sup>1</sup>	52.2% (253/485) [47.61%, 56.69%]	53.8% (112/208) [46.82%, 60.76%]	44.3% (449/1013) [41.24%, 47.45%]	46.3% (216/467) [41.66%, 50.89%]
C [95% Confidence Interval] <sup>1</sup>	19.0% (92/485) [15.57%, 22.75%]	17.3% (36/208) [12.43%, 23.15%]	17.5% (177/1013) [15.18%, 19.95%]	16.3% (76/467) [13.04%, 19.94%]

<sup>1</sup> By Clopper-Pearson exact confidence interval.

Note: N is the total number of subjects; M is the total number of lesions.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

For the following event tables (Tables 4 – 6; Appendix 1 – 2), the denominators include:

- Completers
- Early terminators with the specific event described within the table (e.g., if an early terminator had only a TLR event, he/she would be included in the TVF table but not in the stent thrombosis table).

Early terminators who did not have the specific event described within the table were excluded from the denominators.

Table 4 presents the hierarchical subjects counts of adverse events through 758 days. Data for three periods is presented: the 0 to 393 day period, the 0 to 758 day period and the 394 to 758 day period. The advantage of pooling these studies is the increased numbers of subjects available. The confidence intervals (CI) are presented for descriptive purposes and have not been adjusted for multiple comparisons. To identify clinical endpoints that exhibited potential differences between treatments, the confidence interval of the difference was used. If the confidence interval of the difference did not include zero, the clinical endpoint for the treatment suggested a clinical benefit. In the 2 year follow-up subset, the following clinical endpoints did not have the 0 value in their confidence interval of the difference: MACE from 0 to 393 days; TLR PCI from 0 to 393 days; MACE from 0 to 758 days; and TLR PCI from 0 to 758 days. These endpoints suggested a clinical benefit from the implantation of the XIENCE V in comparison with TAXUS. Both groups had similar outcomes between 394 and 758 days. Non-hierarchical subject counts of adverse events displayed in a similar fashion to Table 4 can be found in Appendix 1. Hierarchical subject counts of adverse events combining TLR (CABG + PCI) and TVR (CABG + PCI) can be found in Appendix 2.

**Table 4 Hierarchical Subject Counts of Adverse Events through 758 Days  
(Intent-to-Treat Population) (Pooled SII + SIII RCT)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>1</sup></b>
<b>0 to 393 days</b>				
MACE (Cardiac Death, MI, TLR)	5.0% (20/403)	12.4% (21/169)	7.2% (41/572)	-7.46% [-12.87%, -2.06%]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	8.4% (34/403)	13.0% (22/169)	9.8% (56/572)	-4.58% [-10.33%, 1.17%]
Cardiac Death	1.2% (5/403)	2.4% (4/169)	1.6% (9/572)	-1.13% [Assump. not met]
QMI	0.2% (1/403)	0.0% (0/169)	0.2% (1/572)	0.25% [Assump. not met]
NQMI	1.5% (6/403)	3.0% (5/169)	1.9% (11/572)	-1.47% [-4.28%, 1.35%]
TLR CABG	0.0% (0/403)	0.0% (0/169)	0.0% (0/572)	0.00% [Assump. not met]
TLR PCI	2.0% (8/403)	7.1% (12/169)	3.5% (20/572)	-5.12% [-9.22%, -1.01%]
TVR CABG, non-target lesion	0.5% (2/403)	0.0% (0/169)	0.3% (2/572)	0.50% [Assump. not met]
TVR PCI, non-target lesion	3.0% (12/403)	0.6% (1/169)	2.3% (13/572)	2.39% [Assump. not met]
<b>0 to 758 days</b>				
MACE (Cardiac Death, MI, TLR)	7.2% (28/387)	13.9% (22/158)	9.2% (50/545)	-6.69% [-12.67%, -0.71%]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	11.4% (44/387)	15.8% (25/158)	12.7% (69/545)	-4.45% [-10.96%, 2.06%]
Cardiac Death	1.8% (7/387)	2.5% (4/158)	2.0% (11/545)	-0.72% [Assump. not met]
QMI	0.3% (1/387)	0.0% (0/158)	0.2% (1/545)	0.26% [Assump. not met]
NQMI	2.6% (10/387)	3.8% (6/158)	2.9% (16/545)	-1.21% [-4.59%, 2.16%]
TLR CABG	0.0% (0/387)	0.0% (0/158)	0.0% (0/545)	0.00% [Assump. not met]
TLR PCI	2.6% (10/387)	7.6% (12/158)	4.0% (22/545)	-5.01% [-9.43%, -0.59%]
TVR CABG, non-target lesion	0.5% (2/387)	0.6% (1/158)	0.6% (3/545)	-0.12% [Assump. not met]
TVR PCI, non-target lesion	3.6% (14/387)	1.3% (2/158)	2.9% (16/545)	2.35% [Assump. not met]

<sup>1</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: Subjects are only counted once in the hierarchical order of Cardiac Death, QMI, NQMI, TLR CABG, TLR PCI, TVR CABG, and TVR PCI.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Table 4 Hierarchical Subject Counts of Adverse Events through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (continued)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>1</sup></b>
<b>394 to 758 days</b> MACE (Cardiac Death, MI, TLR)	2.1% (8/379)	1.3% (2/153)	1.9% (10/532)	0.80% [Assump. not met]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	2.9% (11/379)	3.3% (5/153)	3.0% (16/532)	-0.37% [-3.65%, 2.92%]
Cardiac Death	0.5% (2/379)	0.0% (0/153)	0.4% (2/532)	0.53% [Assump. not met]
QMI	0.0% (0/379)	0.0% (0/153)	0.0% (0/532)	0.00% [Assump. not met]
NQMI	1.1% (4/379)	0.7% (1/153)	0.9% (5/532)	0.40% [Assump. not met]
TLR CABG	0.0% (0/379)	0.0% (0/153)	0.0% (0/532)	0.00% [Assump. not met]
TLR PCI	0.5% (2/379)	0.7% (1/153)	0.6% (3/532)	-0.13% [Assump. not met]
TVR CABG, non-target lesion	0.0% (0/379)	0.7% (1/153)	0.2% (1/532)	-0.65% [Assump. not met]
TVR PCI, non-target lesion	0.8% (3/379)	1.3% (2/153)	0.9% (5/532)	-0.52% [Assump. not met]

<sup>1</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: Subjects are only counted once in the hierarchical order of Cardiac Death, QMI, NQMI, TLR CABG, TLR PCI, TVR CABG, and TVR PCI.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Table 5 presents the stent thrombotic events defined as definite or probable by the ARC definitions by time periods. Early stent thrombosis (0 – 30 days) rates were similar for XIENCE V, 0.5% (2/420) and TAXUS, 0.6% (1/179). Late stent thrombosis (31 – 393 days) rates were similar for XIENCE V, 0.5% (2/397) and TAXUS, 1.2% (2/166). Very late stent thrombosis (394 – 758 days) rates were similar for XIENCE V, 0.3% (1/377) and TAXUS, 0% (0/153). The one very late event (394 – 758 days) reported for XIENCE V came from the SPIRIT II trial. The total late stent thrombosis (31 – 758 days) rates were similar for XIENCE V, 0.8% (3/397) and TAXUS, 1.3% (2/155).

**Table 5 Stent Thrombosis (Definite + Probable) through 758 Days - Per-Subject Analysis (Intent-to-Treat Population) (Pooled SII + SIII RCT) (ARC Definition)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>
<b>Early Stent Thrombosis (0 - 30 days)</b>			
Definite [95% Confidence Interval] <sup>1</sup>	0.5% (2/420) [0.06%, 1.71%]	0.6% (1/179) [0.01%, 3.07%]	0.5% (3/599) [0.10%, 1.46%]
Probable [95% Confidence Interval] <sup>1</sup>	0.0% (0/420) [0.00%, 0.87%]	0.0% (0/179) [0.00%, 2.04%]	0.0% (0/599) [0.00%, 0.61%]
Definite/Probable [95% Confidence Interval] <sup>1</sup>	0.5% (2/420) [0.06%, 1.71%]	0.6% (1/179) [0.01%, 3.07%]	0.5% (3/599) [0.10%, 1.46%]
<b>Late Stent Thrombosis (31 - 393 days)</b>			
Definite [95% Confidence Interval] <sup>1</sup>	0.3% (1/397) [0.01%, 1.40%]	0.0% (0/166) [0.00%, 2.20%]	0.2% (1/563) [0.00%, 0.99%]
Probable [95% Confidence Interval] <sup>1</sup>	0.3% (1/397) [0.01%, 1.40%]	1.2% (2/166) [0.15%, 4.28%]	0.5% (3/563) [0.11%, 1.55%]
Definite/Probable [95% Confidence Interval] <sup>1</sup>	0.5% (2/397) [0.06%, 1.81%]	1.2% (2/166) [0.15%, 4.28%]	0.7% (4/563) [0.19%, 1.81%]
<b>Very Late Stent Thrombosis (394 - 758 days)</b>			
Definite [95% Confidence Interval] <sup>1</sup>	0.3% (1/377) [0.01%, 1.47%]	0.0% (0/153) [0.00%, 2.38%]	0.2% (1/530) [0.00%, 1.05%]
Probable [95% Confidence Interval] <sup>1</sup>	0.0% (0/377) [0.00%, 0.97%]	0.0% (0/153) [0.00%, 2.38%]	0.0% (0/530) [0.00%, 0.69%]
Definite/Probable [95% Confidence Interval] <sup>1</sup>	0.3% (1/377) [0.01%, 1.47%]	0.0% (0/153) [0.00%, 2.38%]	0.2% (1/530) [0.00%, 1.05%]
<b>Total Late Stent Thrombosis (31 - 758 days)</b>			
Definite [95% Confidence Interval] <sup>1</sup>	0.5% (2/378) [0.06%, 1.90%]	0.0% (0/155) [0.00%, 2.35%]	0.4% (2/533) [0.05%, 1.35%]
Probable [95% Confidence Interval] <sup>1</sup>	0.3% (1/378) [0.01%, 1.47%]	1.3% (2/155) [0.16%, 4.58%]	0.6% (3/533) [0.12%, 1.64%]
Definite/Probable [95% Confidence Interval] <sup>1</sup>	0.8% (3/378) [0.16%, 2.30%]	1.3% (2/155) [0.16%, 4.58%]	0.9% (5/533) [0.31%, 2.18%]
<b>Total Stent Thrombosis (0 - 758 days)</b>			
Definite [95% Confidence Interval] <sup>1</sup>	1.1% (4/379) [0.29%, 2.68%]	0.6% (1/155) [0.02%, 3.54%]	0.9% (5/534) [0.30%, 2.17%]
Probable [95% Confidence Interval] <sup>1</sup>	0.3% (1/379) [0.01%, 1.46%]	1.3% (2/155) [0.16%, 4.58%]	0.6% (3/534) [0.12%, 1.63%]
Definite/Probable [95% Confidence Interval] <sup>1</sup>	1.3% (5/379) [0.43%, 3.05%]	1.3% (2/155) [0.16%, 4.58%]	1.3% (7/534) [0.53%, 2.68%]

<sup>1</sup> By Clopper-Pearson exact confidence interval.

Note: All counts presented in this table are subject counts.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Note: None of the adjudicated cases of stent thrombosis per ARC criteria through 758 days in the 2-year follow-up occurred after an intervening target lesion revascularization.

Table 6 presents the stent thrombotic events defined by the protocol definitions by time period. Table 6 shows more protocol defined stent thrombosis events than the ARC definite or probable stent thrombosis frequencies shown in Table 5 because the protocol definition of stent thrombosis is more inclusive than the ARC definite or probable definition. Acute stent thrombosis ( $\leq 1$  day) rates were similar for XIENCE V, 0.2%

(1/422) and TAXUS, 0% (0/179). Subacute stent thrombosis (> 1 – 30 days) rates were similar for XIENCE V, 0.2% (1/420) and TAXUS, 0% (0/179). Late stent thrombosis (31 – 393 days) rates were similar for XIENCE V, 0.5% (2/396) and TAXUS, 1.8% (3/166). Very late stent thrombosis (394 – 758 days) rates were similar for XIENCE V, 0.5% (2/378) and TAXUS, 0% (0/153). The two very late events (394 – 758 days) reported for XIENCE V came from the SPIRIT II trial. There were no reports of very late stent thrombosis from the SPIRIT III trial. The total late stent thrombosis (31 – 758 days) rates were similar for XIENCE V, 1.1% (4/378) and TAXUS, 1.9% (3/155). Although not included in this analysis, the SPIRIT FIRST trial also did not show stent thrombosis events through three years for XIENCE V.

**Table 6 Stent Thrombosis through 758 Days - Per-Subject Analysis (Intent-to-Treat Population) (Pooled SII + SIII RCT) (Protocol Definition)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>
<b>Acute Stent Thrombosis (≤ 1 days)</b> [95% Confidence Interval] <sup>1</sup>	0.2% (1/422) [0.01%, 1.31%]	0.0% (0/179) [0.00%, 2.04%]	0.2% (1/601) [0.00%, 0.92%]
<b>Subacute Stent Thrombosis (&gt; 1 - 30 days)</b> [95% Confidence Interval] <sup>1</sup>	0.2% (1/420) [0.01%, 1.32%]	0.0% (0/179) [0.00%, 2.04%]	0.2% (1/599) [0.00%, 0.93%]
<b>Late Stent Thrombosis (31 - 393 days)</b> [95% Confidence Interval] <sup>1</sup>	0.5% (2/396) [0.06%, 1.81%]	1.8% (3/166) [0.37%, 5.19%]	0.9% (5/562) [0.29%, 2.06%]
<b>Very Late Stent Thrombosis (394 - 758 days)</b> [95% Confidence Interval] <sup>1</sup>	0.5% (2/378) [0.06%, 1.90%]	0.0% (0/153) [0.00%, 2.38%]	0.4% (2/531) [0.05%, 1.35%]
<b>Total Late Stent Thrombosis (31 - 758 days)</b> [95% Confidence Interval] <sup>1</sup>	1.1% (4/378) [0.29%, 2.69%]	1.9% (3/155) [0.40%, 5.55%]	1.3% (7/533) [0.53%, 2.69%]
<b>Total Stent Thrombosis (0 - 758 days)</b> [95% Confidence Interval] <sup>1</sup>	1.6% (6/379) [0.58%, 3.41%]	1.9% (3/155) [0.40%, 5.55%]	1.7% (9/534) [0.77%, 3.18%]

<sup>1</sup> By Clopper-Pearson exact confidence interval.

Note: All counts presented in this table are subject counts.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

One of the limitations presented by a study design that utilizes unbalanced randomization is the ability to detect low frequency events. SPIRIT II had a three to one randomization and SPIRIT III had a two to one randomization. Overall there were 422 XIENCE V subjects and 181 TAXUS included in the 2 year follow-up subset. There is more than a two fold chance of detecting a low frequency event such very late stent thrombosis in the XIENCE V group than the TAXUS group based on the unbalanced randomization schemes. A recent meta-analysis entitled “Incidence, timing, and correlates of stent thrombosis with the polymeric paclitaxel drug-eluting stent: a TAXUS II, IV, V, and VI meta-analysis of 3,445 patients followed for up to 3 years”<sup>1</sup> showed a very late stent thrombotic rate of 0.3% (6/1718) for the 1 to 2 year time period. The data presented in Table 5 and Table 6 are consistent with the data reported in literature and to FDA during the December 2006 Stent Thrombosis Panel Meeting.

<sup>1</sup>Ellis SG, Colombo A, Grube E, Popma J, Koglin J, Dawkins KD, Stone GW. Incidence, timing, and correlates of stent thrombosis with the polymeric paclitaxel drug-eluting stent: a TAXUS II, IV, V, and VI meta-analysis of 3,445 patients followed for up to 3 years. J Am Coll Cardiol. 2007 Mar 13;49(10):1043-51.

For the following Kaplan-Meier Survival Curves (Figures 1-10), the subjects include:

- Completers
- Early terminators

The early terminators were either censored at the time of their termination or if they had an event, at the time of the specific event described within the figure.

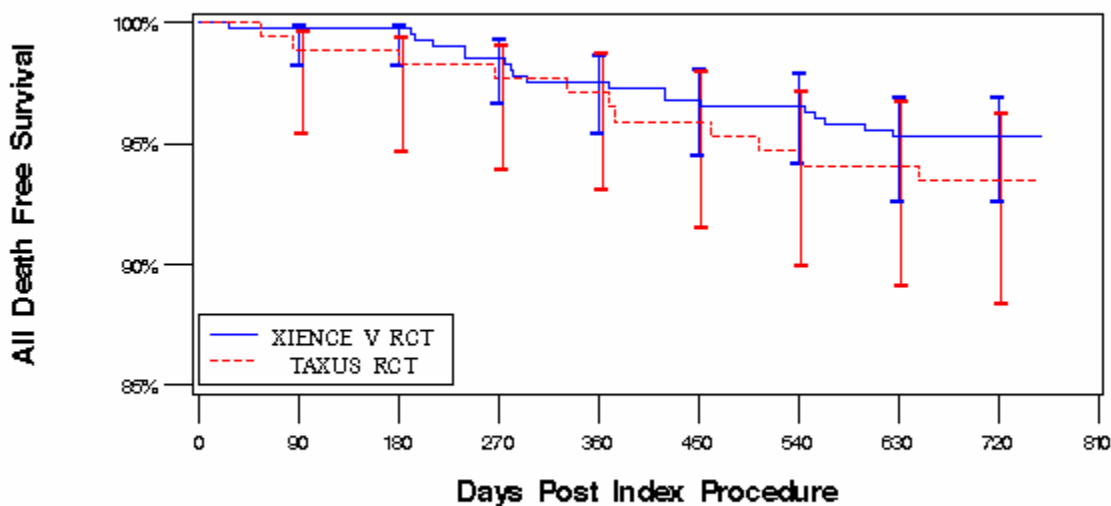
Kaplan-Meier Survival Curves are presented in Figures 1 to 10 as follows:

- Figure 1 Kaplan-Meier Survival Curve: All Death Free Survival through 758 Days
- Figure 2 Kaplan-Meier Survival Curve: Cardiac Death Free Survival through 758 Days
- Figure 3 Kaplan-Meier Survival Curve: MI Free Survival through 758 Days
- Figure 4 Kaplan-Meier Survival Curve: Cardiac Death + MI Free Survival through 758 Days
- Figure 5 Kaplan-Meier Survival Curve: TLR Free Survival through 758 Days
- Figure 6 Kaplan-Meier Survival Curve: MACE Free Survival through 758 Days
- Figure 7 Kaplan-Meier Survival Curve: Late Stent Thrombosis Cumulative Incidence Rate through 758 Days - Per Protocol
- Figure 8 Kaplan-Meier Survival Curve: Late Stent Thrombosis (Definite + Probable) Cumulative Incidence Rate through 758 Days - Per ARC Definition
- Figure 9 Kaplan-Meier Survival Curve: Stent Thrombosis Cumulative Incidence Rate through 758 Days - Per Protocol
- Figure 10 Kaplan-Meier Survival Curve: Stent Thrombosis (Definite + Probable) Cumulative Incidence Rate through 758 Days - Per ARC Definition

Figures 1 to 6 show event free survival curves that favors XIENCE V through 758 days. Figures 7 to 10 show similar stent thrombotic rates regardless of definition through 758 days.

## **Conclusion**

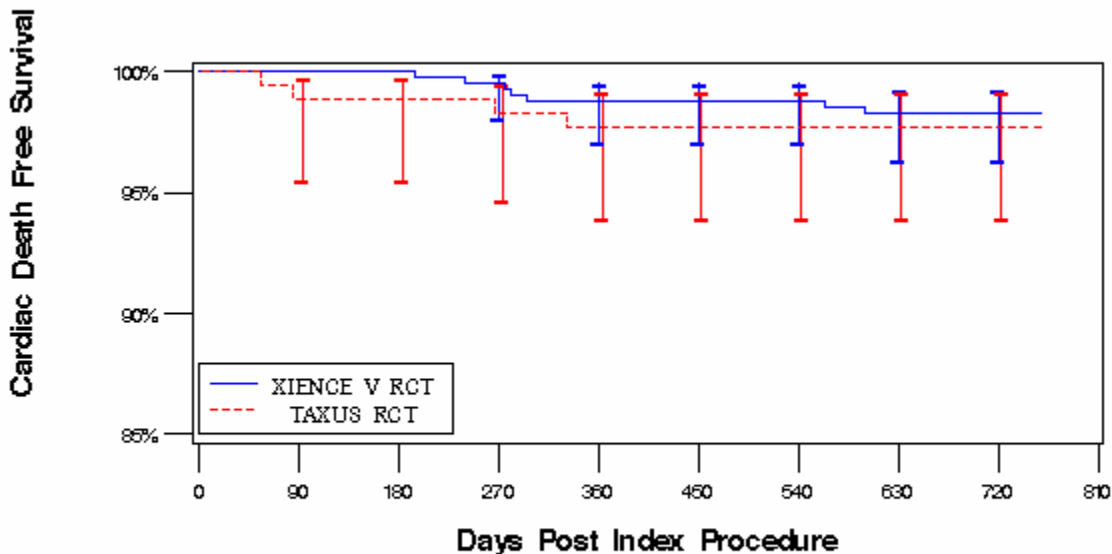
In this meta-analysis of the SPIRIT II and SPIRIT III RCT clinical studies, key clinical endpoints observed in XIENCE V arm were lower than those observed in the TAXUS arm. Therefore, this meta-analysis involving 603 subjects who had completed the 2 year follow-up or were terminated from the study as of October 30, 2007 provides additional evidence regarding the safety and effectiveness of the XIENCE V EECSS through two years, when compared to an approved active control.



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	414	411	401	396	384	383	378	377	377
# Events	0	1	1	6	10	13	14	19	19	19
% Survived	100.0%	99.8%	99.8%	98.5%	97.6%	96.8%	96.6%	95.3%	95.3%	95.3%
% SEM	0.0%	0.2%	0.2%	0.6%	0.8%	0.9%	0.9%	1.1%	1.1%	1.1%
<b>TAXUS:</b> # At Risk	181	173	172	166	164	157	155	154	153	153
# Events	0	2	3	4	5	7	9	10	11	11
% Survived	100.0%	98.9%	98.3%	97.7%	97.1%	95.9%	94.7%	94.1%	93.5%	93.5%
% SEM	0.0%	0.8%	1.0%	1.1%	1.3%	1.5%	1.7%	1.8%	1.9%	1.9%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.816	1	0.3663						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

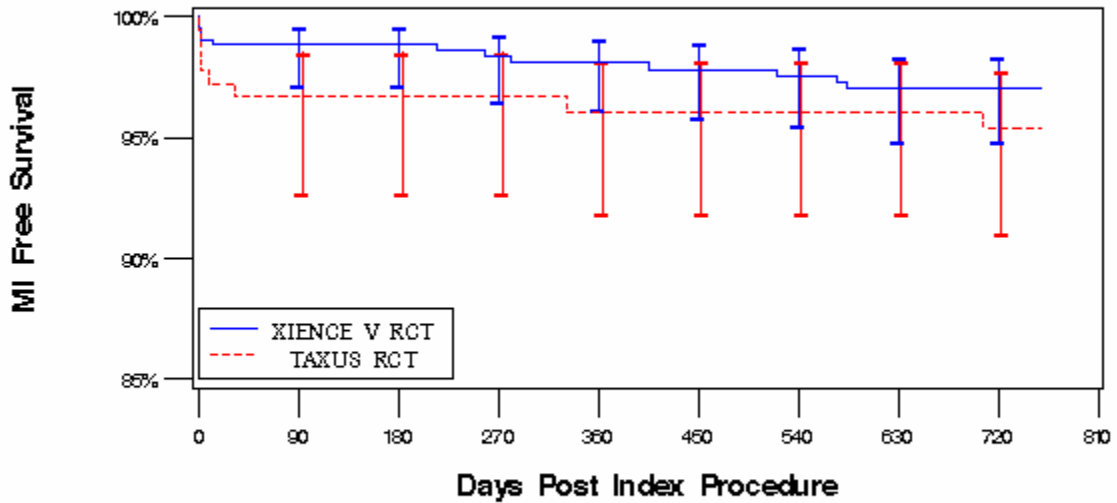
**Figure 1 Kaplan-Meier Survival Curve: All Death Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	414	411	401	396	384	383	378	377	377
# Events	0	0	0	2	5	5	5	7	7	7
% Survived	100.0%	100.0%	100.0%	99.5%	98.8%	98.8%	98.8%	98.2%	98.2%	98.2%
% SEM	0.0%	0.0%	0.0%	0.3%	0.5%	0.5%	0.5%	0.7%	0.7%	0.7%
<b>TAXUS:</b> # At Risk	181	173	172	166	164	157	155	154	153	153
# Events	0	2	2	3	4	4	4	4	4	4
% Survived	100.0%	98.9%	98.9%	98.3%	97.7%	97.7%	97.7%	97.7%	97.7%	97.7%
% SEM	0.0%	0.8%	0.8%	1.0%	1.2%	1.2%	1.2%	1.2%	1.2%	1.2%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.264	1	0.6075						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

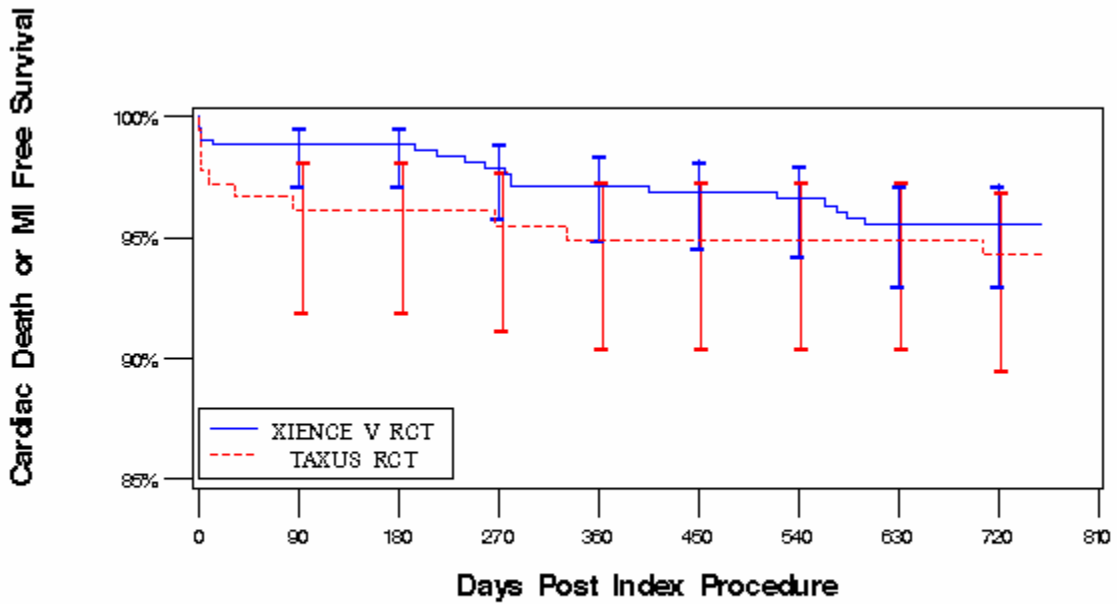
**Figure 2 Kaplan-Meier Survival Curve: Cardiac Death Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	410	407	395	390	377	375	368	367	367
# Events	2	5	5	7	8	9	10	12	12	12
% Survived	99.5%	98.8%	98.8%	98.3%	98.1%	97.8%	97.6%	97.0%	97.0%	97.0%
% SEM	0.3%	0.5%	0.5%	0.6%	0.7%	0.7%	0.8%	0.8%	0.8%	0.8%
<b>TAXUS:</b> # At Risk	181	168	167	161	160	153	151	150	148	148
# Events	1	6	6	6	7	7	7	7	8	8
% Survived	99.4%	96.7%	96.7%	96.7%	96.1%	96.1%	96.1%	96.1%	95.4%	95.4%
% SEM	0.6%	1.3%	1.3%	1.3%	1.5%	1.5%	1.5%	1.5%	1.6%	1.6%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	Log-Rank	1.090	1	0.2965						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

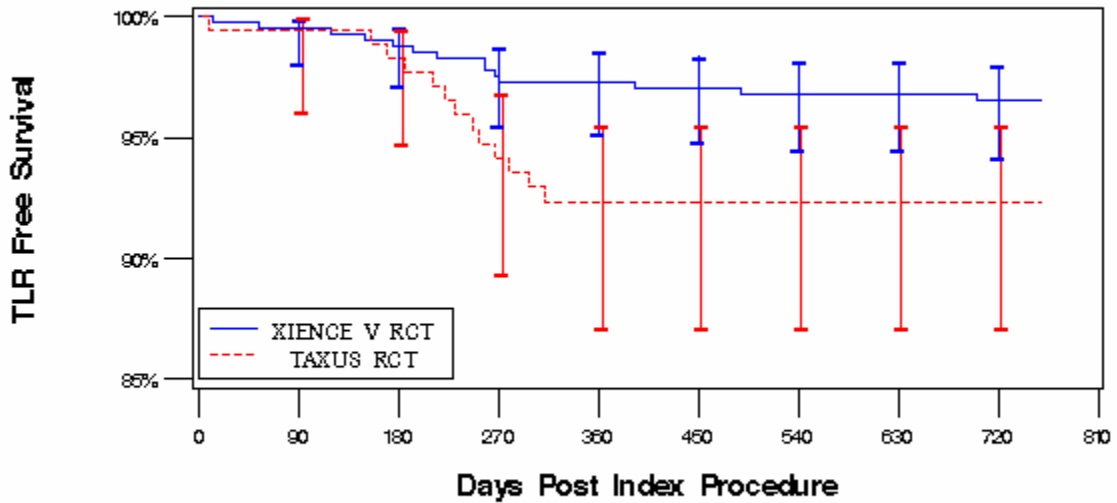
**Figure 3 Kaplan-Meier Survival Curve: MI Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	410	407	395	390	377	375	368	367	367
# Events	2	5	5	9	12	13	14	18	18	18
% Survived	99.5%	98.8%	98.8%	97.8%	97.1%	96.8%	96.6%	95.5%	95.5%	95.5%
% SEM	0.3%	0.5%	0.5%	0.7%	0.8%	0.9%	0.9%	1.0%	1.0%	1.0%
<b>TAXUS:</b> # At Risk	181	168	167	161	160	153	151	150	148	148
# Events	1	7	7	8	9	9	9	9	10	10
% Survived	99.4%	96.1%	96.1%	95.5%	94.9%	94.9%	94.9%	94.9%	94.3%	94.3%
% SEM	0.6%	1.4%	1.4%	1.6%	1.7%	1.7%	1.7%	1.7%	1.8%	1.8%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.565	1	0.4523						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

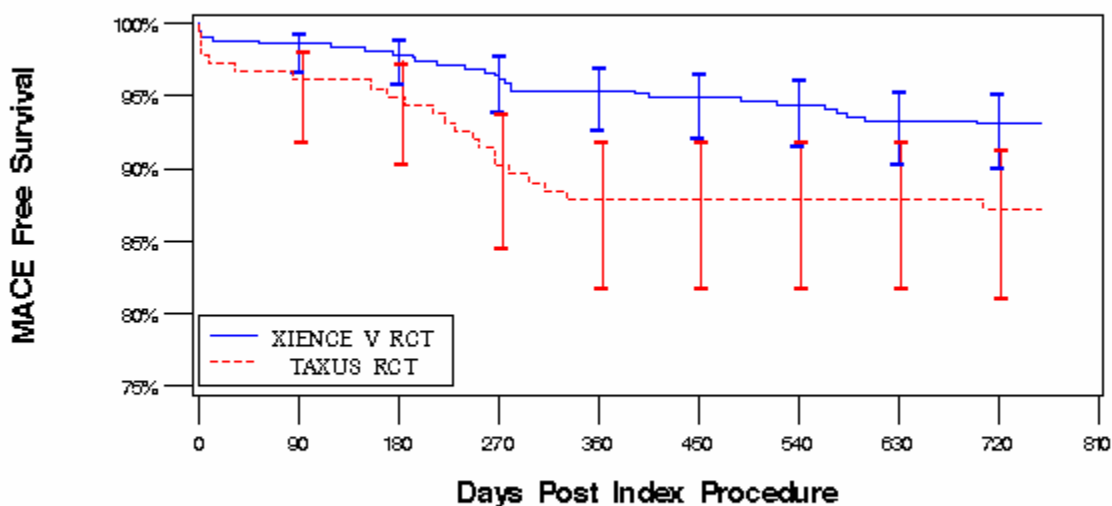
**Figure 4 Kaplan-Meier Survival Curve: Cardiac Death + MI Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	413	407	392	386	374	372	367	365	365
# Events	0	2	5	10	11	12	13	13	14	14
% Survived	100.0%	99.5%	98.8%	97.6%	97.3%	97.1%	96.8%	96.8%	96.5%	96.5%
% SEM	0.0%	0.3%	0.5%	0.8%	0.8%	0.8%	0.9%	0.9%	0.9%	0.9%
<b>TAXUS:</b> # At Risk	181	173	170	157	152	145	143	142	141	141
# Events	0	1	3	10	13	13	13	13	13	13
% Survived	100.0%	99.4%	98.3%	94.1%	92.3%	92.3%	92.3%	92.3%	92.3%	92.3%
% SEM	0.0%	0.6%	1.0%	1.8%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	Log-Rank	4.842	1	0.0278						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Figure 5 Kaplan-Meier Survival Curve: TLR Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

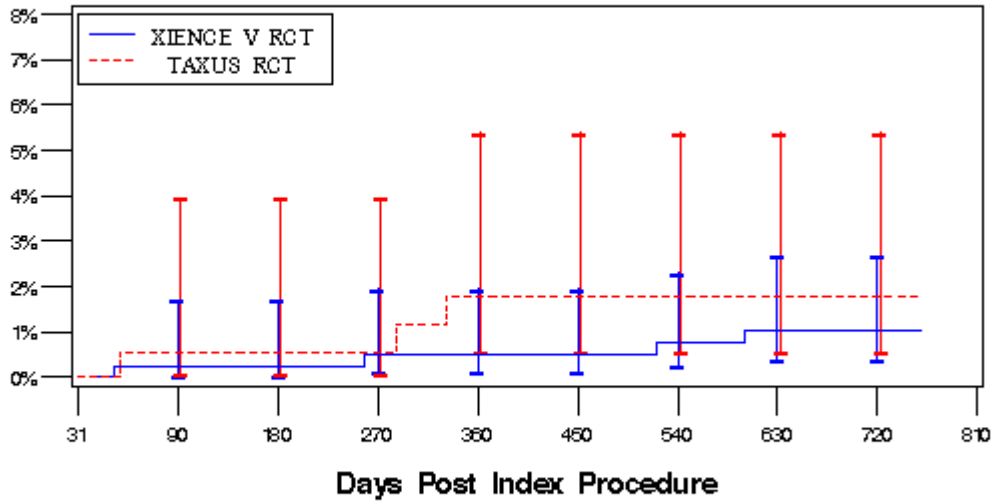


Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	409	403	389	383	370	367	360	358	358
# Events	2	6	9	15	19	21	23	27	28	28
% Survived	99.5%	98.6%	97.9%	96.4%	95.4%	94.9%	94.4%	93.3%	93.1%	93.1%
% SEM	0.3%	0.6%	0.7%	0.9%	1.0%	1.1%	1.1%	1.2%	1.3%	1.3%
<b>TAXUS:</b> # At Risk	181	168	165	152	148	141	139	138	136	136
# Events	1	7	9	17	21	21	21	21	22	22
% Survived	99.4%	96.1%	94.9%	90.2%	87.8%	87.8%	87.8%	87.8%	87.2%	87.2%
% SEM	0.6%	1.4%	1.6%	2.3%	2.5%	2.5%	2.5%	2.5%	2.6%	2.6%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	Log-Rank	5.795	1	0.0161						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Figure 6 Kaplan-Meier Survival Curve: MACE Free Survival through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

Late Stent Thrombosis Cumulative Incidence Rate



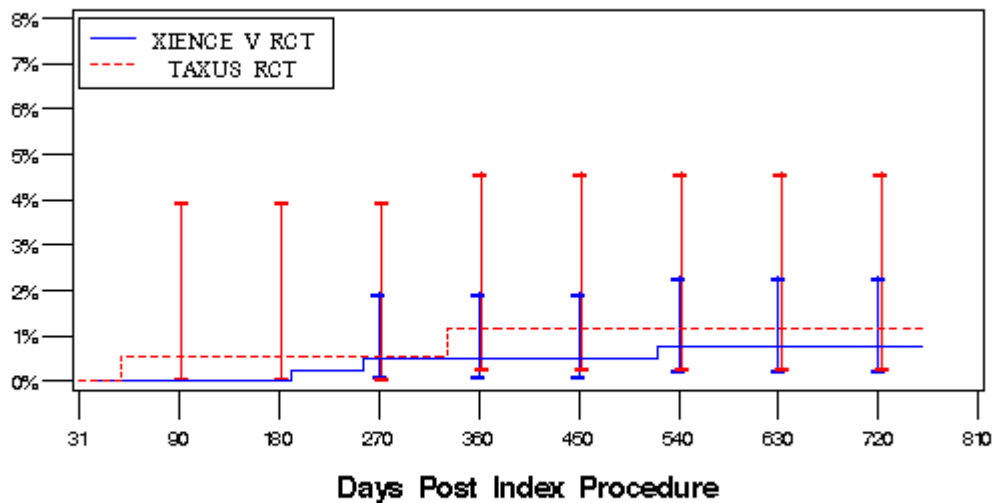
Time After Index Procedure (days)										
	31	90	180	270	360	450	540	630	720	758
<b>XIENCE™ V:</b> # At Risk	416	413	410	399	394	382	380	375	374	374
# Events	0	1	1	2	2	2	3	4	4	4
% Survived	100.0%	99.8%	99.8%	99.5%	99.5%	99.5%	99.2%	99.0%	99.0%	99.0%
% SEM	0.0%	0.2%	0.2%	0.3%	0.3%	0.3%	0.4%	0.5%	0.5%	0.5%
<b>TAXUS®:</b> # At Risk	179	173	172	166	163	156	154	153	152	152
# Events	0	1	1	1	3	3	3	3	3	3
% Survived	100.0%	99.4%	99.4%	99.4%	98.2%	98.2%	98.2%	98.2%	98.2%	98.2%
% SEM	0.0%	0.6%	0.6%	0.6%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.615	1	0.4329						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Note: Only stent thrombosis occurred on or after day 31 was included in the analysis. Subjects early terminated prior to 31 days and did not have stent thrombosis were excluded from the analysis.

**Figure 7 Kaplan-Meier Survival Curve: Late Stent Thrombosis Cumulative Incidence Rate through 758 Days - Per Protocol (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

**Late Stent Thrombosis Cumulative Incidence Rate**



Time After Index Procedure (days)										
	31	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	416	414	411	400	395	383	381	376	375	375
# Events	0	0	0	2	2	2	3	3	3	3
% Survived	100.0%	100.0%	100.0%	99.5%	99.5%	99.5%	99.2%	99.2%	99.2%	99.2%
% SEM	0.0%	0.0%	0.0%	0.3%	0.3%	0.3%	0.4%	0.4%	0.4%	0.4%
<b>TAXUS:</b> # At Risk	179	173	172	166	164	157	155	154	153	153
# Events	0	1	1	1	2	2	2	2	2	2
% Survived	100.0%	99.4%	99.4%	99.4%	98.8%	98.8%	98.8%	98.8%	98.8%	98.8%
% SEM	0.0%	0.6%	0.6%	0.6%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.271	1	0.6024						

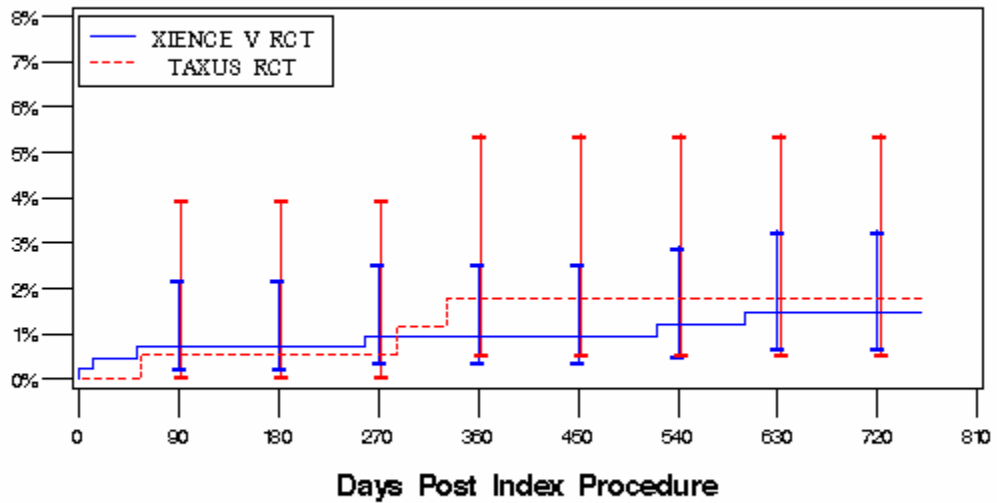
Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

None: None of the adjudicated cases of stent thrombosis per ARC criteria through 758 days in the 2-year follow-up occurred after an intervening target lesion revascularization.

Note: Only definite and probable stent thrombosis occurred on or after day 31 was included in the analysis. Subjects early terminated prior to 31 days and did not have definite or probable stent thrombosis were excluded from the analysis.

**Figure 8 Kaplan-Meier Survival Curve: Late Stent Thrombosis (Definite + Probable) Cumulative Incidence Rate through 758 Days - Per ARC Definition (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

Stent Thrombosis Cumulative Incidence Rate

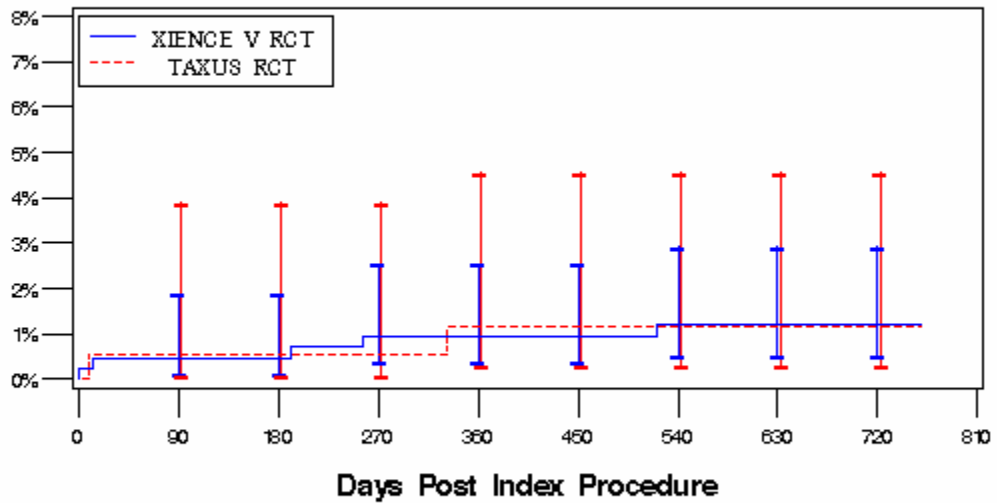


Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V: # At Risk</b>	422	412	409	398	393	381	379	374	373	373
# Events	1	3	3	4	4	4	5	6	6	6
% Survived	99.8%	99.3%	99.3%	99.0%	99.0%	99.0%	98.8%	98.5%	98.5%	98.5%
% SEM	0.2%	0.4%	0.4%	0.5%	0.5%	0.5%	0.5%	0.6%	0.6%	0.6%
<b>TAXUS: # At Risk</b>	181	173	172	166	163	156	154	153	152	152
# Events	0	1	1	1	3	3	3	3	3	3
% Survived	100.0%	99.4%	99.4%	99.4%	98.2%	98.2%	98.2%	98.2%	98.2%	98.2%
% SEM	0.0%	0.6%	0.6%	0.6%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	Log-Rank	0.063	1	0.8023						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Figure 9 Kaplan-Meier Survival Curve: Stent Thrombosis Cumulative Incidence Rate through 758 Days - Per Protocol (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

**Stent Thrombosis Cumulative Incidence Rate**



Time After Index Procedure (days)										
	0	90	180	270	360	450	540	630	720	758
<b>XIENCE V:</b> # At Risk	422	413	410	399	394	382	380	375	374	374
# Events	1	2	2	4	4	4	5	5	5	5
% Survived	99.8%	99.5%	99.5%	99.0%	99.0%	99.0%	98.8%	98.8%	98.8%	98.8%
% SEM	0.2%	0.3%	0.3%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%	0.5%
<b>TAXUS:</b> # At Risk	181	173	172	166	164	157	155	154	153	153
# Events	0	1	1	1	2	2	2	2	2	2
% Survived	100.0%	99.4%	99.4%	99.4%	98.8%	98.8%	98.8%	98.8%	98.8%	98.8%
% SEM	0.0%	0.6%	0.6%	0.6%	0.8%	0.8%	0.8%	0.8%	0.8%	0.8%
<b>Test Between Groups</b>	<b>Test</b>	<b>Chi-Square</b>	<b>DF</b>	<b>p-value</b>						
	<b>Log-Rank</b>	0.003	1	0.9545						

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

Note: None of the adjudicated cases of stent thrombosis per ARC criteria through 758 days in the 2-year follow-up occurred after an intervening target lesion revascularization.

**Figure 10 Kaplan-Meier Survival Curve: Stent Thrombosis (Definite + Probable) Cumulative Incidence Rate through 758 Days - Per ARC Definition (Intent-to-Treat Population) (Pooled SII + SIII RCT) (2-Year Follow-up Subset)**

# Appendix 1

## Appendix 1

### Appendix 1 Non-Hierarchical Subject Counts of Adverse Events through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT)

	XIENCE V 2-Y FU Subset (N=422)	TAXUS 2-Y FU Subset (N=181)	Total (N=603)	Difference [95% CI] <sup>2</sup>
<b>0 to 393 days</b>				
Cardiac Death	1.2% (5/403)	2.4% (4/169)	1.6% (9/572)	-1.13% [Assump. not met]
Myocardial Infraction (MI)	2.0% (8/403)	4.1% (7/169)	2.6% (15/572)	-2.16% [-5.46%, 1.14%]
QMI	0.2% (1/403)	0.6% (1/169)	0.3% (2/572)	-0.34% [Assump. not met]
NQMI	1.7% (7/403)	3.6% (6/169)	2.3% (13/572)	-1.81% [-4.88%, 1.25%]
Revascularization <sup>1</sup>	6.5% (26/403)	9.5% (16/169)	7.3% (42/572)	-3.02% [-8.04%, 2.01%]
CABG	0.5% (2/403)	0.0% (0/169)	0.3% (2/572)	0.50% [Assump. not met]
PCI	6.0% (24/403)	9.5% (16/169)	7.0% (40/572)	-3.51% [-8.49%, 1.47%]
TLR	3.0% (12/403)	7.7% (13/169)	4.4% (25/572)	-4.71% [-9.06%, -0.37%]
CABG	0.0% (0/403)	0.0% (0/169)	0.0% (0/572)	0.00% [Assump. not met]
PCI	3.0% (12/403)	7.7% (13/169)	4.4% (25/572)	-4.71% [-9.06%, -0.37%]
TVR, non-target lesion	3.5% (14/403)	4.1% (7/169)	3.7% (21/572)	-0.67% [-4.16%, 2.83%]
CABG	0.5% (2/403)	0.0% (0/169)	0.3% (2/572)	0.50% [Assump. not met]
PCI	3.0% (12/403)	4.1% (7/169)	3.3% (19/572)	-1.16% [-4.60%, 2.27%]

<sup>1</sup> Revascularization includes both TLR and TVR, non-target lesion.

<sup>2</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Appendix 1 Non-Hierarchical Subject Counts of Adverse Events through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (contined)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>2</sup></b>
<b>0 to 758 days</b> Cardiac Death	1.8% (7/387)	2.5% (4/158)	2.0% (11/545)	-0.72% [Assump. not met]
Myocardial Infraction (MI)	3.1% (12/387)	5.1% (8/158)	3.7% (20/545)	-1.96% [-5.79%, 1.87%]
QMI	0.3% (1/387)	0.6% (1/158)	0.4% (2/545)	-0.37% [Assump. not met]
NQMI	2.8% (11/387)	4.4% (7/158)	3.3% (18/545)	-1.59% [-5.20%, 2.02%]
Revascularization <sup>1</sup>	8.0% (31/387)	12.0% (19/158)	9.2% (50/545)	-4.01% [-9.76%, 1.73%]
CABG	0.8% (3/387)	0.6% (1/158)	0.7% (4/545)	0.14% [Assump. not met]
PCI	7.2% (28/387)	11.4% (18/158)	8.4% (46/545)	-4.16% [-9.74%, 1.43%]
TLR	3.6% (14/387)	8.2% (13/158)	5.0% (27/545)	-4.61% [-9.28%, 0.06%]
CABG	0.0% (0/387)	0.0% (0/158)	0.0% (0/545)	0.00% [Assump. not met]
PCI	3.6% (14/387)	8.2% (13/158)	5.0% (27/545)	-4.61% [-9.28%, 0.06%]
TVR, non-target lesion	4.7% (18/387)	6.3% (10/158)	5.1% (28/545)	-1.68% [-6.02%, 2.66%]
CABG	0.8% (3/387)	0.6% (1/158)	0.7% (4/545)	0.14% [Assump. not met]
PCI	3.9% (15/387)	5.7% (9/158)	4.4% (24/545)	-1.82% [-5.91%, 2.27%]

<sup>1</sup> Revascularization includes both TLR and TVR, non-target lesion.

<sup>2</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Appendix 1 Non-Hierarchical Subject Counts of Adverse Events through 758 Days (Intent-to-Treat Population) (Pooled SII + SIII RCT) (continued)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>2</sup></b>
<b>394 to 758 days</b>				
Cardiac Death	0.5% (2/379)	0.0% (0/153)	0.4% (2/532)	0.53% [Assump. not met]
Myocardial Infraction (MI)	1.1% (4/379)	0.7% (1/153)	0.9% (5/532)	0.40% [Assump. not met]
QMI	0.0% (0/379)	0.0% (0/153)	0.0% (0/532)	0.00% [Assump. not met]
NQMI	1.1% (4/379)	0.7% (1/153)	0.9% (5/532)	0.40% [Assump. not met]
Revascularization <sup>1</sup>	1.6% (6/379)	2.6% (4/153)	1.9% (10/532)	-1.03% [Assump. not met]
CABG	0.3% (1/379)	0.7% (1/153)	0.4% (2/532)	-0.39% [Assump. not met]
PCI	1.3% (5/379)	2.0% (3/153)	1.5% (8/532)	-0.64% [Assump. not met]
TLR	0.5% (2/379)	0.7% (1/153)	0.6% (3/532)	-0.13% [Assump. not met]
CABG	0.0% (0/379)	0.0% (0/153)	0.0% (0/532)	0.00% [Assump. not met]
PCI	0.5% (2/379)	0.7% (1/153)	0.6% (3/532)	-0.13% [Assump. not met]
TVR, non-target lesion	1.1% (4/379)	2.0% (3/153)	1.3% (7/532)	-0.91% [Assump. not met]
CABG	0.3% (1/379)	0.7% (1/153)	0.4% (2/532)	-0.39% [Assump. not met]
PCI	0.8% (3/379)	1.3% (2/153)	0.9% (5/532)	-0.52% [Assump. not met]

<sup>1</sup> Revascularization includes both TLR and TVR, non-target lesion.

<sup>2</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

## **Appendix 2**

**Appendix 2 Hierarchical Subject Counts of Adverse Events through 758 Days  
(Intent-to-Treat Population) (Pooled SII + SIII RCT)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>1</sup></b>
<b>0 to 393 days</b>				
MACE (Cardiac Death, MI, TLR)	5.0% (20/403)	12.4% (21/169)	7.2% (41/572)	-7.46% [-12.87%, -2.06%]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	8.4% (34/403)	13.0% (22/169)	9.8% (56/572)	-4.58% [-10.33%, 1.17%]
Cardiac Death	1.2% (5/403)	2.4% (4/169)	1.6% (9/572)	-1.13% [Assump. not met]
QMI	0.2% (1/403)	0.0% (0/169)	0.2% (1/572)	0.25% [Assump. not met]
NQMI	1.5% (6/403)	3.0% (5/169)	1.9% (11/572)	-1.47% [-4.28%, 1.35%]
TLR (CABG, PCI)	2.0% (8/403)	7.1% (12/169)	3.5% (20/572)	-5.12% [-9.22%, -1.01%]
TVR (CABG, PCI), non-target lesion	3.5% (14/403)	0.6% (1/169)	2.6% (15/572)	2.88% [Assump. not met]
<b>0 to 758 days</b>				
MACE (Cardiac Death, MI, TLR)	7.2% (28/387)	13.9% (22/158)	9.2% (50/545)	-6.69% [-12.67%, -0.71%]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	11.4% (44/387)	15.8% (25/158)	12.7% (69/545)	-4.45% [-10.96%, 2.06%]
Cardiac Death	1.8% (7/387)	2.5% (4/158)	2.0% (11/545)	-0.72% [Assump. not met]
QMI	0.3% (1/387)	0.0% (0/158)	0.2% (1/545)	0.26% [Assump. not met]
NQMI	2.6% (10/387)	3.8% (6/158)	2.9% (16/545)	-1.21% [-4.59%, 2.16%]
TLR (CABG, PCI)	2.6% (10/387)	7.6% (12/158)	4.0% (22/545)	-5.01% [-9.43%, -0.59%]
TVR (CABG, PCI), non-target lesion	4.1% (16/387)	1.9% (3/158)	3.5% (19/545)	2.24% [Assump. not met]

<sup>1</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: Subjects are only counted once in the hierarchical order of Cardiac Death, QMI, NQMI, TLR, TVR, non-target lesion.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.

**Appendix 2 Hierarchical Subject Counts of Adverse Events through 758 Days  
(Intent-to-Treat Population) (Pooled SII + SIII RCT) (continued)**

	<b>XIENCE V 2-Y FU Subset (N=422)</b>	<b>TAXUS 2-Y FU Subset (N=181)</b>	<b>Total (N=603)</b>	<b>Difference [95% CI]<sup>1</sup></b>
<b>394 to 758 days</b>				
MACE (Cardiac Death, MI, TLR)	2.1% (8/379)	1.3% (2/153)	1.9% (10/532)	0.80% [Assump. not met]
TVF (Cardiac Death, MI, TLR, TVR, non-target lesion)	2.9% (11/379)	3.3% (5/153)	3.0% (16/532)	-0.37% [-3.65%, 2.92%]
Cardiac Death	0.5% (2/379)	0.0% (0/153)	0.4% (2/532)	0.53% [Assump. not met]
QMI	0.0% (0/379)	0.0% (0/153)	0.0% (0/532)	0.00% [Assump. not met]
NQMI	1.1% (4/379)	0.7% (1/153)	0.9% (5/532)	0.40% [Assump. not met]
TLR (CABG, PCI)	0.5% (2/379)	0.7% (1/153)	0.6% (3/532)	-0.13% [Assump. not met]
TVR (CABG, PCI), non-target lesion	0.8% (3/379)	2.0% (3/153)	1.1% (6/532)	-1.17% [Assump. not met]

<sup>1</sup> By normal approximation.

Note: Subjects are only counted once for each type of event in each time period.

Note: Subjects are only counted once in the hierarchical order of Cardiac Death, QMI, NQMI, TLR, TVR, non-target lesion.

Note: This table includes TLRs and TVRs on all lesions for subjects with two target lesions treated.

Note: In the analysis for 394 to 758 days, subjects without 2-year follow-up information and without TVF between 394 and 758 days post index procedure are not included in the denominator.

Note: The 2-year follow-up subset includes subjects who had their 2-year visit or early terminated, and whose data were monitored. For subjects who had events, the events were adjudicated by CEC.