Appendix 3

ABSORB III Lead-In Group

Overview

The lead-in group of the ABSORB III Trial, referenced in **Section 5.1.1** of the Sponsor Executive Summary, was designed as a non-randomized group to evaluate the applicability and transferability of the didactic Absorb physician training plan to United States (US) clinical practice in up to 50 subjects. The lead-in group registered subjects prior to the start of the randomized primary analysis group (PAG) and the randomized imaging cohort. The trial design of ABSORB III with the lead-in group and the other cohorts are depicted in **Figure 1**. The primary areas of learning in the usage of Absorb assessed in the lead-in group included good implantation techniques of vessel sizing, lesion preparation, and device delivery and deployment.

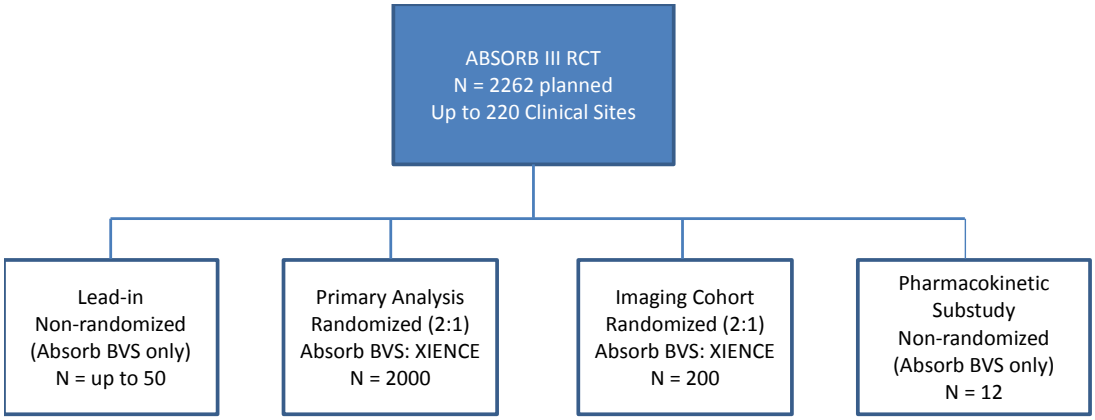

Figure 1 ABSORB III Overall Design

The data from the first 20 subjects registered in the lead-in group met the criteria for successful application and transfer of the Absorb didactic physician training plan to US clinical practice. The registration of the ABSORB lead-in group was completed on April 1, 2013 with a total of 24 patients at 11 investigational sites. As of September 30, 2015, follow-up visits through 2 years had been completed for all Lead-In subjects.

Baseline Demographics and Risk Factors

The key baseline demographics and risk factors are summarized for the ABSORB III Lead-In Group in **Table 1**. The mean age was 63.1 ± 9.2 years, 62.5% (15/24) were male, 33.3% (8/24) were tobacco users, 25.0% (6/24) had any diabetes mellitus, 87.5% (21/24) were hypertensive, and 95.8% (23/24) were dyslipidemic. There were 45.8% (11/24) of subjects who had a prior cardiac intervention and 20.8% (5/24) who had a prior MI. There were 58.3% (14/24) of subjects with stable angina and 20.8% (5/24) of subjects with unstable angina.

Table 1 Key Baseline Subject Characteristics and Risk Factors – Per-Subject Analysis, Lead-In Population

	Absorb (N=24)
Characteristic	
Age (year)	63.1 ± 9.2 (24)
Male Subjects	62.5% (15/24)
Current Tobacco Use	33.3% (8/24)
Any Diabetes Mellitus (DM)	25.0% (6/24)
Hypertension	87.5% (21/24)
Dyslipidemia	95.8% (23/24)
Prior Cardiac Intervention	45.8% (11/24)
Prior MI	20.8% (5/24)
Clinical Presentation	
Stable Angina	58.3% (14/24)
Unstable Angina	20.8% (5/24)
Silent Ischemia	20.8% (5/24)

Lesion and Angiographic Characteristics

The key lesion and angiographic characteristics are summarized in **Table 2**. Of the target lesions, 0% (0/24) were type A, 29.2% (7/24) were type B1, 62.5% (15/24) were type B2, and 8.3% (2/24) were type C according to the American College of Cardiology-American Heart Association (ACC/AHA) classification. The mean lesion length was 12.58 ± 2.19 mm and the mean pre-procedural reference vessel diameter (RVD) was 2.76 ± 0.37 mm. The mean pre-procedural percent diameter stenosis (%DS) was 67.03 ± 9.36 %. The mean pre-procedure minimum lumen diameter (MLD) was 0.89 ± 0.22 mm.

The mean post-procedure in-segment MLD was 2.17 ± 0.42 mm and mean post-procedure in-scaffold/stent MLD was 2.44 ± 0.27 mm. The mean post-procedure in-segment %DS was 22.56 ± 10.33 and the mean post-procedure in-scaffold/stent %DS was 12.26 ± 7.28. The mean in-segment acute gain was 1.27 ± 0.48 mm and the mean in-device acute gain was 1.55 ± 0.39 mm.

Table 2 Key Lesion and Angiographic Characteristics – Per-Subject Analysis, Lead-In Population

	Absorb (N=24) (L=24)
Lesion Characteristics (ACC/AHA Classification)	
Type A	0% (0/24)
Type B1	29.2% (7/24)
Type B2	62.5% (15/24)
Type C	8.3% (2/24)
Pre-Procedure QCA	
Lesion length, mm	12.58 ± 2.19 (24)
Reference vessel diameter, mm	2.76 ± 0.37 (24)
Minimal lumen diameter, mm	0.89 ± 0.22 (24)
% DS	67.03 ± 9.36 (24)
Post-Procedure QCA In-Device	
Minimal lumen diameter, mm	2.44 ± 0.27 (24)
Acute gain, mm	1.55 ± 0.39 (24)
% DS	12.26 ± 7.28 (24)
Post-Procedure QCA In-Segment	
Minimal lumen diameter, mm	2.17 ± 0.42 (24)
Acute gain, mm	1.27 ± 0.48 (24)
% DS	22.56 ± 10.33 (24)

Safety and Effectiveness Results

Acute success results are summarized in **Table 3**. Clinical device success is a per-lesion analysis; whereas, clinical procedure success is a per-subject analysis. In the ABSORB III Lead-in Group, the clinical device success was 100% (24/24). The clinical procedural success rate was 95.8% (23/24) due to one peri-procedural target vessel myocardial infarction (TV-MI).

Table 3 Acute Success

	Absorb (N=24)
Clinical Device Success	100.0% (24/24)
Clinical Procedure Success	95.8% (23/24)

Observed rates of hierarchical target lesion failure (TLF) and non-hierarchical components of TLF (cardiac death, TV-MI and ischemia driven target lesion revascularization (ID-TLR)) through 758 days (2 years plus the 28 day upper end of the follow-up window) are summarized in **Table 4**. A peri-procedure TV-MI was observed in one subject that did not require reintervention; otherwise, there were no occurrences of cardiac death, TV-MI or ID-TLR events through 393 days. An additional TV-MI and ID-TLR in the same subject occurred between 393 days and 758 days, resulting in a hierarchical TLF rate of 8.3% (2/24) at 758 days.

Table 4 Hierarchical TLF and Non-Hierarchical Clinical Outcomes – Per-Subject Analysis, Lead-In Population

	Absorb (N=24)
0 to 37 Days	
TLF (Cardiac Death, TV-MI, TLR)	4.2% (1/24)
Non-Hierarchical Components	
Cardiac Death	0.0% (0/24)
TV-MI	4.2% (1/24)
ID-TLR	0.0% (0/24)
0 to 393 Days	
TLF (Cardiac Death, TV-MI, TLR)	4.2% (1/24)
Non-Hierarchical Components	
Cardiac Death	0.0% (0/24)
TV-MI	4.2% (1/24)
ID-TLR	0.0% (0/24)
0 to 758 Days	
TLF (Cardiac Death, TV-MI, TLR)	8.3% (2/24)
Non-Hierarchical Components	
Cardiac Death	0.0% (0/24)
TV-MI	8.3% (2/24)
ID-TLR	4.2% (1/24)

Stent/scaffold thrombosis (ARC definite/probable) through 758 days is shown in **Table 5**. There were no occurrences of thrombosis through 393 days, with a single occurrence between 393 days and 758 days. The subject had discontinued DAPT on day 590 post-procedure and the thrombosis occurred on day 596. This same subject also had the TV-MI and ID-TLR reported between 393 days and 758 days, resulting in a thrombosis rate of 4.17% (1/24) at 758 days.

Table 5 Stent/Scaffold Thrombosis (Definite/Probable) – Per-Subject Analysis, Lead-In Population

	Absorb (N=24)
Acute (≤ 1 day)	0.0% (0/24)
Acute/Subacute (0 - 30 days)	0.0% (0/24)
Cumulative through 393 Days (0 - 393 days)	0.0% (0/24)
Cumulative through 758 Days (0 - 758 days)	4.17% (1/24)

Summary

The lead-in group of the ABSORB III Trial was designed to assess physician training in the usage of Absorb in terms of vessel sizing, lesion preparation, and device delivery and deployment, as these variables reflect the change in practice that occurs with the use of a polymeric scaffold compared to a metallic stent. Enrolled subjects were of low to moderate risk in risk factors and target lesion complexity. The data from the 24 subjects registered in the lead-in group met the criteria for successful application and transfer of the Absorb didactic physician training plan to US clinical practice. In clinical follow-up through 2 years, the number of TLF and stent/scaffold thrombosis events was low in this small subject population.