Absorb: Clinical Program Overview

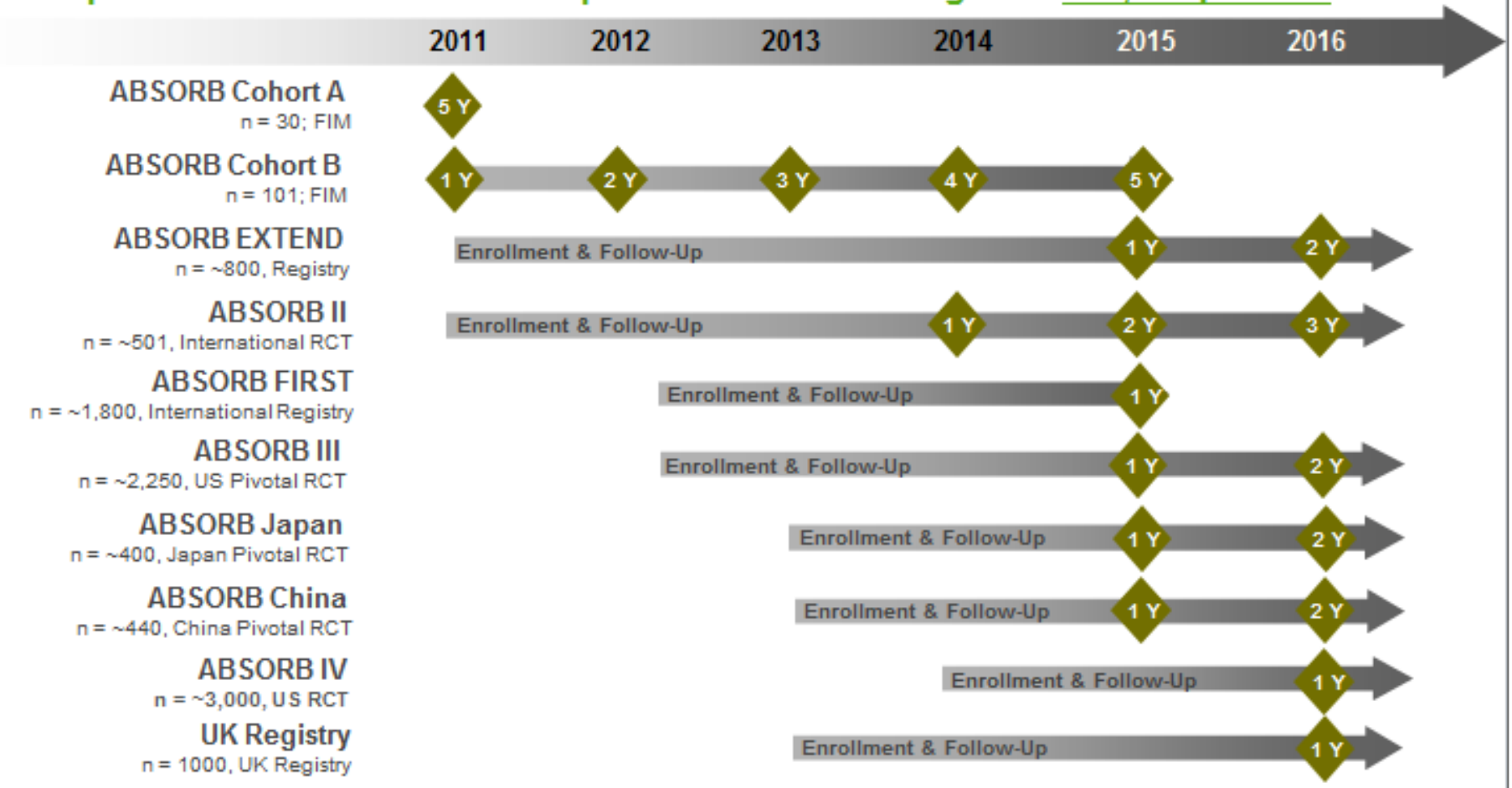
Didier Carrié (Toulouse)

Déjeuner-Débat

Absorb : 3 ans après, pourquoi je suis convaincu

Absorb

Comprehensive Abbott Vascular Sponsored Clinical Program: >10,000 patients



Each trial n reflects total patients. Data effective March 2015

ABSORB : plus de 100 000 patients traités à ce jour dans le monde

Des résultats présentés sur un total de 6232 patients :

- Absorb EXTEND à 1 un an sur la totalité des patients (étude AV -812 pts)
- Absorb FIRST à 1 an (étude AV - 968 pts)
- GHOST EU à 1 an (1477 pts)
- GABI-R à 30 jours (Registre Allemand – 1536 pts)
- REPARA à 30 jours (Registre Espagnol/Portugais – 1439 pts)

ABSORB Cohort A

Clinical Long-term Results Intention-to-Treat

	RESTORATION		RESORPTION	
Hierarchical	**6 Months 30 Patients**	**1 Year 29 Patients****	**2 Year 29 Patients****	**5 Year 29 Patients****
Ischemia Driven MACE***	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Cardiac Death	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
MI	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Q-Wave MI	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Non Q-Wave MI	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Ischemia Driven TLR	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
by PCI	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
by CABG	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

No scaffold thrombosis by ARC or Protocol

*Same patient – this patient also underwent a TLR, not qualified as ID-TLR (DS = 42%). **One patient withdrew consent and missed the 9, 12, 18 month and 2, 3, and 4 year visits; two patients died from a non-cardiac causes, one at 706 days and one at 888 days post procedure. ***MACE – Composite endpoint comprised of cardiac death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) by PCI or CABG.

Serruys, ABSORB Cohort A 5-year results; TCT, 2011

ABSORB Cohort B

Clinical Long-term Results Intention-to-Treat

Non-Hierarchical	30 Days N = 101	1 Year N = 101	2 Years N = 100*	3 Years N = 100*	4 Years N = 99*
Cardiac Death %	0	0	0	0	0
Myocardial Infarction % (n)	2.0(1)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)
Q-wave MI	0	0	0	0	0
Non Q-wave MI	2.0(1)	3.0 (3)	3.0 (3)	3.0 (3)	3.0 (3)
Ischemia driven TLR % (n)	0	4.0 (4)	6.0 (6)	7.0 (7)	7.1 (7)
CABG	0	0	0	0	0
PCI	0	4.0 (4)	6.0 (6)	7.0 (7)	7.1 (7)
Hierarchical MACE % (n)	2.0 (2)	6.9 (7)	9.0 (9)	10.0 (10)	10.1 (10)
Hierarchical TVF % (n)	2.0 (2)	6.9 (7)	11.0 (11)	13.0 (13)**	13.1 (13)***

*One patient lost to FU at 2-year FUP
*One patient missed the 4-year FUP
**Non-TLR TVR at 957 days
***Non-TLR TVR at >957 days

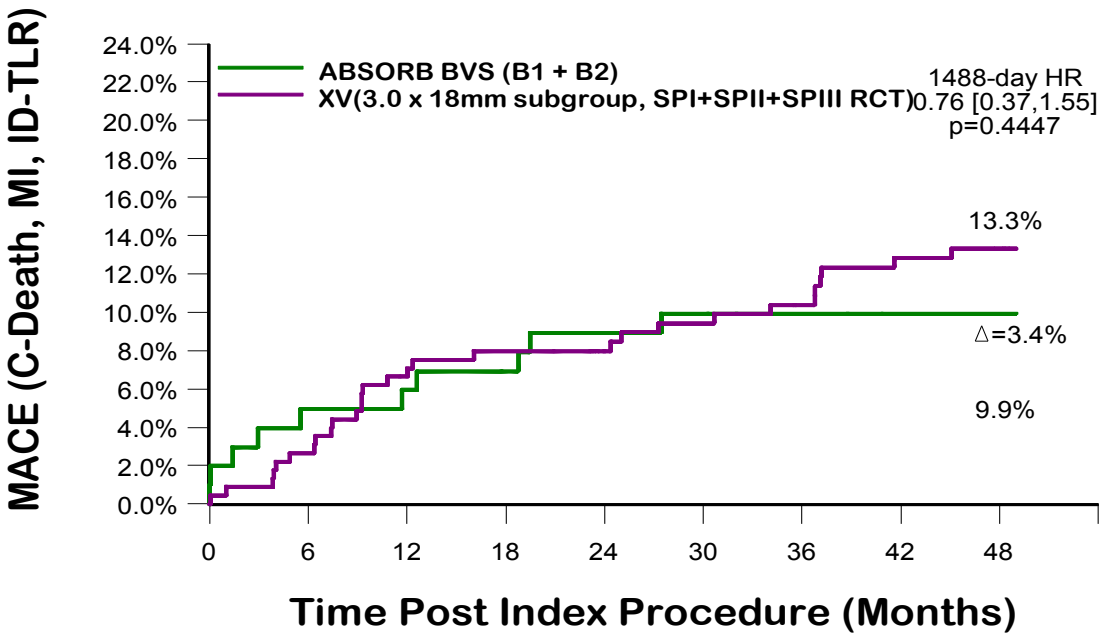
No new MACE between 3 and 4 years
No scaffold thrombosis by ARC or Protocol

MACE: Cardiac death, MI, ischemia-driven TLR, TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

ABSORB Cohort B – 4 year Clinical Results, E. Christiansen, ACC 2014

ABSORB Cohort B

KM Estimate of MACE Rate in Patients Treated with Absorb
Treated with a Single 3.0x 18 mm Metallic XIENCE V



Time After Index Procedure (days)								
	0	**37**	**194**	**284**	**393**	**758**	**1123**	**1488**
Absorb BVS (B1+B2) At Risk	101	99	96	96	94	91	89	86
XIENCE V (3.0 x 18 mm subgroup, SPI +SPII+SPIII RCT) At Risk	227	224	219	211	204	191	182	174

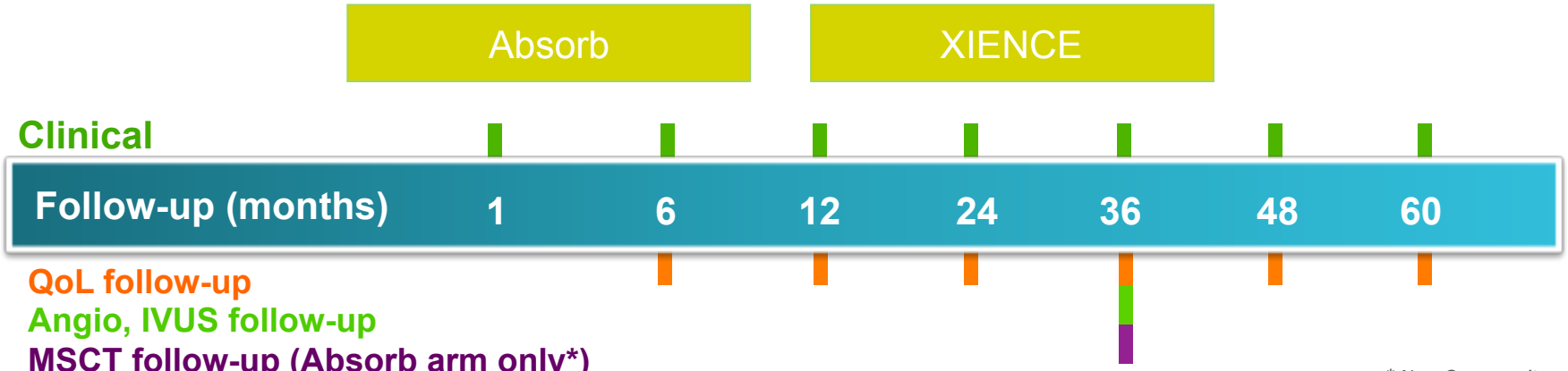
P-values are not from formal hypotheses testing and are displayed for exploratory purpose only.

ABSORB Cohort B – 4 year Clinical Results, E. Christiansen, ACC 2014

ABSORB II

Objective: Evaluate Absorb vs. XIENCE for performance

Design: Randomized 2:1 Controlled Absorb BVS vs. XIENCE, in 501 patients, in 46 sites in Europe & New Zealand



* Non-German sites only.

Co-primary Endpoints:
- Vasomotion at 3 years (superiority)
- Minimum Lumen Diameter (MLD) at 3 years (non-inferiority, reflex to superiority)

Secondary Endpoints:
- Standard clinical endpoints (MACE, TVF, TLF, Cardiac Death, MI, TLR)
- Quality of life (QOL) especially recurring angina
- Device & procedural success

ABSORB II, 1 Year Clinical Results, P.W. Serruys, TCT 2014, The Lancet D-14-05428R1 S0140-6736(14)61455-0

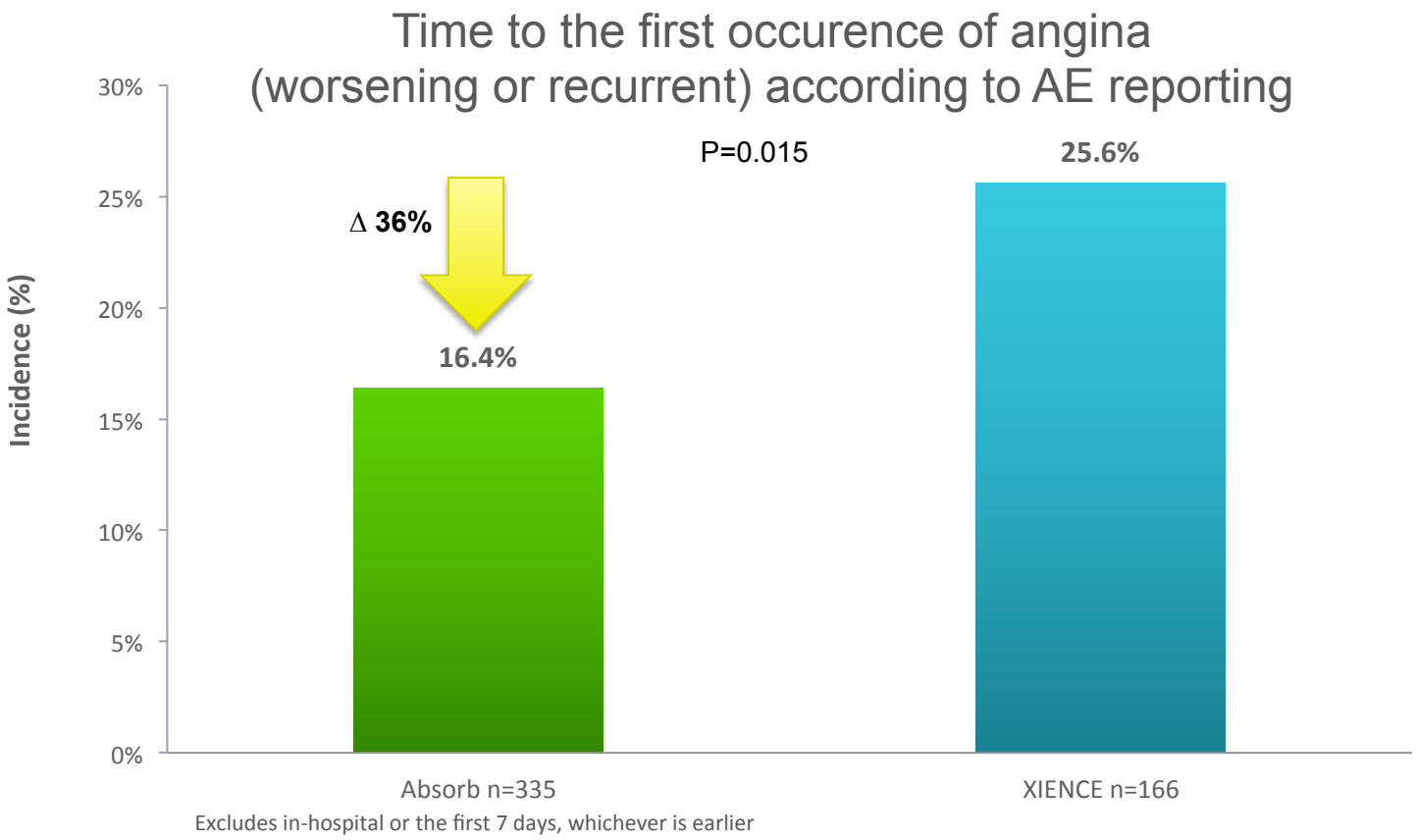
ABSORB II
One Year Clinical Results

	Absorb (N=335 patients)	XIENCE (N=166 patients)	P-value
DoCE (Device-Oriented Composite Endpoint)	**4.8**	**3.0**	**0.35**
Cardiac Death (%)	0	0	1.00
Target Vessel MI (%)	4.2	1.2	0.07
Clinically Indicated TLR (%)	1.2	1.8	0.69
All TLR (%)	1.2	1.8	0.69
Definite Scaffold/Stent Thrombosis (%)	0.6	0.0	1.00
PoCE (Patient-Oriented Composite Endpoint)	**7.3**	**9.1**	**0.47**
All Death (%)	0	0.6	0.33
All MI (%)	4.5	1.2	0.06
All NQMI (%)	3.9	1.2	0.16
All QMI (%)	0.6	0	1.00
All Revascularizations (%)	3.6	7.3	0.08

DoCE - Composite of cardiac death, target vessel MI and clinically indicated target lesion revascularization
PoCE - Composite of all death, all MI and all revascularization

ABSORB II, 1 Year Clinical Results, P.W. Serruys, TCT 2014, The Lancet D-14-05428R1 S0140-6736(14)61455-0

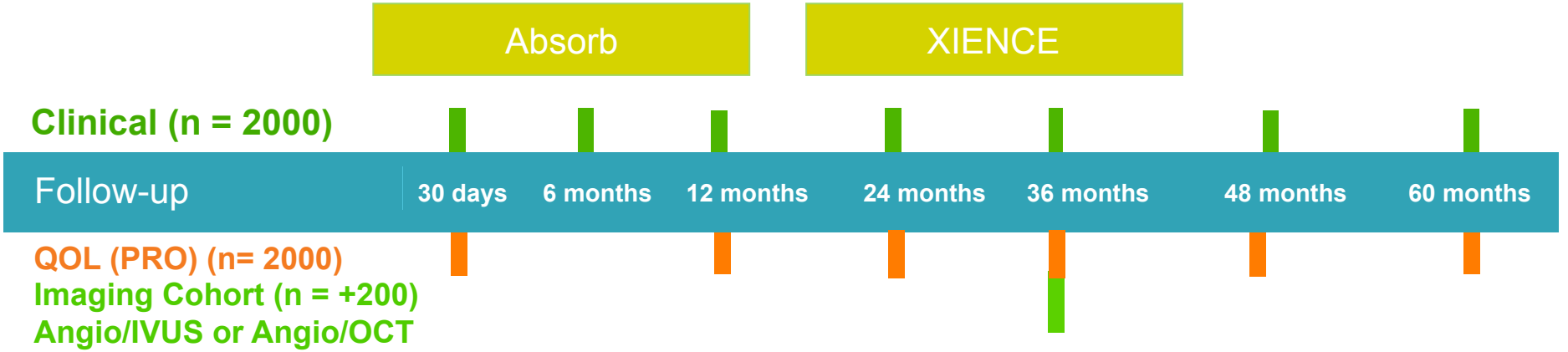
ABSORB II
One Year Angina Outcome



Adapted from ABSORB II, 1 Year Clinical Results, P.W. Serruys, TCT 2014.

ABSORB III

Objective: US Pivotal Trial
Design: Prospective, single blind, randomized 2:1 Absorb vs. XIENCE, in 2000 patients, (+ 200 patients in Imaging Cohort), up to 220 sites (predominantly US)



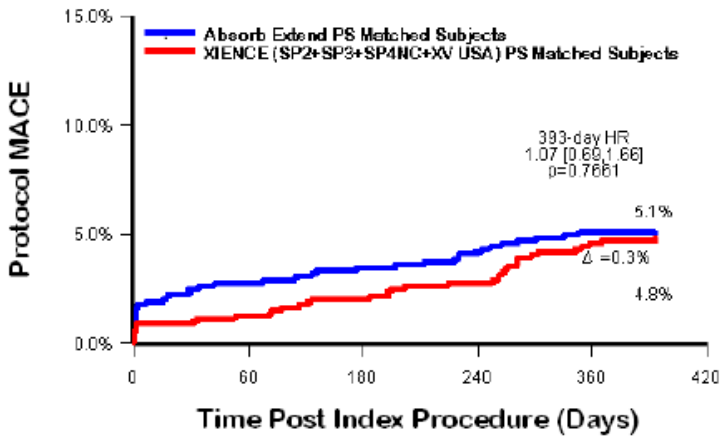
Primary Endpoint:	Target Lesion Failure at 1 year, powered for non-inferiority in 2000 clinical follow-up subjects
Powered Secondary Endpoints:	• Site diagnosed angina at 1 year test for superiority of Absorb to XIENCE (n = 2000) • Nitrate-induces vasomotion at 3 years by QCA, superiority of Absorb to XIENCE (n = 200) • Mean lumen area change from post-procedure to 3 years by IVUS, superiority of Absorb to XIENCE (n = 150) • Diabetic subgroup to support diabetic indication of Absorb

ABSORB EXTEND

Alexandre Abizaid, MD, PhD
On behalf of the ABSORB EXTEND Investigators

KM Curve of MACE through 12 months
Propensity Score Matched: Absorb vs. XIENCE

MACE:
Cardiac death
All MI
ID-TLR



	0	37	194	393
ABSORB EXTEND at Risk	812	790	783	768
XIENCE V (SP2+SP3+SP4NC+XV USA)) at Risk	812	798	772	709

Propensity Score Matched Clinical Outcome 1-year

	Absorb (EXTEND, N = 812)	XIENCE V (SP2,3,4,XV USA N = 812)	P Value
NON-HIERARCHICAL COMPONENTS			
Cardiac Death (%)	0.7	0.6	0.80
Myocardial Infarction (%)	3.3	1.5	0.02
Ischemia Driven TLR (%)	2.3	3.0	0.38
All Revascularizations	4.7	7.1	0.04
MACE (%)	5.0	4.8	0.83
TVF (%)	5.5	6.2	0.57
TLF (%)	5.0	4.7	0.74
Scaffold Thrombosis (ARC Def/Prob) (%)	1.0	0.3	0.11

MACE is the composite of cardiac death, MI (Q-wave and Non-Q wave MI) and TLR.
TVF is the composite of cardiac death, MI (Q-wave and Non-Q wave MI) and TVR.

Investigator Sponsored Trials
Overview and Status Update

Randomized Controlled Trials

Study Title	Design	Number of Patients	Primary Endpoint	Patient FU (Years)
AIDA	All – comers RCT vs. XIENCE	2690	2-Year TVF	5
TROFI II	STEMI RCT vs. XIENCE	190	6-Month neo-intimal healing score	3
PROSPECT II ABSORB	RCT vs. OMT in unstable asymptomatic pts	300	2-Year IVUS MLA	3
PROACTIVE	RCT vs. XIENCE	20	Peri-Proc Platelet Reactivity	1
VANISH	RCT vs. XIENCE	60	Evolution of myocardial blood flow values over time	3
EVERBIO II*	Non-inferiority RCT EES, vs. BES, vs. BVS	240	Late lumen loss at 9 months	5
ISAR ABSORB MI	Randomized, non-inferiority vs EES	260	Percentage diameter stenosis at 6-8 months	1

Update from Sep 2014

Sources: Dr. G. Stone, Bioresorbable Vascular Scaffold: Acute Performance and Safety Symposia, EuroPCR 2014 and NCT01711931 on www.ClinicalTrials .gov viewed 9/5/14.

Investigator Sponsored Trials
Overview and Status Update

Registries

Study Title	Design	Number of Patients	Primary Endpoint	Patient FU (Years)
BVS EXPAND	All – comers Registry (excl STEMI)	300	1 – Year MACE	5
ASSURE	All – comers Registry	180*	Safety and Efficacy	3
ABSORB CTO	Feasibility in CTO	35*	Safety and Performance	2
PABLOS	Feasibililty in Bifurcations	30	Device, Procedural, Main and Side Branch Success	2
IT-DISSAPEARS	MVD and Long Lesion Registry	1000	Safety and Efficacy	5
GABI-R	All – comers Registry	5000	Safety and Efficacy	5
REPARA	All – comers Registry	1500	1- Year MACE	1
POLAR ACS	ACS Registry	100*	Safety, clinical device, procedure success and in-hospital MACE	1
France ABSORB	Feasibility in de novo lesions	2000	1 – Year MACE	1
GHOST	All – comers Registry	consecutive and continuous enrolment	Target Vessel Failure (TVF)	1
Prague 19	STEMI (STEMI Killip I/II)	100	Clinical Outcomes	1

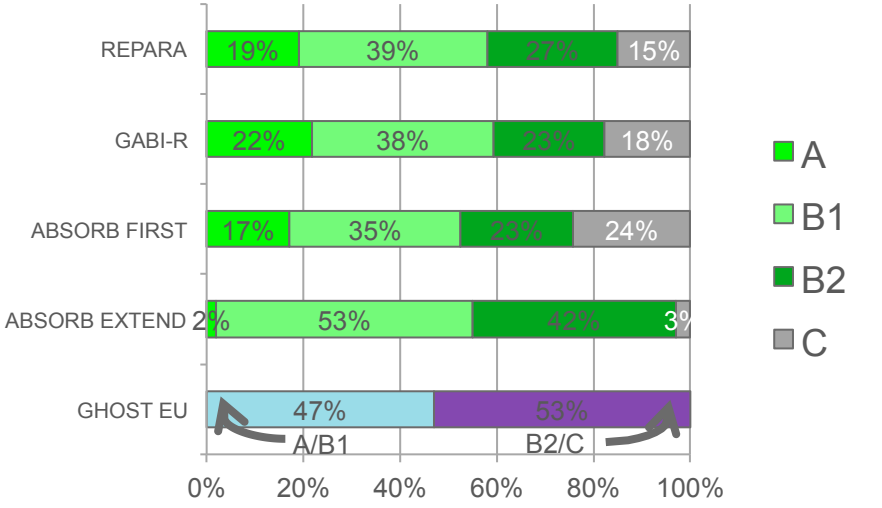
* Enrollment Complete
Update from Sep 2014

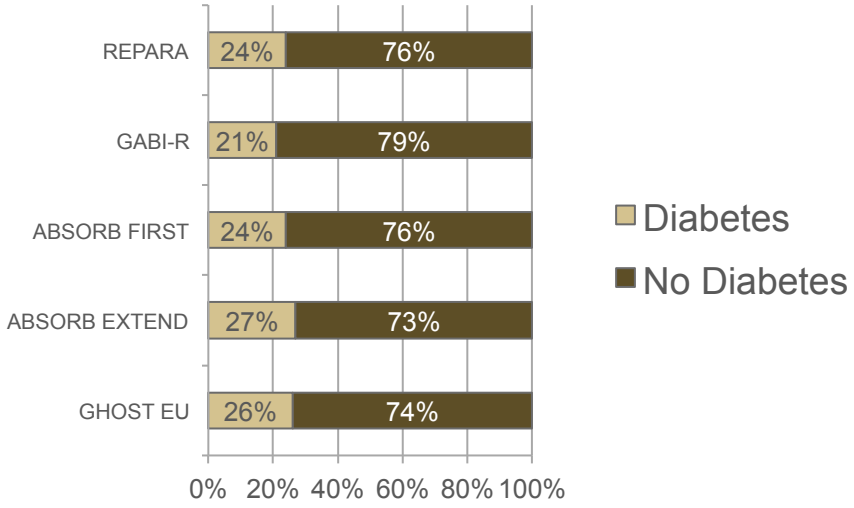
Sources: Dr. G. Stone, Bioresorbable Vascular Scaffold: Acute Performance and Safety Symposia, EuroPCR 2014 and www.clinicaltrials.gov

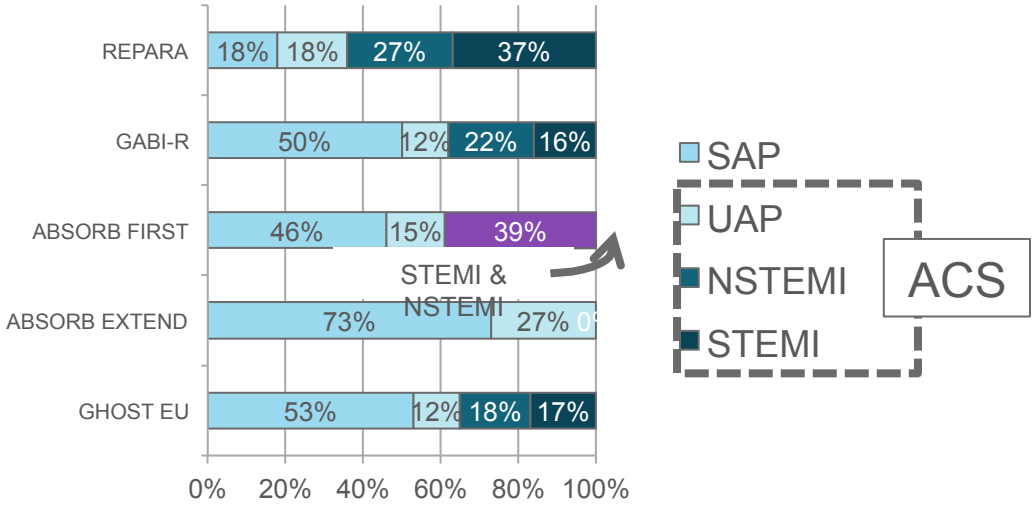
ABSORB dans la vraie vie:
Encore plus de données d'efficacité

GABI-R (1536 patients – 30 jours)
Repara (1439 patients - 30 jours)
Absorb First (968 patients – 1 an)
Ghost EU (1477 patients – 1 an)

Absorb in All Comers patients







Real life population:
> 1500 diabetic patients
> 3000 ACS patients

Absorb
GABI-R 30 Day Data

Pr C. Hamm, on behalf of the Steering-Committee and all GABI-R Investigators

Included patients
from November 2013 until March 2015
N=2003

OCT: 61/1523 (4%)
IVUS: 75/1520 (5%)

30-days FU
N= 1536/1536 eligible (100%)

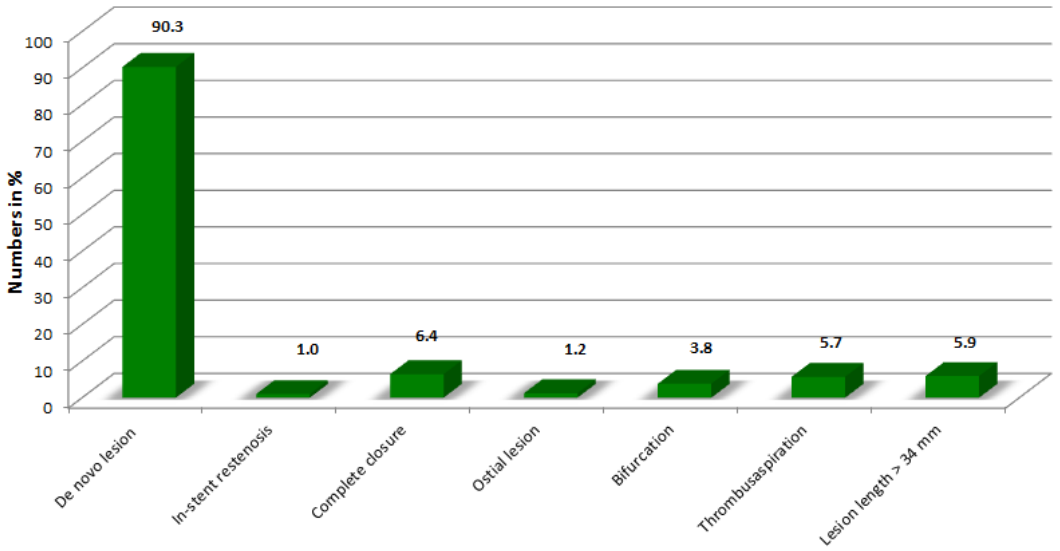
Age, years±SD	62±11 (1.536)
Female	357/1.536 (23%)
Diabetes mellitus	326/1.521 (21%)
On insulin	106/1.521 (7%)
Hyperlipidemia	887/1.468 (60%)
Hypertension	1.150/ 1.509 (76%)
Smoker	846/1.1487 (57%)
Previous PCI	449/1.512 (29%)
Prior CABG	50/1.527 (3%)
Stroke/TIA	65/1.533 (4%)
ACS	763/1.533 (50%)
Unstable angina	185/1.533 (12%)
NSTEMI	340/1.533 (22%)
STEMI	238/1.533 (16%)

Lesion Location	
LMCA	1.7% (26/1527)
LAD	67.5% (1031/1527)
LCX	45.4% (694/1527)
RCA	49.9% (761/1527)

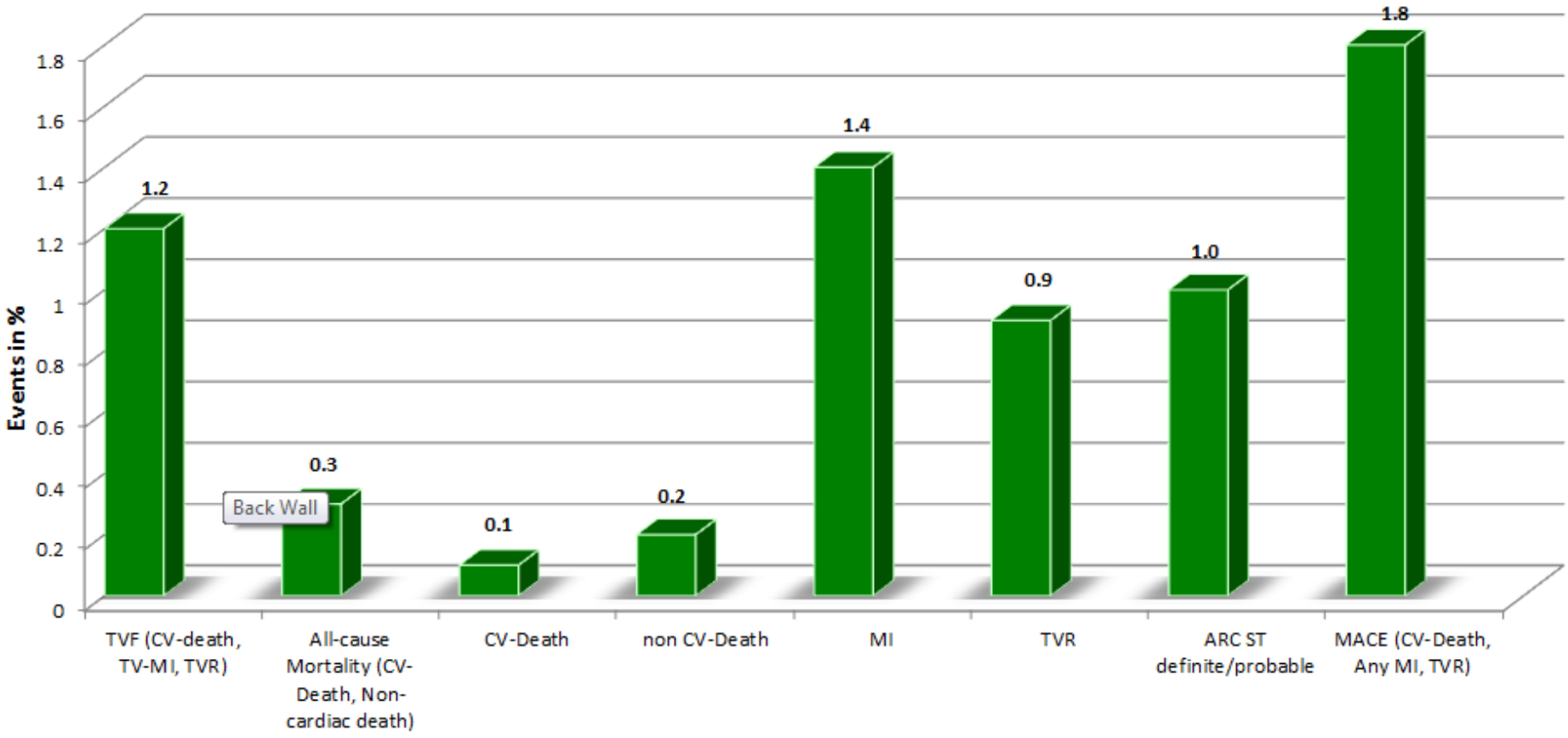
ACC/AHA Lesion complexity	
A	21.9% (437/1991)
B1	37.6% (748/1991)
B2	22.5% (448/1991)
C	18.0% (358/1991)

Patient based	
Radial Access	45.1% (689/1529)
Lesion/Pt.	1,3
Multivessel Disease	50.2% (921/1529)
Hybrid procedure	12.2% (180/1471)
Total scaffold length (mm)	27.6±17.0
Average Scaffold diameter (mm)	3.1±0.4

Lesion based	
Predilation	92.5% (1867/2018)
• NC-Ballon	70.3%
• Semi-compliant	29.7%
Postdilation	66.8% (1345/2013)



Absorb
GABI-R 30 Day Data

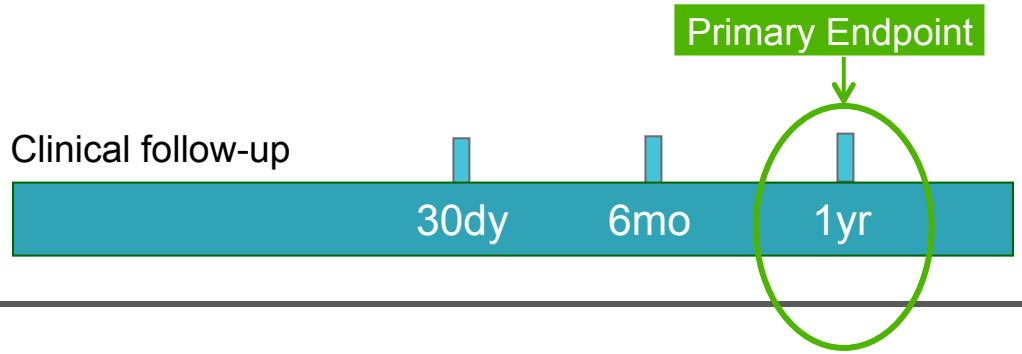


Absorb
REPARA 30 Day Data

Felipe Hernández Hernández, on behalf of the REPARA investigators

Objective: Evaluate the safety and efficacy of BVS usage in real world patients under well-controlled implementation criteria.

Design: Prospective, Open-Label, Multi Center, Iberian registry in 2240 Pts, 60 Spanish sites



Primary Endpoint: MACE rate (major adverse cardiac events) at 12 months of follow-up: Cardiac death; Myocardial infarction; Target lesion revascularisation (TLR) ischemia-driven: Cardiac Death/All MI/ID-TLR

Secondary Endpoints: Components: Death (Cardiovascular, Non-Cardiovascular), Myocardial Infarction (MI: QMI and NQMI, TV,…), Angina, DAPT rates and relationship to events

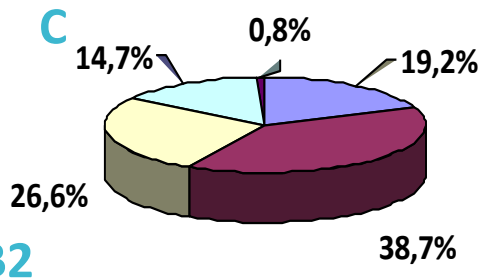
Absorb
REPARA 30 Day Data

1497 Patients at 30 days

Hypertension	52.0%
Dyslipidemia	54.8%
Tobacco use	48.1%
DM	24.4%

Indication	n (%)
•NSTEMI (435) •STEMI (538)	973 (**59.8**)
Unstable angina	293 (**18.0**)

Anatomical characteristics
- Bifurcations 12.9%
- Moderate-severe tortuosity 11%
- Moderate-severe calcification 9.1%



Lesion type

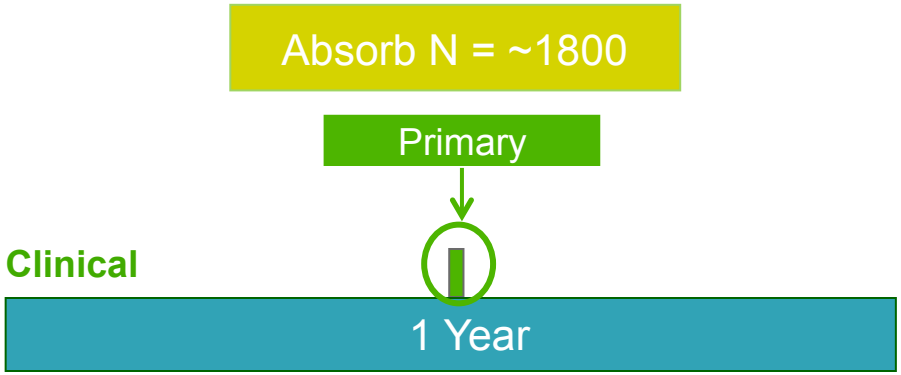
Predilation: 78%
Postdilation: 40%

	Total (n=1479)	%
30-day MYOCARDIAL INFARCTION	23	**1,56**
30-day TLR	12	**0,81**
30-day CARDIAC DEATH	5	**0,34**

ABSORB FIRST

Eric Eeckhout on behalf of the ABSORB FIRST Investigators

Objective:	Evaluate safety and effectiveness of Absorb BVS in more complex lesions and patients in a post-approval, 'real world' setting
Design:	Prospective, open-label, multi-center, single-arm registry in ~1800 patients, in about 90 sites in EMEA, APAC, LA real-world patient population

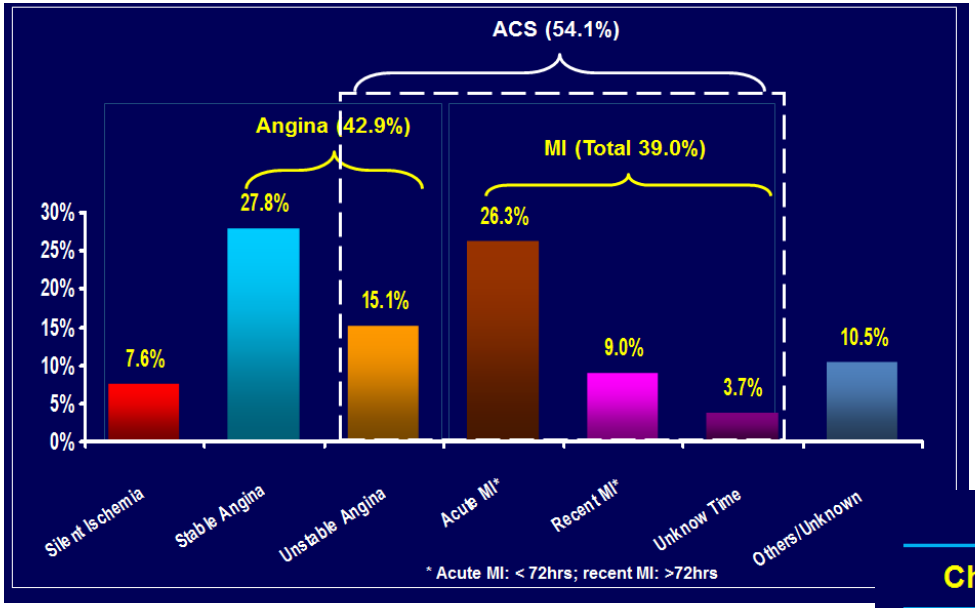


Primary Endpoints:	Death, MI, Revascularization, ST, TLF, MACE, etc. at 12 months; clinical endpoint events are independently adjudicated
Secondary Endpoints:	Device and procedure success Ischemia Driven TVF, TLR, ST, Patient and Physician Questionnaire at 12 months

Absorb First Acute Performance in 1,200 pt, C. Naber, TCT 2014

ABSORB FIRST

958 Patients at 1 Year

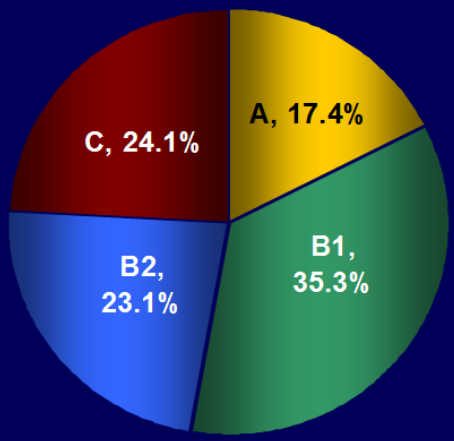


Per Patient Analysis	
# of diseased vessels (Mean ± SD)	1.6 ± 0.8
1 Vessel	55.7%
2 Vessels or more	44.3%

Characteristics	L = 1188
Calcification (Moderate/Severe)	18.8%
Bifurcation	12.9%
Tortuosity	11.3%
Total Occlusion	10.3%
Ostial lesion	5.7%

L: Lesions

Lesion type (AHA/ACC)



→ *B2/C Lesions: 47.2%*

Total occlusion, ostial lesions: exclusion from prior ABSORB trials

ABSORB FIRST

958 Patients at 1 Year

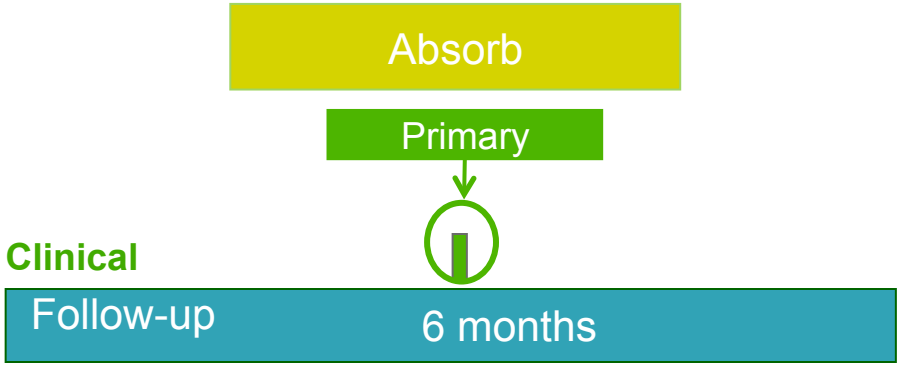
Interim Clinical Outcomes up to 1 Year (N=958)

Clinical Events	In hospital	1 year
All Death	0.2% (2)	1.3% (12)
Cardiac Death	0.0% (0)	0.5% (5)
MI QMI Non-QMI	0.9% (9) 0.2% (2) 0.7% (7)	1.7% (17) 0.4% (4) 1.3% (12)
All Revascularization	0.9% (9)	5.2% (50)
ID-TLR	0.5% (5)	1.4% (13)
MACE	1.0% (10)	2.6% (25)
TLF	0.9% (9)	2.2% (21)
DMR	1.7% (16)	6.8% (65)

Note: Interim clinical outcome data from those 958 patients who complete 1 year follow-up
DMR: all death, all MI, all revascularization

Ghost EU (D. Capodanno)

Objective:	Investigate feasibility and early safety and efficacy outcomes of Absorb in real world population
Design:	Multi-center, all-comers data collection from patients treated with Absorb between November 2011 to January 2014



Combined Endpoints:	• Device Oriented Composite Endpoint: CV death, TV MI, Clinically driven TLR • Patient Oriented Composiite Endpoint: All cause death, any MI, any repeat revascularization • Major Adverse Cardiac Events: CV death, any MI, Clinically driven TLR • Target Vessel Failure: CV death, Target Vessel induced MI, Ciinically driven TVR

Ghost EU, D. Capodanno, EuroIntervention 2014

Patient Population (n=1,477)

Absorb
Ghost EU
1 Y FUp

Overall Patients
N=1,477; 1,736 lesions

30-day FU*
N= 1,444/1,477 (97.8%)

6-month FU*
N=1397/1,477 (94.6%)

12-month FU*
N=1276/1,477 (86.4%)

Age, years±SD	62±11 (1,477)
Male	1180/1,477 (80%)
Diabetes mellitus	**381/1,477 (26%)**
On insulin	134/1,450 (9%)
Hyperlipidemia	778/1,477 (53%)
Hypertension	1070/ 1,477 (72%)
Smoker	448/1,477 (30%)
Previous PCI	**497/1,477 (34%)**
Prior CABG	71/1,477 (5%)
Stroke/TIA	53/1,477 (4%)
ACS	**697/1,477 (47%)**
NSTEMI	**259/1,477 (18%)**
STEMI	**248/1,477 (17%)**
LV ejection fraction <30%	38/1219 (3.1%)
eGFR<60 mL/min	135/934 (14%)

Piera Capranzano, on behalf of the GHOST-EU Investigators

GHOST-EU

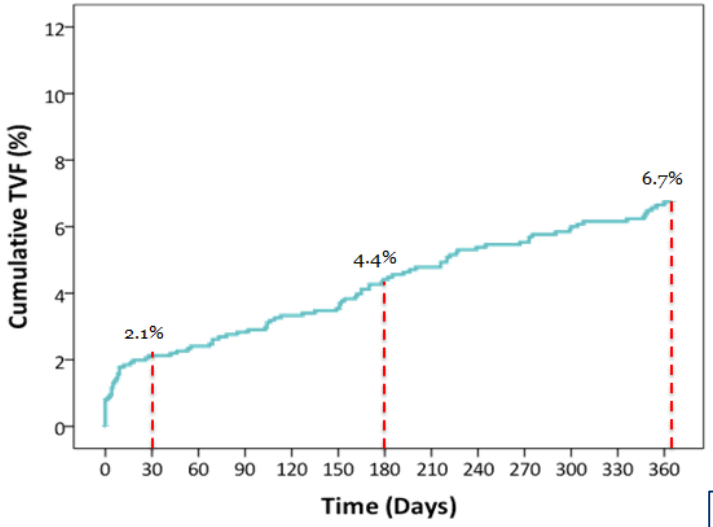
Mean lesion length (n=1,215)	19.5±14.0
Length > 34 mm	139 (11.4%)
Lesion ACC/AHA B2/C	**857/1614 (53.1%)**
Bifurcation	**366 (21.1%)**
CTO	**113/1736 (6.5%)**
ISR	**54/1736 (3.1%)**

	1670/1736 (96.2%)
Cutting balloon	21/1723 (1.2%)
Scoring balloon	47/1722 (2.7%)
Residual DS ≥ 40% after pre-dilatation	254/911 (28%)
Post-Dilatation	908/1736 (52.3%)
Mean Scaffold Diameter/Les	3.1±0.80
Mean scaffold Length/Les (n=1722)	27.6±16.7
N. of scaffold/Les	1.28±0.64
Overlapping/Les	364/1736 (21%)
OCT*	206/1498 (14%)
IVUS*	240/1498 (16%)

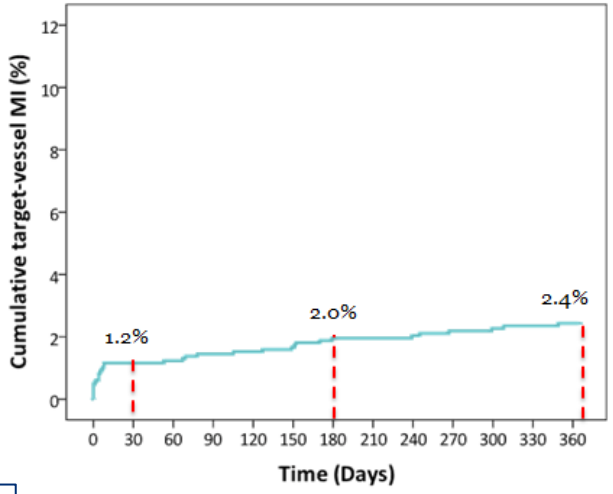
*per patient; DS: diameter stenosis

Absorb

Ghost EU - 1 Y FUp

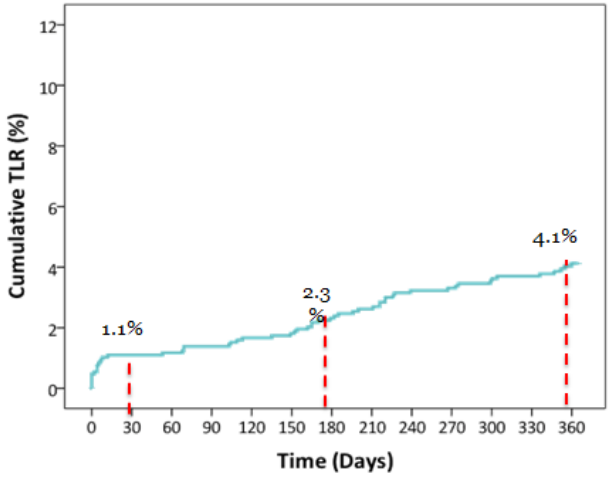


Days	0	90	180	365
Pts at risk	1,477	1,368	1,313	989

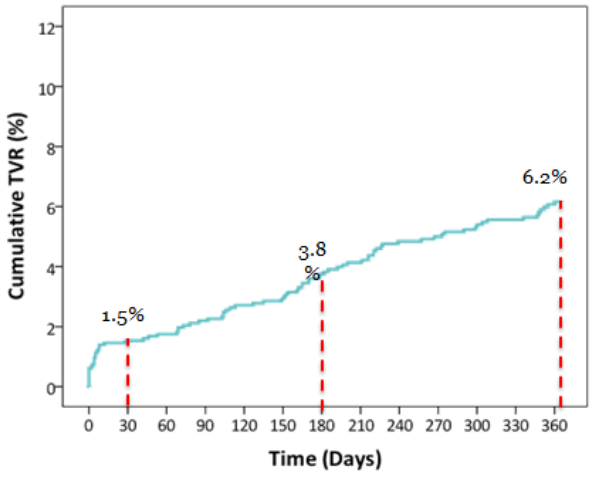


Days	90	180	365
Pts at risk	1,377	1,328	1,009

GHOST-EU



Days	90	180	365
Pts at risk	1,381	1,329	996



Days	90	180	365
Pts at risk	1,331	1,274	963

ABSORB dans la vraie vie:
Quel % de thromboses sur ces 4 études ?

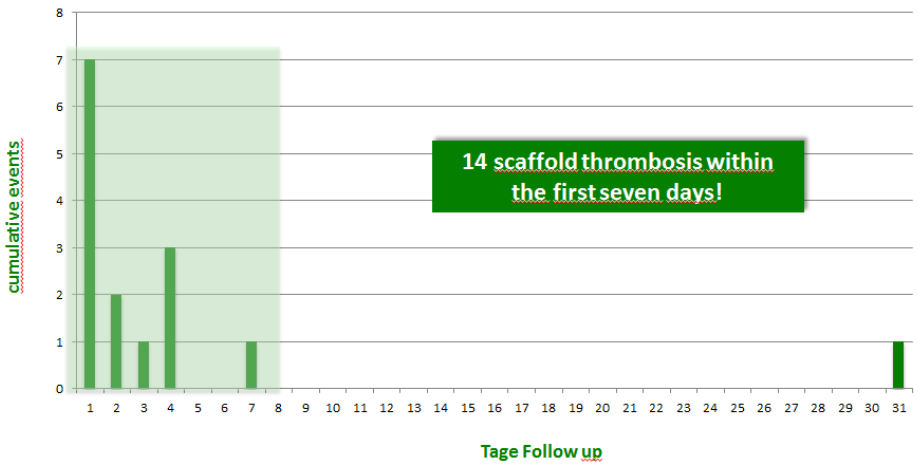
Repara (1439 patients - 30 jours)
GABI-R (1536 patients – 30 jours)
Absorb First (968 patients – 1 an)
Ghost EU (1477 patients – 1 an)

ABSORB
ST @ 30 jours

GABI-R

40 % B2/C
50% SCA

ARC Scaffold thrombosis (def/prob)



ARC ST definite/prob 1%

REPARA

41% B2/C
78% ACS

	Total (n=1479)	%
30-day STENT THROMBOSIS	13	0,88

- ✓ 3 acute ST 23%
- ✓ 4 due to DAPT non-adherence 31%

ABSORB ST @ 1 an

ABSORB First

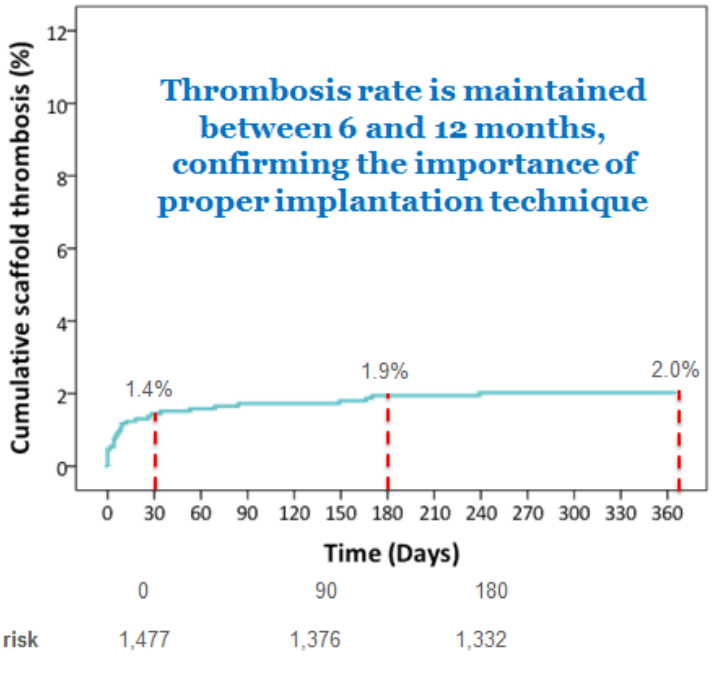
47% B2/C
54% ACS

Definite/Probable Scaffold Thrombosis

Scaffold Thrombosis (Def./Prob.)	Rate
Early (0-30 days)	**0.4%** (4/958)
Acute (< 1 day), 0.0%	
Sub-acute (1-30 days), 0.4%	
Late (30-365 days)	**0.4%** (4/957)
Early & Late (0-365 days)	**0.8%** (8/957)

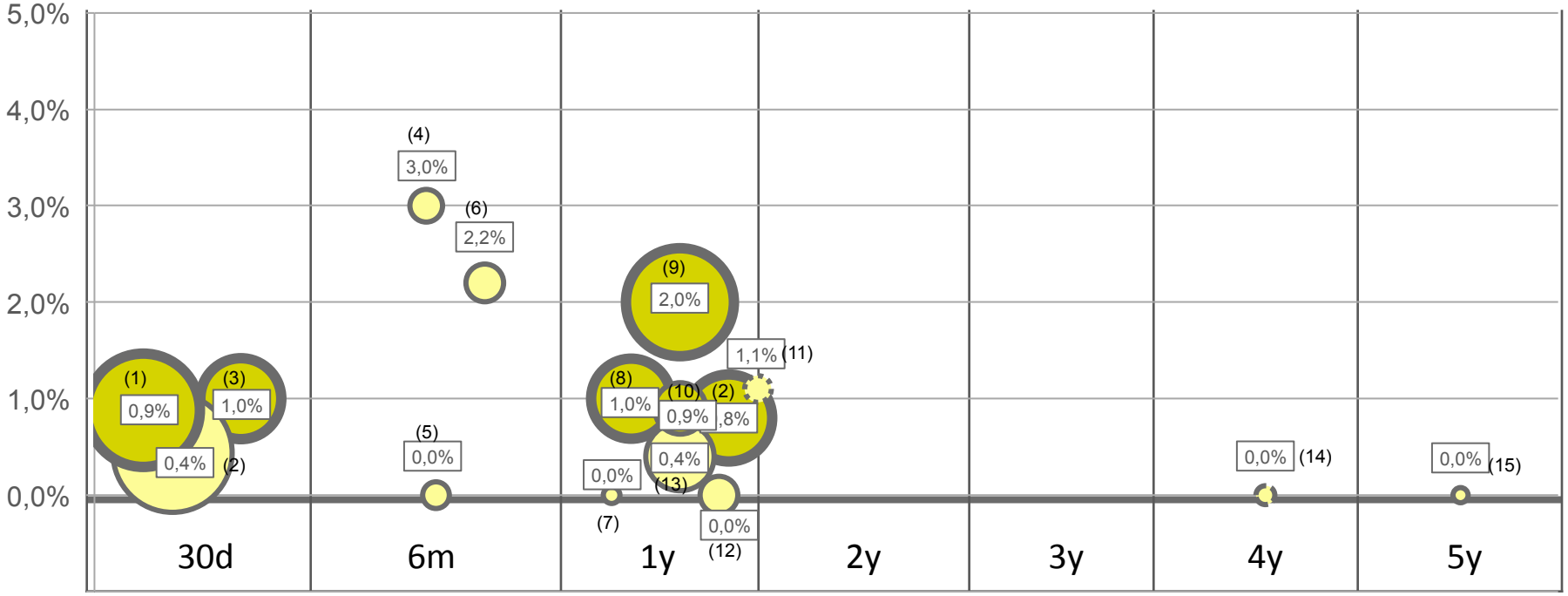
GHOST-EU

53% B2/C
47% ACS



ABSORB Data

Def/Prob Scaffold Thrombosis (Longest Available FU per study)



(1) REPARA: **All Comers (@EuroPCR2015)**
(2) ABSORB FIRST: **All Comers (@EuroPCR2015)**
(3) GABI-R: **All Comers (@EuroPCR2015)**
(4) AMC Registry**: AC (in Eurointervention 2014)**
(5) Dr. Costopoulos on CCI: **All Comers (in CCI2014)**
(6) ABSORB EXPAND: **All Comers (@EuroPCR2014)**
(7) CTO (Dr. Serra): **CTO (on Eurointervention2014)**
(8) ABSORB EXTEND: **mod complexity (@ EuroPCR2015)**
(9) GHOST-EU: **All Comers (@EuroPCR2015)**
(10) ABSORB II**: selected (on Lancet 2014)**
(11) POLAR ACS: **ACS (@ EuroPC2014)**
(12) ASSURE: **All Comers (on Eurointervention2014)**
(13) Polish BVS registry: **all comers (@NFIC2014)**
(14) ABSORB Cohort B: **simple (@ EuroPCR2014)**
(15) ABSORB Cohort A: **simple (@ EuroPCR2011)**

ABSORB Data Compared to DES

ST in studies that have reached 1 year of follow up

Study	Events/Total patients	Incidence
GHOST EU @ 1 year	26/1332	2%
ABSORB-FIRST @ 1 year	8/957	0.8%
Total	34/2289	1.5%
LEADERS – BES	16/804	2.0%
LEADERS – SES	16/801	2.0%
Resolute AC – ZES	14/1134	1.3%
Resolute AC – EES	8/1150	0.7%
COMPARE II – BES	14/1789	0.8%
COMPARE II - EES	9/904	1%

Piera Capranzano, on behalf of the GHOST-EU Investigators
Eric Eeckhout, on behalf of the ABSORB FIRST Investigators

LEADERS 9 months, Serruys, ESC2008, Resolute All Comers 5 year, Windecker, PCR2014; Compare II 3 year, P. Smits, PCR 2014

CONCLUSION
Efficacité et sécurité d'Absorb

Tous ces résultats complètent les premières études Absorb et soulignent l'efficacité et la sécurité d'Absorb.

Les résultats des études « vraies vie » révèlent :

- **un taux de MACE équivalent à celui des DES à 1 an (5-7%)**
- **Des données de ST à 30 jours:**
  - Dans le registre REPARA, malgré le faible de taux de post-dilatation (40%), le taux reste faible (0.9%)
  - Dans le registre GABI-R, avec 67% de post-dilatation, le taux est de 1%
- **Des données de ST à 1 an:**
  - Dans GHOST EU, le taux reste stable entre 6 mois et 1 an (2%) confirmant les évènements précoces liés à la procédure et aux techniques d'implantation.
  - Dans Absorb EXTEND et Absorb FIRST, le taux se situe entre 0.8 et 1.0 %, des valeurs normales et comparables à celle des DES.