A prospective randomized trial of everolimus-eluting stents vs bare metal stents in octogenarians:

XIence or Vision for the **M**anagement of **A**ngina in the elderly – The **XIMA** trial

Adam de Belder
Jose Maria de la Torre Hernandez
On behalf of the **XIMA** Investigators

Sussex Cardiac Centre

Sección de Hemodinámica y Cardiología Intervencionista

Cardiología VALDECILLA SANTANDER

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Abbott Vascular

This trial was funded by an unrestricted educational grant from Abbott Vascular

Background

- Increasingly common clinical scenario – an elderly patient with extensive co-morbidity, refractory angina, complex coronary anatomy, and unsuitable for CABG
- Mean age of patients in trials that influence clinical decision making is 61 years
- Octogenarians often excluded from clinical trials

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

The XIMA dilemma

- Likely to have complex coronary disease with increased risk of restenosis
- **Favours DES**

- Bleeding risks increased in this age group
- Consequences of bleeding much greater in this age group
- Drug compliance and interaction
- Toleration of ISR
- **Favours BMS**

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Hypothesis

- Drug-eluting stenting of coronary disease causing limiting angina will prove superior to bare metal stenting, in terms of a combined endpoint of mortality, MI, CVA, requirement for target vessel revascularisation and severe haemorrhage at one year in patients aged 80 or above.

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Organisation

- PI and UK PI Dr. Adam de Belder
- Co-PI (Spain) Prof. Jose Maria de la Torre Hernandez
- Steering Committee – Dr. Adam de Belder, Prof. Jose Maria de la Torre Hernandez, Dr. David Hildick-Smith, Dr. Ramon Lopez Palop, Dr. Martyn Thomas, Dr. Felipe Hernandez Hernandez, Prof. Nick Curzen
- DSMB – Dr. Derek Robinson, Dr. James Cotton
- Co-ordinating centre and data management – Web-based data system (Dendrite) - Sussex Cardiac Centre, Brighton, RPS Research Iberica SLU, Spain
- Lead research nurse – Nicola Skipper, Nina Cooter
- Statistician – Dr. Derek Robinson
- Clinical Events Committee - (Spain) Javier Goicolea Ruigomez, Luis Martinez Elbal, (UK) Mark de Belder, Andrew Sutton
- Funding: unrestricted educational grant from Abbott Vascular

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Inclusion criteria

- Age≥80
- Stable angina or acute coronary syndrome
- Coronary artery disease requiring stenting:
  - Left main stem stenosis
  - Lesions length ≥15mm long or ≤3mm diameter
  - Lesion at high risk of restenosis (e.g. chronic total occlusion, bifurcation, severe calcification)

Exclusion criteria

- Acute STEMI
- Cardiogenic shock
- Platelet count <50 x $10^9/mm^3$
- Patient life expectancy < 1 year
- Known allergies to clopidogrel, aspirin, heparin, IV contrast or stent drug elutant
- Recent major GI haemorrhage (within 3 months)
- Any previous cerebral bleeding episode
- Participation in another investigational drug or device study
- Patient unable to give consent
- Clinical decision precluding the use of DES

Pharmacological Treatments

- BMS group – 1 month DAPT
- DES group – 12 months DAPT

Endpoint definitions

- Myocardial infarction
  - ESC/ACC 2000 definition:
    - troponin rise and ischaemic symptoms
  - Special circumstances
    - Post-PCI – CK >3x ULN (16-22 hrs post-PCI)
    - Patients with MI on admission (and CK > 500mmol/l)
      - >50% further increase in CK

Endpoint definitions

- Bleeding
  - TIMI
    - Major, Minor, None
    - Major
      - Overt clinical bleeding (or any documented intracranial) associated with a drop in haemoglobin of greater than 5 g/dl (0.5 g/l) or in haematocrit of greater than 15%.

Endpoint definitions

- Target vessel revascularisation
  - vessel requires or undergoes attempted repeat revascularisation with:
    - balloon angioplasty
    - stenting
    - coronary artery bypass grafting

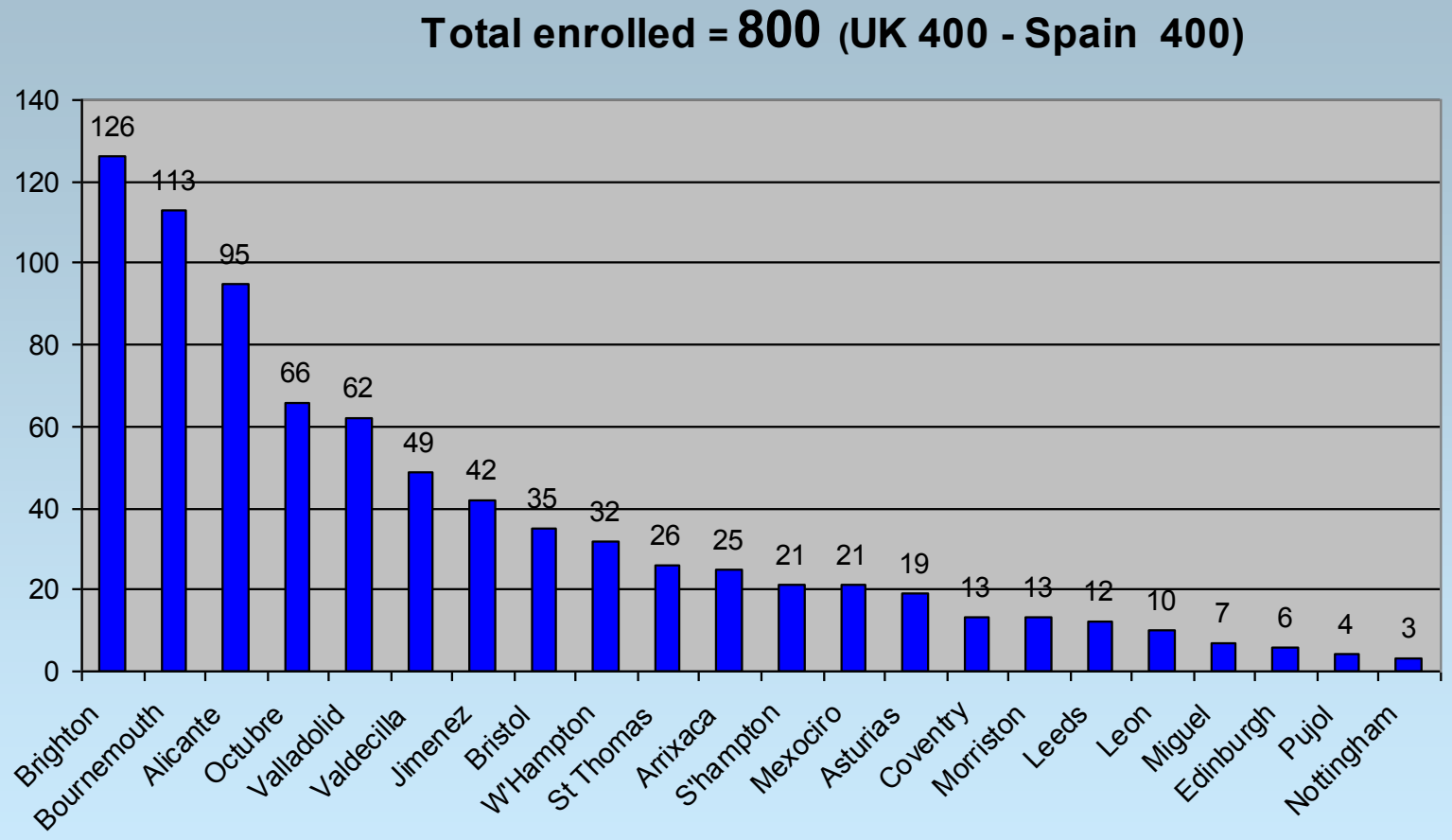
Statistics

- MACE estimates from ARTS I and II and multiple registry data
- Estimated event rates 20% in Vision BMS and 12% in Xience DES
- 80% power with 2-sided significance of 5%
- N=329 in each group

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Enrolment



Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Spanish Recruiters

H. San Juan de Alicante	95	Dr. Ramón López Palop
H. Doce de Octubre	66	Dr. Felipe Hernández
H. Clínico de Valladolid	62	Dr. Federico Gimeno
H. Marqués de Valdecilla	49	Dr. José María de la Torre
H. Juan Ramón Jiménez	42	Dr. José Díaz
H. Virgen de la Arrixaca	25	Dr. Eduardo Pinar
H. Meixoeiro	21	Dr. José Antonio Baz
H. Central de Asturias	19	Dr. Iñigo Lozano
H. de León	10	Dr. Armando Pérez de Prado
H. Miguel Servet	7	Dr. José Antonio Diarte
H. Germans Trias i Pujol	4	Dr. Fina Mauri

Sussex Cardiac Centre

Sección de Hemodinámica y Cardiología Intervencionista

Cardiología VALDECILLA SANTANDER

Sussex Cardiac Centre

Sección de Hemodinámica y Cardiología Intervencionista

Cardiología VALDECILLA SANTANDER

UK Recruiters

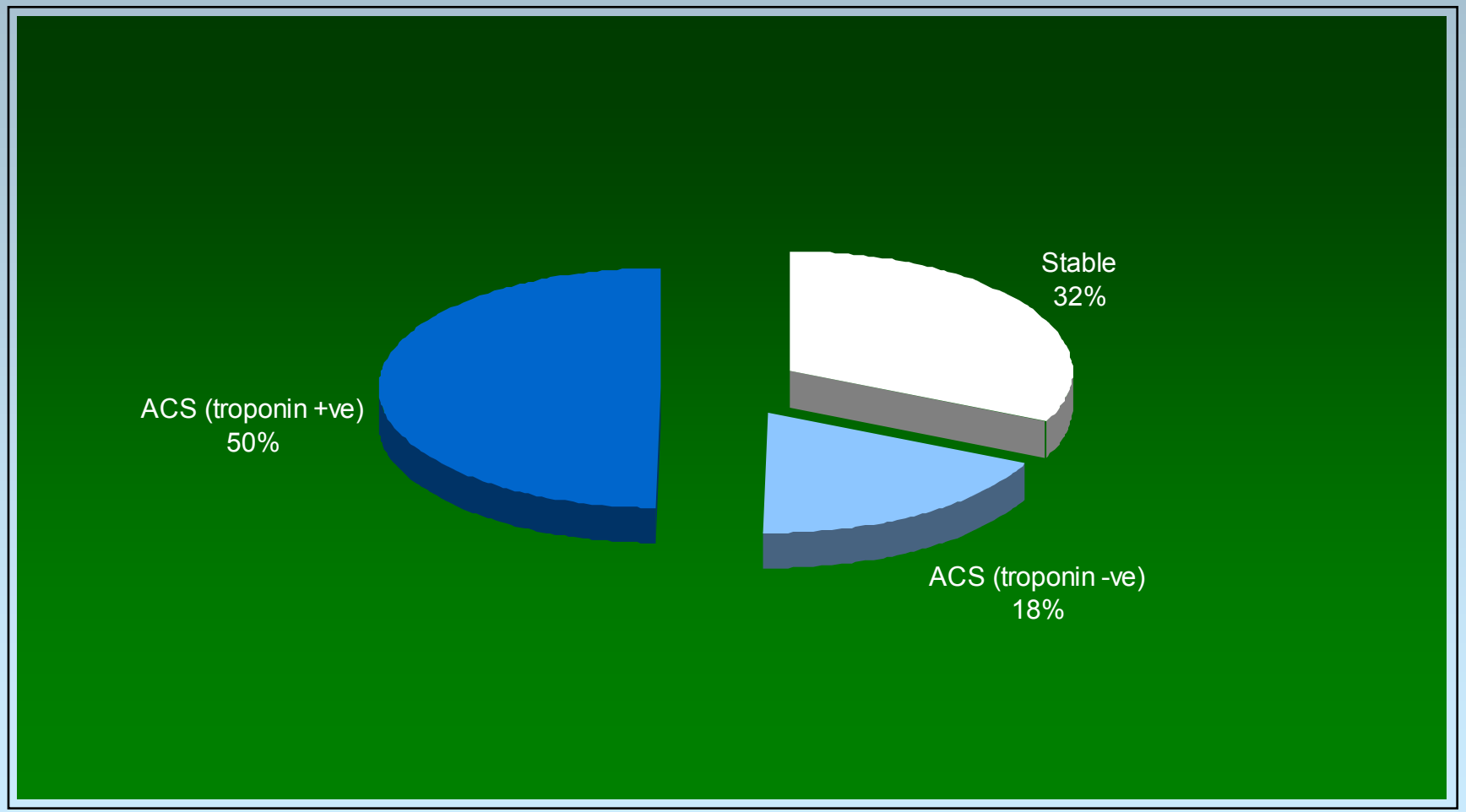
Sussex Cardiac Centre, Brighton	126	Dr. Adam de Belder
Royal Bournemouth Hospital	113	Dr. Peter O'Kane
Bristol Royal Infirmary	35	Dr. Julian Strange
Royal Wolverhampton Hospital	32	Dr. James Cotton
St. Thomas' Hospital	26	Dr. Martyn Thomas
Southampton University Hospital	21	Dr. Nick Curzen
University Hospital, Coventry	13	Dr. Dawn Adamson
Morriston Hospital, Swansea	13	Dr. David Smith
St. James' Hospital, Leeds	12	Dr. Dan Blackman
Royal Infirmary, Edinburgh	6	Dr. Ian Starkey
University Hospital, Nottingham	3	Dr. Robert Henderson

Sussex Cardiac Centre

Demographics

	Vision (BMS) N=401	Xience (DES) N=399	P value
Age yrs (mean±sd)	83.4± 3.1	83.6 ± 3.2	0.35
Female	40.9%	38.9%	0.64
Diabetes	24.2%	25.6%	0.65
Hypertension	77.6%	75.1%	0.42
Hypercholesterolaemia	52.9%	57.6%	0.17
Current smoker	4.0%	5.0%	0.49
Previous CVA/TIA	10.7%	7.8%	0.15
Peripheral vascular disease	12.5%	10.3%	0.33
Creatinine >200um/ml	7.0%	6.0%	0.57
Previous MI	21.5%	29.8%	0.007
Previous PCI	10.2%	12.8%	0.25
Previous CABG	4.2%	7.0%	0.088
LV function <40%	10.1%	13.5%	0.21
On warfarin prePCI	1.3%	2.8%	0.12

Clinical presentation



Procedural details

	Vision (BMS) N=401	**Xience (DES) N=399**	P value
LMS	8.3%	7.6%	P=ns
LAD	63.0%	60.7%	
Cx	30.0%	31.7%	
RCA	35.3%	38.1%	
graft	1.5%	3.6%	
1 vessel PCI	60.5%	62.7%	
2 vessel PCI	31.5%	27.2%	
3 vessel PCI	6.0%	8.4%	
4 vessel PCI	1.5%	1.8%	
5 vessel PCI	0.5%	0%	

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Procedural details

	Vision (BMS) N=401	**Xience (DES) N=399**	P value
Radial approach	58.2%	52.4%	0.12
Rotational atherectomy	12.0%	9.5%	0.26
Complete revascularisation planned?	66.3%	66.5%	0.96
Staged procedure	7.3%	8.3%	0.28
Stented length (mean±SD)	24.0 ±13.4	26.6 ± 14.3	0.011
No. of stents deployed	2.03 ± 1.68	2.13 ± 1.62	0.32
Correct stent deployed	95.0%	93.9%	0.73
Procedural success	97.7%	95.4%	0.075
Use of IIbIIIa inhibitors	1.7%	1.5%	0.79
Days in hospital	6.20± 6.64	7.40±6.33	0.77

Primary endpoint

	Vision (BMS) N=401	Xience (DES) N=399	P value
Death	7.2%	8.5%	0.5
Major haemorrhage	1.7%	2.3%	0.61
MI	8.7%	4.3%	0.01
TVR	7.0%	2.0%	0.0009
CVA	1.2%	1.5%	0.77
Primary endpoint	**18.7%**	**14.5%**	**0.092**

Mortality

	Vision BMS	Xience DES	p
All cause death	7.2%	8.5%	0.5
Cardiac	4.7%	3.3%	0.28
Non-cardiac	2.5%	5.2%	0.04

Major haemorrhage

	Vision BMS	Xience DES	p
Major haemorrhage	1.7%	2.3%	0.61
< 1 month	0.7%	0.5%	1.0
1-6 months	0.7%	0.8%	1.0
6-12 months	0.2%	1.0%	0.22

MI, TVR, CVA

	Vision BMS	Xience DES	p
MI	8.7%	4.3%	0.01
MI <1 month	3.5%	2.5%	0.41
MI 1-12 mnths	5.2%	1.8%	0.006
TVR	7.0%	2.0%	0.0009
CVA	1.2%	1.5%	0.77
CVA (bleed)	0.2%	0.8%	0.37
CVA (ischaemic)	1.0%	0.8%	1.0

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER

Conclusions

This prospective randomised XIMA trial comparing BMS (Vision) and DES (Xience) stents for octogenarians requiring stenting for coronary disease has shown:

- Good clinical results with both DES and BMS
- No difference in mortality between groups at 1 year
- Statistically similar rates of major haemorrhage in both groups despite differing DAPT regimes
- Significantly lower rates of target vessel revascularisation and myocardial infarction among DES-treated patients

Sussex Cardiac Centre

Cardiología VALDECILLA SANTANDER