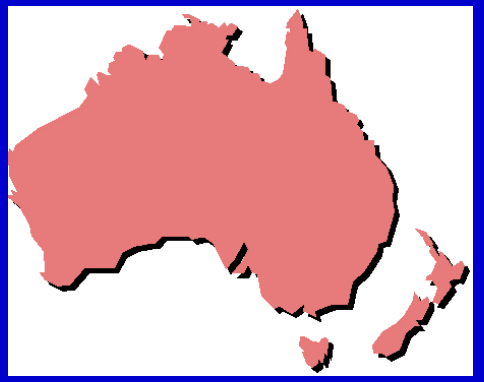
Australia and New Zealand Source Registry Edwards Sapien Aortic Valve

30 day Outcomes

A/ Professor Darren Walters

On behalf of the ANZ Source Investigators

Director of Cardiology
The Prince Charles Hospital
Brisbane, Australia



ANZ Source Registry

- Established to serve as a repository of adjudicated, independently monitored information
- Clinical use and safety and efficacy in ANZ
- Edwards-SAPIEN CE- Marked system for PAVR
- Australian and New Zealand clinical environment.
- Modeled on Source EU protocol

Data Management :

Flinders Cardiovascular Outcomes Research

Prof Derek Chew

Monitoring :

PCRG

Independent Adjudication of death and stroke

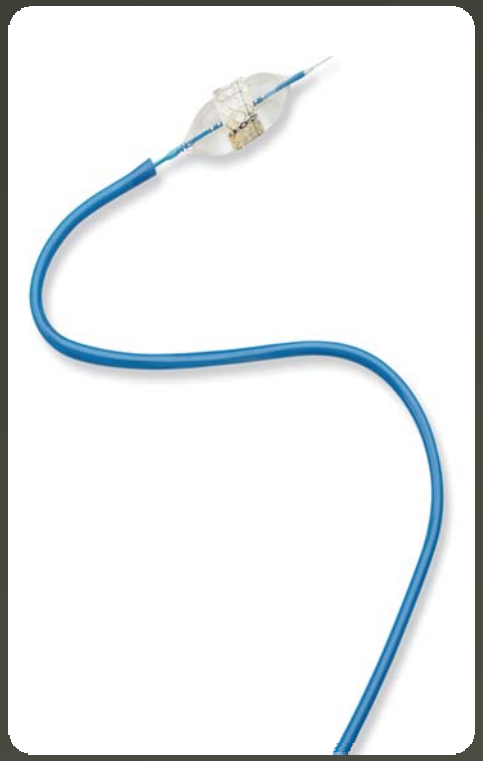
ANZ Source Registry

Three protocol revisions:

- Revision A — SAE/AE monitoring only
- Revision C — Included 100% monitoring
- Revision D — Clarified enrolment to include Heart-team agreement where Euroscore or STS criteria not met but high risk by consensus

Study Devices

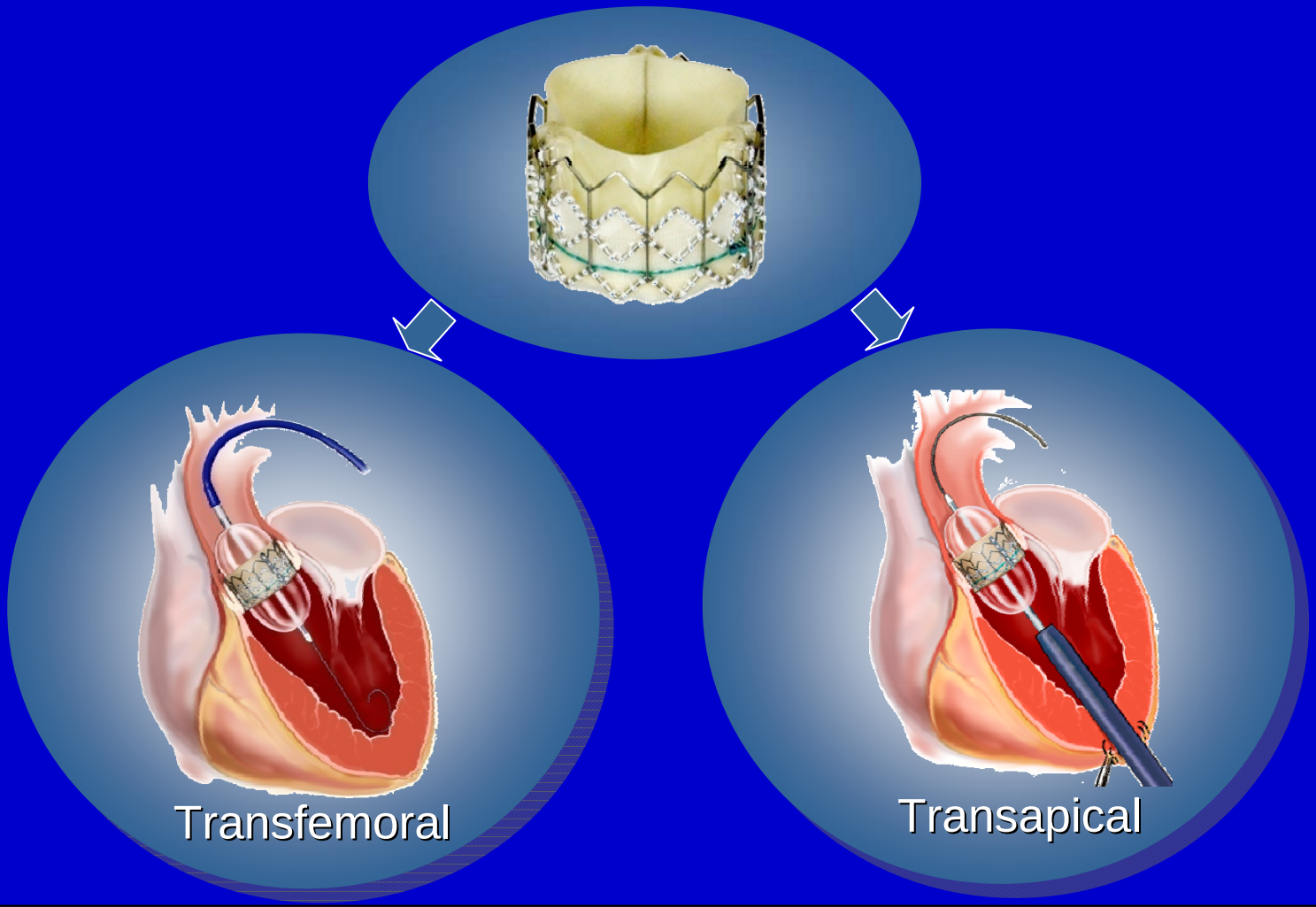
Edwards SAPIEN THV
23 and 26 mm valves



RetroFlex
22 and 24 F sheaths

Ascendra
33 F sheath

TAVR
Transfemoral and Transapical



Criteria

INDICATIONS

1.Symptomatic Degenerative Aortic Stenonosis

2.AVA ≤ 0.8cm2

3.Logistic Euroscore > 20% or STS > 10% or

4.Agreement between Surgeon and Cardiologist : patient not suitable for open surgery due to high risk (Revision D Amendment 5/2010)

www.euroscore.org/calc.html http://209.220.160.181/STSWebRiskCalc261

ANNULUS BY TEE

18 to 22mm = 23mm SAPIEN

21+ to 25mm = 26mm SAPIEN

Trial Design

- Factors might make heart team agree on high risk included but not limited to:
  - Cachexia/Frailty
  - Pulmonary Insufficiency: VMS <1L
  - Home oxygen therapy
  - Previous cardiac surgery
  - Porcelain Aorta
  - Pulmonary hypertension >60 mm Hg
  - Recurrent Pulmonary Embolus
  - RV Insufficiency
  - Thoracic Burning Sequelae Contradicting Open Chest Surgery
  - History of Mediastinum Radiotherapy
  - Severe Connective Tissue Disease
  - Cachexia/Frailty
  - Liver Cirrhosis (Child A or B)
  - Age over 80 yr
  - Age over 90 yr

Consensus risk benefit ratio of open surgery favors TAVR

Criteria

CONTRA - INDICATIONS

The bioprosthesis is contraindicated in patients with:

- Non-valvular aortic stenosis; congenital aortic stenosis, unicuspid, or bicuspid aortic valve; non-calcific acquired aortic stenosis;
- Evidence of intracardiac mass, thrombus,or vegetation
- Untreated clinically significant coronary artery disease requiring revascularization
- Severe deformation of the chest
- Severe coagulation problems
- Active bacterial endocarditis or other active infections
- Previous systemic embolization from the left side of the heart
- Myocardial infarction (MI) within 1 month
- Unstable angina during index hospitalization
- Recent pulmonary emboli
- Cerebrovascular accident (CVA) within 6 months

Criteria

CONTRA - INDICATIONS

- Annulus Ø, (mm) <18 or >25
- Inability to tolerate anticoagulation therapy
- Significant atheroma of the femoral and iliac vessels
- Severe tortuosities of the femoro-iliac vessels
- Femoro-iliac vessels < 7 mm*
- Bilateral iliofemoral bypass
- Hypertrophic cardiomyopathy with or without obstruction (HOCM)
- Severe ventricular dysfunction with ejection fraction < 20%

- The bioprosthesis is not to be used in positions other than the aortic valve

**Smallest diameter > 7mm for 23mm Sapien / > 8 mm for 26 mm Sapien*

Source ANZ Sites

Cases
Initiated on December-2008

Hospital Name (City, Country)

Flinders Medical Center (Sinhal-Bennetts, Adelaide SA)

St. Vincent's Hospital (Baron-Spratt, Sydney, NSW)

Waikato Hospital (Pasupati-El Gamel, Hamilton, New Zealand)

Prince Charles Hospital (Walters-Tesar, Brisbane)

John Hunter (Thambar-James, Newcastle, NSW)

Royal Perth Hospital (Yong-Larbalestier, Perth, WA)

Prince Of Wales (Jepson-Wolfenden,Sydney, NSW)

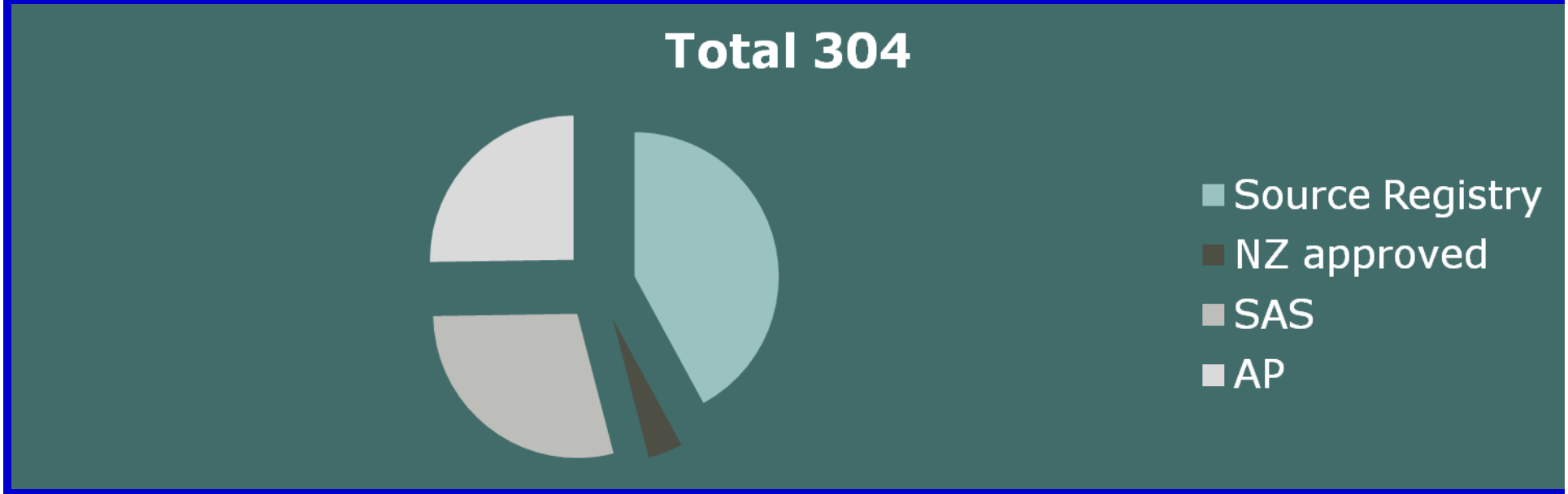
Royal North Shore (Bhindi-Brady,Sydney,NSW)

Patients enrolment

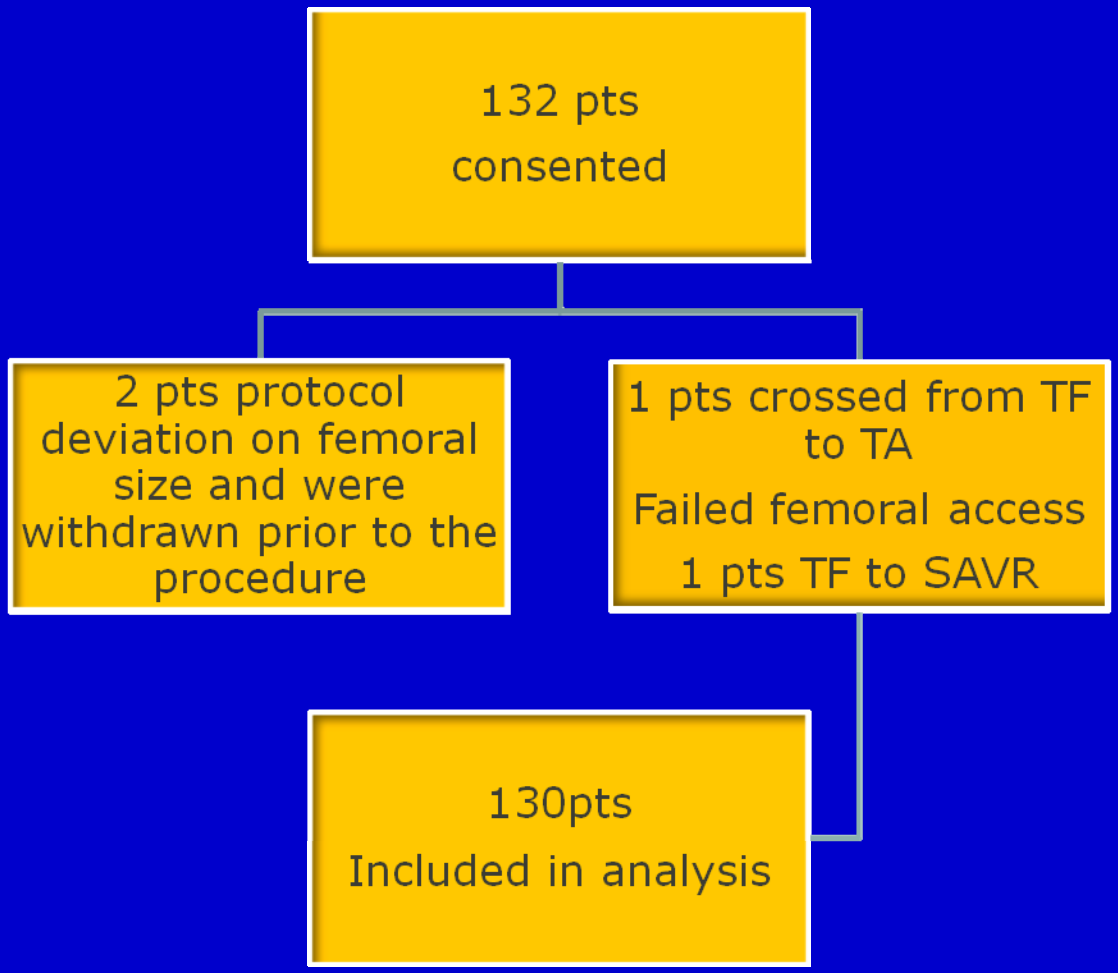
Cases Initiated on December-2008

Hospital Name (City, Country)	CTN
Flinders Medical Center	38
St. Vincent's Hospital	22
Waikato Hospital	17
Prince Charles Hospital	20
John Hunter	11
Royal Perth Hospital	11
Prince Of Wales	8
Royal North Shore	5
Total	**132**

Source - Edwards TAVI in ANZ



Enrolment

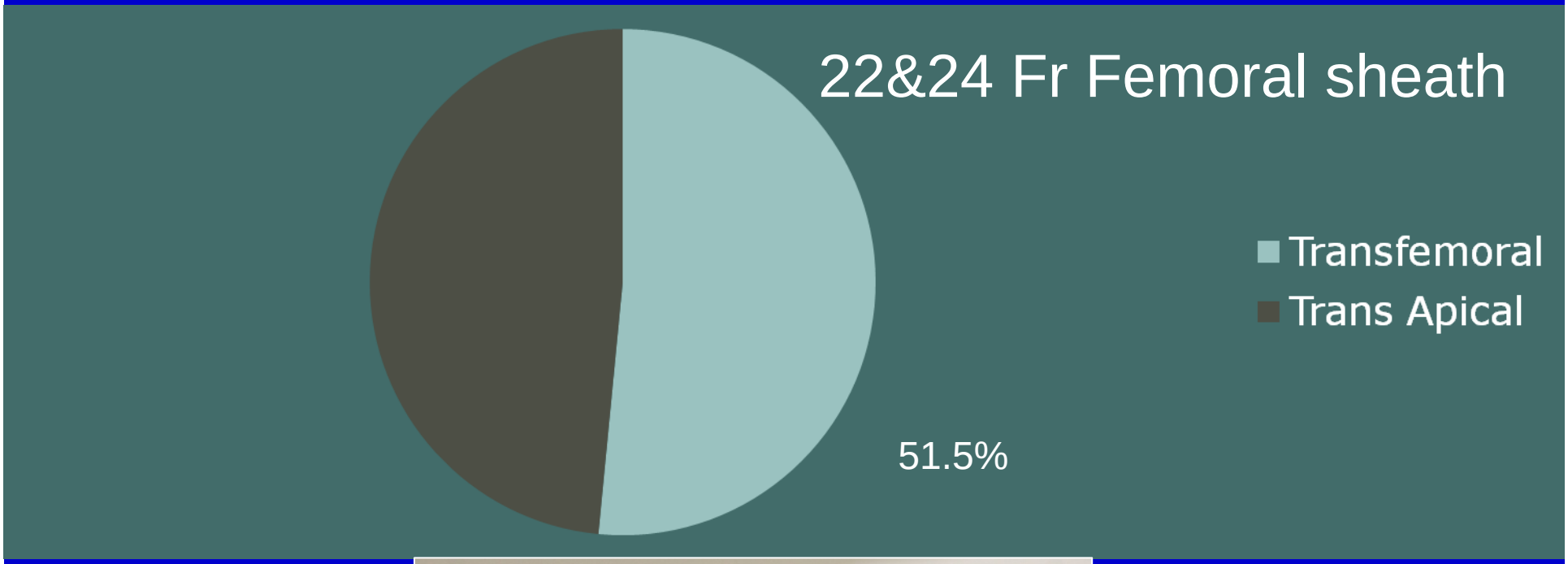

132 pts
consented
2 pts protocol deviation on femoral size and were withdrawn prior to the procedure
1 pts crossed from TF to TA
Failed femoral access
1 pts TF to SAVR
130pts
Included in analysis

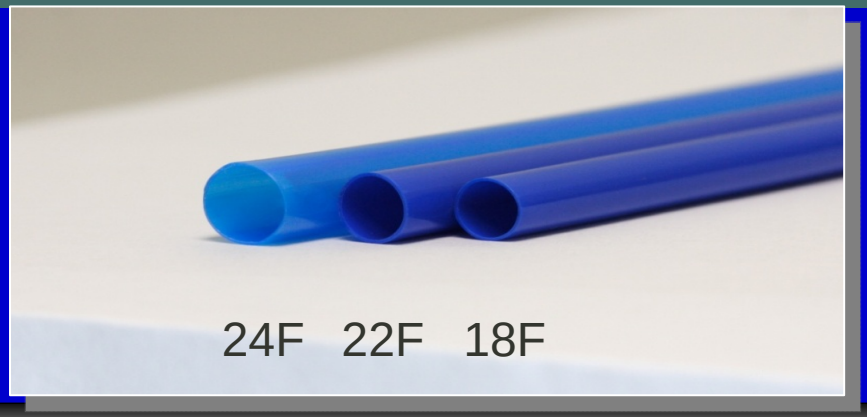
Enrolment

- Revision A 64 pts
- Revision C 63 pts
- Revision D 3 pts

- Monitoring 100% 66 pts
- Monitoring all AE SAE 64 pts

Enrolment by TAVR Route





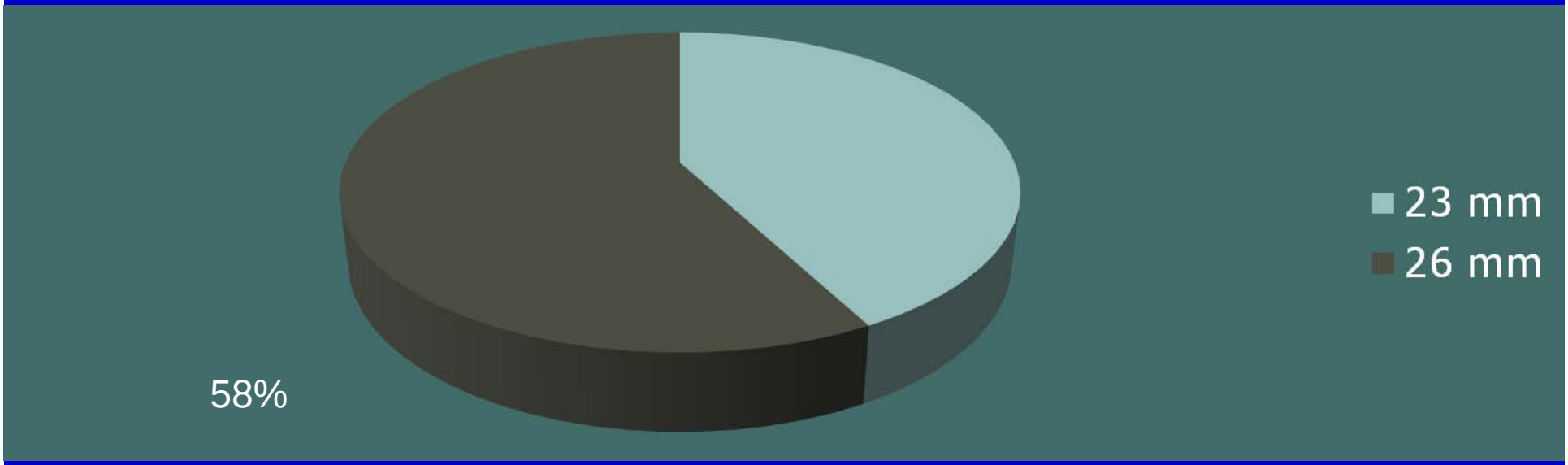
Baseline Demographics and Risk Factors

	TF (n=67)	TA (n=63)	P-Value
Age (yrs)	83.67	81.94	0.252
Female	34.3%	61.9%	0.002
Creatinine (mmol/l)	116.4	115.2	0.904
Logistic EuroSCORE	27.1%	29.1%	0.532
Peripheral Vascular Disease	25.8%	52.4	0.002
Carotid Artery Stenosis (>50%)	5.97%	19.1%	0.024
Incidence of CAD	80.6%	73.0%	0.307
Porcelain Aorta	3.0%	17.5 %	0.006
Prior CABG	40.3%	39.7%	0.943
Mitral valve disease	23.8%	28.6%	0.545

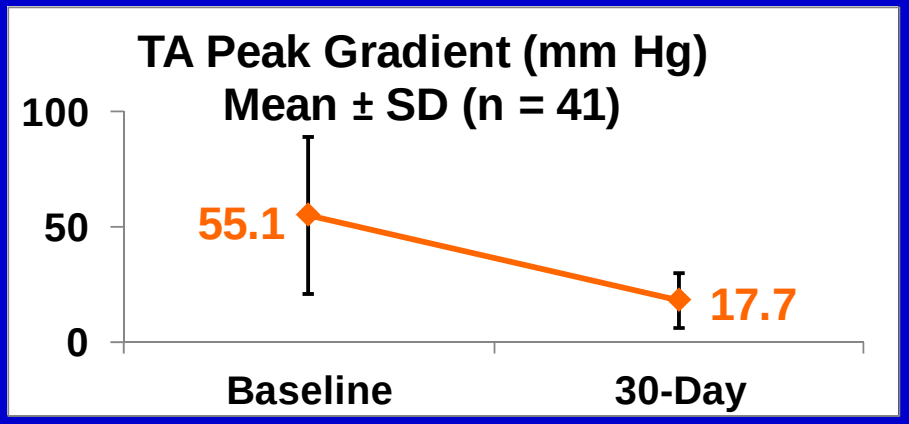
Baseline Demographics and Risk Factors

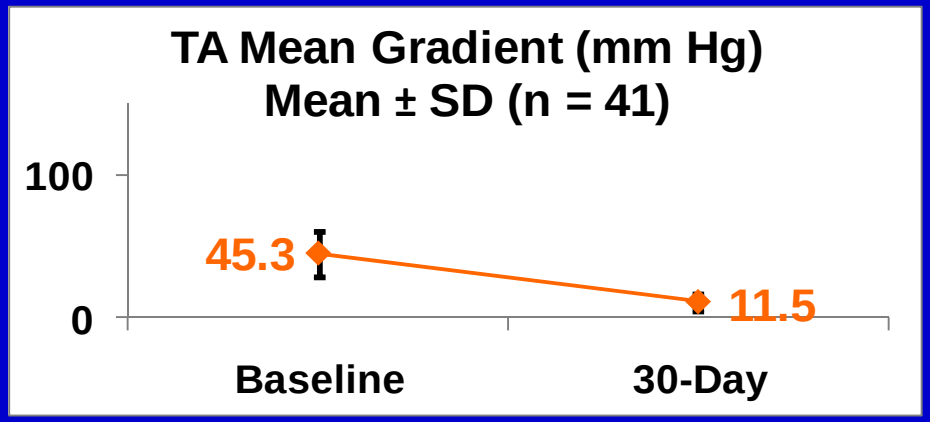
	TF (n=67)	TA (n=63)	P-Value
NYHA (median)	2.83 (n=67)	2.82 (n=60)	0.888
Aortic Valve Area (cm^2)	0.61 (n=56)	0.63 (n=55)	0.552
Peak gradient (mmHg)	49.1 (n=61)	55.1 (n=55)	0.408
Mean gradient (mmHg)	46.7 (n=61)	45.3 (n=59)	0.727
LVEF (%)	58.6 (n=43)	55.2 (n=40)	0.610

Valve Implants

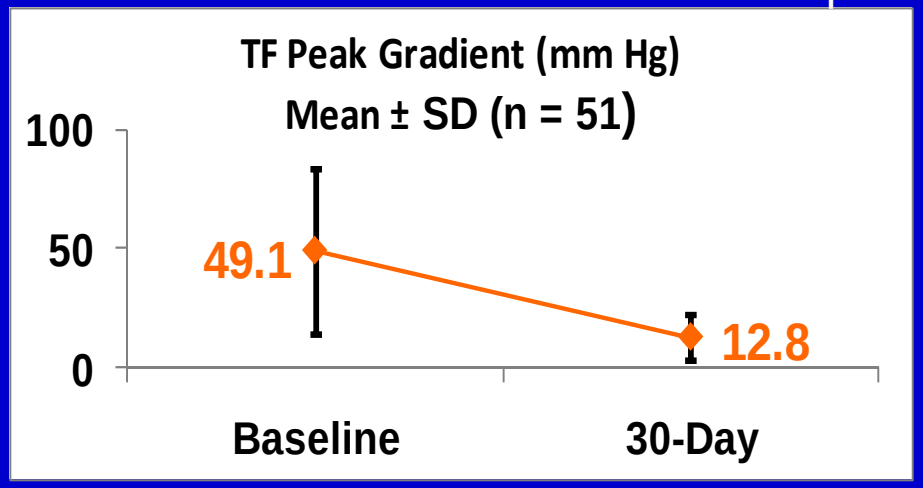


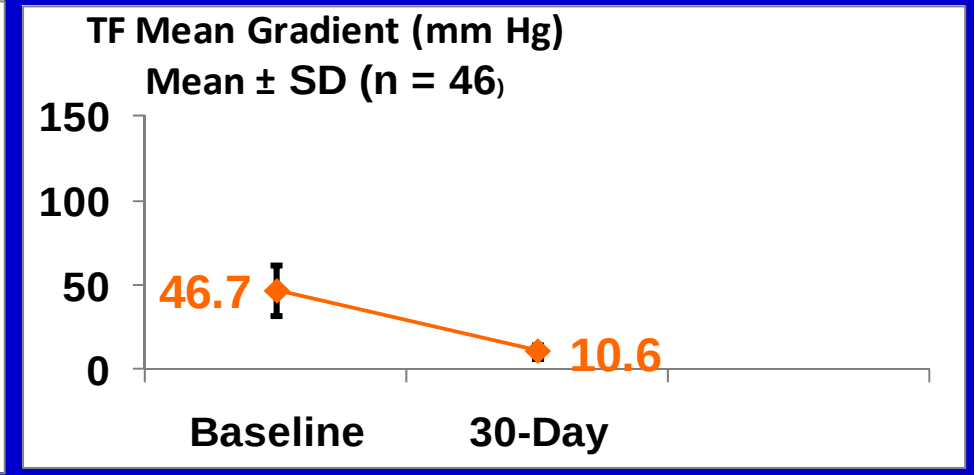
30-Day* Paired Echo Data





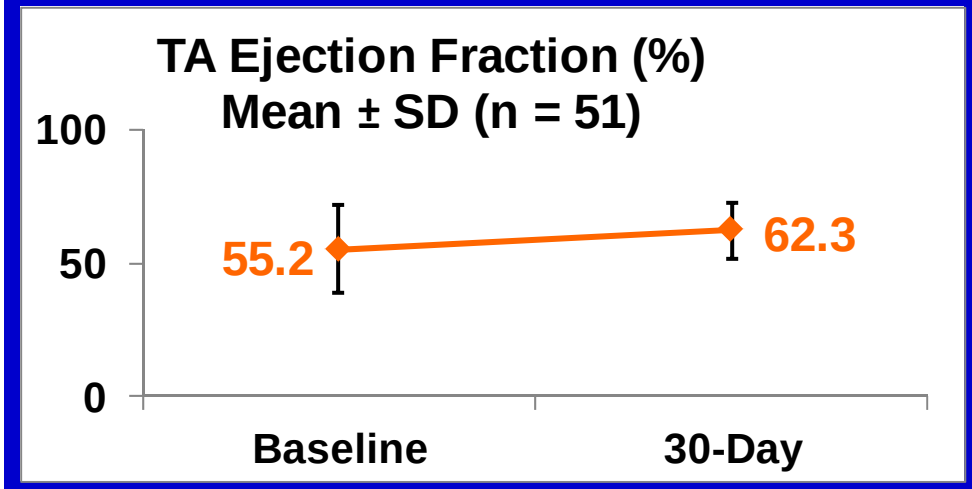
All p<0.001



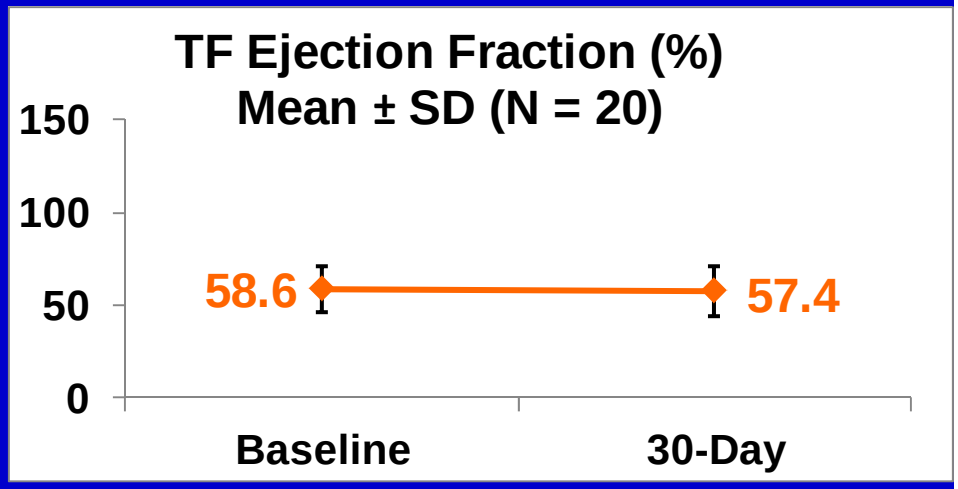


*Include cases with follow-up data between 1-month & 5-month

30-Day* Paired Echo Data



All p=0.053



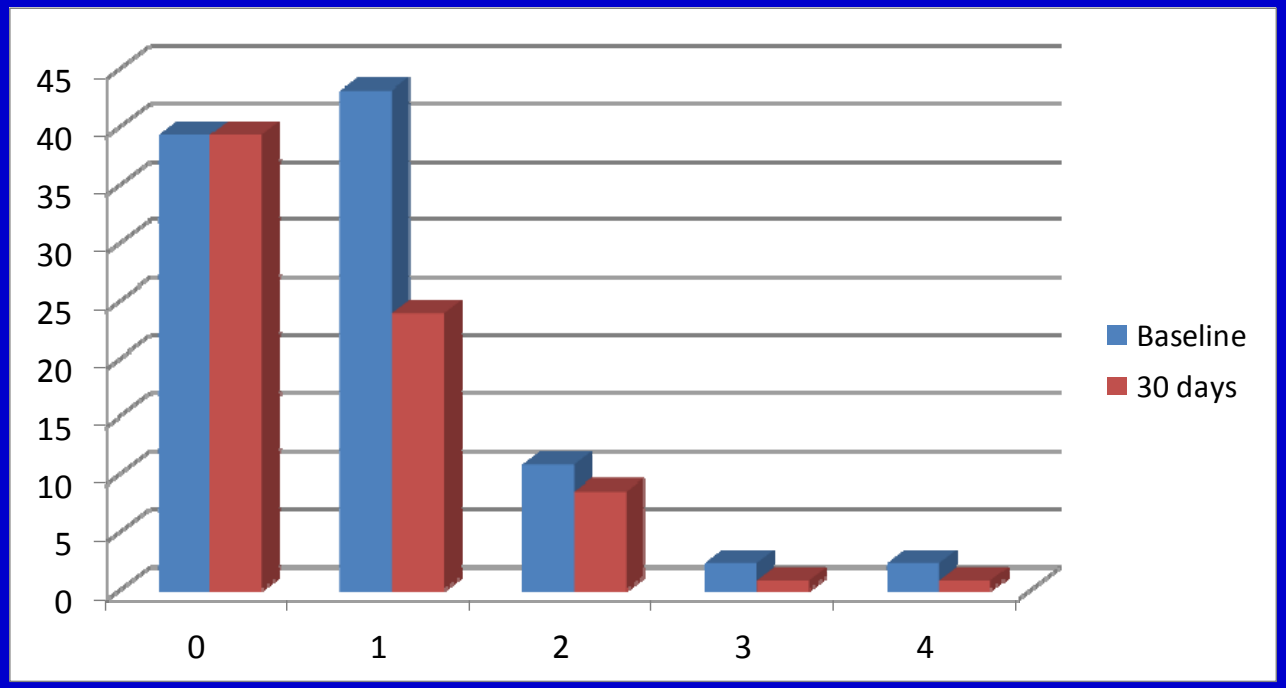
All p=0.345

*Include cases with follow-up data between 1-month & 5-month

Aortic regurgitation at baseline and 30 days

P=0.077

%



Major Complications (30 Days)

	TF % (n=67)	TA % (n=63)	P Value
Death	5.97	9.52	0.449
Stroke	2.99	4.76	0.600
Myocardial infarction	1.49	4.76	0.283
MACCE	8.96	15.87	0.232
Minor Vascular	10.45	1.59	0.036
Major Vascular	4.48	6.35	0.638
Renal function deterioration	11.94	17.46	0.375
Permanent Pacemaker	1.49	7.94	0.081

Major Complications (30 Days)

	TF % (n=67)	TA % (n=63)	Total % (n=129)
Bleed (All)	14.93	19.05	16.92
Minor Vascular	10.45	1.59	6.15
Major Vascular	4.48	6.35	5.38

Defined according to VARC Criteria
Eurointervention:2010:5;673-679.

Major Complications Death
(< 30 days)

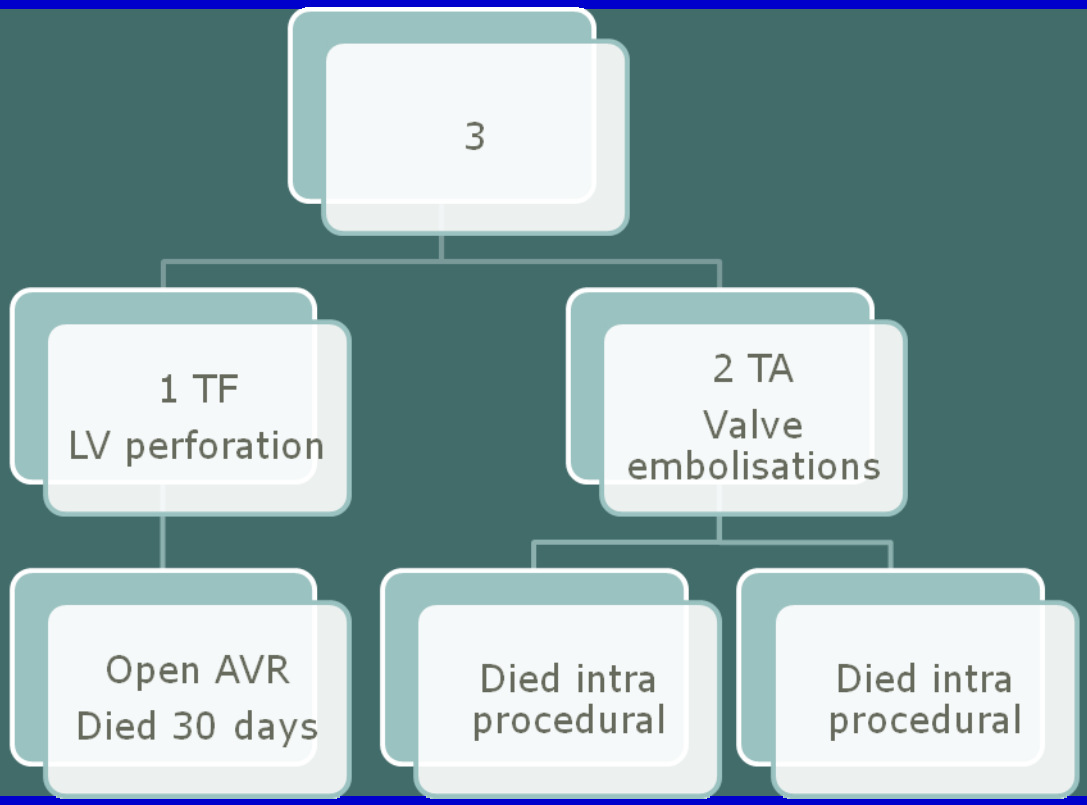
TF x 4

1 annular dissection
1 post sAVR following ventricular perforation during TAVR
1 hemodynamic collapse post op
1 awaiting adjudication ; left main occlusion

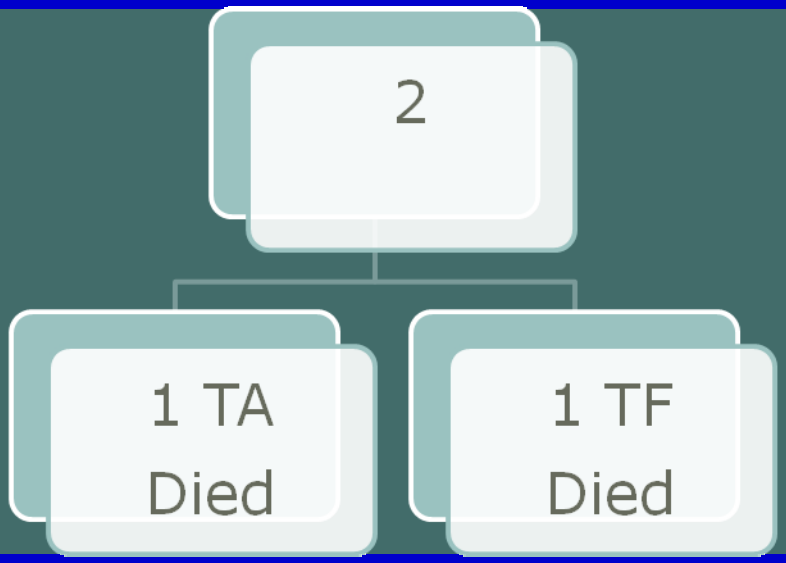
TA x 6

1 left main occlusion
2 following surgical intervention post valve embolisation into ventricle
1 haemorrhage from TA access site
1 day of discharge in hospital arrest post mortem inconclusive
1 awaiting adjudication

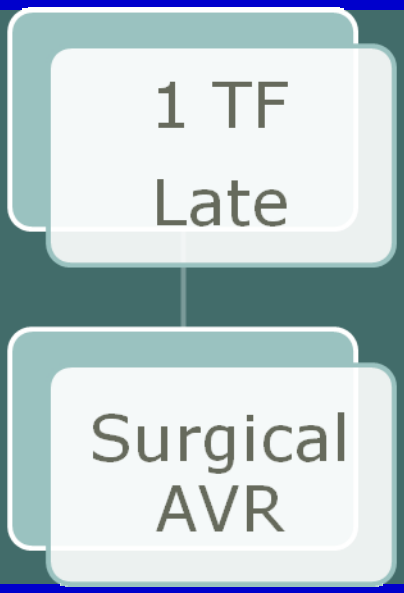
Complications
Surgical conversion



Complications
Coronary Obstruction



Valve Malposition



Baseline Demographics and Risk Factors

	ANZ TF (n=67)	Source TF (n=463)	ANZ TA (n=63)	Source TA (n=575)	Partner A TAVR
Age (yrs)	83.67	81.7	81.94	80.7	83.6
Female	34.3%	55.2%	61.9%	56%	42.2
Logistic EuroSCORE	27.1%	25.7	29.1%	29.2	29.3
Peripheral Vascular Disease	25.4%	10.9%	52.4%	27.5%	43%
Carotid Artery Stenosis (>50%)	5.97%	7.6%	19.1%	17.1%	29.3%
Incidence of CAD	80.6%	47.4%	73.0%	56.0%	74.9%
Porcelain Aorta	2.99%	4.6%	17.5%	11.5%	0.6%
Prior CABG	40.3%	17.6%	39.7%	26.9%	42.6%

Implantation Success

	ANZ TF (n=67)	Source TF (n=463)	ANZ TA (n=63)	Source TA (575)	Partner A TAVR (348)
Acute procedure success	92.5%	95.6%	87.3%	92.9%	94.5%
Conversion to sAVR	1.49%(1)	1.7(2)%	3.17 % (2)	3.5%	2.6%
AR >+2**	1.49% (1)	3.2%	1.59% (1)	5.9%	
Valve migration	1.49% (1)	0.0%	3.17% (2)	0.5%#	2.6%
Coronary obstruction	1.49% (1)	0.7%	1.59% (1)	0.5%	

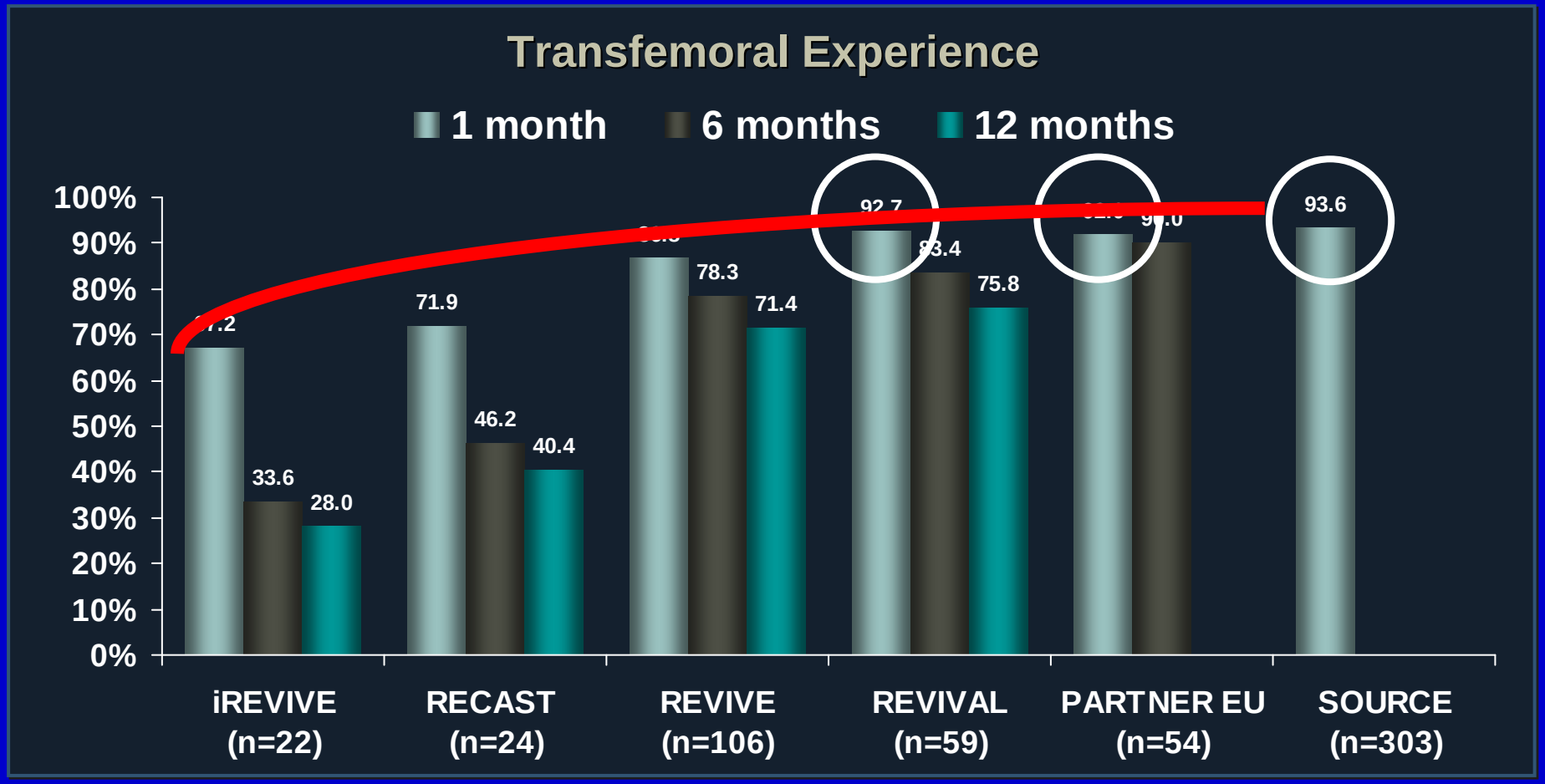
TAVR implanted pt alive at the end of procedure

Major Complications
(< 30 days)

	TF % (n=67)	TA % (n=63)	ANZ Total % (n=130)	EU Total %(n=1038)	Partner A TAVR %(n=348)
Death	5.97	9.52	7.69	8.5	12
Stroke	2.99	4.76	3.85	2.5	5.5
Permanent pacemaker	1.49	7.94	4.62	7.0	3.8
Vascular Major	4.48	6.35	5.38	7.0	11.1

Edwards Transcatheter AVR

Survival at 1, 6 and 12 months



T-AVR Key Issues

- Patient selection beyond the Euroscore/STS
- Procedural performance
  - Hybrid OR
  - TOE/GA/LA
- Procedural Complications
  - Vascular complications- device profile
    - Acceptable with 18 Fr: ?unacceptable with 24 Fr
  - Heart Block – 7.0%-37.5%
    - acceptable with Sapien Platform: ?unacceptable Core Valve
  - Aortic Regurgitation
    - Not yet linked to adverse outcomes

T-AVR Key Issues

- Surgically eligible patient: when not if?
  - Which surgically eligible group: where do we draw the line
    - Critical importance of longevity of device
    - Older patients remain target in medium term
- Quality of life versus survival
- Cost effectiveness compared to standard surgery
- Longevity of device: long term patient follow up essential

Conclusion

- Early learning curve experience in our region appears to demonstrate results similar to the published European Experience.
- Procedural Success acceptable for early experience
- Lower than predicted 30-day mortality
- prospective registry surveillance of procedural success and late outcomes within ANZ essential
- Increased efforts to ensure data quality and trial integrity