AFX System for Endovascular Treatment of Patients with Abdominal Aortic Aneurysms (AAA)

November 2, 2021

Circulatory System Devices Panel

Endologix LLC

Introduction

Matt Thompson, MD

Chief Medical Officer

Endologix

AFX2 is an Effective, Durable, and Necessary Treatment Option for Patients with AAA

- Long-term durability concerns with AFX Strata addressed through updates to labeling, product design and manufacturing
- Clinical evidence from ~3000 patients supports performance and durability of currently available product, AFX2
  - Benefit-risk profile comparable to all other EVAR devices
- Initiatives to guide management of patients with AFX Strata

Evaluating Performance of EVAR Devices

- FDA focused on Type III endoleaks
- EVAR is a complex intervention and no endograft is completely safe or completely effective
- Risk-benefit analysis should include all relevant failure modes and a patient-centric approach
- Single failure modes important as part of a holistic and comparative analysis of endograft performance

Three Different AFX Devices; Each Consists of Implant Design, Manufacturing Process & IFU

AFX2
Feb 2016 – Present

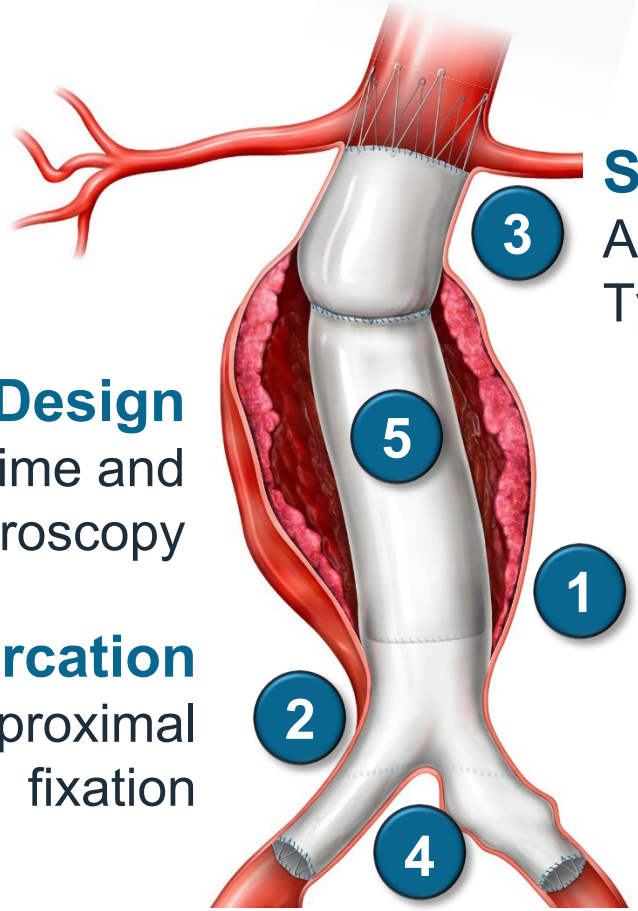
Only Currently Available AFX Device

AFX Duraply
Jul 2014 – May 2020

AFX Strata
Jul 2011 – Dec 2016

- AFX is more than a physical implant
- Combination of elements differentiate AFX devices and impact device performance
  - Implant and delivery system
  - Manufacturing process
  - IFU labeling

AFX Unique Design Offers Advantages in Certain Clinical Situations



Sealing in Proximal Aortic Neck
Achieves effective seal and reduces risk of Type Ia endoleaks in peri-operative period

Unibody Design
Lower operative time and reduced fluoroscopy

7F Contralateral Access
Advantage for patients with narrowed iliac access or peripheral vascular disease

Fixation on Aortic Bifurcation
Offers an alternative to proximal fixation

Preserves Native Aortic Bifurcation
Facilitates retrograde access for treatment of contralateral peripheral vascular disease

Agenda

AFX System Updates, Management of AFX Strata	**Genevieve Dunbar** Senior Director, Regulatory Affairs Endologix
AFX Performance Profile	**Matt Thompson, MD** Chief Medical Officer Endologix
Clinical Perspective	**Christopher Kwolek, MD, MBA** Senior Vascular Surgeon Massachusetts General Hospital

Additional Experts

Chris Mullin
Director, Product Development Strategy
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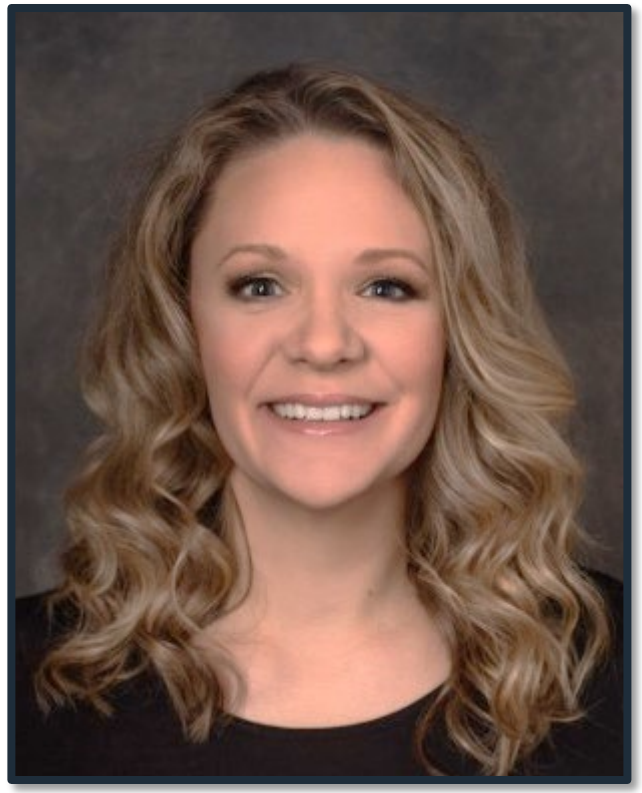
Ken Ouriel, MD
Chief Medical Officer
NAMSA

AFX System Updates, Management of AFX Strata

Genevieve Dunbar

Senior Director Regulatory Affairs

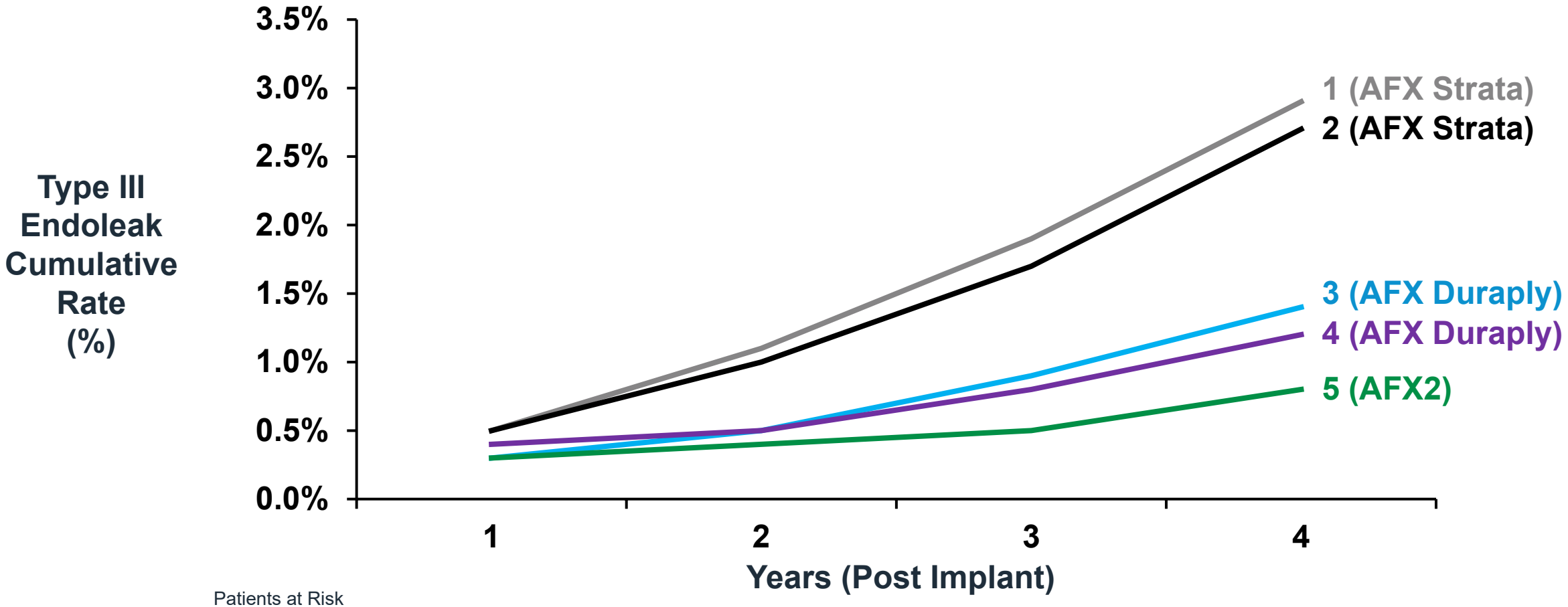
Endologix



Design, Manufacturing, and Labeling Updates from AFX Strata to AFX2

Date	Group	AFX Device	Contributing Factors	Description of Update	Endoleak Addressed
Jul 2011	1	Strata	Baseline	▪ Prior to any updates	N/A
Jan 2013	2	Strata	Inadequate Overlap	▪ Longer bifurcated lengths introduced ▪ IFU update - overlap recommendations	Type IIIa
Jul 2014	3	Duraply	Tear Propagation; Iatrogenic Graft Damage	▪ AFX Duraply new ePTFE processing method ▪ IFU update – guidewire manipulation, ballooning, and vessel calcification	Type IIIb
Sep 2015	4	Duraply	Patient Selection and Disease Progression Impacting Overlap	▪ IFU update – clarify patient selection, procedure planning, and post-operative imaging	Type IIIa
Feb 2016	5	AFX2	Delivery System/Implant Interactions, Incorrect Component Sizing	▪ Improved delivery system ▪ Improved manufacturing method for loading implant ▪ Increased mean thickness of graft material ▪ Introduced sizing algorithm	Type IIIa & IIIb

Each Product Update Reduced Occurrence of Type III Endoleaks



Patients at Risk				
1 (AFX STRATA)	11208	11149	11120	11094
2 (AFX STRATA)	13309	13251	13233	13218
3 (AFX DURAPLY)	8064	8036	8028	8019
4 (AFX DURAPLY)	6660	6643	6640	6633
5 (AFX2)	38465	28990	19370	8838

Complaint data cutoff February 2021

Surveillance and Reintervention Strategy for Patients Implanted with AFX Strata

Surveillance and Reintervention Strategy for Patients Implanted with AFX Strata

- Type III endoleaks are amenable to endovascular repair
- Medical Advisory Boards evaluated patient management, surveillance recommendations and reintervention strategy
- 2018 Field Safety Communication
  - Provided specific guidance for reintervention
  - Emphasized need for patient tailored surveillance
  - Recommended enhanced surveillance for high-risk patients
- Bench and clinical data supports feasibility/durability of AFX-in-AFX
  - IFU update including reline data planned for early 2022; pending review by FDA

Endologix has Continually Monitored and Improved AFX Family of Devices

- Product design, manufacturing, and labeling updates successful in reducing rate of Type III Endoleaks
- AFX2 addresses concerns previously identified
- Multiple actions provide information to physicians to guide management of patients with AFX Strata

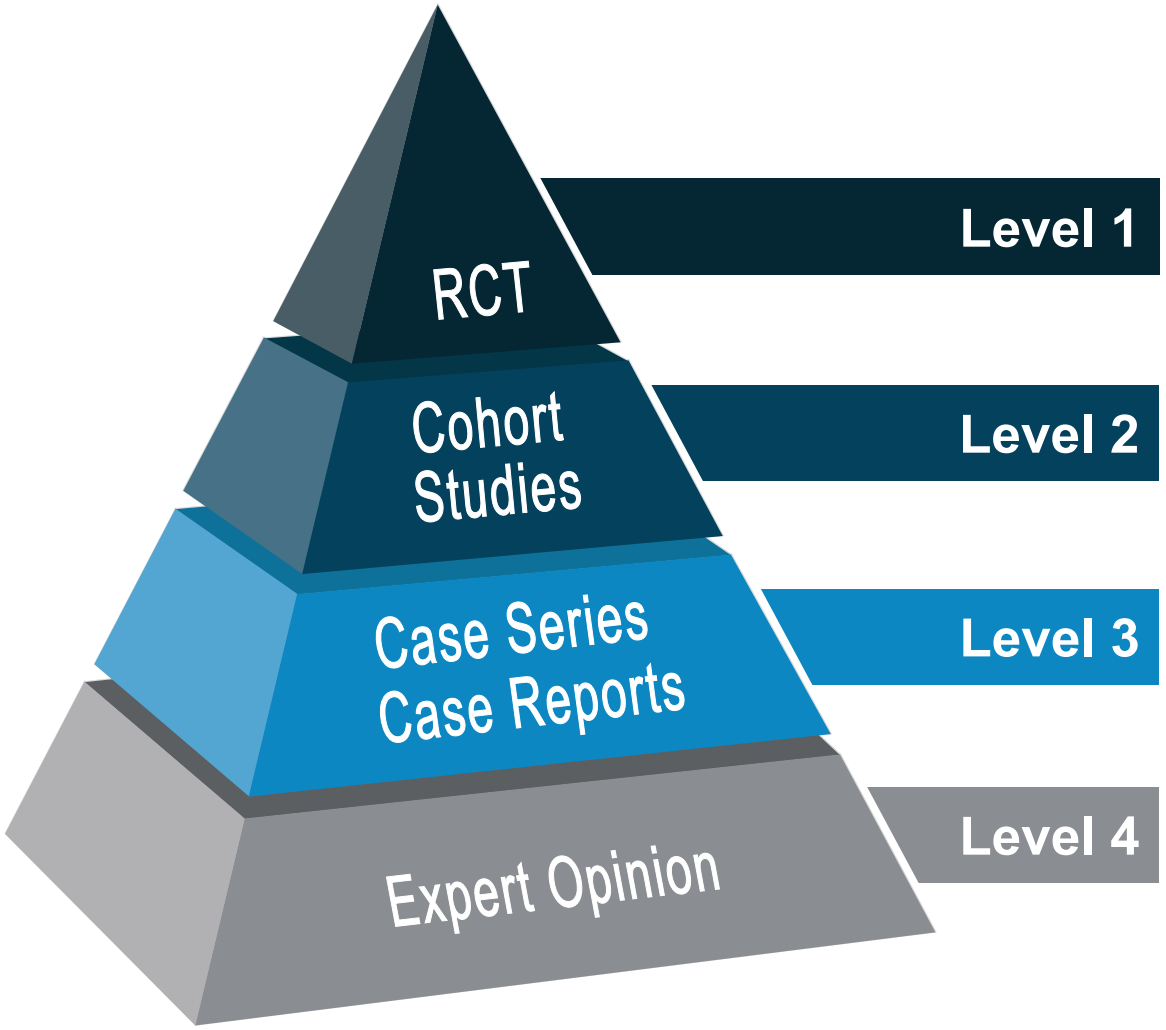
AFX Performance Profile

Matt Thompson, MD

Chief Medical Officer

Endologix

Available Evidence Provides Robust Evaluation of AFX Device Performance

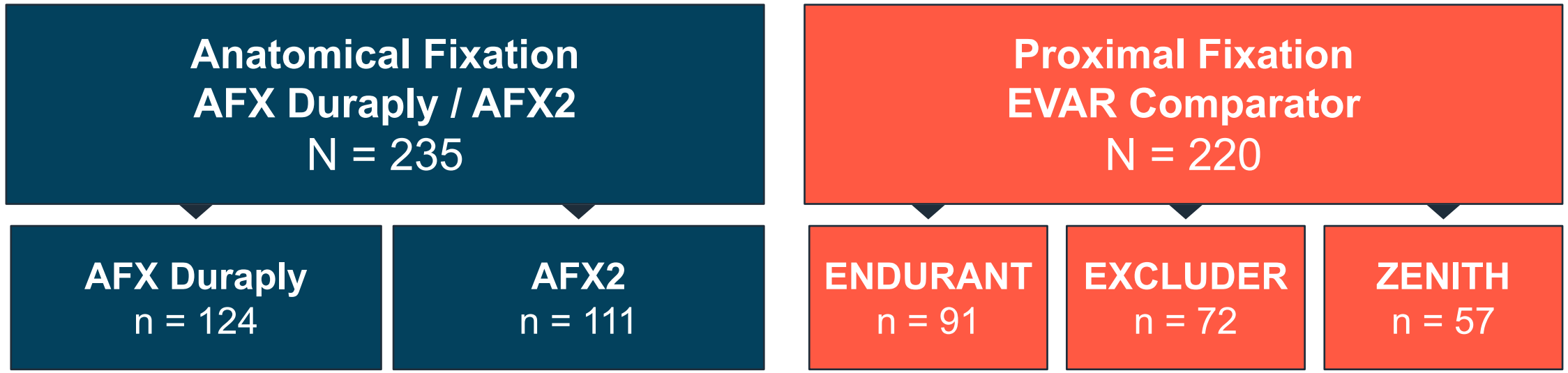


LEOPARD RCT

Medicare Data
Vascular Quality Initiative (VQI)

Multicenter Series

LEOPARD: Only Prospective, Multicenter, RCT Comparing EVAR Devices (N=455 Patients)



- 105 investigators enrolled patients at 56 sites
- Follow-up based on institutional standard of care, ongoing up to 5 years
- All adverse events independently adjudicated
- CT imaging reviewed by core lab

LEOPARD: Primary Composite Endpoint

Primary Endpoint

- Freedom from aneurysm-related complications (ARC) at 1 year
  - Peri-operative death (< 30 days)
  - Endograft limb occlusion
  - Post-operative endoleaks
  - Aneurysm enlargement (≥ 5 mm)
  - Migration (≥ 10 mm)
  - Conversion to open surgical repair
  - Aneurysm rupture
  - Reintervention

Secondary Endpoints
(Reported as a non-composite Kaplan-Meier Estimates)

- All-cause mortality
- Major adverse events
- Aneurysm-related mortality
- Endoleaks classified by type
- Individual components of ARC
- AAA-related secondary procedures

LEOPARD: 3-Year Timepoint Represents True Estimate of Available Follow-Up Data

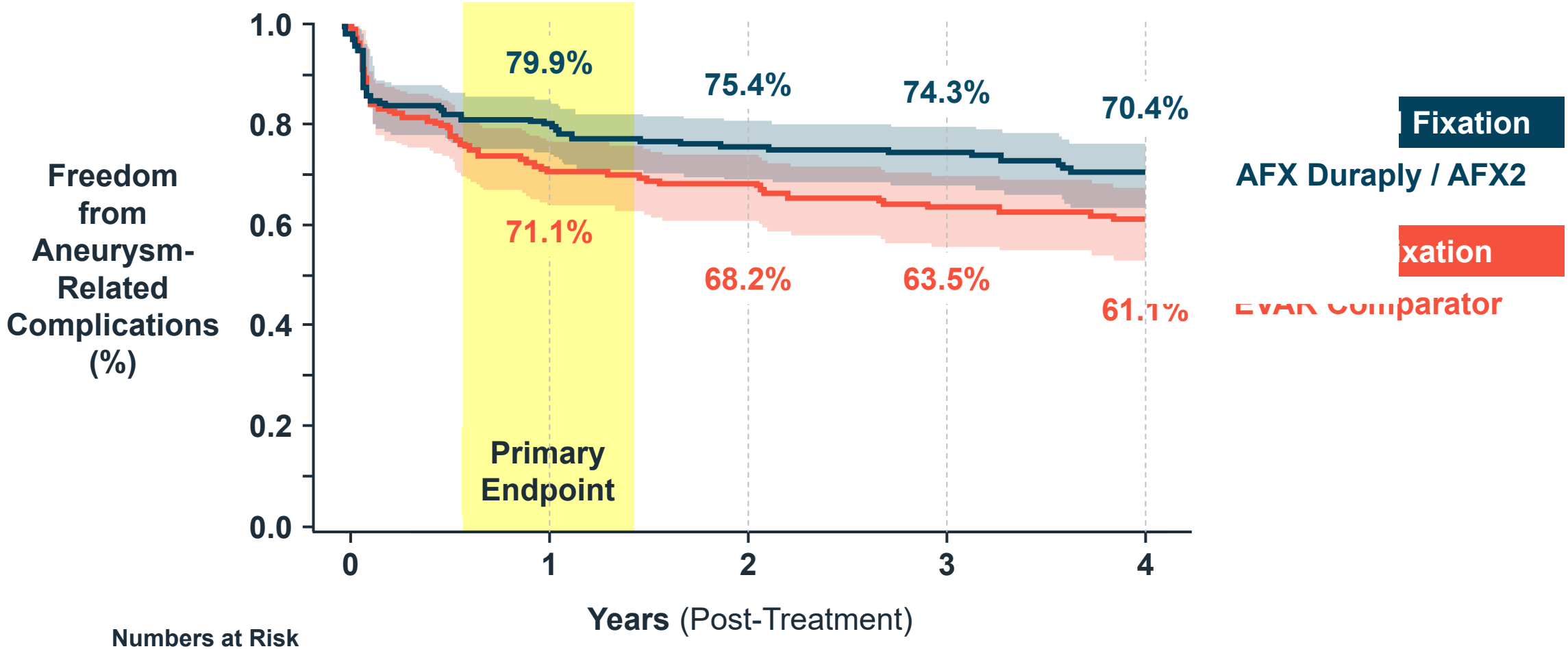
	Anatomical Fixation AFX DURAPLY / AFX2 N = 235				Proximal Fixation EVAR Comparator N = 220			
	Eligible for Follow-Up	Clinical Follow-Up	Site Imaging Results	CT Core Lab Reviewed	Eligible for Follow-Up	Clinical Follow-Up	Site Imaging Results	CT Core Lab Reviewed
1 Year	**218**	194 **(89%)**	190 **(87%)**	150 **(69%)**	**194**	180 **(93%)**	175 **(90%)**	141 **(73%)**
2 Year	**198**	184 **(93%)**	174 **(88%)**	134 **(68%)**	**175**	159 **(91%)**	150 **(86%)**	122 **(70%)**
3 Year	**181**	156 **(86%)**	149 **(82%)**	112 **(62%)**	**155**	138 **(89%)**	128 **(83%)**	106 **(68%)**
4 Year	**145**	117 **(81%)**	113 **(78%)**	89 **(61%)**	**129**	107 **(83%)**	102 **(79%)**	86 **(67%)**
5 Year	**80**	61 **(76%)**	52 **(85%)**	37 **(61%)**	**84**	74 **(88%)**	64 **(76%)**	46 **(55%)**

As requested by FDA, these data were provided to FDA on September 22, 2021

Sequence of Events that Resulted in LEOPARD Enrollment Stopping

LEOPARD	▪ Prespecified powering to assess non-inferiority (NI) and superiority ▪ Estimated sample size N=804
2015	▪ Enrollment began
2016	▪ AFX Strata devices recalled
2017	▪ OUS Regulatory requests ▪ Seeking confirmation that AFX Strata issues resolved ▪ LEOPARD most pertinent dataset to address questions ▪ Descriptive analysis performed; N=246 at 1 year ▪ Sample size re-evaluated; N > 2000 needed for superiority ▪ Enrollment stopped at N=455; adequate power for NI claim

LEOPARD: Aneurysm-Related Complications



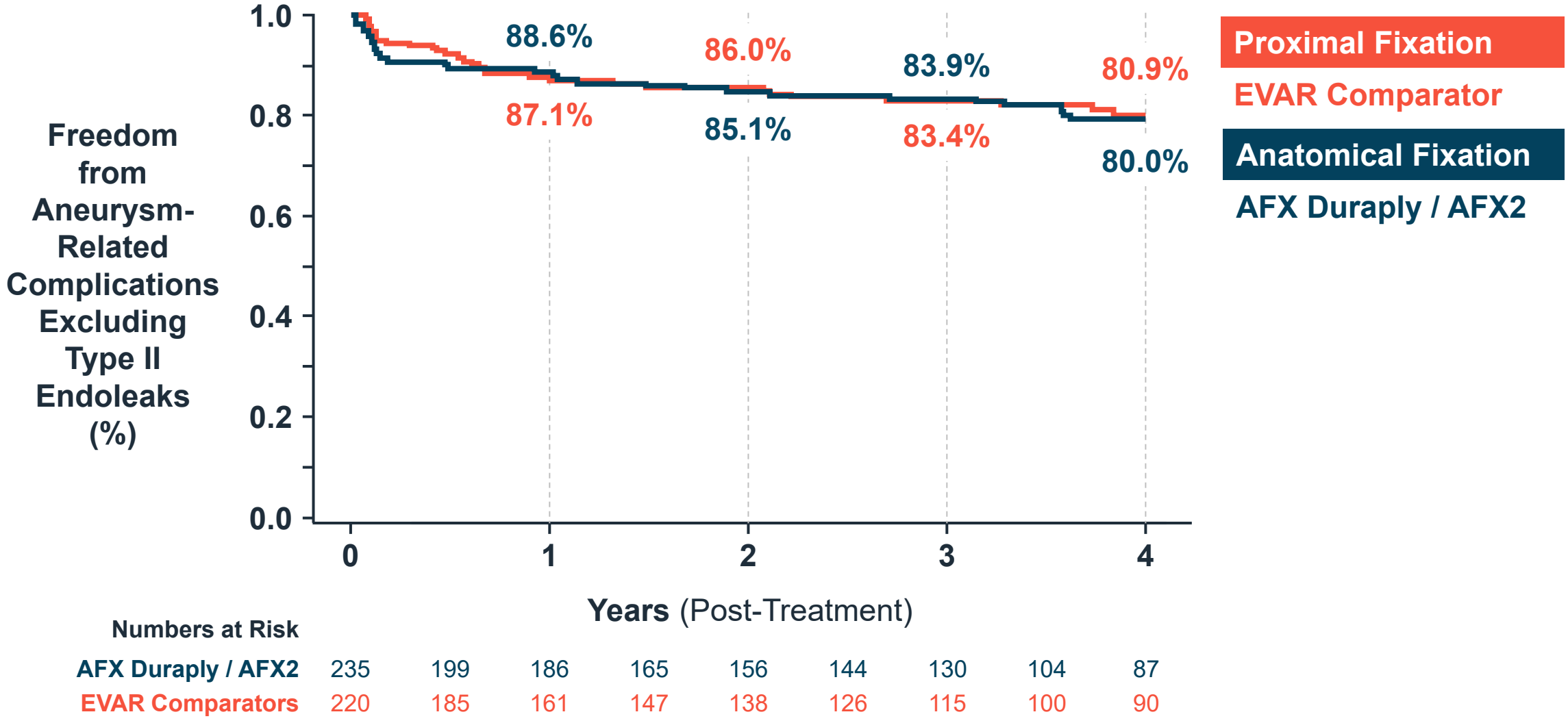
Numbers at Risk

AFX Duraply / AFX2	235	182	169	149	141	130	116	92	77
EVAR Comparators	220	159	129	117	108	97	87	77	70

Core Lab Reported + Site Reported Data

Data extract date August 31, 2021

LEOPARD: ARC Excluding Type II Endoleaks



Numbers at Risk									
AFX Duraply / AFX2	235	199	186	165	156	144	130	104	87
EVAR Comparators	220	185	161	147	138	126	115	100	90

Core Lab Reported + Site Reported Data

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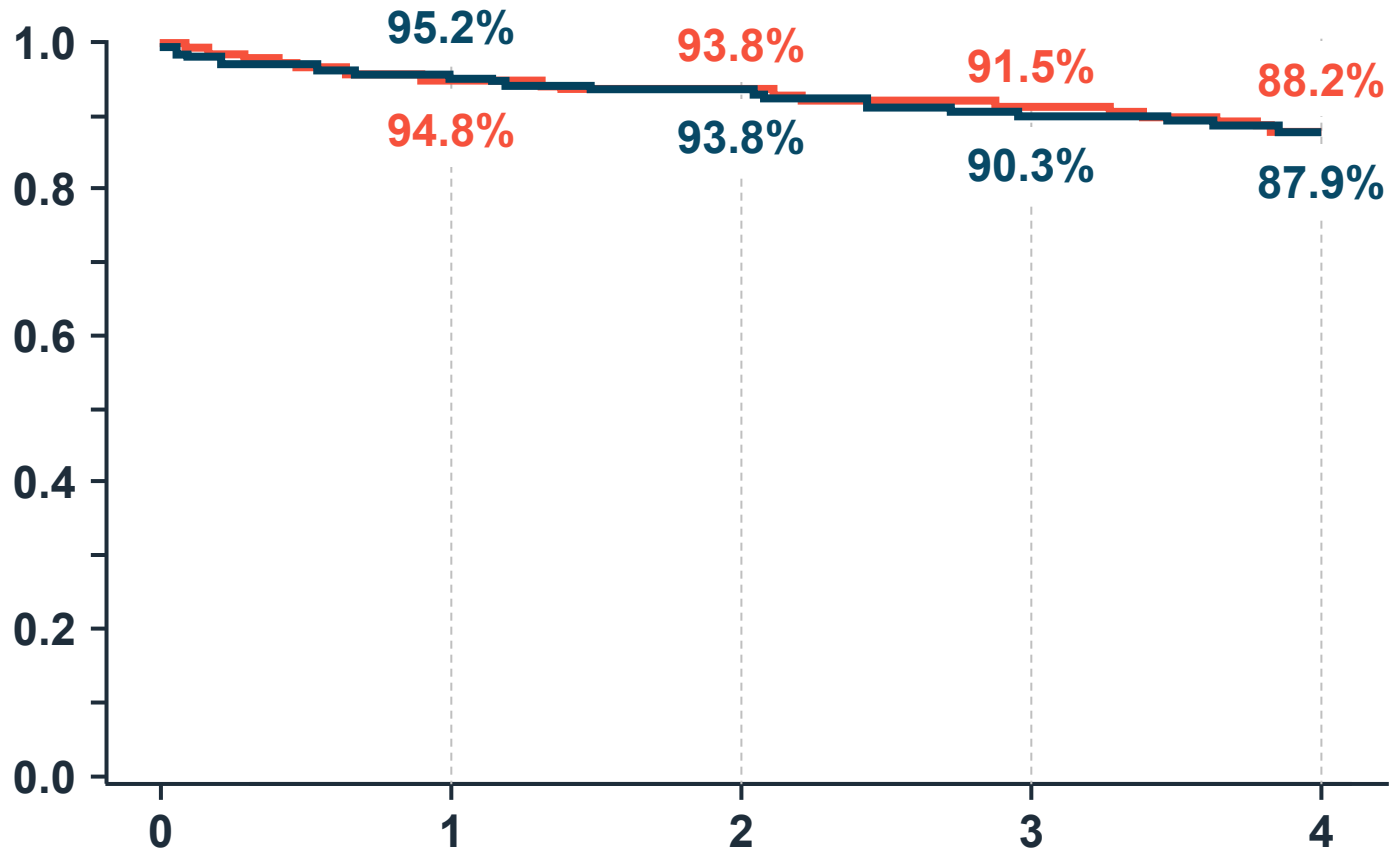
LEOPARD: Freedom from Reinterventions



Freedom from Reintervention (%)

Proximal Fixation
EVAR Comparator

Anatomical Fixation
AFX Duraply / AFX2

Numbers at Risk

AFX Duraply / AFX2	235	221	210	197	191	176	168	155	141
EVAR Comparators	220	201	189	181	175	160	151	136	125

Core Lab Reported + Site Reported Data

Data extract date August 31, 2021

LEOPARD: Secondary Endpoints at 4 Years

4-Year Freedom from Outcomes	Anatomical Fixation AFX Duraply / AFX2	Proximal Fixation EVAR Comparator
Rupture	98.9%	99.3%
All-cause mortality	77.5%	77.9%
Aneurysm related mortality	97.1%	98.5%
Type Ia endoleaks	99.2%	98.5%
Type IIIa endoleak	100%	100%
Type IIIb endoleak	98.7%	100%
Open conversion	100%	98.0%
Occlusion	97.8%	95.3%

Core Lab Reported + Site Reported Data

Data extract date August 31, 2021

LEOPARD: High Level Evidence Comparing Mid- to Long-Term Outcomes of EVAR

- Freedom from aneurysm-related complications comparable between AFX and comparator endografts
- Post hoc analysis of secondary endpoints
  - Endografts have different spectra of failure modes
  - Comparable overall performance
- 4-year data continue to support risk / benefit profile of AFX

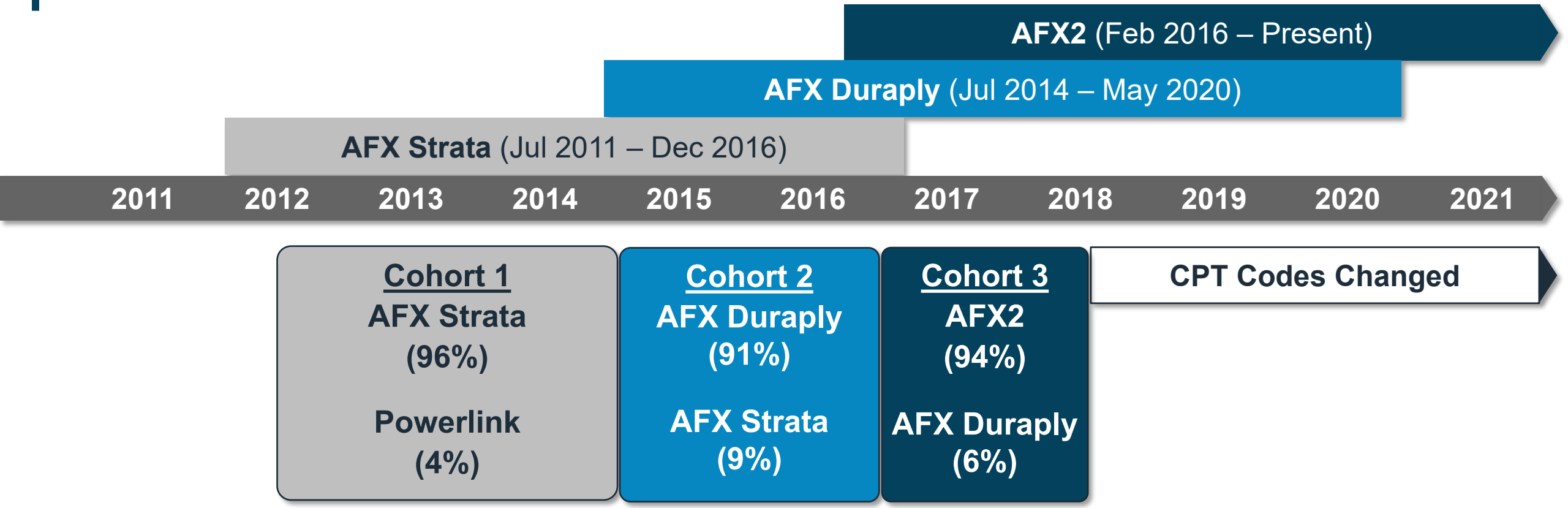
Medicare / CMS and VQI

Medicare Beneficiaries Provide Comparative Performance of AFX

- Patients undergoing elective aneurysm between 2012 and 2018
- Follow-up through October 2020
- Two distinct groups identified using CPT codes
  - Unibody grafts (AFX)
  - Single / double docking limb devices (proximally fixated grafts – other EVAR devices)
- Outcomes of interest: Peri-operative, all-cause mortality, aortic-related reintervention and post-EVAR aortic rupture

As requested by FDA, these data were provided to FDA on September 22, 2021

Three Time Cohorts to Comparatively Evaluate AFX Strata, AFX Duraply, and AFX2



Medicare / CMS Dataset Includes > 32,000 Patients who Underwent EVAR

	AFX N = 4,729	All Other EVAR Devices N = 27,302
Cohort 1 (AFX Strata)	**1,498**	**8,256**
Cohort 2 (AFX Duraply)	**1,713**	**9,390**
Cohort 3 (AFX2)	**1,518**	**9,656**

Baseline Demographics and Disease Characteristics Between Groups

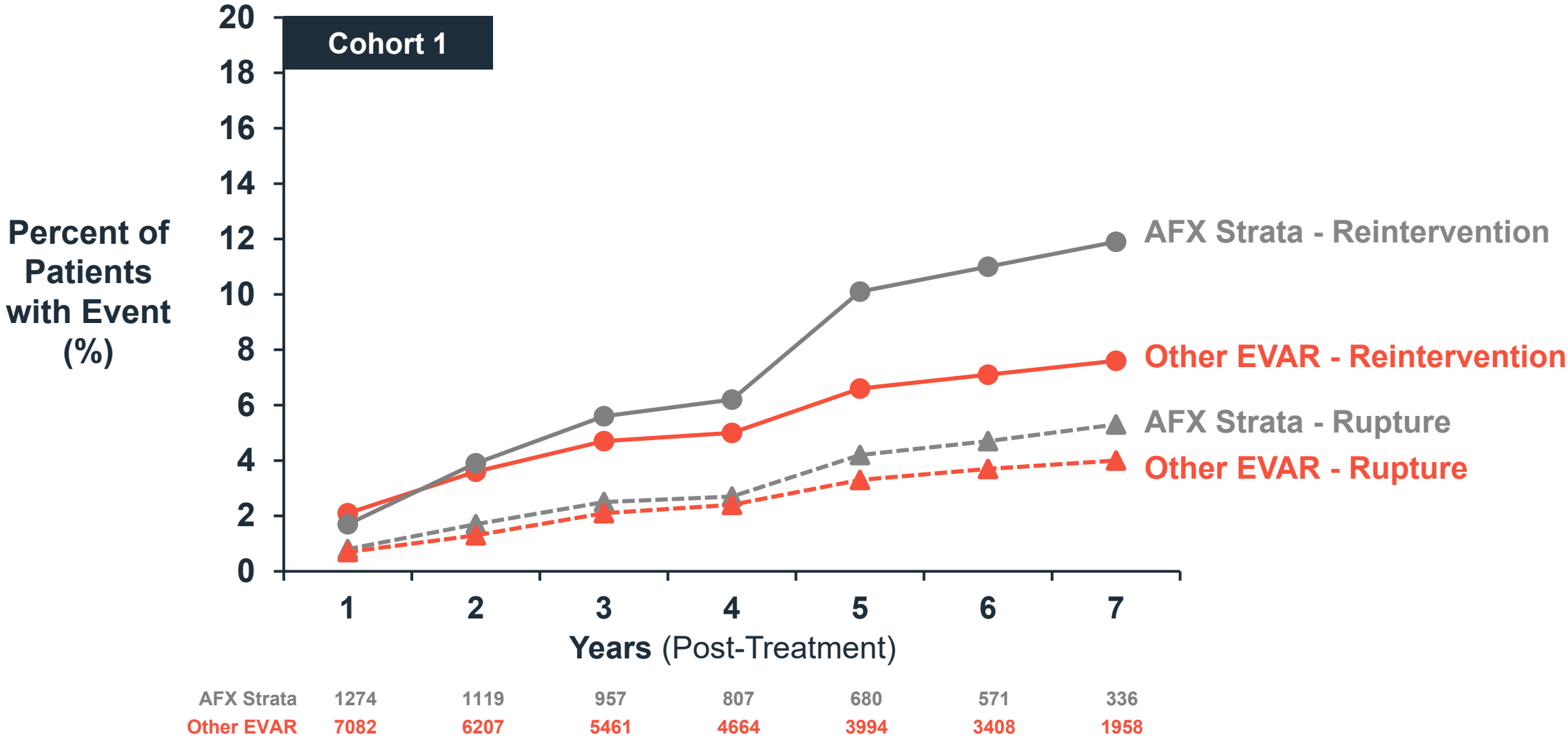
- Mean age approximately 76 years across all groups
- Higher proportion of females received AFX
  - ~23% in AFX2 group
  - ~18% in comparator group
- Higher proportion of significant co-morbidities in AFX patients
- Peripheral vascular disease highest among AFX patients
  - ~45% in AFX2 group
  - ~35% in comparator group

Medicare Beneficiary Peri-Operative Outcomes Similar Across All Time Points

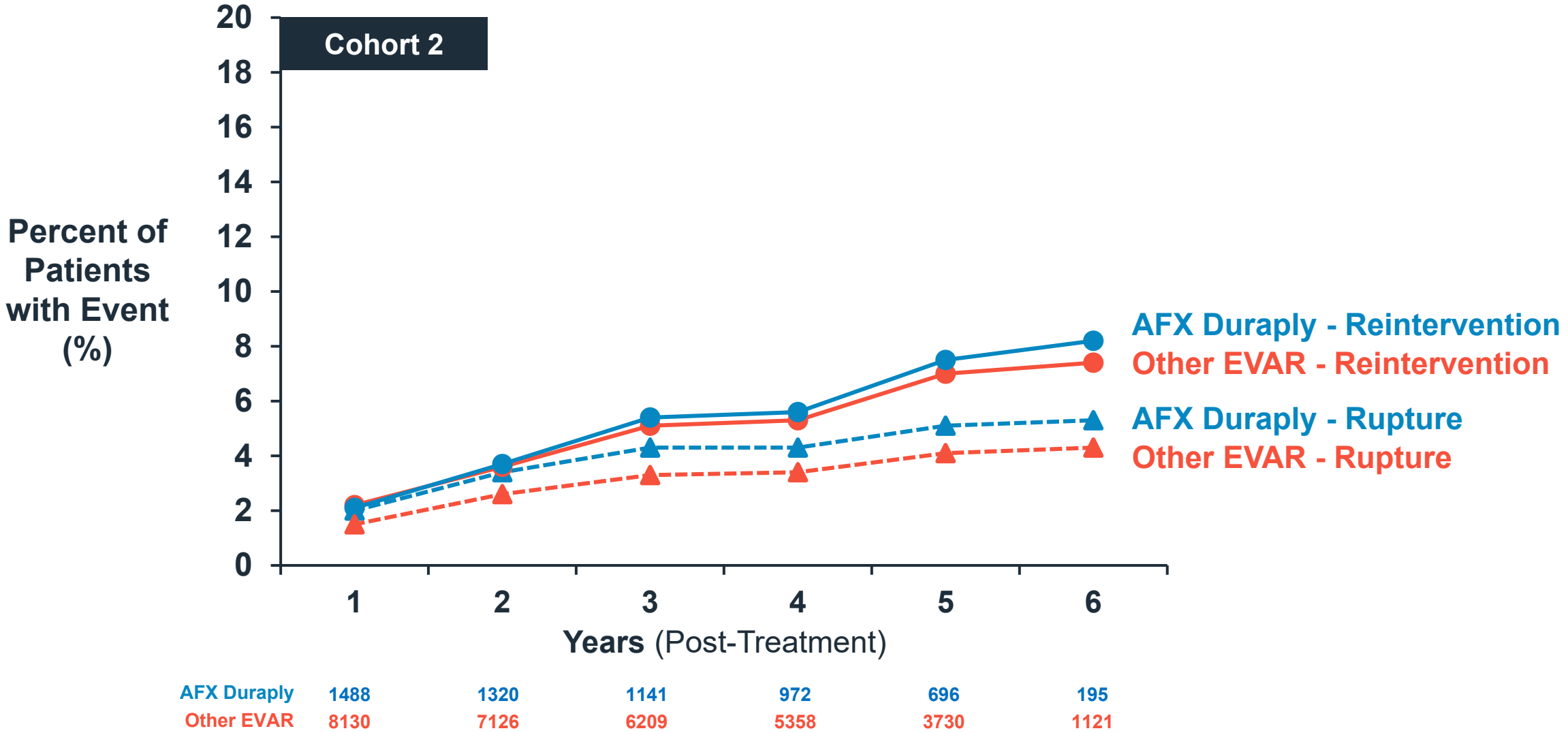
Peri-Operative Mortality	AFX	All Other EVAR Devices
Cohort 1 (AFX Strata)	**1.8%** (27 / 1498)	**1.9%** (157 / 8256)
Cohort 2 (AFX Duraply)	**1.5%** (25 / 1713)	**1.6%** (147 / 9390)
Cohort 3 (AFX2)	**1.8%** (27 / 1518)	**1.6%** (154 / 9656)

- No difference in peri-operative complications
  - Including acute renal failure, myocardial infarction, mesenteric ischemia, pneumonia, or DVT
- Higher rates of embolectomy in AFX2 group (1.1%) vs comparator (0.5%)

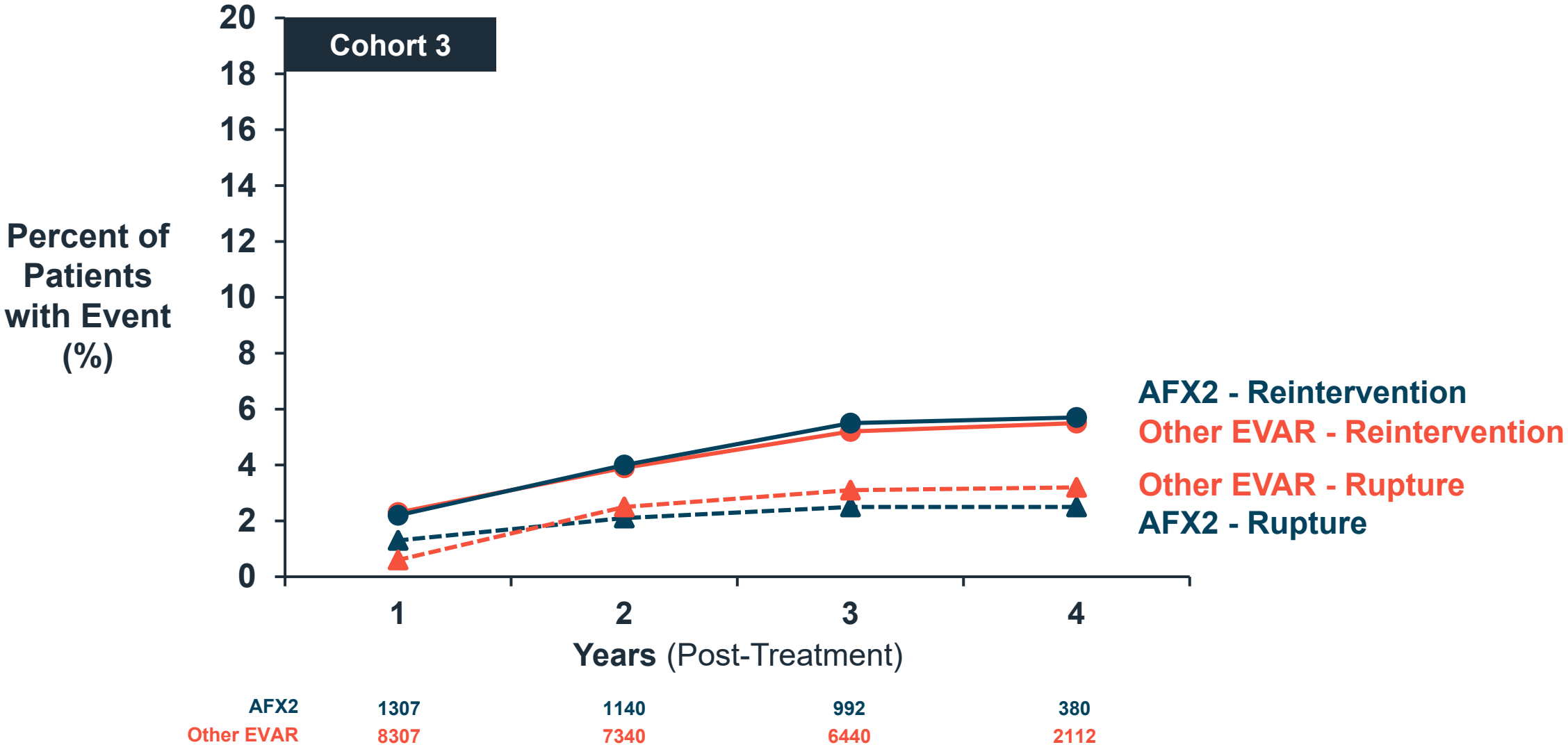
Reintervention and Rupture Rates Higher with AFX Strata



Reintervention and Rupture Rates Similar Between AFX Duraply and Other EVAR



Reintervention and Rupture Rates for AFX2 Similar to All Other EVAR Devices



Medicare Data Demonstrate Continuous Improvement of the AFX Product Line

- Patient groups treated with AFX have different characteristics than those treated with other EVAR devices
- Peri-operative outcomes similar between treatment groups
- Data consistent with internal complaint trending
- Support that prior concerns have been resolved
- Medicare: AFX2 similar reintervention rate and trends toward lower rupture rates compared with proximally fixated endografts
- Some limitations of Medicare analysis addressed by VQI-VISION

VQI: Large Dataset Providing Unbiased Assessment of EVAR Device Performance

- Provides robust peri-operative data and 1-year follow-up
- Established in 2011 by Society for Vascular Surgery
  - 36,256 patients
  - > 1,600 surgeons at 331 centers across US
- Able to differentiate AFX2 from other endografts
  - N=1,030 AFX2
  - N=35,226 all other EVAR devices

Data extract date March 31, 2021

VQI: AFX2 Performs Well in Peri-Operative Phase

30-Day outcomes	AFX2 N = 1,030	All Other EVAR Devices N = 35,226
Procedure time (min), mean ± SD	108 ± 65	124 ± 66*
Contrast use (ml), mean ± SD	74 ± 53	92 ± 54*
Any endoleak	8.3%	23.2%*
Type Ia	0.7%	2.8%*
Type Ib	0.6%	0.7%
Type II	4.1%	13.8%*
Type IIIa	0.2%	0.2%
Type IIIb	0%	0.1%
Peri-operative mortality	0.6%	0.7%

* $p < 0.001$

Data cutoff March 31, 2021

VQI: Rate of Endoleaks, Reintervention, and Mortality at 1 Year Similar Across Groups

1-Year outcomes	AFX2 N = 1,030	All Other EVAR Devices N = 35,226
Any endoleak	9.0%	16.5%*
Type Ia	0.9%	0.8%
Type Ib	0.3%	0.7%
Type II	3.5%	12.1%*
Type IIIa	0.9%	0.2%
Type IIIb	0%	0.1%
Freedom from reintervention	97.9%	97.2%
Freedom from mortality	92.3%	92.6%

* $p < 0.001$

Data cutoff March 31, 2021

VQI Demonstrate AFX2 has Significant Advantages in Peri-Operative Endoleak

- VQI: AFX2 provides significant advantages in peri-operative outcomes
- Endoleak rate lower with AFX2 peri-operatively and at 1 year
- Acute results have clinical significance

Midterm Outcomes of Patients Receiving AFX2 for Treatment AAA

Retrospective Multicenter Analysis

Endologix Sponsored

Endologix Sponsored Retrospective, Multicenter Study of AFX2 in 5 US Centers

- All consecutive patients receiving AFX endograft for elective infra-renal AAA repair
- Jan 2016 – Dec 2020
- N=405 patients
- Vast majority received AFX2

1. **Freeman Heart and Vascular Institute,** Joplin, MO
2. **Cooper University Healthcare,** Camden, NJ
3. **Baptist Memorial Hospital,** Memphis, TN
4. **Mercy Hospital,** Springfield, MO
5. **Advent Health,** Orlando, FL

As requested by FDA, these data were provided to FDA on September 22, 2021

Multicenter Series: Low Rate of Endoleaks and Rupture with AFX2

3-Year freedom from outcomes	Multicenter Series*	LEOPARD
	AFX2 N = 405	AFX Duraply / AFX2 N = 235
All-cause mortality	81.3%	84.1%
Aneurysm-related mortality	98.2%	98.2%
Open conversion	98.8%	100%
Aortic rupture	100%	99.5%
Type Ia endoleak	99.4%	100%
Type III endoleak	98.9%	99.5%
Device-related reintervention	91.7%	90.3%

*Not core lab adjudicated

LEOPARD data extract date August 31, 2021

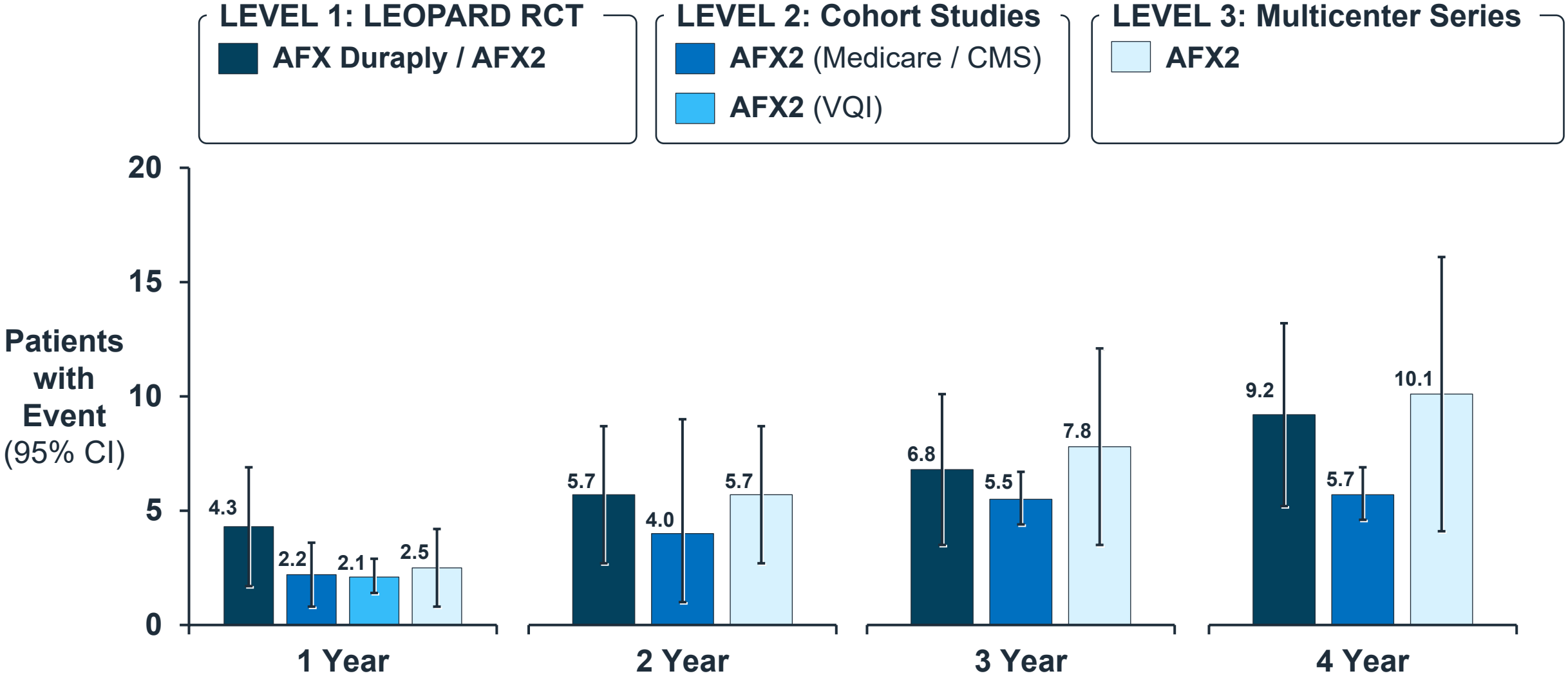
Summary of Results from Multicenter Series

- Retrospective study with large sample size
- AFX demonstrated satisfactory results with an acceptable risk / benefit profile
- All aortic-related outcomes are good
- Outcomes consistent with LEOPARD trial

Endologix Clinical Compendium

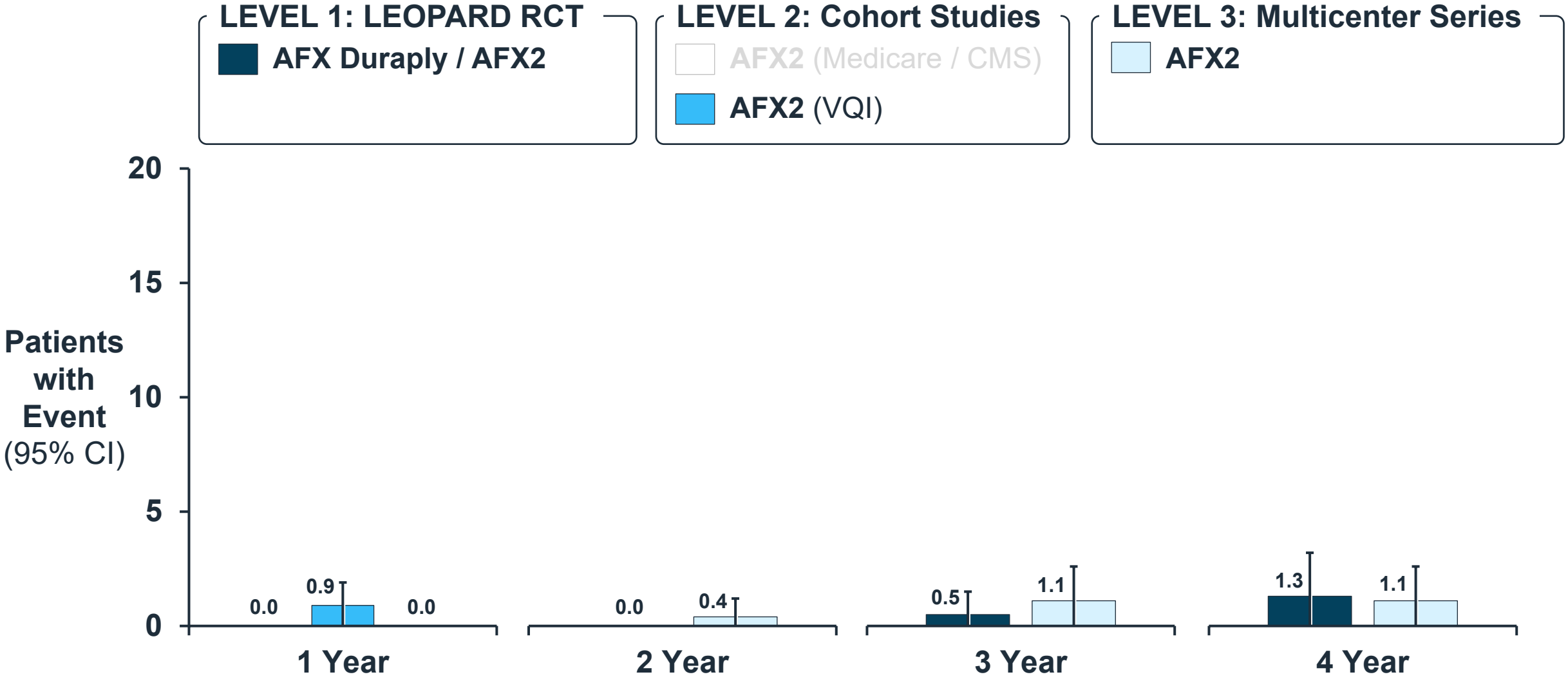
Degree of Concordance

Rate of Device-Related Reinterventions for AFX2 Consistently Low Across Data Sets



LEOPARD data extract date August 31, 2021

Low Rate of Type III Endoleak with AFX2 Across Compendium of Clinical Data



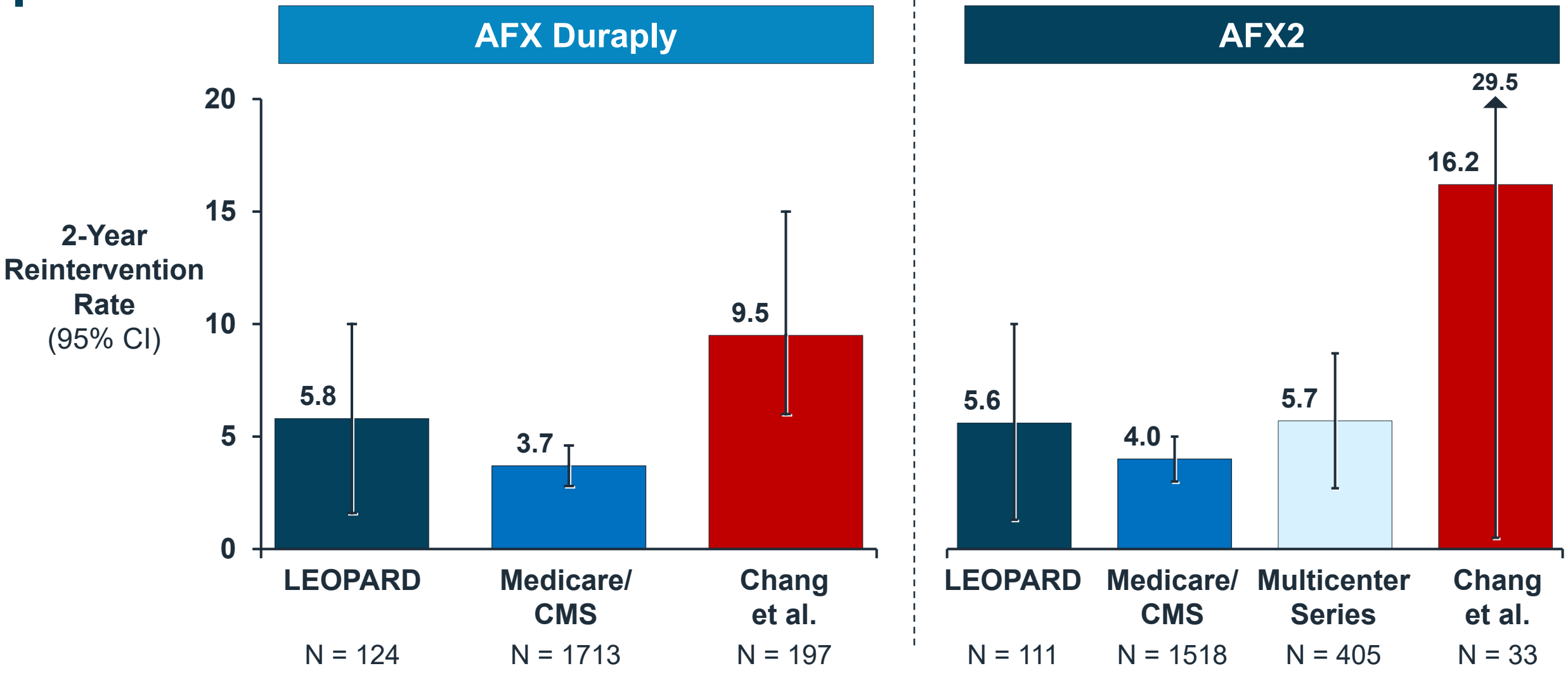
LEOPARD data extract date August 31, 2021

Studies Quoted by FDA Provide Limited Data on AFX Performance After Product Updates

Author	Type	AFX Strata Patients (N)	AFX Duraply Patients (N)	AFX2 Patients (N)
Lemmon et al.	Article	83	0	0
Barleben et al.	Abstract	107	0	0
Ta et al.	Abstract	122	0	0
Wanken et al.	Abstract	67	51*	0
Chang et al.	Retrospective Series	375	197	33

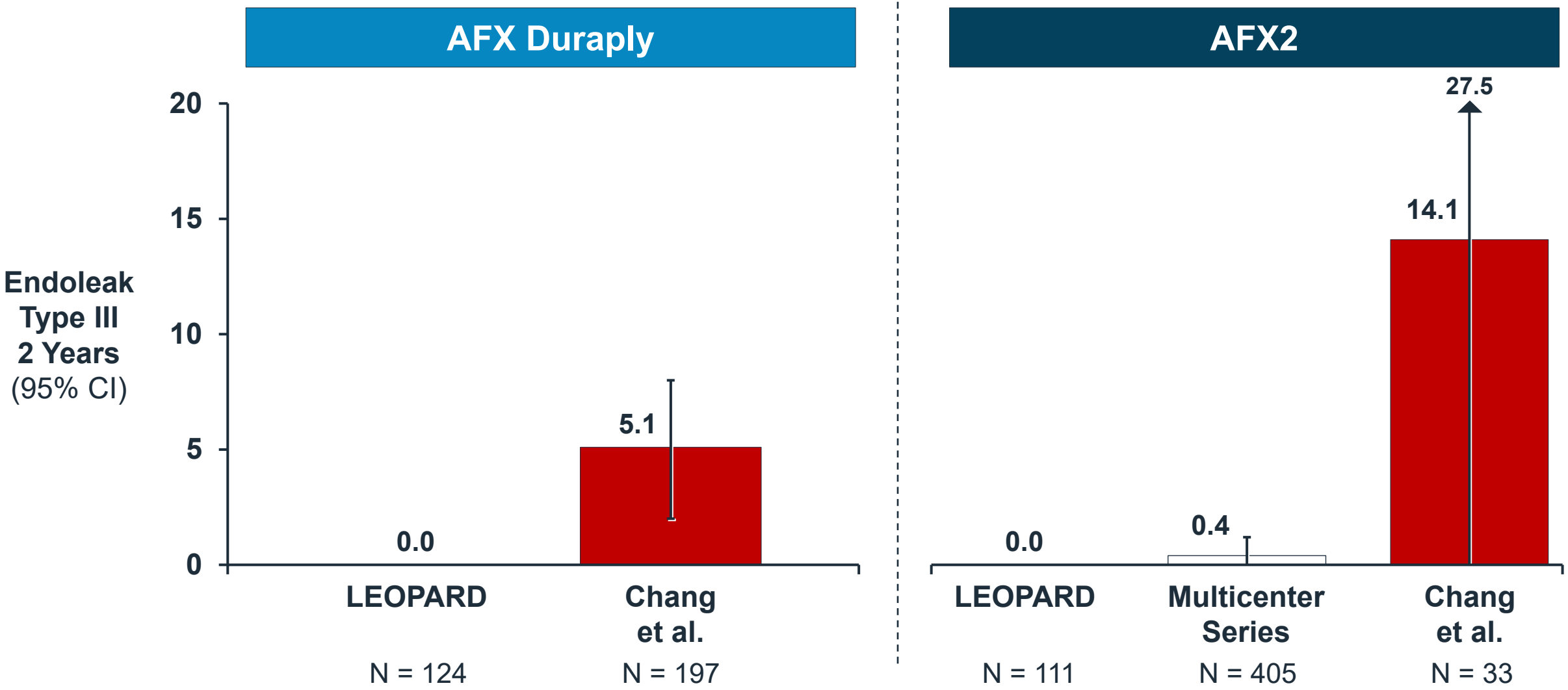
* Includes mix of AFX Duraply and IntuiTrak endografts – Proportion in each group not identified

Reintervention Rates Reported by Chang et al. are Discordant with All Other Data Sources



LEOPARD data extract date August 31, 2021

Chang et al. Reported Significantly Higher Rate of Type III Endoleaks



LEOPARD data extract date August 31, 2021

Summary of Evidence Support AFX Performance Profile

- AFX2 is completely differentiated by labelling, manufacturing, and design updates
- Clinical compendium of ~3000 patients treated with AFX2
  - Demonstrates favorable benefit-risk profile
  - Comparable outcomes with all other EVAR grafts
- Type III endoleak rate less than 1.5% at 4 years (LEOPARD & Multicenter Series)
- Longer term data will be acquired from LEOPARD study, Medicare or linkage (VQI-VISION) analysis

Clinical Perspective

Christopher Kwolek, MD

Senior Vascular Surgeon

Massachusetts General Hospital

Associate Professor of Surgery

Harvard Medical School

Technological Advancements have Resulted in Improved Patient Outcomes with EVAR

- Less invasive than surgery
- Reduced hospital stays
- Patients receiving EVAR device require life-long follow-up
  - > 30% require reintervention within 10 years of implant[1]
- Informed consent process should clearly outline overall benefit-risk of all treatment options

1. Columbo, 2021

LEOPARD: Prospective RCTs Provides Most Robust Assessment of Device Performance

4-Year freedom from outcomes	Anatomical Fixation AFX Duraply / AFX2	Proximal Fixation EVAR Comparator
Aneurysm related complication	70.4%	61.1%
Reintervention	87.9%	88.2%
Rupture	98.9%	99.3%
Type Ia endoleaks	99.2%	98.5%
Type IIIa endoleak	100%	100%
Type IIIb endoleak	98.7%	100%
All-cause mortality	77.5%	77.9%
Aneurysm related mortality	97.1%	98.5%

Core Lab Reported + Site Reported Data

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Lower-Level Data Sources Provide Supportive Information

- Do not provide details necessary to draw definitive conclusions
  - Limited anatomic data
  - Limited details on patient demographics and vascular characteristics
  - No confirmation of clinical events through core lab adjudication
- Discordant outcomes make interpretability of lower levels of evidence difficult

Unique Properties of AFX System Make it an Important Option for Treatment of AAA

Clinical Scenario	Advantages of AFX2
Challenging Contralateral Access Narrowed iliac access or presence of significant peripheral vascular disease	▪ 7 French contralateral access ▪ Hydrophilic sheath remains in place during delivery
Urgent Repair Required Repair of ruptured aneurysm or need for minimal fluoroscopy or contrast volume	▪ Technically straightforward procedure ▪ No sheath exchange allows components to be quickly and accurately deployed ▪ Low operative time and reduced fluoroscopy
Proximal Neck Thrombosis Ability to achieve adequate fixation and good seal compromised	▪ Only anatomically fixated EVAR device ▪ Fabric moves independently from stent cage allowing it to conform to irregularities of proximal neck ▪ Reduced risk of Type Ia endoleak
Aortoiliac Occlusive Disease	▪ Allows for preservation of native bifurcation

Overall Performance and Durability of AFX Comparable with Other EVAR Devices

- LEOPARD provides high-quality evidence that AFX2 addresses concerns with earlier generations
  - AFX2 is only available AFX device
- Lower-levels of evidence provide supportive evidence
  - Discordant results make it challenging to draw definitive conclusions

AFX2 provides unique and much needed treatment option for patients with abdominal aortic aneurysms

AFX System for Endovascular Treatment of Patients with Abdominal Aortic Aneurysms (AAA)

November 2, 2021

Circulatory System Devices Panel

Endologix LLC