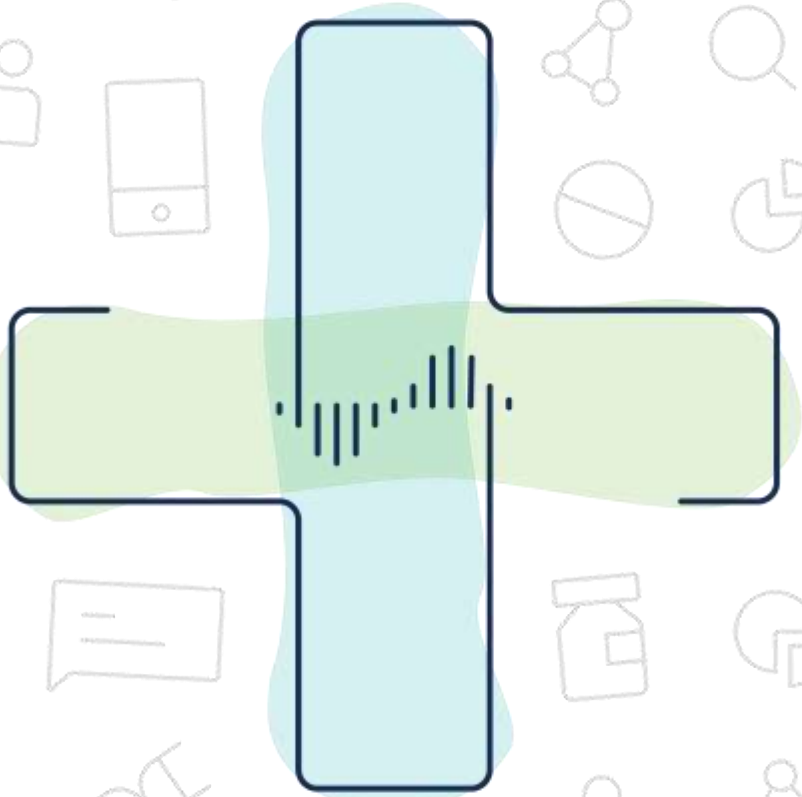
Factor XIa Inhibitors for NVAF:

Current Perspectives from Cardiologists

January 2024



ZoomRx

Key Findings

Current Landscape: *Eliquis leads the pack*

- Eliquis is currently the top choice for stroke prevention in NVAF, being used in 56% of patients, followed by Xarelto at 26%
- Mirroring usage, 77% of cardiologists perceive Eliquis as performing “extremely well”, while only 47% have equally positive perceptions of Xarelto
- Eliquis’ twice daily dosing is considered its only major drawback, while safety & efficacy-related unmet needs are noted for Xarelto

Future Perspectives: *Awareness of FXIa inhibitors on the horizon are modest, with some aware of early clinical setbacks*

- Only 50% of cardiologists are aware of in-development FXIa inhibitors, with asundexian, abelacimab and milvexian being the top 3 recalled pipeline therapies
- 40% of cardiologists are both aware and familiar with asundexian’s latest clinical data, and most of those (6 out of 10) are specifically aware of the halting of OCEANIC-AF due to inferior data vs Eliquis

Respondent Profile

Unique Respondents

30 **Unique Cardiologists**

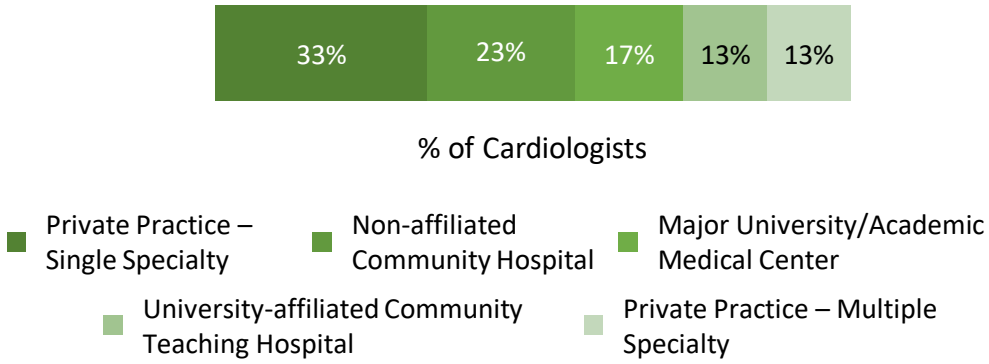
Avg. Years of Experience
(n = 30)

14

Average No. of NVAF Patients Treated in Last 3 Months
(n = 30)

146

Practice Setting
(n = 30)

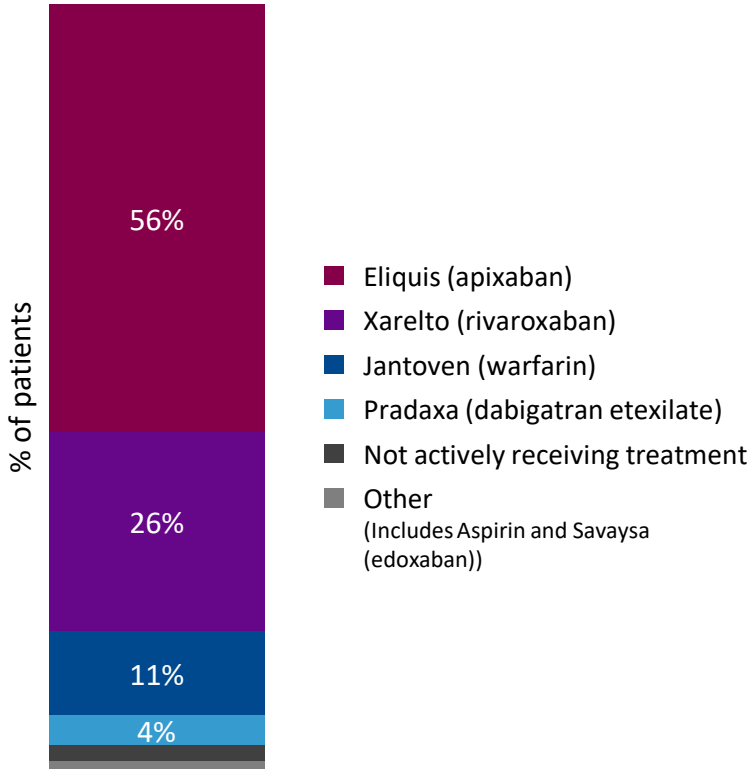


Question text in speaker notes | n refers to the number of cardiologists

Eliquis is used for 56% of NVAF patients for stroke prevention, and the majority of Cardiologists perceive it favorably

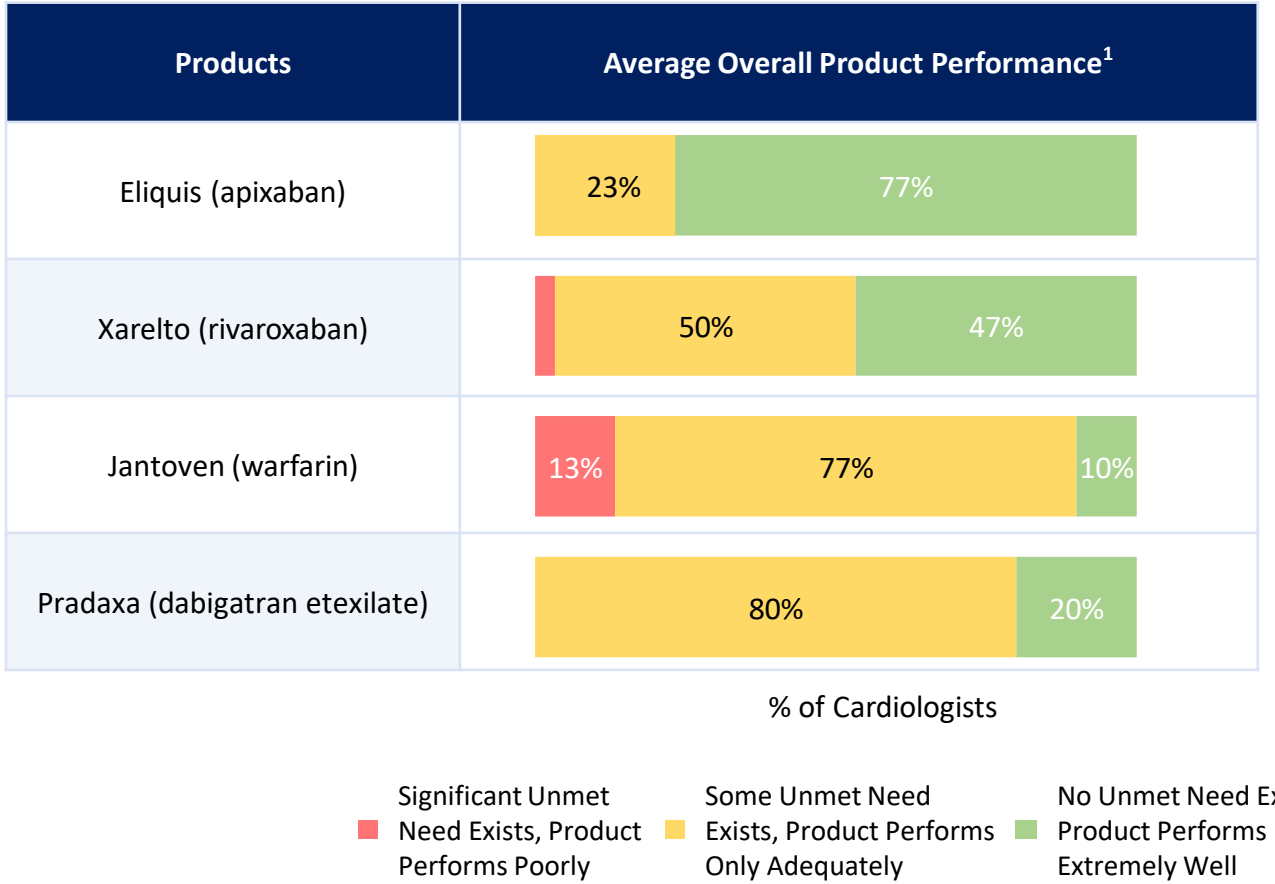
Current Treatment for Stroke

(n = 30) | (p = 4390)



Overall Product Performance & Unmet Needs

(n = 30)



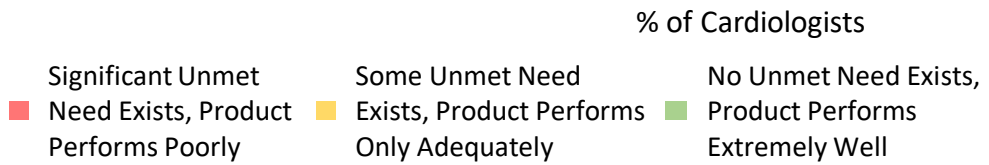
Question text in speaker notes | n refers to the number of cardiologists | p refers to the number of patients | [1]Overall Product Performance Rating is computed as the geometric mean of the ratings received across the six product performance attributes

Eliquis' twice daily dosing is considered its only major unmet need

Product Performance – Eliquis

(n = 30)

Attributes	Eliquis
Efficacy: reducing risk of stroke / systemic embolism	97%
Efficacy: reducing all-cause mortality	13% / 83%
Tolerability	17% / 83%
Safety: minimizing the rate of bleeding	20% / 80%
Safety: other / unrelated to bleeding	23% / 77%
Dosing	43% / 57%



Reasons for Eliquis Having Significant Unmet Needs [Unaided][2]

HCP: *"I think the only unmet need specifically with Eliquis is probably twice daily dosing. And any way that a future inhibitor such as a Factor XI inhibitor could reduce bleeding, even though its bleeding profile is probably the best of all oral anticoagulants."*

HCP: *"The unmet need for Eliquis is in terms of taking the medication twice daily, which becomes a challenge in terms of compliance for some of the patients."*

HCP: *"Concomitant use of antiplatelets with Eliquis -- def increased risk of bleeding. Cost. BID dosing."*

HCP: *"Generally a good medication but affordability can be a concern"*

HCP: *"Eliquis overall does a pretty good job with preventing, bleeding and clotting. I think the only unmet need would be in obese patients."*

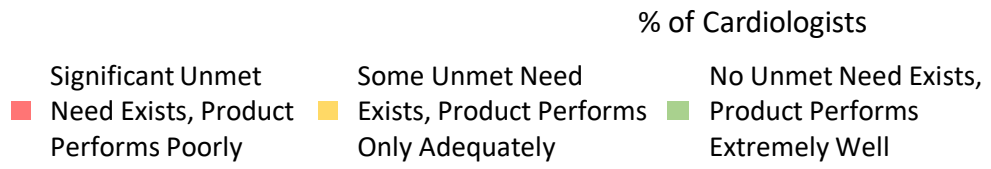
Question text in speaker notes | Data points sorted in descending order of "No Unmet Need Exists, Product Performs Extremely Well" | [2]Question asked to cardiologists who indicate that unmet needs exist

Safety concerns rank high among Xarelto's unmet needs, although its once daily dosing is perceived well

Product Performance – Xarelto

(n = 30)

Attributes	Xarelto
Dosing	23% / 77%
Efficacy: reducing risk of stroke / systemic embolism	40% / 60%
Tolerability	43% / 53%
Safety: minimizing the rate of bleeding	7% / 43% / 50%
Efficacy: reducing all-cause mortality	50% / 47%
Safety: other / unrelated to bleeding	53% / 43%



Reasons for Xarelto Having Significant Unmet Needs [Unaided][2]

HCP: *"I think Xarelto has great once a day dosing. However, I think unmet need exists in regards to the PK-PD data in regards to a high peak and low trough. Also, the fact that there is bleeding in comparison to other DOACs may be higher, and also the fact that the renal excretion of this medication may lead to that."*

HCP: *"The greatest unmet needs with the use of rivaroxaban relate to its lack of superior efficacy in terms of reducing the risk of stroke or systemic embolism compared to warfarin in its pivotal phase three trial for nonvalvular atrial fibrillation, as well as the opportunity to reduce risks of major and clinically relevant non-major bleeding."*

HCP: *"Xarelto, I have a bigger concern in patients who have GI bleed. So that is the bigger unmet need for Xarelto in patients."*

HCP: *"Cost. Bleeding concerns still persists. Some people still have CVA/TIA on a standard dose therapy. Risk of bleeding with concomitant use of antiplatelets/NSAIDs/alcohol etc. "*

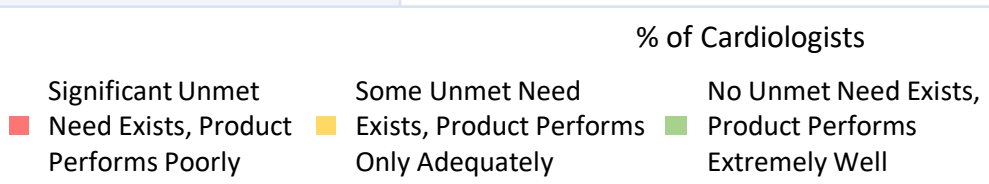
Question text in speaker notes | Data points sorted in descending order of "No Unmet Need Exists, Product Performs Extremely Well" | [2]Question asked to cardiologists who indicate that unmet needs exist

Cardiologists perceive significant unmet needs concerning warfarin's dosing regimen and its tolerability

Product Performance – Warfarin

(n = 30)

Attributes	Warfarin
Efficacy: reducing risk of stroke / systemic embolism	60% / 40%
Tolerability	20% / 50% / 30%
Efficacy: reducing all-cause mortality	7% / 67% / 27%
Safety: other / unrelated to bleeding	7% / 77% / 17%
Safety: minimizing the rate of bleeding	13% / 73% / 13%
Dosing	33% / 63% / 3%



Reasons for Warfarin Having Significant Unmet Needs [Unaided][2]

HCP: *"Warfarin has multiple problems. First of all, the dosing is to be adjusted based on levels, frequent monitoring is a problem. Furthermore, sometimes people are sub-therapeutic, sometimes they are supratherapeutic. So, bleeding and clotting, both are a major unmet need for Warfarin."*

HCP: *"The problem with warfarin and several unmet needs include the fact that there are multiple drug-drug interactions, the fact that with green vegetables or other things with vitamin K, there are food-drug interactions, and the fact that bleeding is higher, particularly intracranial bleeding."*

HCP: *"Standard challenges with warfarin – fluctuation in INR levels and dosing and dietary restrictions."*

HCP: *"The dietary restrictions, frequent monitoring, and complicated dosing regimens requiring frequent adjustments make this an undesirable medication."*

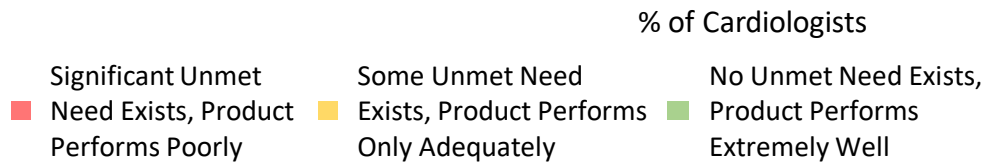
Question text in speaker notes | Data points sorted in descending order of "No Unmet Need Exists, Product Performs Extremely Well" | [2]Question asked to cardiologists who indicate that unmet needs exist

Minimizing safety concerns, particularly related to GI side effects and risk of bleeding, is considered Pradaxa's top unmet need

Product Performance – Pradaxa

(n = 30)

Attributes	Pradaxa
Efficacy: reducing risk of stroke / systemic embolism	53% / 47%
Efficacy: reducing all-cause mortality	60% / 37%
Tolerability	7% / 63% / 30%
Dosing	7% / 63% / 30%
Safety: other / unrelated to bleeding	77% / 20%
Safety: minimizing the rate of bleeding	7% / 73% / 20%



Reasons for Pradaxa Having Significant Unmet Needs [Unaided][2]

HCP: *"The unmet needs with Pradaxa include the tartaric acid core that's necessary for absorption and stomach side effects, which can be a major limitation in its use. The other unmet need is the twice dosing and its renal excretion, and the fact that it has really never been studied, but only modelled in the 75 milligrams, twice daily dosing regimen in the United States."*

HCP: *"Dosing BID. Risk of bleeding compared to the Xa inhibitors is high. Cost."*

HCP: *"GI intolerance is a major problem with 30 % patients discontinuing it."*

HCP: *"Pradaxa has twice daily dosing and the market share is low because of patient preference and insurance preference."*

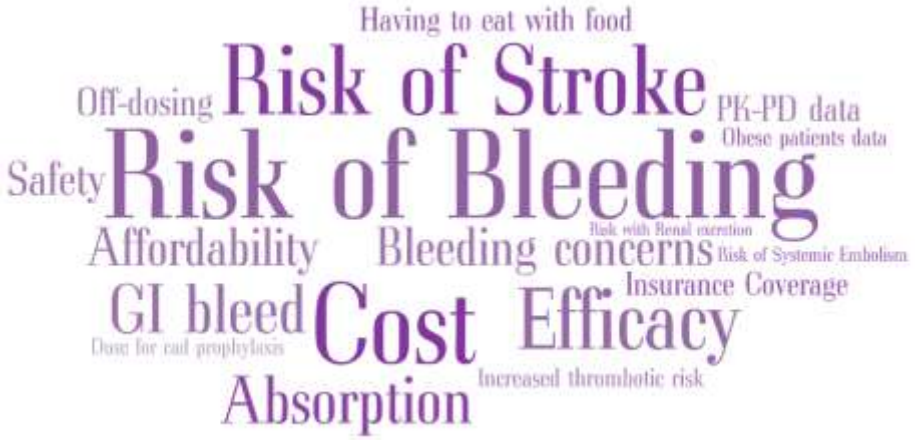
HCP: *"Unmet needs exist with the use of dabigatran, primarily related to its twice-daily dosing. In addition to this, there are opportunities to improve its bleeding rate, specifically with regard to GI bleeding."*

Question text in speaker notes | Data points sorted in descending order of "No Unmet Need Exists, Product Performs Extremely Well" | [2]Question asked to cardiologists who indicate that unmet needs exist

While Eliquis lacks optimal dosing, safety-related concerns are top of mind for Xarelto; convenience issues are top of mind with warfarin

Descriptions of Unmet Needs [Unaided][2]

Xarelto (rivaroxaban)



Eliquis (apixaban)

Jantoven (warfarin)

Pradaxa (dabigatran etexilate)

Question text in speaker notes | [2]Question asked to cardiologists who indicate that unmet needs exist

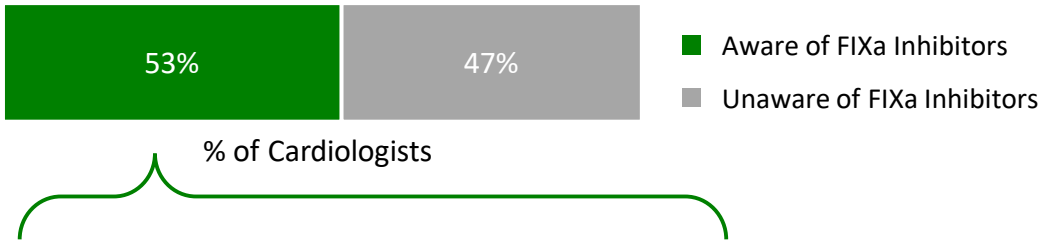
Roughly half of cardiologists are aware of in-development FXIa inhibitors; asundexian, abelacimab and milvexian are the most recalled therapies

Factor Xia Inhibitors Awareness

(n = 30)

Awareness of In-Development Factor Xia (FXIa) Inhibitors

(n = 30)



FXIa Inhibitors Awareness [Unaided]

(n = 15*)[3]

Inhibitors	Awareness of Inhibitors
asundexian	47%
milvexian	40%
abelacimab	33%
Osocimab	7%
Other^	7%
Don't Know / Can't Recall	27%

% of Cardiologists

In-Development FXIa Inhibitors Awareness [Aided]

(n = 30)

Inhibitors	Awareness of Inhibitors
asundexian	40%
abelacimab	30%
milvexian	27%
Osocimab	7%
IONIS-FXIRX	7%
Fesomersen	7%
Xisomab	3%
None of the above	50%

% of Cardiologists

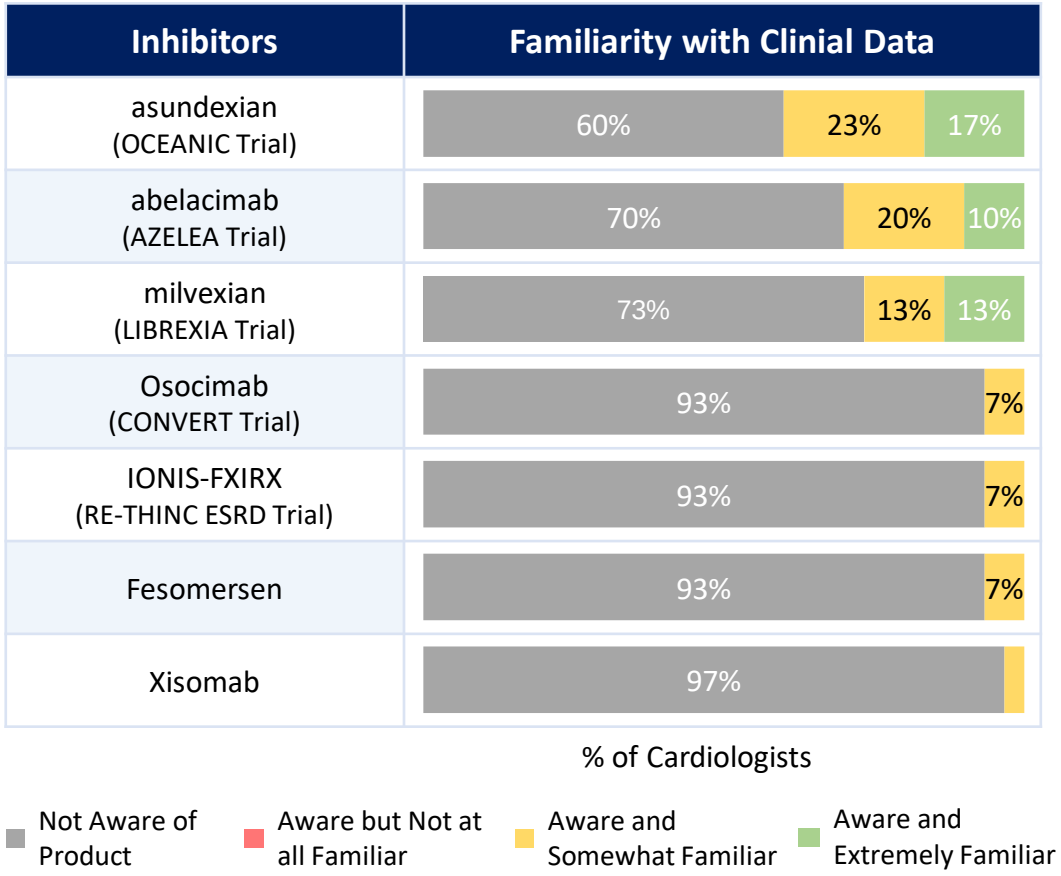
* Low sample size | Question text in speaker notes | [3]Local outliers removed | ^Other refers to "ASO investigators phase 2 mononucleotides antibodies small molecule"

Cardiologists indicate being more familiar with asundexian, abelacimab and milvexian's latest clinical data, although overall familiarity is low

Level of Familiarity with Clinical Data

(n = 30)

Level of Familiarity with Clinical Data [Aided]



Awareness of Latest Clinical Data [Unaided]

(Asked only to respondents who indicate being familiar with clinical data)

Inhibitors	HCPs on the Latest Clinical Developments – Verbatims
asundexian	*"The OCEANIC-AF trial was halted early due to lack of efficacy"*
asundexian	*"This is a small molecule inhibitor of Factor 11a. Oral daily dosing being studies for pts with AF / CVA / MI. PACIFIC AF / AMI / CVA"*
abelacimab	*"AZELEA-TIMI 71 stopped early due to lower bleeding risk and comparable ischemic outcomes"*
abelacimab	*"abelacimab had recent phase 2 trial data presented with significantly lower bleeding compared to rivaroxaban."*
milvexian	*"This is being studied for stroke and in pts with total knee replacement surgery."*
milvexian	"milvexian *has an ongoing phase 3 trial in patients with atrial fibrillation."*
Osocimab	*"IV and SubQ formulation being studied. Being studies for total knee replacement and in pts with ESRD on HD"*
Fesomersen	*"SubQ weekly formulation for ESRD on HD patients eval"*
Xisomab	*"IV single dose formulation for cancer related VTE tx and safety in ESRD on HD patients"*

Question text in speaker notes | Data points sorted in descending order of "Extremely Familiar"

Out of 10 cardiologists who indicated some awareness of asundexian, 6 were also aware of the halting of OCEANIC-AF due to inferior efficacy compared to Eliquis

Asudenxian's Latest Clinical Data Comparing its Efficacy with Eliquis'

When the 10 cardiologists who indicated being aware of asundexian and familiar with asundexian's latest clinical data were asked what they know about the latest clinical development of asundexian:

3 cardiologists **mentioned the clinical data failure** due to inferior efficacy *(without any prompts)*

3 cardiologists **mentioned the clinical data failure** only **when prompted[4]** and asked specifically about their familiarity / awareness of efficacy data comparing asundexian & Eliquis

4 cardiologists remained **unaware** of the clinical data failure **even when prompted[4]** and asked explicitly about their awareness of efficacy data comparing asundexian & Eliquis

HCP: *"The oceanic-AF trial was halted early due to lack of efficacy."*

HCP: *"Asudexian had its phase 3 atrial fibrillation study stopped prematurely in patients with atrial fibrillation."*

HCP: *"It had its A-fib study stopped due to lack of efficacy."*

HCP: *"Phase 3 AF study using asundexian called OCEANIC-AF was stopped due to inferior efficacy as mentioned above compared to Eliquis for the prevention of CVA/systemic embolism. Most data is not published yet to look at data in detail. Oceanic stroke trial continues."*

HCP: *"I hear that it will be at least as effective with less bleeding"*

HCP: *"Inferior efficacy but lower bleeding rates"*

Question text in speaker notes | [4]Prompt questions are generated using AI as a follow-up to the primary unaided question on awareness of latest clinical developments of products

Questions?
Get in touch

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