

REVIEW

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Asundexian: a systematic review of safety, efficacy, and pharmacological insights in thrombosis

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Abstract

Background Asundexian, a novel oral Factor XIa (FXIa) inhibitor, targets the intrinsic coagulation pathway to prevent thrombosis while potentially reducing bleeding risk compared to direct oral anticoagulants (DOACs) and vitamin K antagonists (VKAs). This systematic review synthesizes clinical evidence on its safety, efficacy, and pharmacological properties in managing arterial and venous thrombotic events.

Methods Following PRISMA guidelines, we searched PubMed, Embase, Scopus, Cochrane Library, ClinicalTrials.gov, and Web of Science for clinical trials and observational studies on asundexian until January 2025. Inclusion criteria included studies reporting safety, efficacy, and pharmacokinetics/pharmacodynamics (PK/PD) outcomes. Two reviewers independently screened studies and extracted data, with quality assessed using the Cochrane Risk of Bias 2 tool.

Results Eleven trials ($n > 21,000$, phases 1–3) were included. Asundexian suppressed FXIa activity, with phase 2 trials (e.g., PACIFIC-AF, PACIFIC-STROKE) showing reduced bleeding compared to apixaban. However, the phase 3 OCEANIC-AF trial was terminated early due to inferior efficacy in atrial fibrillation, with higher stroke/systemic embolism rates (2.5%) versus apixaban. PK/PD data support once-daily dosing with minimal drug interactions. Safety concerns include potential abnormal uterine bleeding, with limited data.

Conclusion Asundexian shows promise in reducing bleeding but lacks efficacy in high-risk settings like atrial fibrillation. Ongoing trials are needed to define its role in specific thrombotic conditions.

Clinical trial number Not applicable.

Keywords Asundexian, Factor XIa inhibitor, Anticoagulation, Thrombosis

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Introduction

Thrombosis is a significant global health burden, contributing to conditions such as atrial fibrillation (AF), myocardial infarction, deep vein thrombosis, pulmonary embolism, and stroke [1]. It is a leading cause of cardiovascular mortality, with acute arterial and venous thromboses driving significant morbidity in developed countries [1–3]. Imbalances in coagulation, triggered by vascular injury or inflammation, can lead to pathological clot formation and cardiovascular morbidity [4, 5].

Current anticoagulant therapies include parenteral agents such as unfractionated heparin and low-molecular-weight heparins, as well as oral anticoagulants including direct oral anticoagulants (DOACs; e.g., dabigatran, apixaban, rivaroxaban, and edoxaban) and vitamin K antagonists (VKAs; e.g., warfarin) [6–8]. DOACs are the mainstay for preventing and managing thromboembolic diseases, while VKAs remain an alternative when DOACs are contraindicated [9]. However, both carry significant bleeding risks, including intracranial and gastrointestinal hemorrhage, necessitating safer alternatives [10, 11].

Factor XIa (FXIa) has emerged as an attractive therapeutic target for anticoagulation owing to its unique role within the intrinsic pathway of the coagulation cascade [12]. In contrast to DOACs, which inhibit pivotal downstream enzymes such as Factor Xa or thrombin (Factor IIa) and thereby affect both thrombosis and hemostasis, FXIa inhibitors act upstream, primarily attenuating thrombus propagation rather than initiation of hemostatic clot formation [13]. The tissue factor–dependent extrinsic pathway, which mediates physiological hemostasis following vascular injury, remains largely preserved under FXIa inhibition. By selectively blocking FXIa, agents such as asundexian diminish pathologic thrombus formation driven by intrinsic pathway activators, including neutrophil extracellular traps (NETs) and polyphosphates, while maintaining normal hemostatic function [14]. This mechanistic selectivity provides a plausible explanation for the lower bleeding rates observed in early clinical trials. Asundexian, a potent and orally bioavailable FXIa inhibitor, represents one of the most advanced agents in this emerging drug class, alongside milvexian and abelacimab [13, 14]. These novel anticoagulants aim to achieve effective thromboprophylaxis with an improved safety profile across arterial and venous thrombotic disorders, including stroke, myocardial infarction, and venous thromboembolism. This systematic review synthesizes clinical evidence on the safety, efficacy, and pharmacological profile of asundexian in thrombosis management.

Methodology

Research question and aim

This systematic review addresses the question, “What are the safety, efficacy, and pharmacological characteristics of asundexian in the prevention and treatment of arterial and venous thrombotic events?” The aim is to synthesize clinical evidence on asundexian’s role in preventing and treating these conditions and evaluate its potential as a novel anticoagulant compared to existing therapies.

Study protocol and registration

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study protocol, detailing the research question, objectives, inclusion/exclusion criteria, and methodological framework, was registered with PROSPERO (CRD42025634031).

Search strategy

A literature search was performed across PubMed/MEDLINE, Embase, Scopus, Google Scholar, Cochrane Library, ClinicalTrials.gov, and Web of Science to identify studies evaluating the safety, efficacy, and pharmacological profile of asundexian in the prevention or treatment of arterial and venous thrombotic events. The search spanned database inception to January 2025. The strategy used Medical Subject Headings (MeSH) terms and free-text keywords, including: “safety,” “drug safety,” “efficacy,” “treatment efficacy,” “anticoagulants,” “biomarkers,” “pharmacokinetics,” “pharmacodynamics,” “thrombosis,” “factor XIa inhibitor,” and “asundexian.” Boolean operators (“AND,” “OR”) refined the search. Filters limited results to clinical trials and observational studies (cross-sectional, cohort, case-control designs) in English. Figure 1 illustrates the PRISMA flowchart for study selection.

Inclusion/exclusion criteria

Studies were included if they:

- Investigated asundexian therapy for preventing or treating arterial (e.g., stroke, myocardial infarction) or venous (e.g., venous thromboembolism) thrombotic events.
- Reported safety outcomes (e.g., major/minor bleeding events) and efficacy outcomes (e.g., stroke rates, systemic embolism, or other thrombotic events).
- Evaluated pharmacokinetics (e.g., plasma concentrations, bioavailability) or pharmacodynamics (e.g., FXIa inhibition, aPTT prolongation) relevant to asundexian’s clinical use.

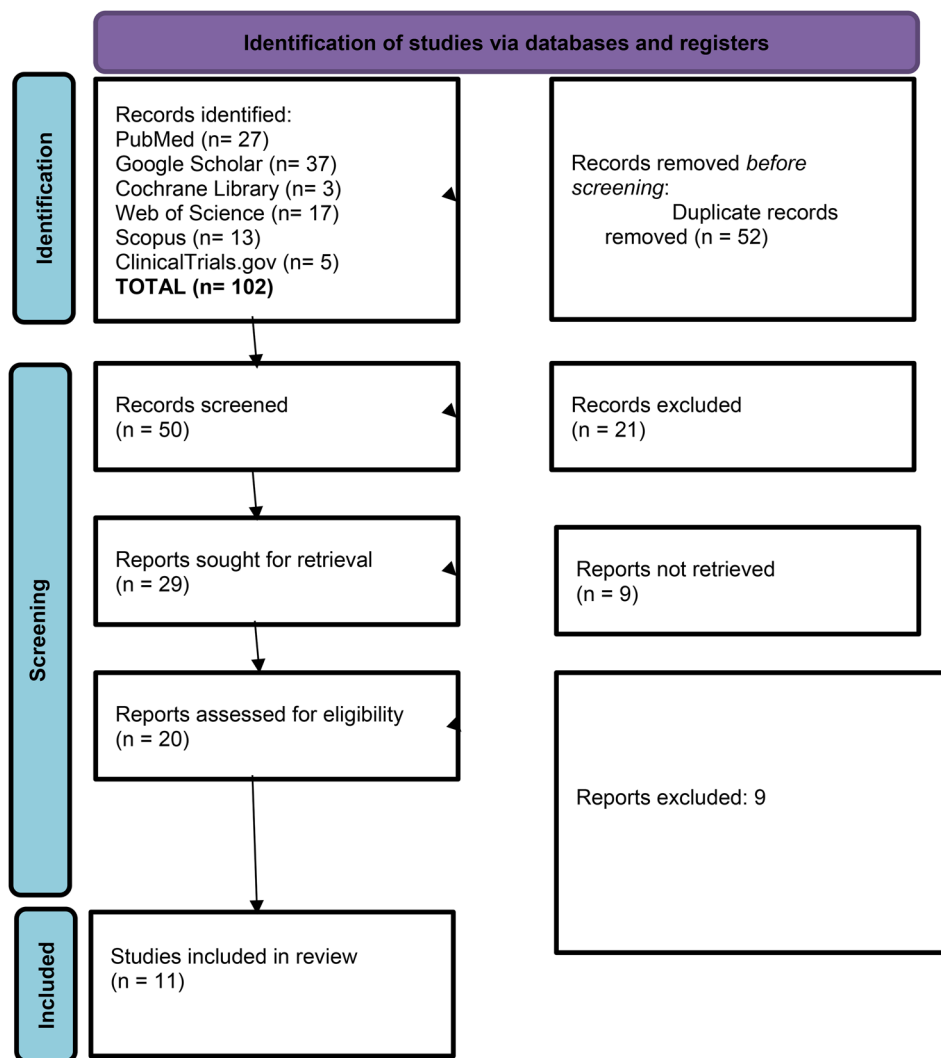


Fig. 1 PRISMA flow diagram for study selection

Studies were excluded if they:

- Were in-vitro or animal studies.
- Were published in languages other than English.

Study selection

Two independent reviewers (EK, NA) conducted title/abstract screening, followed by full-text screening. Discrepancies were resolved through discussion or consultation with a third reviewer (GO). Two reviewers (AM, RP) extracted data using a standardized form capturing study design, population, intervention, outcomes, and quality metrics.

Quality assessment

The risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, evaluating domains such as

randomization, blinding, and outcome reporting. Figure 2 summarizes the risk of bias across studies.

Data synthesis

Data were synthesized qualitatively due to heterogeneity in trial designs, populations, and endpoints (e.g., stroke prevention in AF versus myocardial infarction). A narrative synthesis integrated findings on safety, efficacy, and pharmacological outcomes, with tables summarizing key trial characteristics and results.

Results

Characteristics of included studies

This systematic review included 11 clinical trials [15–25], spanning phase 1 to phase 3, evaluating asundexian in preventing and treating arterial and venous thrombotic events. These trials enrolled over 21,000 participants, with study sizes ranging from 57 in phase

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Brase et al, 2024	+	+	+	+	+	+
Kubitza et al, 2021	-	+	+	+	+	-
Kanefendt et al, 2023	+	+	-	+	+	-
Chen et al, 2024	+	+	X	+	+	+
Thomas et al, 2021	+	+	+	+	+	+
Piccini et al, 2024	+	+	+	+	+	+
Piccin et al, 2022	+	-	-	X	+	X
Shoamanesh et al, 2022	+	+	+	+	+	+
Rao et al, 2022	+	+	+	+	+	+
Smith et al, 2024	+	+	+	+	+	+
Balali et al, 2024	+	+	+	+	+	+

Domains:
D1: Bias arising from the randomization process.
D2: Bias due to deviations from intended intervention.
D3: Bias due to missing outcome data.
D4: Bias in measurement of the outcome.
D5: Bias in selection of the reported result.

Judgement
X High
- Some concerns
+ Low

Fig. 2 Cochrane risk of bias 2 (RoB 2) quality assessment

1 safety studies to 14,810 in the phase 3 OCEANIC-AF trial. Asundexian was administered orally at 5–150 mg (commonly 10, 20, or 50 mg once daily), with treatment durations from single-dose pharmacokinetic studies up to 1 year in phase 2 and 3 trials. Table 1 summarizes study designs, populations, interventions, and outcomes, highlighting phase 1 trials for pharmacokinetics/pharmacodynamics (PK/PD), phase 2 for dose-finding, and phase 3 for clinical endpoints.

Efficacy

Asundexian's efficacy in preventing arterial and venous thrombotic events varied across trials, with results summarized below.

Stroke prevention

In the PACIFIC-STROKE trial (Shoamanesh et al., 2022 [21]; Balali et al., 2024 [25]), 1,808 patients with acute non-cardioembolic ischemic stroke received asundexian (50 mg daily) or placebo. Asundexian achieved a 7.1% relative risk reduction (RRR) in recurrent ischemic stroke (non-significant), with greater benefit in patients with large-artery atherosclerosis compared to those with small subcortical infarcts. Similarly, Smith et al., 2024 [22] reported a trend toward reduced stroke/infarcts with asundexian 50 mg (HR 0.71, 95% CI 0.45–1.11).

Myocardial infarction

The PACIFIC-AMI trial (Rao et al., 2022 [23]) enrolled 1,601 patients with acute myocardial infarction. Asundexian (50 mg) showed no significant reduction in the composite endpoint of cardiovascular death, myocardial infarction, or stroke versus placebo. However, it was associated with lower bleeding rates compared to standard anticoagulation.

Atrial fibrillation

The PACIFIC-AF trial (Piccini et al., 2022 [20]) included 862 patients with atrial fibrillation (CHA₂DS₂-VASc score 2–4). Asundexian (20 or 50 mg) had a 53% lower bleeding rate than apixaban but showed a non-significant increase in ischemic strokes, indicating uncertain stroke prevention efficacy. The phase 3 OCEANIC-AF trial (Piccini et al., 2024 [16]) ($n = 14,810$) was terminated early due to inferior efficacy, with asundexian (50 mg) associated with a higher stroke/systemic embolism rate (2.5%) versus apixaban (HR 3.79, 95% CI 2.46–5.83).

Safety profile

Bleeding risk

In PACIFIC-AF (Piccini et al., 2022 [20]), asundexian (20 or 50 mg) significantly reduced major or clinically relevant non-major (CRNM) bleeding compared to apixaban (HR 0.47, 95% CI 0.23–0.95). Conversely, OCEANIC-AF

Table 1 Characteristics of included studies

S/N	Authors & Year	Study Design	Sample Size	Clinical Condition	Age (Mean)	Intervention	Comparator	Efficacy Outcomes	Safety Outcomes	Pharmacokinetics (PK)	Pharmacodynamics (PD)	Other Notes
1	Braset al., 2024 [15]	Phase 1, multicenter, randomized, placebo-controlled (Study 1); non-randomized, non-blinded (Studies 2, 3)	57 (Study 1); ≥6/group (Study 2)	Hypertension, dyslipoproteinemia, CKD, liver impairment	≥ 18–≤80 yrs	Asundexian, single oral dose, 25 mg	Placebo (Study 1); matched controls (Studies 2, 3)	Prolonged aPTT; reduced FXIa activity	Well tolerated; minor sex-based PK differences	Cmax: 386–504 µg/L; Tmax: 2–4 h; t1/2: 14.9–23.8 h	FXIa activity decreased concentration-dependently; aPTT ratio: ~1.4–1.9	Negligible first-pass metabolism; metabolized by CES1 (47%), CYP3A4 (13%); 37% excreted unchanged
2	Kubitza et al., 2021 [17]	Phase 1, randomized, multi-part, single-blind, placebo-controlled	112 (48 randomized)	Healthy volunteers	18–45 yrs	Asundexian, 25, 50, 100 mg OD; 25 mg BID	Placebo; midazolam (Part C)	FXIa inhibition and aPTT prolongation dose-dependent	Mild TEAEs (headache, nasopharyngitis); no significant bleeding	Cmax, AUC dose-proportional; Tmax: 2–4 h; t1/2: 15.8–17.8 h	aPTT prolongation, FXIa inhibition dose-dependent	No CYP3A4 interaction; supports phase 2 exploration
3	Kanefend et al., 2023 [18]	Phase 1, single-center, randomized, crossover	60	Healthy white men	18–45 yrs	Asundexian, 25 or 50 mg (IR/ASD tablets)	Placebo, standard tablets	High bioavailability; no food/pH effects	Mild TEAEs (headache, gastrointestinal)	Cmax: 716 µg/L (Study 2); Tmax: 2–4.5 h; t1/2: 14–17 h	Platelet aggregation inhibition; PT/INR unchanged	Minimal variability; no impact from meals/pH
4	Chen et al., 2024 [19]	Phase 1, randomized, placebo-controlled, dose-escalation	60	Healthy Chinese/Japanese men	Chinese: 30.3 yrs; Japanese: 28.7 yrs	Asundexian, 25, 50, 100 mg single/multiple doses	Placebo	Dose-proportional exposure; consistent aPTT prolongation	Mild TEAEs (triglycerides, lipase increase)	Cmax, AUC dose-proportional; Tmax: 3.5–4.5 h; t1/2: 15.2–18.6 h	FXIa inhibition rapid, dose-dependent	Supports once-daily dosing; ongoing OCEANIC-STROKE
5	Thomas et al., 2021 [24]	Phase 1, randomized, two-part	86	Healthy men	18–45 yrs	Asundexian, 5–150 mg single dose	Placebo	Dose-dependent FXIa inhibition; aPTT increase	Mild TEAEs (dysgeusia, nausea, vertigo)	Cmax dose-dependent; Tmax: 1–3.97 h; t1/2: 14.2–17.4 h	FXIa inhibition consistent; PT/INR unaffected	Minimal meal effects; phase 2 candidate

Table 1 (continued)

S/N	Authors & Year	Study Design	Sample Size	Clinical Condition	Age (Mean)	Intervention	Comparator	Efficacy Outcomes	Safety Outcomes	Pharmacokinetics (PK)	Pharmacodynamics (PD)	Other Notes
6	Piccini et al., 2024 [16]	Phase 3, international, double-blind	14,810	Atrial fibrillation (AF), CKD, stroke/TIA	73.9 yrs	Asundexian, 50 mg OD	Apixaban	Higher stroke/systemic embolism (HR 3.79, 95% CI 2.46–5.83)	Major bleeding higher (1.3% vs. 0.4%)	–	–	Terminated early
7	Piccini et al., 2022 [20]	Phase 2b, randomized, double-blind, dose-finding	862	AF	73.7 yrs	Asundexian, 20 or 50 mg OD	Apixaban	53% lower bleeding; uncertain stroke prevention	Major/CRNM bleeding lower (HR 0.47, 95% CI 0.23–0.95)	–	–	–
8	Shoamaneh et al., 2022 [21]	Phase 2b, randomized, double-blind, placebo-controlled	1,808	Non-cardioembolic ischemic stroke	67 yrs	Asundexian, 10, 20, or 50 mg OD	Placebo	7.1% RRR in stroke (non-significant)	Major/CRNM bleeding comparable	–	–	–
9	Rao et al., 2022 [23]	Phase 2, double-blind, placebo-controlled, dose-ranging	1,601	Acute myocardial infarction (AMI)	68 yrs	Asundexian, 10, 20, or 50 mg OD	Placebo	No significant CV event reduction	Lower bleeding vs. standard therapy	–	–	Dose-related FXIa decrease
10	Smith et al., 2024 [22]	Phase 2, placebo-controlled, double-blind, randomized	1,808	Non-cardioembolic ischemic stroke	≥ 45 yrs	Asundexian, 10, 20, or 50 mg OD + antiplatelet	Placebo + antiplatelet	Trend toward reduced stroke/farcts (HR 0.71, 95% CI 0.45–1.11)	–	–	–	–
11	Balali et al., 2024 [25]	Phase 2b, international, double-blind, randomized	1,746	Non-cardioembolic ischemic stroke	67 yrs	Asundexian, 10, 20, or 50 mg OD	Placebo + antiplatelet	7% recurrent stroke/TIA	No increase in microbleeds (10.2% vs. 10.5%)	–	–	–

(Piccini et al., 2024 [16]) reported higher major bleeding with asundexian (1.3%) versus apixaban (0.4%), contributing to trial termination. Limited data suggest a potential risk of abnormal uterine bleeding (AUB) with FXIa inhibitors, particularly in women with FXI deficiency, but asundexian-specific AUB data are lacking [26].

Other safety considerations

Asundexian's tolerability was assessed across diverse populations, including those with hepatic impairment, chronic kidney disease, and cardiovascular risk factors. Brase et al., 2024 [15] found no significant cardiac repolarization or QT prolongation, supporting cardiovascular safety. Kubitz et al., 2021 [17] and Kanefendt et al., 2023 [18] reported mild treatment-emergent adverse events (TEAEs), primarily headache (4.2%) and gastrointestinal symptoms (3.8%), with no serious adverse events in healthy volunteers or patients with mild-to-moderate hepatic/renal impairment.

Pharmacological insights

Asundexian's pharmacokinetic (PK) profile is linear across 5–150 mg, with peak plasma concentrations within 2–4 h (Kubitz et al., 2021 [17]; Thomas et al., 2021 [24]). Food, tablet formulation, and gastric pH minimally affect bioavailability, supporting once-daily dosing (Kanefendt et al., 2023 [18]). Metabolism involves carboxylesterase 1 (47%), CYP3A4 (13%), and 37% unchanged excretion, reducing drug-drug interaction risks (Brase et al., 2024 [15]). This profile suggests safety in hepatic/renal impairment. Pharmacodynamically, asundexian induces dose-dependent FXIa inhibition, leading to prolongation of aPTT without affecting PT or INR [17]. These laboratory effects reflect target engagement but do not directly predict clinical bleeding outcomes. Consistent PD effects across ethnic groups (Chen et al., 2024 [19]) support generalizability.

Discussion

This systematic review synthesized evidence from 11 clinical trials [15–25], involving over 21,000 participants, to evaluate the efficacy, safety, and PK/PD of asundexian, a novel oral FXIa inhibitor, in the prevention and treatment of arterial and venous thrombotic events. The findings show asundexian's potential as an anticoagulant with a favorable bleeding profile in specific contexts but reveal significant efficacy limitations, particularly in high-risk conditions like AF.

Asundexian's efficacy in preventing thrombotic events varied across clinical contexts. In the PACIFIC-STROKE trial (Shoamanesh et al., 2022 [21]; Balali et al., 2024 [25]), asundexian (50 mg daily) achieved a modest, non-significant 7.1% relative risk reduction (RRR) in recurrent ischemic stroke among 1,808 patients with

non-cardioembolic stroke. Subgroup analyses revealed a more pronounced benefit in patients with large-artery atherosclerosis than those with small vessel disease [21]. This heterogeneity may stem from FXIa's greater contribution to thrombus formation in large-artery atherosclerosis, where shear stress and platelet activation dominate, versus small vessel disease, which involves distinct pathophysiological mechanisms [26]. These findings suggest asundexian could be tailored to specific stroke etiologies, a hypothesis supported by Smith et al., 2024 [22], who reported a trend toward reduced stroke/infarcts with asundexian (HR 0.71, 95% CI 0.45–1.11). In contrast, the PACIFIC-AMI trial (Rao et al., 2022 [23]) found no significant reduction in cardiovascular events among 1,601 patients with acute myocardial infarction, suggesting that in high-risk arterial thrombosis, where tissue factor-driven thrombin generation is pronounced, FXIa inhibition alone may be insufficient, and broader blockade of the coagulation cascade (at Factor Xa or thrombin) may be required for adequate antithrombotic protection. In AF, the PACIFIC-AF trial (Piccini et al., 2022 [20]) demonstrated a 53% lower bleeding rate but uncertain stroke prevention, while the OCEANIC-AF trial (Piccini et al., 2024 [16]) was terminated early due to a higher stroke/systemic embolism rate (2.5%) versus apixaban (HR 3.79, 95% CI 2.46–5.83). This inferior efficacy contrasts with abelacimab, another FXIa inhibitor, which has shown promising stroke prevention in AF, suggesting potential differences in potency, dosing, or trial populations [27]. The variability in asundexian's efficacy shows the need to delineate FXIa's role across thrombotic conditions and identify patient subgroups where its mechanism is most effective.

Asundexian's primary advantage lies in its favorable bleeding profile, attributed to selective FXIa inhibition that limits interference with normal hemostatic clot formation. In contrast, DOACs such as apixaban and rivaroxaban inhibit central enzymes (Factor Xa or thrombin) that participate in both physiological hemostasis and pathologic thrombosis, thereby increasing bleeding risk [28]. The PACIFIC-AF trial reported a significant reduction in major or clinically relevant non-major (CRNM) bleeding (HR 0.47, 95% CI 0.23–0.95) [20], highlighting asundexian's potential for patients at high bleeding risk, such as those with prior gastrointestinal hemorrhage or elderly populations. However, the OCEANIC-AF trial's higher major bleeding rate (1.3% vs. 0.4% with apixaban) [16] suggests that patient-specific factors, such as AF-related comorbidities (e.g., hypertension, diabetes) or trial-specific dosing regimens, may influence safety outcomes. This discrepancy warrants further investigation into the contexts where asundexian's bleeding advantage is consistent. Additionally, FXIa inhibitors may increase the risk of abnormal uterine bleeding (AUB), particularly

in women with FXI deficiency, as observed in broader anticoagulant studies [29]. The lack of asundexian-specific AUB data is a critical gap, given AUB's significant impact on quality of life and adherence to anticoagulation therapy [30]. For example, Patel et al., 2023 noted that two-thirds of women starting anticoagulation for venous thromboembolism experienced AUB-related quality-of-life declines, emphasizing the need for targeted studies in female populations [31].

Asundexian's PK/PD profile enhances its clinical appeal. Its linear pharmacokinetics (peak concentration within 2–4 h), minimal hepatic metabolism (47% carboxylesterase 1 [CES1], 13% CYP3A4, 37% unchanged excretion), and low drug-drug interaction risk support once-daily dosing, particularly in patients with hepatic or renal impairment (Brase et al., 2024 [15]; Kanefendt et al., 2023 [18]). Dose-dependent FXIa inhibition, prolonging aPTT without affecting PT or INR, underlies its bleeding advantage in trials like PACIFIC-AF [17]. The consistency of PD effects across ethnic groups (Chen et al., 2024 [19]) suggests broad applicability, but the disconnect between robust PD effects and limited clinical efficacy in OCEANIC-AF raises questions about FXIa inhibition's sufficiency in high-thrombotic-risk settings. AF-related thrombi, often driven by stasis and endothelial dysfunction, may require additional anticoagulant mechanisms (e.g., Factor Xa inhibition) for adequate protection [32].

The findings highlight a critical balance between efficacy and safety in anticoagulation therapy. Asundexian's lower bleeding risk, compared to DOACs, comes at the expense of reduced thrombotic protection, particularly in AF, where abelacimab and milvexian may offer advantages [33]. This trade-off prompts a fundamental question: can FXIa inhibitors achieve robust thromboembolism prevention and minimal bleeding? Current evidence suggests asundexian may be best suited for patients with high bleeding risk but lower thrombotic burden, such as those with non-cardioembolic stroke due to large-artery atherosclerosis or patients requiring anticoagulation but with a history of bleeding events. Compared to milvexian, which is under investigation for similar indications, asundexian's once-daily dosing and minimal metabolism offer practical advantages, but its efficacy limitations necessitate head-to-head comparisons [33]. Clinically, asundexian could fill a niche for patients where DOACs are contraindicated (e.g., severe renal impairment) or bleeding risks outweigh thrombotic risks, pending further validation.

Future research should focus on several key areas. First, refining patient selection criteria is critical to identify subgroups benefiting from FXIa inhibition, such as those with large-artery atherosclerosis or low-to-moderate thrombotic risk. The ongoing OCEANIC-STROKE trial

may provide clarity on asundexian's role in non-cardioembolic stroke prevention. Also, combination strategies, such as asundexian with low-dose antiplatelets (e.g., aspirin) or reduced-dose DOACs, could enhance efficacy without compromising safety, as explored in trials like COMPASS for rivaroxaban [34]. Studies on AUB are essential to quantify its incidence and impact in women receiving asundexian, informing sex-specific prescribing guidelines. Fourth, long-term safety and efficacy data must address the gaps left by OCEANIC-AF's early termination, particularly in real-world settings. Moreover, comparative trials with other FXIa inhibitors (e.g., abelacimab, milvexian) could elucidate mechanistic or dosing differences driving efficacy variations.

Limitations of the review

Limitations should be acknowledged. Heterogeneity across studies regarding patient populations, dosing regimens, and trial endpoints limits direct comparisons. Second, the early termination of key phase 3 trials introduces uncertainty regarding long-term outcomes. Moreover, real-world data on asundexian remain limited, and post-marketing surveillance will be crucial in assessing its safety in diverse clinical settings.

Conclusion

Asundexian, a selective FXIa inhibitor, represents a promising advancement in anticoagulation by aiming to reduce thrombotic risk with a lower bleeding burden. This review highlights its potential, particularly in non-cardioembolic ischemic stroke, where early-phase trials show encouraging safety and efficacy. However, recent findings from phase 3 trials such as OCEANIC-AF raise concerns about its effectiveness in AF, with increased thromboembolic risk compared to apixaban. These mixed results show the need for further research to clarify its optimal clinical role, refine patient selection, and evaluate long-term outcomes. Despite these challenges, FXIa inhibition remains a compelling strategy for improving anticoagulation therapy.

Abbreviations

AF	Atrial Fibrillation
DOAC	Direct Oral Anticoagulant
FXIa	Factor XIa
INR	International Normalized Ratio
ISTH	International Society on Thrombosis and Haemostasis
OAC	Oral Anticoagulant
PK/PD	Pharmacokinetics/Pharmacodynamics
RCT	Randomized Controlled Trial
TAVI	Transcatheter Aortic Valve Implantation
VKA	Vitamin K Antagonist

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None.

Author contributions

GO conceptualised the study; ZSA, RP, NA-H, EK, NA, GO, AG, AM, HS were involved in the literature review; EK, NA, and AM extracted the data from the reviewed studies; ZSA, RP, NA-H, EK, NA, GO, AG, AM, HS wrote the final and first drafts. ZSA, RP, NA-H, EK, NA, GO, AG, AM, HS read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations**Ethical approval and consent to participate**

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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