Dermatology Reports

https://journals.pagepress.net/dr

eISSN 2036-7406

Please cite this article as:

Oshima Y, Hashimoto T, Miyama H, Fujimoto T. Efficacy and safety of topical sofpironium bromide in treating primary axillary hyperhidrosis: systematic review and meta-analysis of randomized controlled trials. *Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10853*

Received: 9 March 2026; Accepted: 18 May 2026.

Efficacy and safety of topical sofpironium bromide in treating primary axillary hyperhidrosis: systematic review and meta-analysis of randomized controlled trials

Yuichiro Oshima,[1] Takashi Hashimoto,[2] Hiroshi Miyama,[2] Tomoko Fujimoto[3]

[1]Department of Dermatology, Aichi Medical University School of Medicine, Aichi; [2]Medical Affairs Department, Kaken Pharmaceutical Co., Ltd., Tokyo; [3]Ikebukuro Nishiguchi Fukurou Dermatology Clinic, Tokyo, Japan

Correspondence: Yuichiro Oshima, Department of Dermatology, Aichi Medical University School of Medicine, 1-1 Yazakokarimata, Nagakute, 480-1195 Aichi, Japan. E-mail: y45123@aichi-med-u.ac.jp. Tel.: +81-561-62-3311

Key words: sofpironium bromide; primary axillary hyperhidrosis; systematic review; meta-analysis; randomized controlled trial.

Contributions: Takashi Hashimoto, Hiroshi Miyama: article screening and supervision. All authors contributed to the conceptualization and methodology of the study and critically reviewed and approved the manuscripts.

Conflict of interest: Yuichiro Oshima and Tomoko Fujimoto have received payments for lectures from Kaken Pharmaceutical Co., Ltd; Takashi Hashimoto and Hiroshi Miyama are employees of Kaken Pharmaceutical Co., Ltd. Medical writing support was provided by Medical Professional Relations Inc., with funding from Kaken Pharmaceutical Co., Ltd.

Ethics approval and consent to participate: not applicable.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Funding: this study was funded by Kaken Pharmaceutical Co., Ltd. (Tokyo, Japan).

Acknowledgments: the authors would like to acknowledge Mr. Akihiko Uegaki of Medical Professional Relations Inc. for the systematic review and medical writing support.

Abstract

This systematic review and meta-analysis aimed to comprehensively evaluate the efficacy and safety of topical sofpironium bromide in patients with primary axillary hyperhidrosis (PAH) in various published randomized controlled trials (RCTs). The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. We systematically searched PubMed, Scopus, Web of Science, Embase, and Medline databases through April 30, 2025, using keywords related to sofpironium and PAH. The odds ratio (OR) or mean difference (MD) was calculated using a random effects model with 95% confidence interval (CI). Three RCTs of sofpironium were included in the meta-analysis, with 1,209 patients with PAH. Sofpironium, compared to the vehicle, showed statistically significant improvement in the Hyperhidrosis Disease Severity Measure–Axillary (HDSM-Ax) score (OR=2.35, 95% CI [1.82 to 3.04]), Hyperhidrosis Disease Severity Scale (HDSS) score (OR=2.02, [1.46 to 2.79]), Dermatology Life Quality Index (DLQI) score (MD=−2.75, [−3.58 to −1.92]), and gravimetric sweat production (MD=−26.39, [−44.65 to −8.12]). The incidences of anticholinergic adverse events (AEs) and application site AEs were statistically higher in patients treated with sofpironium. Sofpironium is an effective treatment for PAH associated with significant improvements in sweat reduction and QOL for patients, although the drug also has risks of anticholinergic or application-site AEs.

Introduction

Primary focal hyperhidrosis (PFH) is defined as a condition characterized by excessive sweating in localized sites, such as the head/face, palmar, plantar, and axillary regions, through which patients experience difficulties in daily activities with or without heat or mental burden.[1] In some patients with PFH, the disease severely affects their daily life, including emotional well-being, interpersonal relationships, leisure activities, personal hygiene, work and productivity, and self-esteem.[2] Many patients with PFH suffer from these adverse effects of the disease, with a reported PFH prevalence of 10.0% in Japan.[3] The disease is particularly prevalent among young people in their 20s to 30s,[3] and is thought to have a negative impact on their work lives. A cost-of-illness survey for axillary hyperhidrosis in Japan estimates that the overall work impairment of working patients is 30.52%, and the societal cost of productivity loss is ¥312 billion per month.[4] The Japanese guideline recommends two topical anticholinergic drugs, sofpironium bromide gel (hereafter referred to as “sofpironium”) and glycopyrronium tosylate hydrate wipes, as the first-line treatment for primary axillary hyperhidrosis (PAH) in addition to conventional topical aluminum chloride.[1]

Systematic reviews and meta-analyses provide a more comprehensive view of the evidence on the

efficacy and safety of a medication by combining the results of multiple studies and enable health care providers to reach more robust conclusions and make more informed decisions based on the available evidence.[5] One systematic review without meta-analysis has reported the efficacy and safety of sofpironium for treating PAH and concludes that sofpironium provides notable improvements in symptom severity, sweat reduction, and quality of life (QOL), with mostly mild localized adverse events (AEs).[6] We were the first to conduct a systematic review and meta-analysis to more robustly evaluate the efficacy and safety of topical sofpironium in patients with PAH in various published randomized controlled trials (RCTs).

Materials and Methods

We followed the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) to conduct this systematic review and meta-analysis.[7]

Search strategy

We systematically searched the PubMed, Scopus, Web of Science, Embase, and Medline databases from the inception until April 30, 2025, using a combination of keywords related to sofpironium and primary hyperhidrosis: ((“Sofpironium bromide” OR Sofpironium OR Sofdra OR SB OR “BBI 4000” OR “BBI-4000” OR Ecclock) AND (Hyperhidrosis)). Duplicates were removed from all the articles searched for these keywords. Next, title and abstract screening was performed using the Rayyan software package.[8] The full-text screenings were conducted independently by two reviewers. Any disagreements were resolved through consultation with a third reviewer.

Study selection and eligibility criteria

The inclusion criteria were as follows: i) RCTs that use sofpironium as an intervention *vs.* a placebo; ii) RCTs that evaluate the efficacy of sofpironium using the Hyperhidrosis Disease Severity Measure–Axillary (HDSM-Ax) score; and iii) RCTs evaluating the quantitative suppression of perspiration by sofpironium. We excluded review articles, case/cohort studies, uncontrolled studies, non-English articles, and RCTs not evaluated in patients with PAH.

Data extraction

Two independent authors extracted the data from the studies using a pre-specified data extraction form. Specific data were extracted, including study characteristics, efficacy outcomes, and treatment-emergent adverse events (TEAE).

Quality assessment

Two researchers independently assessed the quality of the included studies using a Cochrane risk-of-bias tool for randomized control trials (RoB 2)[9] and classified the bias of each study as having a "low risk", "some concerns", or "high risk".

Statistical analysis

Analyses were performed according to the Cochrane Handbook for Systematic Reviews of Interventions (version 6.5).[10] A meta-analysis with a random-effects model was performed using R software (version 4.3.1).

Results

Article search results

The PRISMA flow diagram of the study selection process is shown in Figure 1. Our search strategy yielded a total of 207 articles containing potentially relevant study information. After removing the duplicates, 118 articles remained. Following screening of titles and abstracts, 20 articles were selected for a full-text review. Of these, three articles reporting the results of RCTs were included in the systematic review and meta-analysis.[11-13]

Characteristics of the included studies

Our study included three RCTs that included 1,209 patients with PAH. All patients received sofpironium or a vehicle for the treatment of PAH, and the efficacy and safety of sofpironium were compared with those of the vehicle. A summary of the included RCTs and baseline patient characteristics in the studies is shown in Tables 1 and 2.

Quality assessment of the included studies

Of the three RCTs, two showed a low risk of bias, and another was judged to have some concerns in the RoB 2 assessment (Table 3).

Efficacy outcomes

Responders for the HDSM-Ax score

Figure 2 shows a forest plot comparing the proportion of patients who achieved a ≥1-point improvement (Pariser 2025 and Kirsch 2020) or a ≥1.5-point improvement (Yokozeki 2021) on the HDSM-Ax score between the treatment of sofpironium and the vehicle. A statistically significant difference was observed in the overall effect in favor of the sofpironium group compared to the vehicle group (odds ratio [OR]=2.35, 95% confidence interval [CI] [1.82 to 3.04]). The pooled results were homogeneous (I^2=0%, p=0.88).

Responders for the Hyperhidrosis Disease Severity Scale score

The proportion of patients who achieved a score of 1 or 2 (Yokozeki 2021) or a ≥1-point improvement (Kirsch 2020) on the Hyperhidrosis Disease Severity Scale (HDSS) score was compared between the treatment of sofpironium and vehicle. A statistically significant difference was observed in the overall effect in favor of the sofpironium group compared to the vehicle group (OR=2.02, 95% CI [1.46 to 2.79]). The pooled results were homogeneous (I^2=0%, P=0.68) (Figure 3).

Change in Dermatology Life Quality Index score

The mean difference (MD) of changes in the Dermatology Life Quality Index (DLQI) score was compared between the sofpironium and vehicle treatments. A statistically significant difference was observed in the overall effect in favor of the sofpironium group compared to the vehicle group (MD=−2.75, 95% CI [−3.58 to −1.92]). The pooled results were homogeneous (I^2=0%, p=0.50) (Figure 4).

Change in gravimetric sweat production

The gravimetric sweat production (GSP) was evaluated in two RCTs using a standard method with axillary filter paper. The MD of changes in GSP was compared between the sofpironium and vehicle treatments. A statistically significant difference was observed in the overall effect in favor of the sofpironium group compared to the vehicle group (MD=−26.39, 95% CI [−44.65 to −8.12]). The pooled results were homogeneous (I^2=0%, p=0.86) (Figure 5).

Safety outcomes

The overall risk of TEAE incidence was unfavorable in the sofpironium group compared to the vehicle group (OR=7.63, 95% CI [4.75 to 12.25]), with no significant heterogeneity detected in the pooled results (I^2=2%, p=0.40) (Figure 6). The overall risks were also unfavorable in the sofpironium group regarding the incidence of dry mouth (OR=15.63, 95% CI [6.47 to 37.73]) (Figure 7), vision blurred (OR=8.06, 95% CI [1.86 to 34.84]) (Figure 8), mydriasis (OR=7.20, 95% CI [1.53 to 33.86]) (Figure 9), application site dermatitis (OR=6.41, 95% CI [2.42 to 16.94]) (Figure 10), and application site erythema (OR=3.05, 95% CI [1.98 to 4.69]) (Figure 11), with no significant heterogeneity. In particular, anticholinergic TEAEs were more prevalent in patients treated with higher concentrations of sofpironium (Figures 7-9).

Discussion

This study provides the first findings of a systematic review and meta-analysis that evaluates the efficacy and safety of topical sofpironium in patients with PAH. Furthermore, the inclusion of RCTs only for the analysis also enhances the strength of our findings, which provides significant insights into the treatment benefit of the drug. We reviewed and analyzed data from three RCTs identified from a systematic literature review strategy, and the RCTs included a total of 1,209 patients with PAH. Our findings indicate that sofpironium is effective in treating patients with PAH, although the drug also has the risk of AEs that may be due to its anticholinergic effects or may occur at the site of drug application.

Meta-analysis of efficacy outcomes included the HDSM-Ax, HDSS, DLQI score, and GSP. In all these efficacy outcomes, statistically significant differences were observed in the overall effects in favor of the sofpironium group compared to the vehicle group, indicating the benefit of sofpironium treatment for patients with PAH.

The HDSM-Ax score is a validated, 11-item, patient-reported outcome measure of symptom severity and frequency.[14] Among the three RCTs included in our analysis, the HDSM-Ax was used in two RCTs (Yokozeki 2021 and Kirsch 2020), whereas the simplified version of the HDSM-Ax score consisting of a 7-item measure[11] was used in one RCT (Pariser 2025). HDSM-Ax is reported to be a well-defined and reliable measure of primary PAH severity, and a 1-point change in HDSM-Ax score represents a clinically meaningful change.[15] The findings of this meta-analysis suggest that sofpironium treatment provides clinically significant benefits in terms of symptom severity and frequency in patients with PAH.

The HDSS score is used to assess the severity of PFH based on the patient's subjective symptoms: a score of 3 or 4 indicates severe hyperhidrosis, a score of 2 indicates moderate hyperhidrosis, and a score of 1 indicates the absence of hyperhidrosis.[16] Patients with an HDSS score of 3 or 4, indicating severe hyperhidrosis, were enrolled in two RCTs (Yokozeki 2021 and Kirsch 2020). PAH is a refractory disease that not only limits daily and social activities but also causes psychological and emotional distress.[17,18] Sofpironium treatment may provide clinical benefits to patients with PAH who experience limitations in activity and distress caused by severe hyperhidrosis symptoms.

The DLQI is designed to evaluate the skin disease-related quality of life (QOL), and responses to 10 questions are scored and summed to obtain the DLQI score.[19] The DLQI score, with minor modifications for PAH, which makes it more terminologically suitable for disease assessment, was evaluated in two RCTs (Yokozeki 2021 and Kirsch 2020). Hyperhidrosis creates significant emotional, physical, or social discomfort, negatively impacting a patient's QOL.[20,21] Therefore, improvement in QOL with sofpironium treatment is a clinically important benefit for patients with

PAH. Varella *et al.* reported a statistical correlation between the HDSS and QOL questionnaire scores in patients with hyperhidrosis.[22] Given that sofpironium also reduced the HDSS score in our analysis, the drug may improve QOL by suppressing hyperhidrosis symptoms in patients with PAH.

Additionally, a greater improvement in the change in GSP with sofpironium treatment also supports the robustness of the efficacy of sofpironium for the treatment of PAH, considering that GSP is an objective evaluation index, unlike the HDSM-Ax, HDSS, and DLQI scores, which are based on the patient's subjective judgment.

Meta-analysis of safety outcomes included the incidence of TEAE and anticholinergic-related AEs such as dry mouth, blurred vision, mydriasis, and application site AEs of dermatitis and erythema. In all safety outcomes, significantly higher incidences were observed in the sofpironium group than in the vehicle group, indicating the risk of AEs associated with sofpironium treatment in patients with PAH.

Sofpironium is an M3 muscarinic receptor ligand that has been developed as a retro-metabolically designed drug and inhibits M3 muscarinic receptors in eccrine glands at the application site.[23,24] Based on its mechanism of action against hyperhidrosis through M3 receptors, sofpironium also poses a risk of anticholinergic AEs. Most anticholinergic TEAEs were mild or moderate according to the severity, with a controllable risk in all three included RCTs. This may be due to the topical administration of sofpironium as well as the nature of the retro-metabolically designed drug, which is assumed to decrease the anticholinergic activity in the blood.[23,24] However, in only one RCT (Pariser 2025), severe dry mouth was reported (incidence: 0.8%).

In the meta-analysis, anticholinergic TEAEs were more prevalent in patients treated with higher concentrations of sofpironium, suggesting that the risk is dose dependent. Thus, it is important to administer the drug in compliance with the approved dose. Although anticholinergic AEs are thought to be caused by sofpironium absorbed into the blood after application, anticholinergic AEs in the eye may also be caused by touching the eyes with hands that have the applied drug on the axilla. Therefore, the following care should be taken while administering the drug: do not apply the drug directly with the hand; if the drug attaches to the hand, wash it immediately; in case the drug accidentally enters the eyes, wash them with water immediately. To reduce the exposure to anticholinergics, a topical formulation of sofpironium was designed for convenient application.

The severity of the reported application site AEs related to sofpironium treatment was mostly mild or moderate, with an acceptable or controllable profile in all three included RCTs. Sofpironium is associated with a risk of dermatitis and erythema at the application site; however, this risk is plausible because it is intended for topical use.

This study had some limitations. First, the number of studies included in our analysis was limited, and only three RCTs were identified throughout the screening process. A previous systematic review of sofpironium treatment for PAH includes five studies, not limited to RCTs, and the findings are consistent with our study.[6] Second, the treatment duration was 6 weeks in all three RCTs included, and the period was not sufficient to consider the long-term efficacy and safety of sofpironium in the treatment of PAH. Long-term evaluation has been conducted in a phase 3, 52-week, open-label study in Japan,[25] as an extension of the preceding 6-week phase 3 RCT included in this analysis (Yokozeki 2021). Extension phase 3 demonstrates that the efficacy of sofpironium is maintained during the 52-week treatment period, and no new safety risks are observed. Third, no publication bias analysis could be performed because of the small number of included RCTs, according to the report of Egger *et al.*, which indicates unreliable publication bias assessment by funnel plot asymmetry for <10 pooled studies.[26]

Conclusions

In conclusion, topical sofpironium bromide is an effective treatment for PAH associated with significant improvements in sweat reduction and QOL for patients. Although the drug also has the risk of anticholinergic AEs or application site AEs, they are primarily mild to moderate, with an acceptable or controllable profile. These findings support the use of topical sofpironium bromide to manage PAH in clinical practice. Further RCTs and long-term studies are needed to confirm these findings and optimize the use of the drug.

References

1. Fujimoto T, Yokozeki H, Nakazato Y, et al. Guidelines of the Japanese dermatological association, clinical guidelines for primary focal hyperhidrosis (revised edition in 2023). Jpn J Dermatol 2023;133:157-88 (Article in Japanese).
2. Hamm H. Impact of hyperhidrosis on quality of life and its assessment. Dermatol Clin 2014;32:467-76.
3. Fujimoto T, Inose Y, Nakamura H, et al. Questionnaire-based epidemiological survey of primary focal hyperhidrosis and survey on current medical management of primary axillary hyperhidrosis in Japan. Arch Dermatol Res 2023;315:409-17.
4. Murota H, Fujimoto T, Oshima Y, et al. Cost-of-illness study for axillary hyperhidrosis in Japan. J Dermatol 2021;48:1482-90.
5. Murad MH, Montori VM, Ioannidis JPA, et al. How to read a systematic review and meta-analysis and apply the results to patient care: users' guides to the medical literature. JAMA

2014;312:171-9.
6. Odat RM, Aldalati AY, Hammadeh BM, et al. Efficacy and safety of sofpironium in treatment of primary hyperhidrosis: a systematic review. J Dermatolog Treat 2025;36:2441258.
7. Page MJ, McKenzie JE, Bossuyt PM, et al. Updating guidance for reporting systematic reviews: development of the PRISMA 2020 statement. J Clin Epidemiol 2021;134;103-12.
8. Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan-a web and mobile app for systematic reviews. Syst Rev 2016;5:210.
9. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019;366:l4898.
10. Higgins JPT, Thomas J, Chandler J, et al., editor(s). Cochrane Handbook for Systematic Reviews of Interventions version 6.5 (updated August 2024). Cochrane, 2024. Available from: www.cochrane.org/handbook
11. Pariser D, Glaser DA, Rosso JD, et al. Sofpironium topical gel, 12.45%, for the treatment of axillary hyperhidrosis: Pooled efficacy and safety results from 2 phase 3 randomized, controlled, double-blind studies. J Am Acad Dermatol 2025;93:82-8.
12. Yokozeki H, Fujimoto T, Abe Y, et al. A phase 3, multicenter, randomized, double-blind, vehicle-controlled, parallel-group study of 5% sofpironium bromide (BBI-4000) gel in Japanese patients with primary axillary hyperhidrosis. J Dermatol 2021;48:279-88.
13. Kirsch B, Smith S, Cohen J, et al. Efficacy and safety of topical sofpironium bromide gel for the treatment of axillary hyperhidrosis: A phase II, randomized, controlled, double-blinded trial. J Am Acad Dermatol 2020;82:1321-7.
14. Kirsch BM, Burke L, Hobart J, et al. The Hyperhidrosis Disease Severity Measure-Axillary: conceptualization and development of item content. J Drugs Dermatol 2018;17:707-14.
15. Hobart J, Burke L, Kirsch B, et al. Hyperhidrosis Disease Severity Measure-Axillary (HDSM-Ax): evaluation of measurement performance. J Drugs Dermatol 2021;20:410-8.
16. Solish N, Bertucci V, Dansereau A, et al. A comprehensive approach to the recognition, diagnosis, and severity-based treatment of focal hyperhidrosis: recommendations of the Canadian Hyperhidrosis Advisory Committee. Dermatol Surg 2007;33:908-23.
17. Strutton DR, Kowalski JW, Glaser DA, et al. US prevalence of hyperhidrosis and impact on individuals with axillary hyperhidrosis: results from a national survey. J Am Acad Dermatol 2004;51:241-8.
18. Hornberger J, Grimes K, Naumann M, et al. Recognition, diagnosis, and treatment of primary focal hyperhidrosis. J Am Acad Dermatol 2004;51:274-86.
19. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.

20. Nawrocki S, Cha J. The etiology, diagnosis, and management of hyperhidrosis: A comprehensive review: Etiology and clinical work-up. J Am Acad Dermatol 2019;81:657-66.
21. Parashar K, Adlam T, Potts G. The Impact of hyperhidrosis on quality of life: a review of the literature. Am J Clin Dermatol 2023;24:187-98.
22. Varella AYM, Fukuda JMF, Teivelis MP, et al. Translation and validation of Hyperhidrosis Disease Severity Scale. Rev Assoc Med Bras (1992) 2016;62:843-7.
23. Wu WM, Buchwald P, Mori N, et al. Pharmacokinetic and pharmacodynamic evaluations of the zwitterionic metabolite of a new series of N-substituted soft anticholinergics. Pharm Res 2005;22:2035-44.
24. Wu WM, Wu J, Mori N, et al. Stereoisomers of N-substituted soft anticholinergics and their zwitterionic metabolite based on glycopyrrolate--syntheses and pharmacological evaluations. Pharmazie 2008;63:200-9.
25. Fujimoto T, Abe Y, Igarashi M, et al. A phase III, 52-week, open-label study to evaluate the safety and efficacy of 5% sofpironium bromide (BBI-4000) gel in Japanese patients with primary axillary hyperhidrosis. J Dermatol 2021;48:1149-61.
26. Egger M, Smith GD, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-34.

Table 1. Summary of the three included RCTs.

RCT ID	Phase	Country	Treatment comparison	Period	No. of PFH patients (randomized)	Inclusion for PFH severity	Primary endpoint	Conclusion
Pariser 2025	3	USA	Vehicle	6 weeks	348	HDSM-Ax: 3 or 4 GSP: ≥150 mg (in both axillae)	(Co-primary endpoint) ≥2-point improvement from baseline to end of treatment on HDSM-Ax, and GSP at treatment end	Sofpironium topical gel, 12.45%, applied topically once daily before bedtime is effective and well-tolerated for treatment of primary axillary hyperhidrosis in patients ≥9 years old
			Sofpironium 15%*		353			
Yokozeki 2021	3	Japan	Vehicle	6 weeks	140	HDSM-Ax: 2 to 4 HDSS: 3 or 4 GSP: ≥50 mg (in each axilla)	Proportion of patients who satisfied both criteria with a HDSS of 1 or 2 at the end of treatment and ≥50% reduction in total GSP at the end of treatment relative to baseline	5% sofpironium was confirmed to be effective and safe in Japanese patients with primary axillary hyperhidrosis
			Sofpironium 5%*		141			
Kirsch 2020	2	USA	Vehicle	6 weeks	57	HDSM-Ax: 3 or 4 HDSS: 3 or 4 GSP: ≥150 mg (in both axillae)	(Co-primary endpoint) Percentage of patients exhibiting ≥1-point improvement on HDSM-Ax, and change in HDSM-Ax	Sofpironium bromide gel produced meaningful reductions in hyperhidrosis severity and had an acceptable safety profile
			Sofpironium 5%*		57			
			10%*		57			
			15%*		56			

*Shown as a dose of sofpironium bromide; GSP, gravimetric sweat production; HDSM-Ax, Hyperhidrosis Disease Severity Measure–Axillary; HDSS, Hyperhidrosis Disease Severity Scale; PFH, primary focal hyperhidrosis; RCT, randomized controlled trial.

Table 2. Baseline patient characteristics in the included RCTs.

RCT ID	Treatment comparison	No. of PFH patients (evaluated)	Age (years), median (range)	Female (%)	PAH severity at baseline
Pariser 2025	Vehicle	348	31.0 (11~71)	58.0	ND
	Sofpironium 15%*	353	31.0 (10~76)	53.8	ND
Yokozeki 2021	Vehicle	140	36.0 (13~72)	70.7	HDSM-Ax: 3.04±0.572[#] HDSS: 3 (67.1%) or 4 (32.9%) DLQI: 10.9±4.42[#] GSP: 226.3±128.88 mg[#]
	Sofpironium 5%*	141	35.0 (13~72)	69.5	HDSM-Ax: 3.06±0.514 HDSS: 3 (67.4%) or 4 (32.6%) DLQI: 11.7±4.96[#] GSP: 228.0±167.10 mg[#]
Kirsch 2020	Vehicle	57	30.0±8.6[#]	53	HDSM-Ax: 3.39±0.29[#] GSP: 279.4±178.8 mg[#]
	Sofpironium 5%*	57	30.8±10.2[#]	44	HDSM-Ax: 3.49±0.32[#] GSP: 274.3±191.4 mg[#]
	10%*	57	33.7±11.3[#]	39	HDSM-Ax: 3.50±0.29[#] GSP: 288.5±195.6 mg[#]
	15%*	54	30.7±9.2[#]	46	HDSM-Ax: 3.57±0.31[#] GSP: 311.1±187.2 mg[#]

*Shown as a dose of sofpironium bromide; [#]mean ± standard deviation; ND, not described; DLQI, Dermatology Life Quality Index; GSP, gravimetric sweat production; HDSM-Ax, Hyperhidrosis Disease Severity Measure–Axillary; HDSS, Hyperhidrosis Disease Severity Scale; PFH, primary focal hyperhidrosis; RCT, randomized controlled trial.

Table 3. Risk of bias assessment of the included RCTs.

RCT ID	Risk of bias					
	Domain 1	**Domain 2**	**Domain 3**	**Domain 4**	**Domain 5**	**Overall**
Pariser 2025	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Yokozeki 2021	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Kirsch 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Domain 1: bias arising from the randomization process; Domain 2: bias due to deviation from intended intervention; Domain 3: bias due to missing outcome data; Domain 4: bias in measurement of the outcome; Domain 5: bias in selection of reported results. RCT, randomized controlled trial.

Figure 1. PRISMA flow diagram for the selection of articles containing relevant study information.

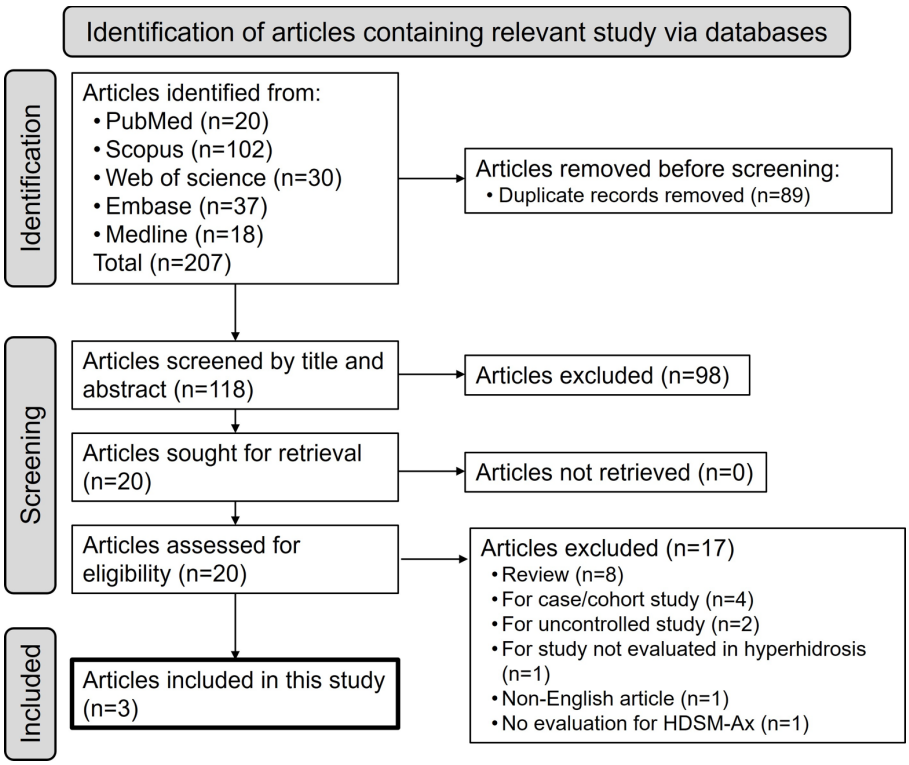

Figure 2. Forest plot of the responders for the HDSM-Ax score.

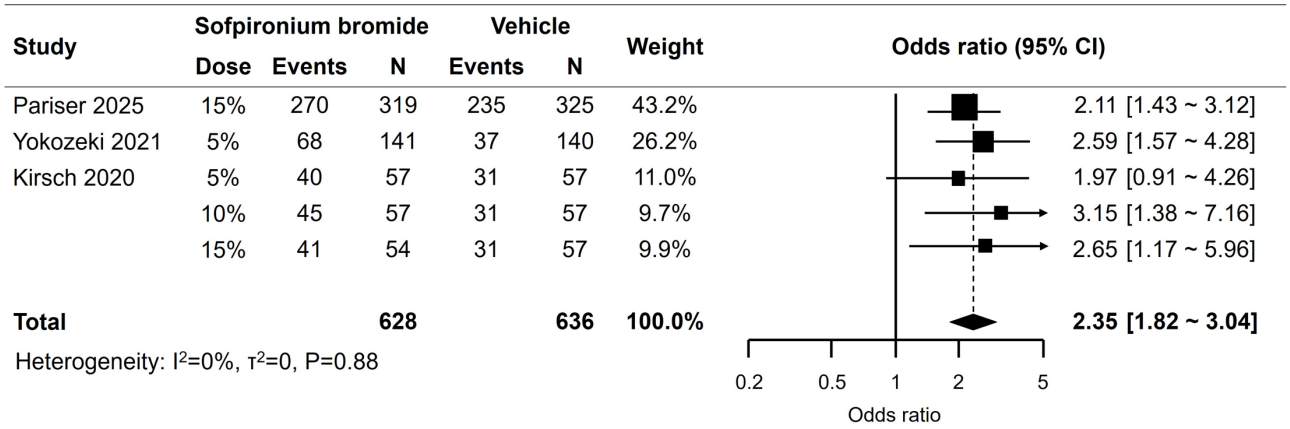

Figure 3. Forest plot of the responders for the HDSS score.

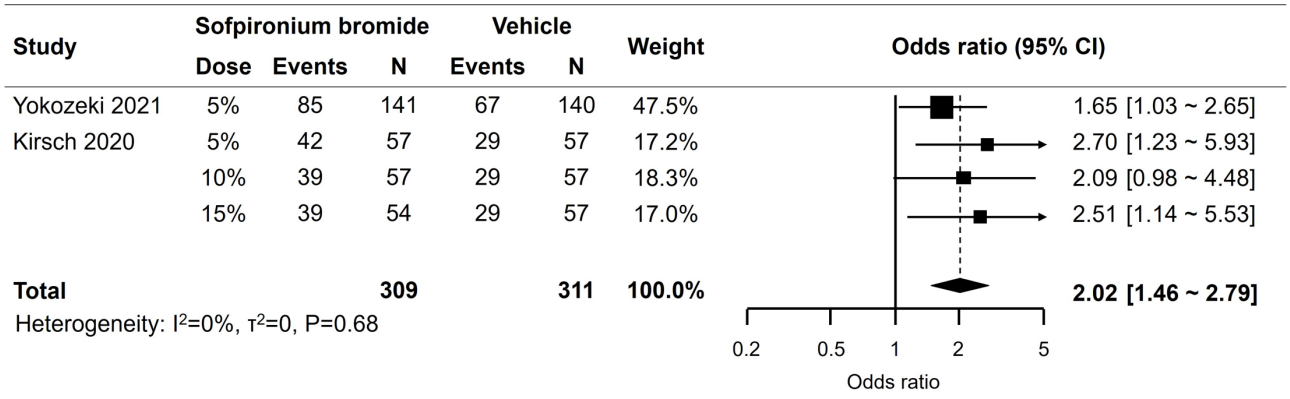

Figure 4. Forest plot of the responders for the DLQI score.

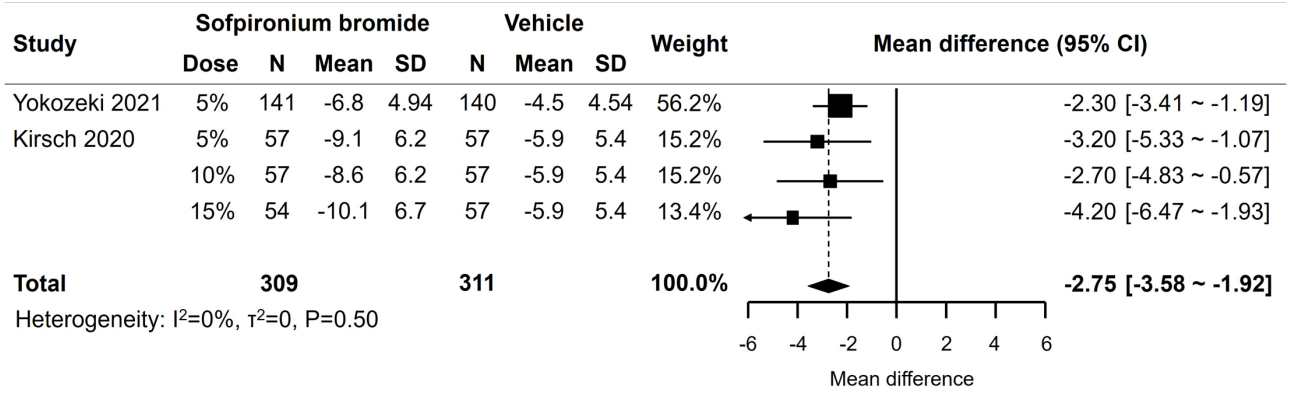

Figure 5. Forest plot of the change in GSP.

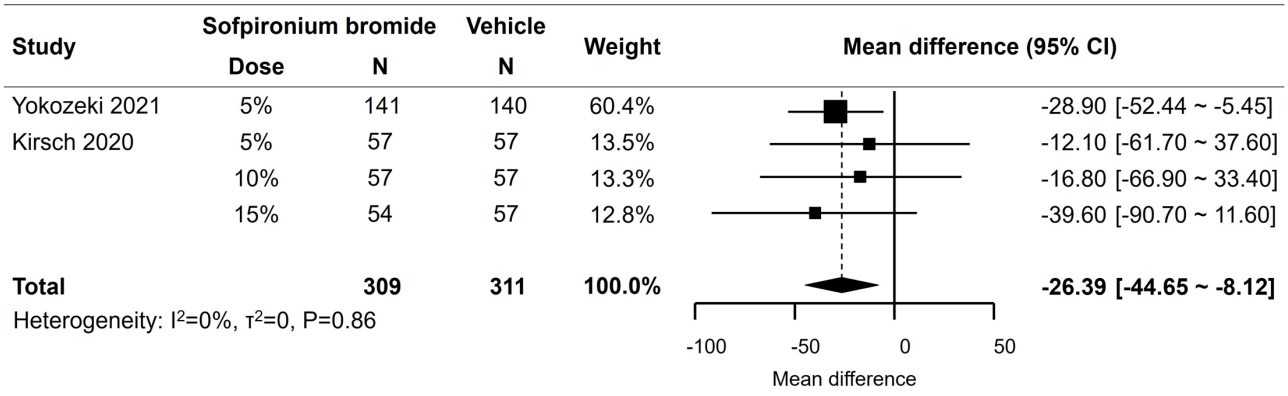

Figure 6. Forest plot for the incidence of TEAE.

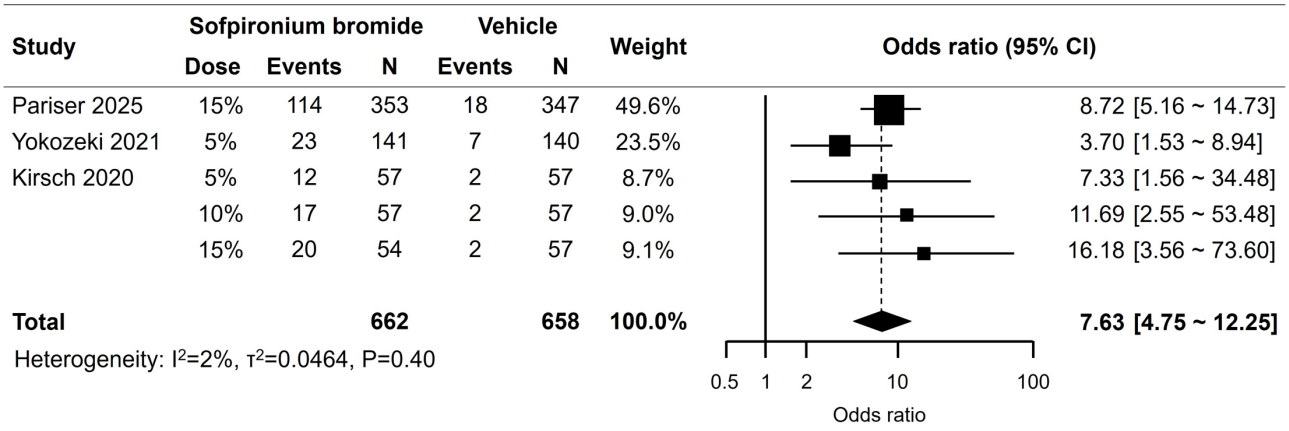

Figure 7. Forest plot for the incidence of dry mouth.

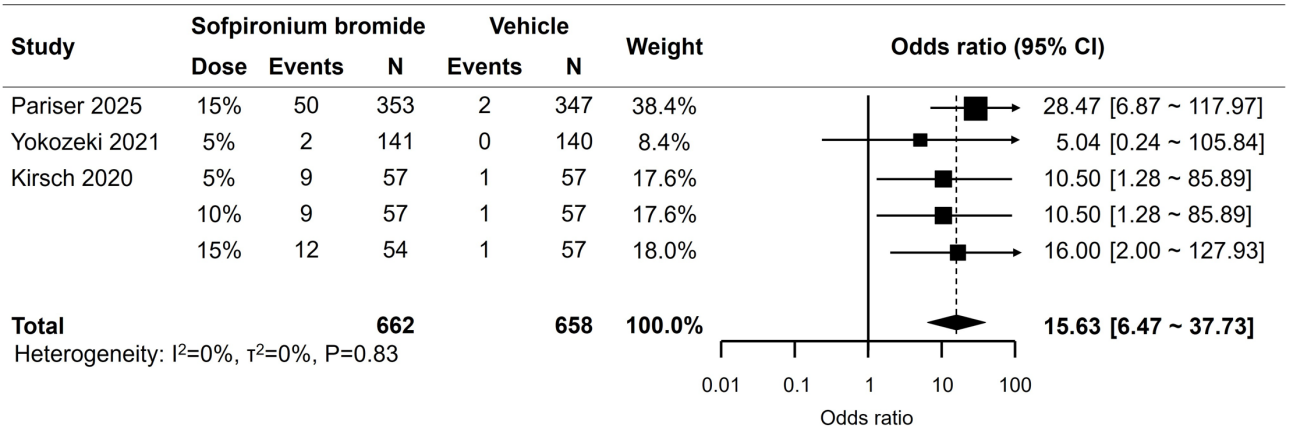

Figure 8. Forest plot for the incidence of blurred vision.

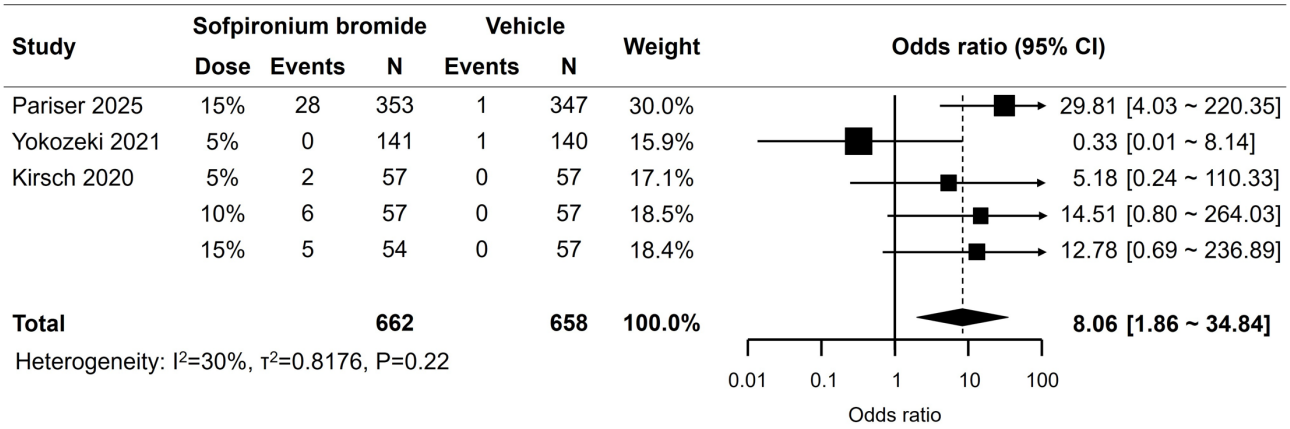

Figure 9. Forest plot for the incidence of mydriasis.

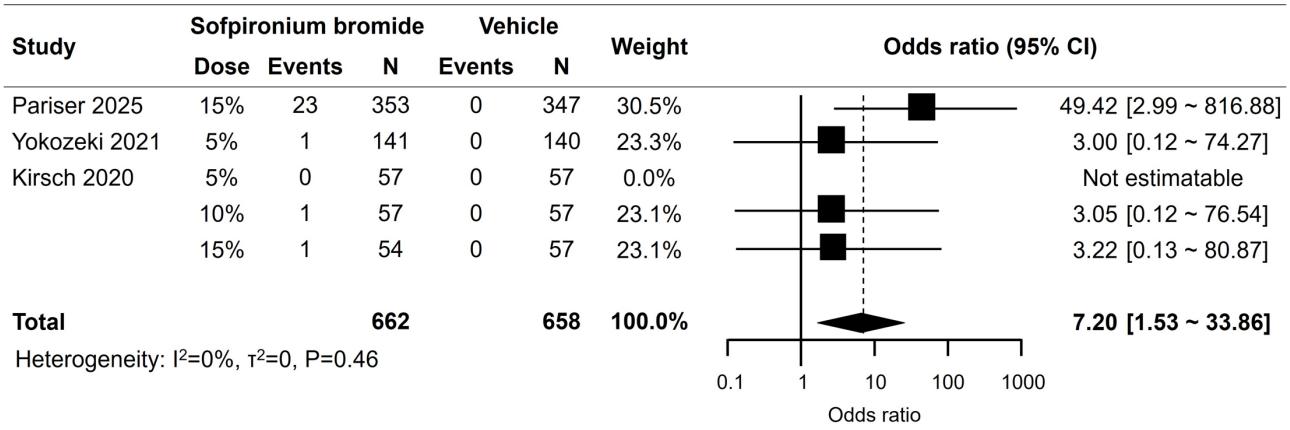

Figure 10. Forest plot for the incidence of application site dermatitis.

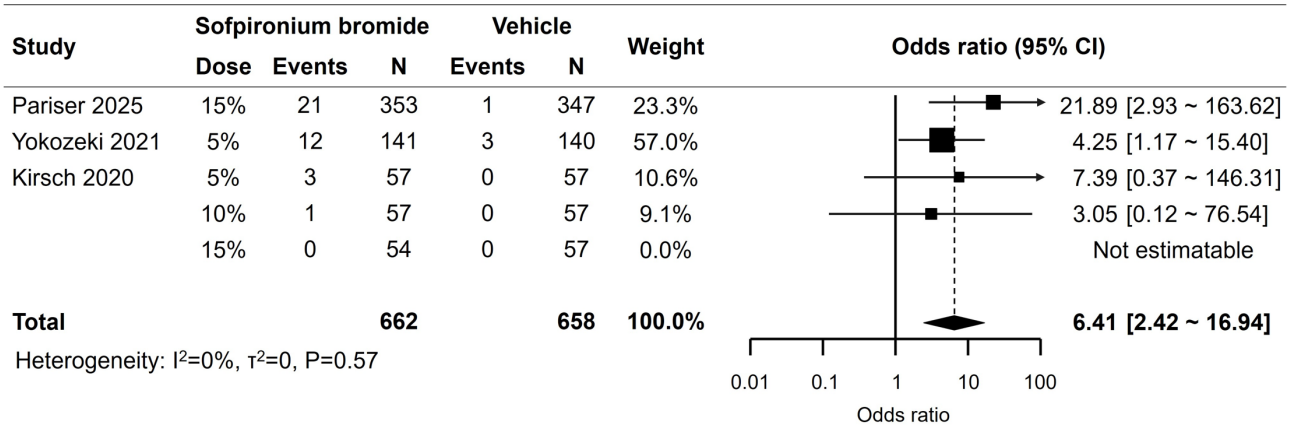

Figure 11. Forest plot for the incidence of application site erythema.