INPLASY

Clinical and functional outcomes of Stallergenes Greer index of reactivity liquid sublingual immunotherapy in allergic asthma: a product-specific systematic review and meta-analysis of randomized placebo-controlled trials

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ADMINISTRATIVE INFORMATION

Support - Stallergenes Greer.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690052

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 September 2026 and was last updated on 11 September 2026.

INTRODUCTION

Review question / Objective What is the efficacy and safety of Stallergenes Greer index of reactivity (IR) liquid sublingual immunotherapy (IR-SLIT-liquid; Staloral®) compared with placebo in patients with allergic asthma?

Rationale Allergen immunotherapy (AIT) is an established treatment for IgE-mediated allergic respiratory diseases. However, evidence regarding its efficacy in allergic asthma remains heterogeneous, particularly for clinically relevant and functional outcomes such as asthma symptoms, medication use, and lung function.

Previous systematic reviews have pooled different AIT products, formulations, routes of administration, dosing regimens, and treatment schedules, potentially limiting the clinical interpretability of pooled estimates. Furthermore, evidence regarding lung function outcomes, particularly forced expiratory volume in one second (FEV_1), remains limited and fragmented.

International recommendations increasingly emphasize that evidence for allergen immunotherapy should be evaluated at the individual-product level rather than assuming a class effect. Therefore, this systematic review will specifically evaluate Stallergenes Greer IR liquid sublingual immunotherapy (IR-SLIT-liquid; Staloral®), with the aim of providing a product-specific synthesis of its efficacy and safety in patients with allergic asthma.

Questo razionale riproduce il punto centrale del vostro lavoro: le precedenti meta-analisi hanno avuto problemi di eterogeneità tra prodotti e scarsità di dati quantitativi, in particolare per FEV_1.

Condition being studied Allergic asthma.

METHODS

Search strategy Search strategies combined controlled vocabulary terms, where applicable, and free-text terms related to:

allergic asthma;
allergen immunotherapy;
sublingual immunotherapy;
SLIT;
Stallergenes;
Staloral;
index of reactivity/IR;
relevant allergen extracts.

Search strategies will be adapted to the syntax and controlled vocabulary of each database.

The complete electronic search strategies will be reported in the Supplementary Material of the systematic review.

Participant or population Patients of any age with allergic asthma associated with sensitization to a clinically relevant allergen and treated with Stallergenes Greer IR-SLIT-liquid.

Studies including patients with concomitant allergic rhinitis or rhinoconjunctivitis will also be eligible, provided that asthma-specific outcomes are reported or can be extracted.

No restrictions will be applied according to age, sex, asthma severity, or allergen source.
PICO summary

Population: Patients with allergic asthma.
Intervention: Stallergenes Greer IR-SLIT-liquid (Staloral®).
Comparator: Placebo.
Outcomes: Asthma symptom score, asthma medication score, FEV_1, and safety outcomes.

Intervention Sublingual allergen immunotherapy with Stallergenes Greer index of reactivity (IR) liquid formulations (IR-SLIT-liquid; Staloral®), irrespective of allergen source, administered dose, treatment schedule, or treatment duration.

Comparator Placebo.

Study designs to be included Randomized placebo-controlled clinical trials.

Eligibility criteria Studies will be eligible if they meet the following criteria:

randomized placebo-controlled clinical trials;
inclusion of patients with allergic asthma treated with Stallergenes Greer IR-SLIT-liquid (Staloral®);
reporting of at least one asthma-related efficacy or safety outcome of interest; and
availability of sufficient quantitative information to calculate an effect estimate or allow such information to be derived from the reported data.

Studies evaluating multiple SLIT products will be excluded unless data for Stallergenes Greer IR-SLIT-liquid can be extracted separately. Studies not reporting asthma-related outcomes will be excluded.

No restrictions will be applied according to language, publication year, age, allergen source, treatment duration, or treatment schedule.

Information sources A comprehensive literature search was conducted in MEDLINE (via PubMed), Web of Science, and Cochrane Library from database inception to July 2025.
ClinicalTrials.gov was additionally searched to identify ongoing, completed, or unpublished randomized controlled trials and to retrieve supplementary information on potentially eligible studies.
The electronic literature search will be updated before completion of the systematic review to identify additional potentially eligible studies published or registered since the original search.
No language restrictions will be applied.
Reference lists of eligible studies and relevant systematic reviews will also be manually screened to identify additional potentially eligible studies.

Main outcome(s) Asthma symptom score

Differences between IR-SLIT-liquid and placebo in asthma symptom scores, assessed using the symptom scoring systems reported in the individual randomized controlled trials.

When different symptom scoring systems are used across studies, results will be expressed as standardized mean differences (SMDs) with corresponding 95% confidence intervals (CIs).

Asthma medication score

Differences between IR-SLIT-liquid and placebo in asthma medication use, according to the medication scoring systems reported in the individual trials.

When different medication scoring systems are used across studies, results will be expressed as

standardized mean differences (SMDs) with corresponding 95% CIs.

Lung function

Differences between IR-SLIT-liquid and placebo in forced expiratory volume in one second (FEV_1), preferentially expressed as percentage of predicted FEV_1 when available.

When sufficiently comparable scales are reported across studies, pooled effects will be expressed as mean differences (MDs) with corresponding 95% CIs.

Questi sono i tre outcome sui quali è effettivamente costruita la quantitative synthesis del lavoro.

Additional outcome(s) Safety outcomes will include:
overall adverse events;
treatment discontinuations;
treatment discontinuations due to adverse events.

Other asthma-related clinical outcomes, including asthma control and exacerbations, will be considered when available. These outcomes will be quantitatively synthesized only if sufficiently homogeneous data are available; otherwise, they will be summarized narratively.Safety.

Data management All records identified through the electronic searches will be imported into Rayyan, which will be used for reference management, duplicate removal, and study selection.
Two reviewers will independently screen titles and abstracts for potential eligibility. Potentially eligible studies will subsequently undergo independent full-text assessment.
Disagreements regarding study eligibility will be resolved through discussion and consensus.
Reasons for exclusion at the full-text stage will be documented.
The study selection process will be reported using a PRISMA flow diagram.

Data extraction
Two reviewers will independently extract data using a standardized data extraction form.
Extracted information will include:

study design and publication characteristics;
study population and patient characteristics;
age;
allergen source;
sample size;
intervention and comparator characteristics;
administered dose;
treatment schedule;
treatment duration;
outcome definitions and measurement instruments;
efficacy outcome data;
safety data.

Disagreements will be resolved through discussion and consensus.
When standard deviations (SDs) are not directly reported, they will be estimated from available summary statistics using established methods. When standard errors (SEs) are reported, SDs will be calculated using the formula:
$SD = SE \times \sqrt{n}$
Where necessary and sufficiently reliable, numerical outcome data may be extracted from graphical representations.

Quality assessment / Risk of bias analysis Risk of bias in individual randomized controlled trials will be independently assessed using the Cochrane Risk of Bias 2 (RoB 2) tool.

The following domains will be considered:

bias arising from the randomization process;
bias due to deviations from intended interventions;
bias due to missing outcome data;
bias in measurement of the outcome;
bias in selection of the reported result.

An overall risk-of-bias judgement will be assigned to each relevant outcome according to RoB 2 guidance.

Disagreements between reviewers will be resolved through discussion and consensus.

The overall certainty of evidence for the main efficacy outcomes will be assessed according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

The following domains will be considered:

risk of bias;
inconsistency;
indirectness;
imprecision;
publication bias.

The certainty of evidence will be categorized as high, moderate, low, or very low.

Summary of Findings tables will be prepared using GRADEpro GDT.Sensitivity analyses will be conducted, where feasible, to assess the robustness of pooled effect estimates.

These may include leave-one-out analyses and influence diagnostics to identify individual studies exerting a disproportionate influence on the pooled treatment effect or between-study heterogeneity.

Baujat plots and other appropriate influence diagnostics may be used to explore the contribution of individual studies to heterogeneity and overall effect estimates.

Strategy of data synthesis For continuous outcomes measured using different instruments or scoring systems, treatment effects will be summarized using standardized mean differences (SMDs) with corresponding 95% confidence intervals.

When outcomes are reported using sufficiently comparable measurement scales, mean differences (MDs) with corresponding 95% confidence intervals will be calculated.

For dichotomous outcomes, including adverse events and treatment discontinuations, treatment effects will be expressed as risk ratios (RRs) with corresponding 95% confidence intervals.

Meta-analyses will be conducted using random-effects models to account for anticipated clinical and methodological heterogeneity among trials.

Statistical heterogeneity will be quantified using the I^2 statistic.

Where quantitative synthesis is considered inappropriate because of insufficient data or substantial clinical or methodological heterogeneity, findings will be summarized narratively.

Statistical analyses will be performed using R, primarily employing the metafor package, and Python where appropriate.

Subgroup analysis Where sufficient data are available, subgroup analyses and/or meta-regression analyses will be performed to explore potential sources of heterogeneity and effect modification.

Potential study-level covariates will include:

age;
allergen source;
treatment duration;
treatment schedule;
yearly administered dose;
cumulative dose.

Meta-regression analyses will only be performed when considered statistically appropriate according to the number of available studies and will be interpreted as exploratory.

Sensitivity analysis Sensitivity analyses will be conducted, where feasible, to assess the robustness of pooled effect estimates.

These may include leave-one-out analyses and influence diagnostics to identify individual studies exerting a disproportionate influence on the pooled treatment effect or between-study heterogeneity.

Baujat plots and other appropriate influence diagnostics may be used to explore the contribution of individual studies to heterogeneity and overall effect estimates.

Language restriction No.

Country(ies) involved Italy, France.

Other relevant information This protocol is being registered retrospectively. The original literature search was conducted in July 2025. Protocol registration was not completed at the initial stage of the review. The literature search will be updated before completion of the systematic review to identify additional potentially eligible studies published or registered since the original search.

Keywords Allergic asthma; allergen immunotherapy; sublingual immunotherapy; SLIT; Staloral; index of reactivity; symptom score; medication score; FEV_1; randomized controlled trial; systematic.

Dissemination plans The findings of this systematic review and meta-analysis will be submitted for publication in a peer-reviewed scientific journal and may also be presented at relevant national and international scientific conferences.

Contributions of each author

Author 1 - Danilo Di Bona - Conceptualization and design of the systematic review; development of the methodology; literature screening and study selection; data extraction; risk-of-bias and certainty-of-evidence assessment; statistical analysis and interpretation of findings; drafting and

critical revision of the manuscript; supervision of the review.
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Author 2 - Andrea Di Biase - Literature screening and study selection; data extraction; risk-of-bias assessment; contribution to data analysis and interpretation of findings; critical revision of the manuscript.
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