

CONFLICT OF INTERESTS

The authors have no conflict of interest to declare.

ETHICAL APPROVAL

Clinical features were collected through a standardized form. Written informed consents were obtained from all patients according to the French legislation and the principles of the Declaration of Helsinki. The study was approved by the research ethics committee from the Hôpitaux Universitaires de Strasbourg, France (N°ID RCB 2008-A01295-50).

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Intranasal antihistamine and corticosteroid to treat allergic rhinitis: A systematic review and meta-analysis

To the Editor,

Recently, combination therapy with intranasal corticosteroid (INCS) and intranasal antihistamine (INAH) has been recommended as an alternative to INCS monotherapy for patients with allergic rhinitis;¹ however, only one meta-analysis compared treatment outcomes between fluticasone/azelastine combination therapy and fluticasone monotherapy, groups; other INCS/INAH combination therapies and INCS monotherapies were not evaluated.²

The PubMed, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, Scopus, and MEDLINE databases were

systematically searched for both randomized controlled trials (RCTs) and non-RCTs, in accordance with the recommendations of the Cochrane handbook.³ In total, 19,685 studies were initially identified and retrieved, of which 19,643 were excluded after title and abstract screening. The remaining 42 studies were assessed for eligibility; 28 were removed after full-text screening. The reasons for exclusion, and the PRISMA flow chart for study selection, are presented in Figure S1. Ten studies that evaluated differences in symptom scores, and 12 that described adverse events, were included (some studies reported both types of data). All studies were RCTs. In total, 13

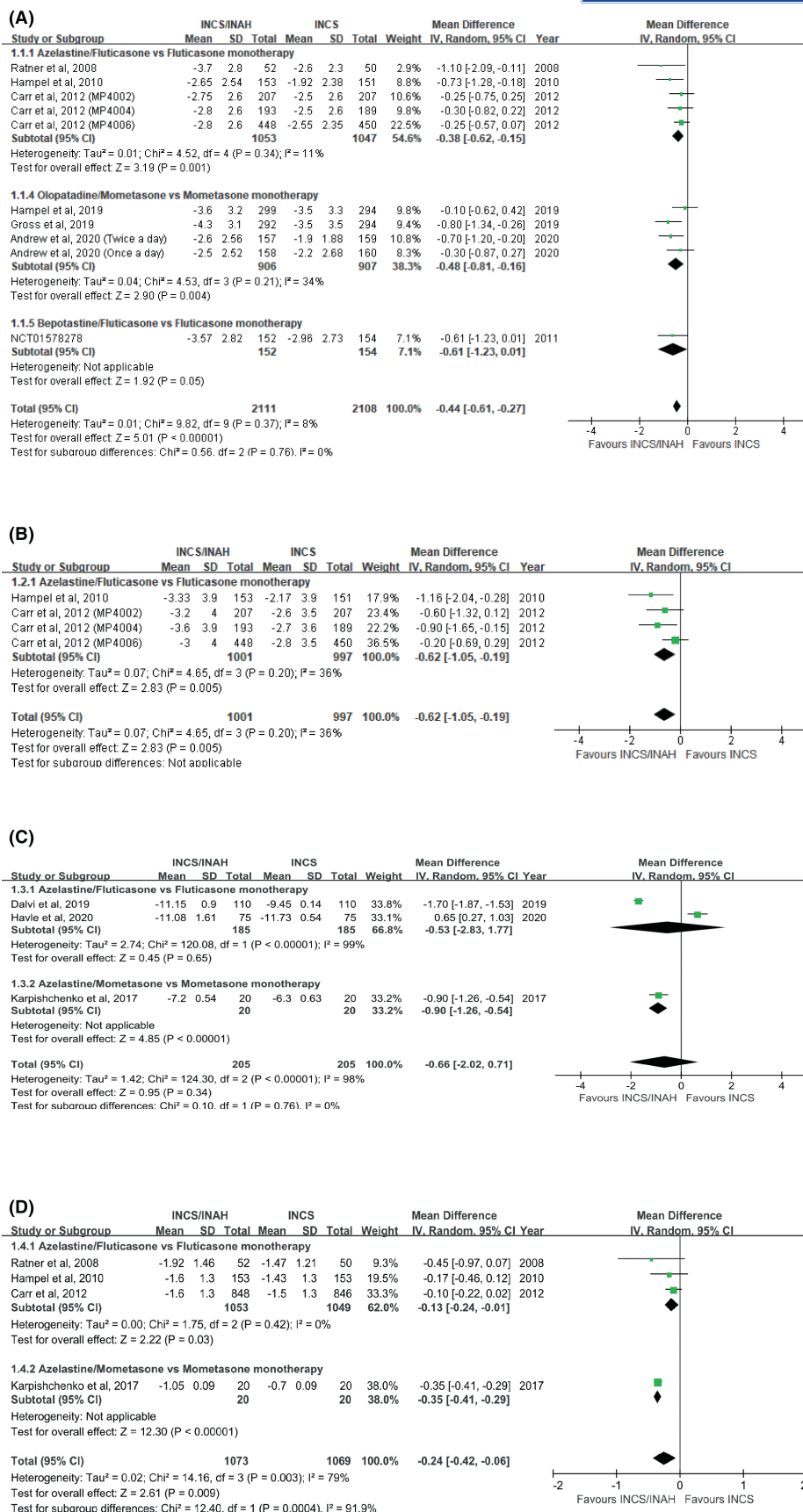


FIGURE 1 Comparison of changes in symptom scores after treatment between INCS/INAH combination therapy and INCS monotherapy. (A) TNSS; (B) TSS; (C) TOSS; (D) RQLQ. INAH, intranasal antihistamine; INCS, intranasal corticosteroid; RQLQ, rhinoconjunctivitis quality of life questionnaire; TNSS, total nasal symptom score; TOSS, total ocular symptom score; TSS, total symptom score

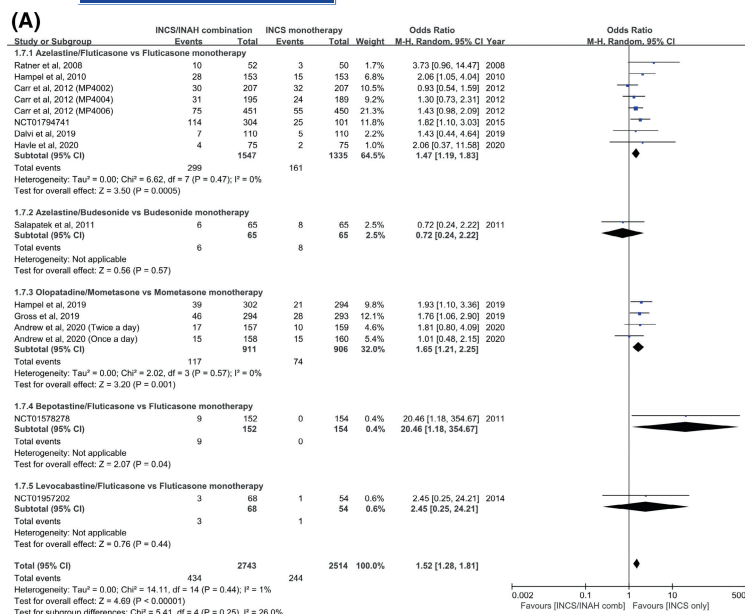
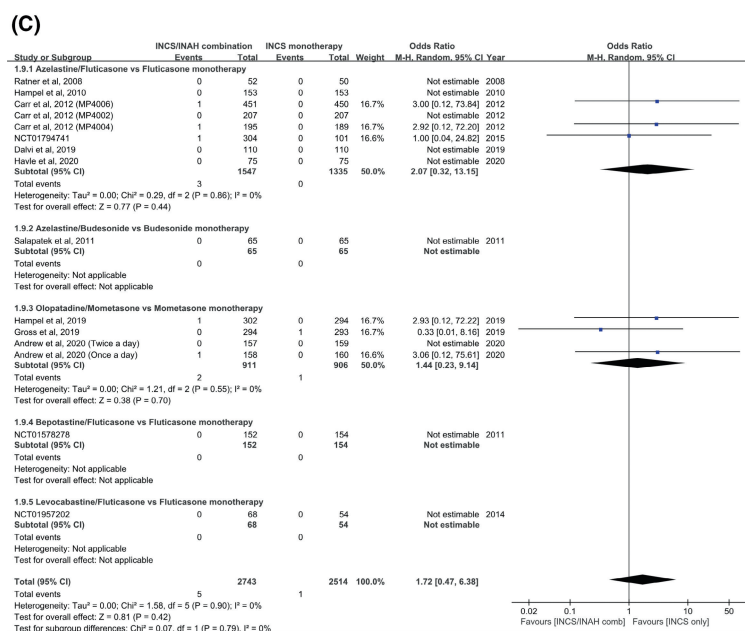
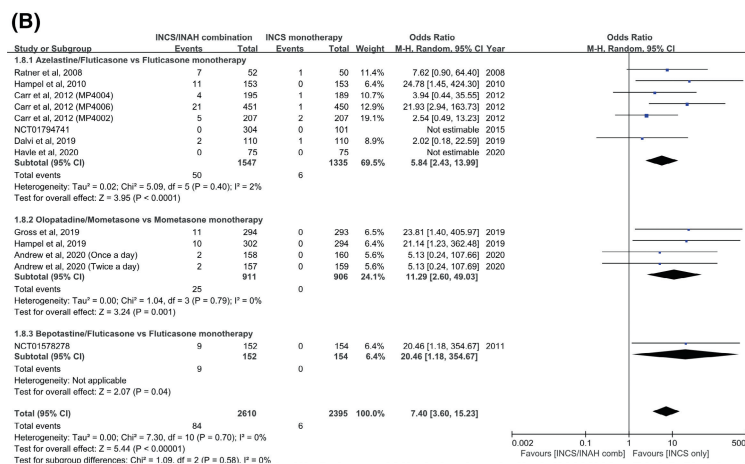


FIGURE 2 Comparison of frequencies of adverse events after treatment between INCS/INAH combination therapy and INCS monotherapy. (A) TEAEs; (B) dysgeusia; (C) SAEs. INAH, intranasal antihistamine; INCS, intranasal corticosteroid; SAEs, serious adverse events; TEAEs, treatment emergent adverse events



studies were included. The characteristics of the studies are shown in Table S1. The risks of bias data are presented in Figures S2 and S3.

Compared to INCS monotherapy, INCS/INAH combination therapy reduced the mean morning and evening 12-h reflective total nasal symptom score (TNSS) more significantly (MD -0.44, 95% CI -0.61 to -0.27, $P < 0.00001$, $I^2 = 8\%$), as well as the total ocular symptom score (MD -0.62, 95% CI -1.05 to -0.19, $P = 0.005$, $I^2 = 36\%$), but not the total symptom score (MD -0.66, 95% CI -2.02 to 0.71, $P = 0.34$, $I^2 = 98\%$). The INCS/INAH combination significantly improved the total mean Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) score compared to INCS monotherapy (MD -0.24, 95% CI -0.42 to -0.06, $P = 0.009$, $I^2 = 79\%$) (Figure 1 and Table S2). In sensitivity analysis, the TNSS, TSS, and RQLQ scores differed significantly between the two treatments (Figures S4–S6).

INCS/INAH combination therapy was associated with a significantly greater risk of treatment-emergent adverse events (TEAEs) than INCS monotherapy (RR 1.52, 95% CI 1.28 to 1.81, $P < 0.00001$, $I^2 = 1\%$), especially in terms of dysgeusia (bad/bitter taste in the mouth/throat)⁴ (RR 7.40, 95% CI 3.60 to 15.23, $P < 0.00001$, $I^2 = 0\%$), but not serious adverse events (RR 1.72, 95% CI 0.47 to 6.38, $P = 0.42$, $I^2 = 0\%$) (Figure 2). In sensitivity analysis, INCS/INAH combination therapy also significantly increased the risk of TEAEs (excluding studies with uncertain bias due to deviation from the planned intervention, missing outcome data, or both) (Figure S7) and dysgeusia (excluding studies with uncertain bias due to deviation from the planned intervention and missing outcome data, but not both) (Figure S8).

INCS/INAH combination therapy was significantly better for alleviating nasal and ocular symptoms and improving quality of life than INCS monotherapy in AR patients. However, the thresholds of minimal clinically important differences (0.28 for TNSS and 0.5 for RQLQ)^{5,6} were not exceeded. Moreover, INCS/INAH combination therapy was associated with a higher rate of adverse events (such as dysgeusia). Our meta-analysis had some limitations. First, there were uncertainties related to bias arising from the randomization process in most studies, as well as deviation from the intended intervention and missing outcome data in some studies (Figures S2 and S3). Second, there was possible publication bias; eight clinical trials did not post their results to clinical registries (Figure S1). Further studies are required to verify the potential therapeutic utility of INCS/INAH combination therapy compared to INCS monotherapy.

FUNDING INFORMATION

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest in relation to this study.

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SUPPORTING INFORMATION

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Presentation of airway and general symptoms in COVID-19 caused by dominant SARS-CoV-2 variants: A follow-up on ARIA consensus

To the Editor,

Several SARS-CoV-2 variants have occurred since the beginning of the COVID-19 pandemic. Mutated variants of concerns (VOC; World Health Organization nomenclature) have a variable contamination rate and virulence. COVID-19 symptoms are polymorphic and vary according to VOC.¹ A consensus effort from the ARIA group (*Allergic Rhinitis and its Impact on Asthma*) has been shown that symptoms from common cold, allergic rhinitis, and COVID-19 are likely to be differentiated in a panel of 15 items.²

Although papers have described major clinical manifestations in these new variants,^{3,4} there is no consensus on important symptom changes caused by VOC Delta and Omicron. Following the methods

of the first EAACI-ARIA-GA¹LEN paper,² we assessed globally how physicians seeing COVID-19 patients are rating various symptoms induced by different VOC.

2 | METHODS

A bibliographic survey identified common symptoms induced by VOC Delta and Omicron. Then, a Delphi questionnaire regarding key symptoms associated with SARS-CoV-2 infection was developed based on the items from ARIA-EAACI-GA2LEN consensus² and from literature. Symptoms included common cold (upper airway),

TABLE 1 Tasks of the questionnaire

Symptom	Occurrence	Expected VAS
Runny nose, sneezing, stuffy nose, nasal pruritus, facial/nasal pain, ocular itch, ocular pain, Ocular redness, >3 nasal symptoms, smell dysfunction, taste dysfunction, dyspnea, cough, wheezing, sore throat, headache, fatigue, fever, duration of illness >1 week, undulating symptoms, gastrointestinal symptoms, skin symptoms, body/muscle ache, arthralgia, altered consciousness	Choice between: (none, very rare, possible, common, always) or (yes, no)	(grade from 0–10)

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