Indirect treatment comparison of budesonide oral suspension vs dupilumab in paediatric patients with EoE

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INTRODUCTION

- Eosinophilic esophagitis (EoE) is a chronic, progressive, immune-mediated oesophageal disease, characterised clinically by symptoms of oesophageal dysfunction and histologically by eosinophil-predominant inflammation[1].
- Until the recent approval of the budesonide oral suspension (BOS), EoE treatment consisted of budesonide ODT, licensed only in adults, dupilumab, licensed in paediatric patients subject to weight and treatment-eligibility criteria, proton pump inhibitors, and dietary restrictions[2,3].
- Paediatric patients with EoE faced a substantial unmet need, as, until BOS approval, no approved treatment was suitable across the full paediatric population[3,4]. As a consequence, many patients continued to rely on restrictive dietary elimination strategies and off-label treatments.
- Budesonide oral suspension (BOS), developed following EMA's interest in a paediatric formulation of budesonide, demonstrated significant efficacy versus placebo in paediatric EoE in the PEDEOS-1 trial [EudraCT No: 2017-003737-29][5].
- However, no head-to-head studies comparing BOS with dupilumab in paediatric EoE are available.

OBJECTIVE

This study aimed to compare the efficacy of BOS versus dupilumab via an indirect treatment comparison (ITC) using the Bucher methodology.

METHODS

Literature review

- A structured literature review was performed to identify randomised clinical trials (RCTs) of dupilumab in paediatric EoE patients, to compare with BOS in the PEDEOS-1 study.
- Three RCTs (PEDEOS-1 for BOS, and LIBERTY EoE TREET and EoE KIDS for dupilumab met the inclusion criteria for the ITC (Figure 2).

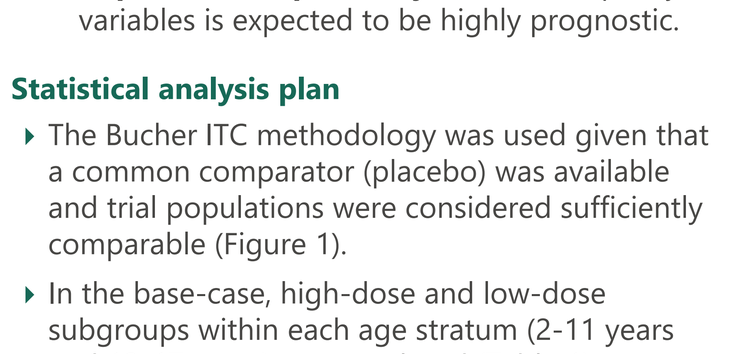
Comparability assessment

- Baseline characteristics and outcome measures were compared across the three trials. Comparability was assessed under three categories:
  - **No comparability issue expected**: comparable values within ~20% difference
  - **Some potential comparability issue**: large discrepancy (>20%) in a variable that is not considered highly prognostic
  - **Important comparability issue**: discrepancy in variables is expected to be highly prognostic.

Statistical analysis plan

- The Bucher ITC methodology was used given that a common comparator (placebo) was available and trial populations were considered sufficiently comparable (Figure 1).
- In the base-case, high-dose and low-dose subgroups within each age stratum (2-11 years and 12-17 years) were analysed (Table 1).
- Odds ratios were estimated using the standard Bucher method. Because there were no responders in the placebo arm of PEDEOS-1, Haldane–Anscombe continuity corrections were applied in the PEDEOS-1 trial in the base case.
- Sensitivity analyses tested Haldane–Anscombe in both trials and Firth penalised logistic regression (Table 2).

Figure 1. Bucher ITC Network Diagram

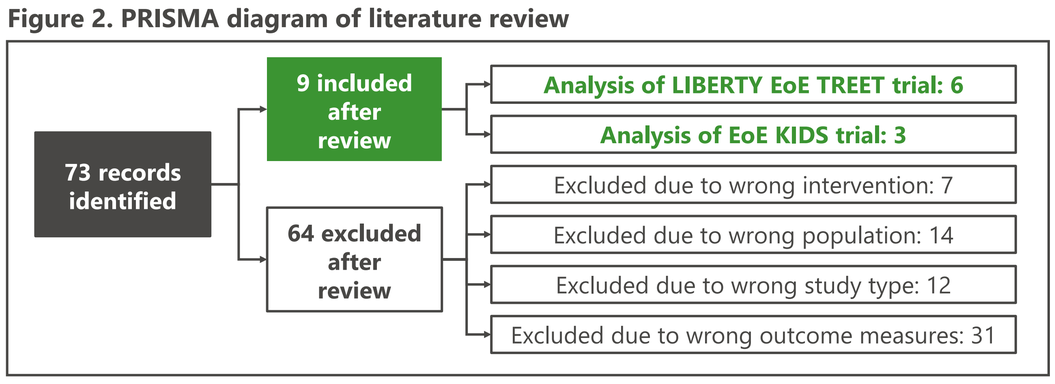


RESULTS

Literature review

In total, 9 publications describing two trials: EoE KIDS (2024) in children aged 1–11 years [EudraCT No: 2019-003078-24][6] and LIBERTY EoE TREET in adolescents aged 12–17 years [EudraCT No: 2018-000844-25][7] were identified.

Figure 2. PRISMA diagram of literature review



Comparability assessment

- The trial characteristics and eligibility criteria were sufficiently comparable.
- Histologic remission was selected as the endpoint for ITC, as it was the (co)-primary endpoint in all trials, and the definition was considered comparable. Histological remission was assessed separately by age and dosing subgroup. PEDEOS-1 defined histological remission as <16 eos/mm^2, corresponding to approximately <5 eos/hpf. Values were converted to eos/hpf to align reporting units with the dupilumab trials, which used ≤6 eos/hpf.

ITC results

- Across paediatric age strata and dosing subgroups, BOS provides at least comparable and numerically higher rates of histological remission compared to dupilumab (Table 1; OR>1 favours BOS). In all subgroups, except the low-dose subgroup aged 2–11 years, ITC results numerically favoured BOS versus dupilumab (base-case ORs of 1.15 and 4.69 in the 2–11-year and 12–17-year populations, respectively), although confidence intervals were wide due to the limited sample sizes.
- Sensitivity analyses consistently showed numerically favourable results for BOS compared with dupilumab (Table 2 & Table 3; 1 - OR>1 favours BOS).

Comparison	Population	Dose	OR	95% CI	BOS vs placebo	Dupilumab vs placebo
PEDEOS-1 vs EoE KIDS	2-11 years	Overall	1.15	0.03, 42.54,p = 0.94	21/28 (75%) vs 0/13 (0%)	43/68 (63.2%) vs 1/34 (2.9%)
		Low dose	0.69	0.02, 27.78, p = 0.84	9/14 (64.3%) vs 0/13 (0%)	25/37 (67.6%) vs 1/34 (2.9%)
		High dose	2.56	0.05, 128.90, p = 0.64	12/14 (85.7%) vs 0/13 (0%)	18/31 (58.1%) vs 1/34 (2.9%)
PEDEOS-1 vs LIBERTY EoE TREET	12–17 years	Overall	4.69	0.17, 128.07, p = 0.36	21/28 (75%) vs 0/13 (0%)	32/64 (50%) vs 2/35 (5.7%)
		Low dose	4.19	0.14, 128.41, p = 0.41	9/14 (64.3%) vs 0/13 (0%)	15/26 (57.7%) vs 2/26 (7.7%)
		High dose	8.25	0.24, 283.00, p = 0.24	12/14 (85.7%) vs 0/13 (0%)	13/27 (48.1%) vs 2/26 (7.7%)

Table 1. ITC base-case analysis results (Haldane-Anscombe correction only in PEDEOS-1)

Comparison	Population	Dose	Odds ratio	95% CI
PEDEOS-1 vs EoE KIDS	2–11 years	Overall	1.72	0.06, 52.79, p = 0.76
		Low dose	1.02	0.03, 34.65, p = 0.99
		High dose	3.87	0.09, 164.21, p = 0.48
PEDEOS-1 vs LIBERTY EoE TREET	12–17 years	Overall	5.78	0.22, 148.6, p = 0.29
		Low dose	5.11	0.18, 147.68, p = 0.34
		High dose	10.22	0.32, 330.65, p = 0.19

Table 2. ITC sensitivity analyses results (Haldane-Anscombe correction in both trials)

Comparison	Population	Dose	Odds ratio	95% CI
PEDEOS-1 vs EoE KIDS	2–11 years	Overall	1.72	0.06, 52.79, p = 0.76
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Table 3. ITC sensitivity analyses results (Firth penalised logistic regression)

CONCLUSIONS

- These findings suggest that BOS provides at least comparable, and potentially greater, histological efficacy compared with dupilumab in paediatric patients with EoE.
- This potential clinical benefit is particularly relevant in paediatric EoE, where treatment options remain limited by age, weight, formulation and route of administration; BOS offers a standardised, age-appropriate oral treatment across the paediatric age range without injection burden.
- Interpretation of the findings is limited by the small sample sizes, particularly in the placebo arms, which resulted in sparse event data and necessitated the use of statistical adjustment methods.

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Abbreviations: BOS: budesonide oral suspension; CI: confidence interval; EMA: European Medicines Agency; EoE: eosinophilic oesophagitis; eos/hpf: eosinophils per high-power field; ITC: indirect treatment comparison; ODT: orodispersible tablet; OR: odds ratio; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: randomised controlled trial.

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