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THE AUTHORS RESPOND

We have read the letter from Martin et al in critique of our article, "A cost comparison of benralizumab, mepolizumab, and dupilumab in patients with severe asthma: A US third-party payer perspective,"[1] which was recently published in *J Manag Care Spec Pharm*. We appreciate the careful examination of our model inputs and assumptions and welcome the opportunity to engage in dialogue around this important topic.

Martin and colleagues have raised several concerns regarding the methodology we used to conduct a comparison of costs associated with 3 biologics (benralizumab, mepolizumab, and dupilumab) used for the treatment of severe eosinophilic asthma. First, the authors mention inconsistencies between our stated cost-minimization approach and the analysis we conducted, arguing that we "state that similar effectiveness for all three biologics is assumed in the absence of head-to-head trials… Since similar effectiveness was not modeled, a cost-effectiveness rather than a cost-minimization approach should have been taken." As stated in the Introduction of our article, a published Institute for Clinical and Economic Review report of clinical trial evidence and a recent indirect comparison indicated that effectiveness was similar between biologics.[2] The indirect comparison adjusted for differences across study populations in age, asthma severity, and phenotype. The analysis adjusted for these differences and provided some evidence of similarity among biologics in exacerbation rates, forced expiratory volume in the first second of expiration, asthma control, and serious adverse events.[3] We adopted a cost-minimization approach based on the assumptions that although clinical effectiveness is similar between biologics, administration modes and schedules are different and have an important impact on resource use and costs. Our model and the article present cost comparison results for a scenario in which equal (rather than similar) efficacy is assumed across all biologics. Assuming therapeutic equivalence (without taking into consideration reductions in exacerbations and oral corticosteroid [OCS] dependence difference), the administration plus drug cost for benralizumab was lower than that of the other 2 products in both the 2- and 4-year analyses. This is shown in Figure 2A in the original article and is consistent over the 2- and 4-year scenarios and across both comparisons between benralizumab vs mepolizumab ($8,957 difference over 2 years and $23,061 difference over 4 years) and benralizumab vs dupilumab (difference of $6,844 over 2 years and difference of $17,242 over 4 years). Indeed, although our analysis also considered cost offsets from reduced exacerbations and OCS use (shown separately in Figure 2B in the original article), results showed that these were not the main drivers of cost minimization. Rather, the administration and biologic costs were the main driver of results.

Second, Martin et al call into question the studies chosen for inclusion as model inputs for effectiveness. The authors assert that we did not describe how studies were chosen; on the contrary, we have clearly stated in the article that the effectiveness data are based on results from published clinical trials, including SIROCCO, CALIMA, BORA, and MELTEMI for benralizumab; MENSA, COSMOS, and COSMEX for mepolizumab; and LIBERTY QUEST and TRAVERSE for dupilumab (listed in the footnotes of Supplementary Tables 1 and 2).[1] The "internal, unpublished analyses" on n = 77 patients with blood eosinophils of at least 150 cells/μL comprised patients enrolled in MELTEMI with registration dosing (Q8W); these data are presented in Supplementary Table 1. Importantly, the data for patients with blood eosinophils of at least 300 cells/μL, which have been published in MELTEMI,[4] showed similar results. Benralizumab real-world evidence (RWE) data came from the published ZEPHYR 1 study.[5] For the mepolizumab RWE data, we did not include the REALITI-A study[6] because this article was published in 2022, after the time that our model was developed in 2021. The data from Llanos et al[7] were the best published data available at the time. However, when applying the newly published 43% OCS reduction

Xiao Xu, PhD
BioPharmaceuticals Market Access and Pricing, AstraZeneca, Gaithersburg, MD; BioPharmaceuticals Global Medical Affairs, AstraZeneca, Gaithersburg, MD

Rohit Katial, MD
BioPharmaceuticals Global Medical Affairs, AstraZeneca, Gaithersburg, MD

Caroline Schaefer, MBA
Product Development & Market Access Consulting, Labcorp Drug Development, Gaithersburg, MD

Agota Szende, PhD, MSc
Product Development & Market Access Consulting, Labcorp Drug Development, Leeds, UK

Eduardo Genofre, MD, PhD, and Yen Chung, PharmD
BioPharmaceuticals US Medical Affairs, AstraZeneca, Wilmington, DE

rate with mepolizumab for year 1 and year 2, the model estimates that in the RWE data–based scenario, the marginal cost difference in total health care costs per patient over 2 years comparing benralizumab with mepolizumab would be $10,662 instead of the original estimate of $11,592, as seen in Figure 3. This change in results does not alter the conclusions of the article.

Furthermore, we clearly stated in the Methods that, given the lack of head-to-head clinical trials, "an approach was taken to source model inputs from similar subgroups across trials." The characteristics of the patient population from the source of effectiveness data for benralizumab on OCS dependency (PONENTE[8]) are representative of the OCS-dependent population as defined by guidelines[9,10]; therefore, the evaluation of aggressive OCS elimination questioned by Martin et al represents a more rigorous outcome. As 4-year OCS elimination data were available for mepolizumab, and with the rationale of using the best available peer-reviewed published data at the time of study conduct, we chose to use these data rather than assume constant OCS elimination. Indeed, these data favored mepolizumab as patients eliminated OCS use; this would not have been the case if we had assumed the same constant for mepolizumab.

Finally, to account for uncertainty in model parameter estimates and to test the robustness of model results, we conducted 1-way and probabilistic sensitivity analyses around key model parameters in the base-case scenario (see Sensitivity Analyses in the Results section of the article) and the model results and conclusions were consistent across scenarios. As reported in the article, RWE-based data were only available for the comparison between benralizumab and mepolizumab over a 2-year time horizon. One-way sensitivity analysis also indicated that results and conclusions were consistent across the RWE scenarios (data available on request).

In summary, based on the model inputs and sensitivity analyses described herein, we believe that our methodology is valid and that the estimated differences in treatment costs to third-party payers have been adequately substantiated.

DISCLOSURES

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Drs Xu, Chung, Genofre, and Katial are or were AstraZeneca employees at the time this research was conducted and may hold stock. Ms Schaefer and Dr Szende are or were employees of Labcorp Drug Development (now Fortrea), which received funding from AstraZeneca to perform this research, at the time this research was conducted.

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