

Efficacy and safety of ribosome-component immune modulator for preventing recurring respiratory infections in socialized children

To the Editor

RE: Fiocchi A, et al. Efficacy and safety of ribosome-component immune modulator for preventing recurrent respiratory infections in socialized children. *Allergy Asthma Proc* 33:197–204, 2012.

In the study by Fiocchi *et al.*¹ the methods and the results require some further clarification.

First, the primary outcome was “the comparison of the overall duration of the respiratory infectious episodes between ribosome-component immune modulator (RCIM) and placebo at 6 months, separately for children with five or less recurrent respiratory infectious episodes in the preceding year (group A) and for those with more than five episodes (group B).”

Subgroup analysis (for group A and group B) was provided for by the study design.

Subgroup analysis in clinical trials can be only for exploratory or supportive use, unless specific analysis “for confirmatory use” would be planned before.

Formal rules for planning, analysis, and reporting were defined.²

In this study, subgroup analysis is not “for confirmatory use.” No particularly important subgroup-specific outcome was defined and no basal risk, α_2 -error, statistical power, or subgroup-specific sample size were calculated correctly and reported.

Children were randomly assigned to treatment or to placebo but no randomization was applied to the subgroup A or B allocation.

Second, there are no results of the comparison of the overall duration of the recurrent respiratory infections between RCIM group (A + B) and placebo, but no subgroup analysis is possible without a previous statistical analysis of the corresponding results in the entire sample.

Third, the multivariate logistic regression analysis was performed to evaluate the risk of developing rhinitis during 6 months.

During 6 and 12 months of treatment with RCIM, however, frequency (%) of occurrence of rhinitis wasn't significantly different between the two treatment groups (47/81 versus 56/77 and 47/81 versus 53/77, respectively; Fig. 3).

Why and how was a multivariate logistic regression analysis performed on a variable that wasn't

significantly different between the two treatment groups?

Fourth, the authors conclude that RCIM “significantly reduces...the frequency of recurrences of upper and lower respiratory tract infections in...,” but no data were reported in the Results section on the frequency of RRI in children “5 years of age and with a lower usual frequency of respiratory infections.” However, the frequency of recurrences of upper and lower respiratory tract infections in all children wasn't significantly different between the two treatment groups (Fig. 3).

Fifth, after all, the clinical relevance of the results consists in reducing of 1 day (media) the duration of RRI, mainly rhinitis, in children with less than five episodes of respiratory infections per year. How much the use of medical resources, costs of care and medication, lost school days, and parental absence from work would really decrease?

Sincerely,
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Giovanni Simeone, M.D.
Maria Carmen Verga, M.D.

REFERENCES

1. Fiocchi A, Omboni S, Mora R, et al. Efficacy and safety of ribosome-component immune modulator for preventing recurrent respiratory infections in socialized children. *Allergy Asthma Proc* 33:197–204, 2012.
2. Moyé LA. In *Multiple Analyses in Clinical Trials—Fundamentals for Investigators*. Chapter 11: Subgroups III: Confirmatory Analyses. New York, NY: Springer-Verlag, N.Y. Inc. 303–328, 2003. (ISBN 10918937.)

Response

Reply to the Editor:

In reply to correspondence to editor by M. Bergamini, *et al.* regarding “Efficacy and safety of ribosome-component immune modulator for preventing recurrent respiratory infections in socialized children.”¹

Dr. Bergamini and his colleagues have raised thought-provoking issues about our article, “Efficacy and safety of ribosome-component immune modulator for preventing recurrent respiratory infections in socialized children.” They also shed light on several aspects that we had difficulty with during writing the article.

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