EFFECTIVENESS AND SAFETY OF PEGVISOMANT: META-ANALYSIS OF OBSERVATIONAL LONGITUDINAL STUDIES

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OBJECTIVES

Acromegaly is an endocrine rare disease that often requires drug treatment. Pegvisomant is one of the most effective medical therapy to treat this disease (efficacy of up to 97% according to clinical trial[1]), and it has been on the market for more than 10 years. Therefore, we aimed to gather evidence regarding the effectiveness and safety of pegvisomant by reviewing real-world observational longitudinal studies.

METHODS

A systematic review was conducted with a meta-analysis of event rates (95% confidence interval – CI) using a random effects model. Sensitivity and subgroup analyses were performed. Heterogeneity was assessed using Chi-square and I^2 statistical tests, and was considered substantial at $p < 0.05$ and high at $I^2 > 75\%$(Comprehensive Meta-analysis 2.0). The systematic review was conducted in accordance to PRISMA, MOOSE, and Cochrane recommendations (PROSPERO CRD42017060756). PubMed, Scopus, Web of Science, and SciELO databases were used to search for literature. Methodological quality of the studies was assessed by New Castle-Ottawa Scale. Longitudinal observational studies in patients using pegvisomant for the treatment of acromegaly were included.

RESULTS

Initially, 552 papers were retrieved from the databases. Of these, 14 were included in the quantitative analysis (Fig 1). The overall rate of patients with disease control (i.e., normal values of IGF-1 for sex and age) was of 60.9% (51.8–69.3%; 95% CI; I^2 = 80%) – Fig 2a. When considering only patients under monotherapy, the control rate was 71.7% (64.0–78.4%; 95% CI; I^2 = 10%) – Fig 2b. Tumor growth was estimated in 7.3% (4.7–11.1%; 95% CI; I^2 = 58%) and elevation of transaminases in 3.0% (1.7–5.2%; 95% CI I^2 = 55%) – Fig 3. Removal of studies and changes to the statistical model and methods revealed no significant differences as compared with the original meta-analyses. Subgroup analyses were performed with studies reporting disease control data over 1 to 5 years, with event rates ranging from 57% to 65%. The studies showed consistent methodological quality, with no major deficiencies in the description of patient inclusion criteria or data collection. The follow-up period was considered proper in all studies (≥6 months). Few patient withdrawals were reported.

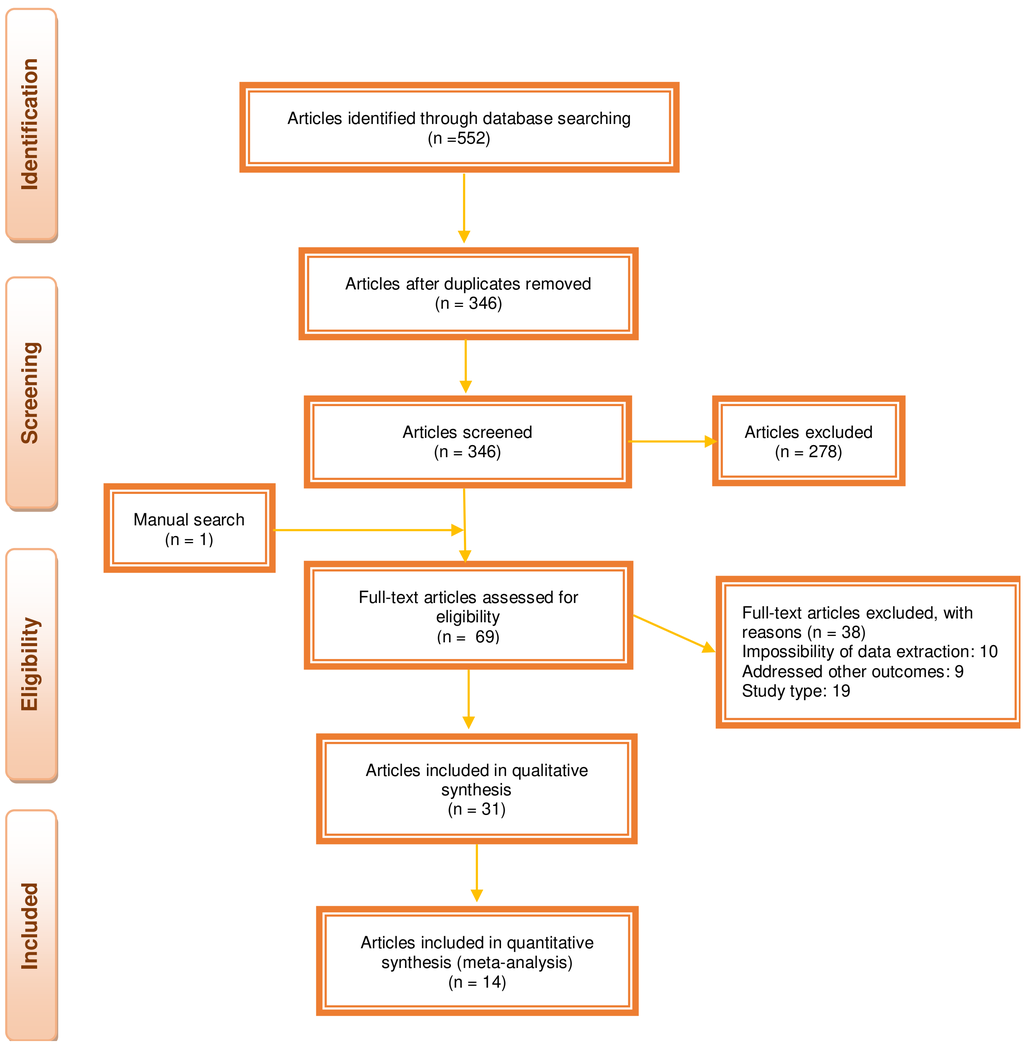

Fig. 1 PRISMA flowchart diagram of study selection

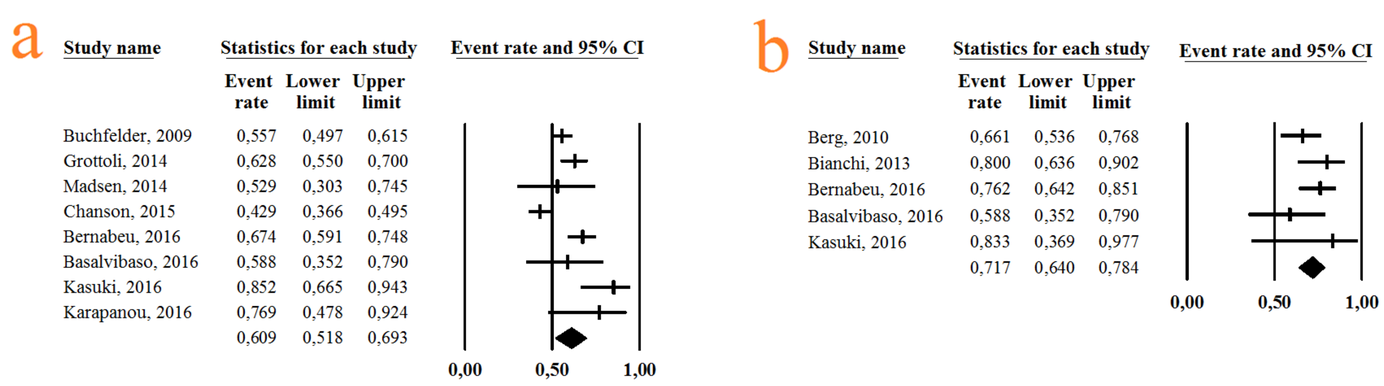

Fig. 2 Meta-analysis results for the rate of patients achieving IGF-1 control under pegvisomant therapy (a) and under pegvisomant monotherapy (b)

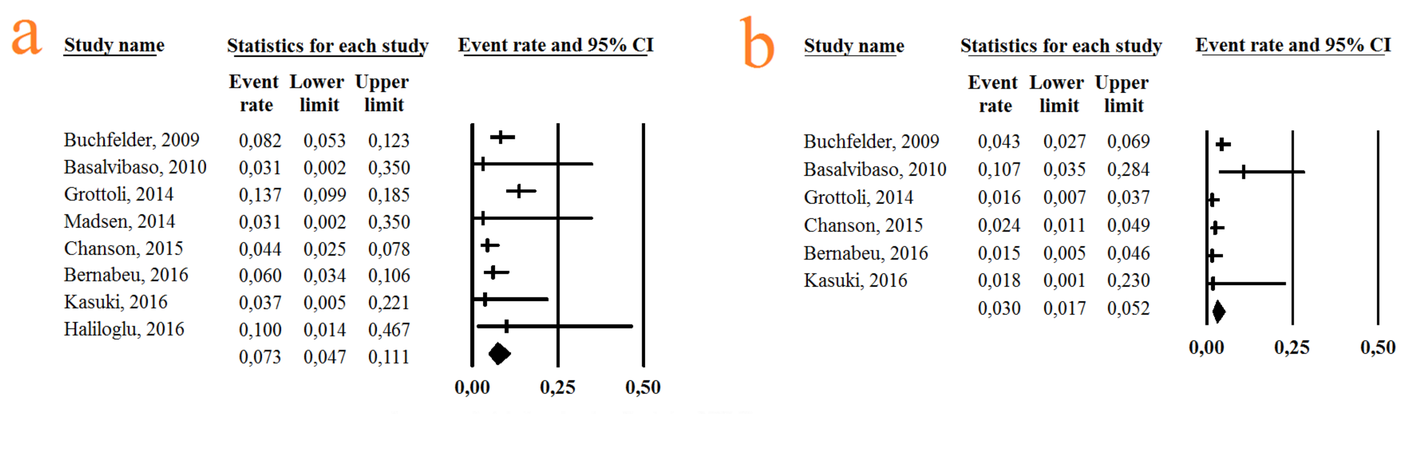

Fig. 3 Meta-analysis results for safety outcomes. Tumor growth verified by local magnetic resonance imaging (a) and elevation of transaminases (b)

CONCLUSIONS

The real-world data showed that the effectiveness of pegvisomant is not as high as reported in interventional studies. Best rates of disease control were observed when pegvisomant was used as a monotherapy. Subgroup analyses showed that the effectiveness of pegvisomant is stable over the years, which is important given the chronicity of the disease. No serious or frequent adverse events were observed. Pegvisomant seems to be an effective and safe drug; however, given its high cost, further economic studies are required.

REFERENCES

1. P.J., Trainer, PJ *et al*. Treatment of acromegaly with the growth hormone-receptor antagonist pegvisomant. N. Engl. J. Med 342(16), 1171–1177 (2000)

ACKNOWLEDGEMENTS

CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico
CAPES