**EFFICACY AND EFFECTIVENESS OF PEGVISOMANT MONOTHERAPY IN TREATMENT PATIENTS WITH ACROMEGALY – SYSTEMATIC REVIEW WITH META-ANALYSIS**

**INTRODUCTION**

Acromegaly is a rare disease associated with multiple comorbidities, an impaired quality of life and an increased rate of mortality. The diagnosis of acromegaly is usually delayed. The goal of treatment is to reverse the effect of the overproduction of growth hormone (GH) and to normalize IGF-1 concentration. The current therapeutic options for acromegaly are surgery, radiotherapy and/ or medical treatment (dopamine agonists (DA), somatostatin analogues (SSA)). Pegvisomant (PEG), growth hormone antagonist, is an effective option in patients who have had an inadequate response to previous treatments.

**OBJECTIVES**

The aim of this systematic review was assessment of efficacy and effectiveness of pegvisomant in the treatment of adult patients (age ≥ 18 years) with acromegaly. The type of treatment with PEG is serum IGF-1 levels normalization.

**METHODS**

The review was conducted according to the Cochrane Collaboration guidelines and polish recommendations of The Agency for Health Technology Assessment and Tariff System. The following databases were searched up to 06 February 2018: Medline (via Pubmed), Embase, Cochrane Library. The clinical trials registries were searched and the bibliographies of published studies were checked. Studies selected for inclusion were based on a pre-defined protocol with the following PICOS scheme:

- **Population**: Adult patients with acromegaly who have had an inadequate response to surgery and/or radiotherapy and in whom an appropriate medical treatment with somatostatin analogues did not normalize IGF-1 concentrations or was not tolerated.
- **Intervention**: Pegvisomant monotherapy.
- **Comparators**: Technologies with effectiveness of the placebo (i.e. placebo or continuation of treatment with somatostatin analogues, despite their prior ineffectiveness).
- **Outcome**: IGF-1 normalization.
- **Study**: RCT, non-RCT (experimental studies), real-world data (observational and postmarketing studies).

Data were independently extracted by two investigators. Calculations (statistical aggregation) were performed using the StatsDirect® 3 statistical package and Review Manager 5.3.

**RESULTS**

Out of 1753 publications screened, 104 publications were analyzed in full-text, of which 14 publications met the criteria for inclusion (Figure 1). Nine studies containing a total of 1900 patients were included to analysis (Table 1). At 3 months of therapy, IGF-1 level was reported normal in 64% patients (Trainer 2000). After 18 months (van de Leij 2001) 97% of patients achieved IGF-1 normalization (Figure 2). The results from real-world data confirm the high effectiveness of the PEG therapy. Calculated weighted average percentages of normalization of IGF-1 after 6 and 12 months and at least 5 years were, as follows: 55% (95% CI: 51%, 59%); 62% (95% CI: 59% 64%) and 73% (95% CI: 68% 78%) (Table 3, Figure 3).

**CONCLUSIONS**

All the identified scientific evidence confirmed effectiveness of PEG administered as monotherapy in nearly 1900 acromegalic patients, in the long-term follow-up (to 11 years of therapy). Presented analysis showed that pegvisomant monotherapy is effective treatment of acromegaly, with 73% of patients achieving a normal IGF-1 level, by 5 years of therapy. Pegvisomant is currently the only drug recommended by clinical guidelines for the treatment of acromegalic patients, who have had an inadequate response to surgery and/or radiotherapy and in whom first-line medical treatment did not normalize IGF-1 concentrations or was not tolerated.