INDIRECT TREATMENT COMPARISON OF ANTICALCITONIN GENE RELATED PEPTIDE PATHWAY ANTIBODIES IN CHRONIC MIGRAINE

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BACKGROUND AND IMPORTANCE

Erenumab, fremanezumab, galcanezumab and eptinezumab → monoclonal antibodies targeting calcitonin gene-related peptide pathway (anti-CGRP), used as preventive treatment in chronic migraine (CM).

AIM AND OBJECTIVES

To evaluate whether anti-CGRP drugs could be declared equivalent therapeutic alternatives (ETA) in CM, through an adjusted indirect treatment comparison (ITC).

MATERIAL AND METHODS

Bibliographic search of randomized clinical trials (RCTs) in Pubmed database (20/05/2019).

- Inclusion criteria: phase II/III RCTs of anti-CGPR with similar population, follow-up duration and comparator treatment. CM was defined as ≥15 headache days/month, of which ≥8 were migraine-days (event duration ≥4 hours).

- Exclusion criteria: RCTs with different clinical CM context and other CM definition.

Efficacy endpoint → reduction ≥50% migraine days/month (from beginning of treatment until 12 weeks).

ITC → developed using Bucher’s method.

Δ → maximum difference as clinical criterion of equivalence. Calculated according to ETA guide: use was made of half of absolute risk reduction (ARR) obtained in the meta-analysis of RCTs included in ITC (pooled ARR=20%; Δ=10%).

RESULTS

- 6 RCTs found: erenumab (n=3), fremanezumab (n=2), galcanezumab (n=1) and eptinezumab (n=0).
- Selected: 1 study of erenumab and 1 of fremanezumab. The rest were not included in ITC (non-compliance of inclusion criteria).

- Trials included were three-arm (control and two different drug regimens), double-blind and placebo-controlled RCTs.
- Results of ITC:

<table>
<thead>
<tr>
<th>Reduction ≥50% migraine days/month</th>
<th>Erenumab 70mg</th>
<th>Erenumab 140mg</th>
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<tbody>
<tr>
<td>ARR (95%CI)</td>
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<tr>
<td>Fremanezumab quarterly</td>
<td>3% (-7.56% to 13.56%)</td>
<td>2% (-8.64% to 12.64%)</td>
</tr>
<tr>
<td>Fremanezumab monthly</td>
<td>6% (-4.59% to 16.59%)</td>
<td>5% (-5.66% to 15.66%)</td>
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In all cases, there were no statistically significant differences. The most part of the 95%CI was within calculated Δ margins.

CONCLUSION AND RELEVANCE

ITC showed no statistically significant differences in reduction of ≥50% migraine days/month between erenumab and fremanezumab. Probable clinical equivalence was found between erenumab and fremanezumab. These drugs could be considered ETA in CM. Further studies are necessary to include galcanezumab and eptinezumab in ITC.