

IMPROVEMENT IN DEPRESSIVE AND ANXIETY SYMPTOMS DURING EPTINEZUMAB TREATMENT: A POST-HOC ANALYSIS FROM THE TACHIS STUDY

E. Maria Piella[1], A. Mario Chiarandon[1], V. Batti[1], D. Antonio Montisano[2], L. Francesco Iannone[3], C. Fasano[4], G. Sebastianelli[5], G. Coppola[5], D. Ferrandi[6], C. Lanni[7], M. Pia Prudenzano[8], M. De Tommaso[9], P. Merlo[10], A. Viganò[10], F. De Cesaris[11], A. Chiarugi[11], A. Munafò[11], F. Pistoia[12], R. Ornello[12], S. Sacco[12], A. Doretti[13], L. Grazzi[2], F. Lo Castro[14], R. Allamprese[14], R. De Icco[15|16], G. Vaghi[15|16], C. Tassorelli[15|16], G. Avino[17], M. Romozzi[18], C. Vollono[18], P. Calabresi[18], S. Battistini[19], A. Rufa[19], M. Albanese[20], M. Trimboli[21], G. Carlucci[4], M. Silvestro[22], A. Russo[22], M. Valente[23], L. Fofi[24], M. Marcosano[24], P. Geppetti[25], C. Altamura[24], F. Vernieri[24], E. Rubino[1], I. Rainero[1], S. Guerzoni[14]

[1]Department of Neuroscience "Rita Levi Montalcini", University of Turin, Italy; [2]Headache Center, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy; [3]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Italy; [4]NEUROFARBA Department, University of Florence - Neurologia, AOU Careggi, Italy; [5]Sapienza University of Rome, Department of Medico-Surgical Sciences and Biotechnologies, Polo Pontino, Latina, Italy; [6]AOU Alessandria, SC Neurologia, Italy; [7]Psicologia AOU Alessandria, Italy; [8]Clinica Neurologica "L. Amaducci", Azienda Ospedaliero-Universitaria Consorziale di Bari, Italy; [9]Neurophysiopathology Unit, Department of Translational Biomedicine and Neuroscience, University of Bari Aldo Moro, Italy; [10]UO di Neurologia, Humanitas Gavazzeni, Bergamo, Italy; [11]Headache center and Clinical pharmacology unit, AOU Careggi, Florence, Italy; [12]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, Italy; [13]Department of Neurology and Laboratory of Neuroscience, IRCCS Istituto Auxologico Italiano, Milano, Italy; [14]Digital and Predictive Medicine, Pharmacology, Clinical Metabolic Toxicology--Headache Center and Drug Abuse, Laboratory of Clinical Pharmacology and Pharmacogenomics, AOU Policlinico, Modena, Italy; [15]Department of Brain and Behavioral Sciences, University of Pavia, Italy; [16]Headache Science and Neurorehabilitation Unit, IRCCS Mondino Foundation, Pavia, Italy; [17]SOC Neurologia, Ospedale di Prato, Italy; [18]Fondazione Policlinico Universitario A. Gemelli IRCCS, Università Cattolica del Sacro Cuore, Roma, Italy; [19]Department of Medical, Surgical and Neurological Sciences, University of Siena, Italy; [20]Unit of Neurology, Department of Systems Medicine, University of Rome Tor Vergata, Italy; [21]Headache Center, Unit of Neurology, AOU Renato Dulbecco, Catanzaro, Italy; [22]Inter-departmental Program of Headache Medicine and Primary Pain Syndromes, Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy; [23]DMED, University of Udine and Clinical Neurology, Udine University Hospital, Italy; [24]Fondazione Policlinico Universitario Campus Bio-Medico, Roma e Università Campus Bio-Medico di Roma, Italy; [25]Department of Molecular Pathobiology and Pain Research Center, College of Dentistry, New York University, NY, USA

Background. Depression and anxiety disorders are common migraine comorbidities contributing substantially to disease burden. Whether mood improvement during anti-calcitonin gene related peptide pathway treatments is entirely attributable to reductions in headache frequency remains unclear. We evaluated longitudinal changes in self-reported depressive and anxiety symptoms during eptinezumab treatment and their relationship with clinical outcomes.

Methods. This post-hoc analysis of the TACHIS study, a prospective, multicenter, real-world study, included patients with episodic or chronic migraine who started eptinezumab across 23 Italian headache centers. Depressive and anxiety symptoms were assessed at baseline and after 12 and 24 weeks using the validated Hamilton Depression Rating Scale (HAM-D) and Hamilton Anxiety Rating Scale (HAM-A). Migraine outcomes included monthly headache days (MHDs), acute medication days (AMDs), the Migraine Disability Assessment (MIDAS), the Headache Impact Test-6 (HIT-6) and the Migraine-Specific Quality of Life Questionnaire (MSQ). Longitudinal changes were evaluated using mixed-effects models adjusted for demographic and clinical covariates.

Results. A total of 128 patients were included (82.0% female; mean age 46.9±12.4 years). 24 patients (18.8%) had pre-existing psychiatric comorbidities, including depression, anxiety, personality disorders, and bipolar disorder. Linear mixed-effects models demonstrated significant reduction in MHDs and AMDs, migraine-related disability (MIDAS and HIT-6 questionnaires), and migraine-specific quality of life (MSQ) during eptinezumab treatment (all $p<0.001$ compared to baseline).Mean HAM-D scores decreased from 14.6±6.4 at baseline to 11.7±7.3 at 12 weeks and 11.6±7.3 at 24 weeks ($p<0.001$), while HAM-A scores decreased from 17.5±10.2 to 11.8±9.8 and 11.2±8.9, respectively ($p<0.001$). Most of the improvement in depressive and anxiety symptoms occurred within the first 12 weeks of treatment and was maintained through week 24. After adjustment for clinical covariates, changes in MHDs were not independently associated with changes in HAM-D and HAM-A scores. Conversely, a weak but significant association was observed between reductions in HAM-D and MIDAS scores ($\rho=0.294$; $p=0.045$).

Conclusions. Eptinezumab treatment was associated with early and sustained reduction in depressive and anxiety symptoms. These improvements were not independently associated with reductions in MHDs, suggesting that mood changes may not be solely driven by headache frequency. Further studies are needed to clarify the mechanisms underlying this association.

On behalf of the Italian Headache Registry (RICe) Study Group.