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BRIEF COMMUNICATION

One year experience with erenumab: real-life data in 30 consecutive patients

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Monoclonal antibodies (mAb) against calcitonine gene–related peptide (CGRP) and its receptors (CGRP/CGRP-R mAb) represent a novel therapeutic option for migraine prophylaxis [1]. Erenumab, the only fully human CGRP-R mAb, is the first mAb approved as migraine specific treatment in both episodic migraine (EM) and chronic migraine (CM). Although independent real-life studies confirmed erenumab efficacy and safety in difficult to treat EM and CM patients [2, 3] with a 6-month follow-up; in Italy, this therapeutic option is not used yet in routine practice due to the lack of regulation in drug reimbursement by the national health system.

We present a prospective interventional study conducted on consecutive patients diagnosed with EM and CM aimed to assess the efficacy and safety of erenumab (70 and 140 mg) in a real-life scenario. Our study included 30 patients consecutively treated with erenumab from April 2019 to May 2020, diagnosed according to the International Classification of Headache Disorders third version (ICHD-3) with EM with more than 6 days with migraine (at least 4 of severe intensity) per month and CM; both groups had a documented unresponsiveness to at least 2 preventative treatments prescribed at our Headache Centre. All the patients were treated with erenumab 70 mg monthly for 3 months; after that, patients with poor response switched to erenumab 140 mg monthly. Patients were allowed to start, continue, or discontinue oral migraine preventative treatment on clinical basis. Data on monthly headache days (MHD), monthly severe migraine days (MSMD), and monthly acute medication days (MAMD) have been collected with structured diaries during a run-in period of 28 days before treatment (baseline) and during follow-up. Main outcomes included the changes from baseline in MHD, MSMD, and MAMD at 3rd month (30 patients), at 6th month (28 patients), and at 12th month (16 patient). Statistical analysis have been performed comparing median of MHD, MSMD, and MAMD with nonparametric tests (significant p value was set < 0.05 and calculated with SPSS Statistic ver 22). Secondary outcomes included descriptive data: the incidence of any side effect and of treatment discontinuation due to any reason; the percentage of responders (MHD reduction $\geq 50\%$) at 3rd, 6th, and 12th month with respect to all the patients at that time-point follow-up plus whatever patients that had interrupted treatment before; the percentage of patients needing switch from 70 to 140 mg overtime.

Out of the 30 patients treated with erenumab, 9 patients were diagnosed with EM (30%) and 21 with CM (70%), 27 (90%) female, and 3 (10%) male, with mean (standard deviation) age of 44 (11%). Demographic and clinical data are summarized in Table 1. All the 30 patients completed 3 month therapy; 28 completed 6 month therapy (2 patient discontinued at 4th and 5th month respectively); data of 16 patients have been collected up to 12 month therapy (2 further patients discontinued at 7th month and 1 patient at 8th month; a follow-up from 6th to 11th month was ongoing for 9 patients in May 2020). At baseline median MMD was 19.5 (IQR 15), median MSMD was 10 (IQR 9), and median MAMD was 10 (IQR 9). At each time-point follow-up (3rd, 6th, and 12th month) median of MHD, MSMD, and MAMD resulted significantly reduced compared to baseline (Table 1). Five patients (16,7%) interrupted erenumab treatment overtime: 1 patient after 4 month therapy for pregnancy planning (while responded to treatment with erenumab 70 mg); 1 patient after 5 month therapy for poor compliance to injection and to follow-up schedule; 1 patient at 7th month therapy for severe adverse event (i.e., orticarioid rush) while she was responding to treatment with erenumab 70

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Table 1 Demographic and clinical characteristics of the study sample

Age, mean (SD)			44 (11.5)		
Female, *n* (%)			27 (90)		
Chronic migraine, *n* (%)			21 (70)		
- with MO, *n* (% of CM)			6 (28.5)		
Episodic migraine, *n* (%)			9 (30)		
On preventative treatment at baseline, *n* (%)			9 (30%)		
Time (no of patients)		Baseline (30)	3rd month (30)	6th month (28)	12th month (16)
MHD:	median (IQR)	19,5 (15)	11 (12)*	8 (10) *	6 (7) *
	mean ± SD	19.6 ± 7.3	11.9 ± 8.8	10.6 ± 9.	7.9 ± 6.9
MSMD:	median (IQR)	10 (9)	4 (6) *	4 (8) *	2.5 (6.75) **
	mean ± SD	11.3 ± 6.2	4.9 ± 4.8	5.7 ± 5.5	3.6 ± 3.5
MAMD:	median (IQR)	10 (9)	3.5 (6) **	4 (8) ***	3 (7.75) *
	mean ± SD	10.1 ± 5.5	5.9 ± 6.6	6.4 ± 6.9	4.4 ± 4.0

SD, standard deviation; *IQR*, interquartile range; *MO*, medication overuse; *MHD*, monthly headache days; *MSMD*, monthly severe-migraine days; *MAMD*, monthly acute medication days; A single asterisk (*) is a statistically significance difference ($p < 0{,}0001$) comparing median values with baseline at Wilcoxon test; a double asterisk (**) is a statistically significance difference ($p < 0{,}001$) comparing median values with baseline at Wilcoxon test; a triple asterisk (***) is a statistically significance difference ($p < 0{,}01$) comparing median values with baseline at Wilcoxon test. Mean values have been reported to allow a comparison with literature data

mg; 1 patient at 7th month for complete unresponsiveness also to erenumab 140 mg for 3 months; 1 further patient for poor response (< 30%) at 9th month also with erenumab 140 mg continued for 5 months. Side effects consisted in orticariod rush in 2 patients (6,7%)—1 patients presented it only in the injection site and without need for discontinuation and in 1 patient presented a diffuse rush needing drug discontinuation (this patient had a past medical history of atopic dermatitis); 3 patients complained constipation (10%); 2 patients referred pain in injection site for 24–48 h (6,7%); 1 patient complained diffuse skin itch for 24 h after only one injection (3%). Thus, treatment discontinuation for adverse events presented only in one patient (3%) for a severe orticarioid rush. MHD reduction ≥ 50% was obtained in 15 out of 30 patients (50%) after 3 month of therapy and in 19 (63,3%) at 6th month. Patients with MHD reduction ≥ 50% at 12th month were 11 (52.4%) out of 21 (16 patients reaching 12th month follow-up plus 5 patients that had interrupted the treatment before). At 6th month, 15 out of 28 patients (53.6%) have required dose switch from 70 to 140 mg; at 12th month, 11 out of 16 patients (68.7%) received erenumab 140 mg. Our real-life single center study in consecutive patients diagnosed with both EM and CM, selected for previous inefficacy to preventative treatments confirmed the efficacy of erenumab and its safety (only 3% discontinued for adverse events). Most of our patient series had CM (70 %) with medication overuse (28.5% of CM patients). The efficacy results of our real-life experience with erenumab in migraine prophylaxis, as already demonstrated in previous real-life studies [2, 3], seems to be higher with respect to the results observed in clinical trials. Our study reported real-life data with a follow-up of 12 months, although in a small sample of 16 patients. Further studies are needed to identify potential predictors of response and to clarify the best treatment duration needed to maintain a positive effect also after erenumab withdrawal.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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