Efficacy of fremanezumab in patients with migraine and documented inadequate response to 2, 3, or 4 classes of migraine preventive treatments: results of the international, multicenter, randomised, placebo-controlled FOCUS study

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Methods: For 12 weeks of double-blind treatment, patients were randomised (1:1:1) to monthly fremanezumab (Month 1: CM, 675 mg; EM, 225 mg; Months 2 and 3: 225 mg), quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), or matched placebo. Changes from baseline in monthly average migraine days for 12 weeks were evaluated by sex and age. Results: Of 838 randomized patients, 50%, 32%, and 18% had inadequate response to 2, 3, and 4 preventive medication classes, respectively. Changes from baseline in monthly average migraine days over 12 weeks were significantly greater with monthly and quarterly fremanezumab, respectively, vs placebo among patients with inadequate response to 2 (LSMD vs placebo: −3.7, −2.9, 3 (−2.9, −3.3), or 4 (−5.4, −5.3) medication classes (all P < 0.0001). Proportions of patients who achieved ≥50% reductions in migraine days at 12 weeks were significantly greater with monthly and quarterly fremanezumab, respectively, vs placebo among patients with inadequate response to 2 (41% and 39% vs 11%), 3 (28% and 32% vs 7%), or 4 (32% and 27% vs 4%) classes (all P < 0.002).

Discussion: For migraine patients with documented inadequate response to 2, 3, or 4 classes of migraine preventive medications, reductions in monthly average migraine days were significantly greater with both fremanezumab vs placebo.

Impact of age and sex on efficacy of fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive treatments: results of the international, multicentre, randomised, placebo-controlled FOCUS study

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Methods: Patients were randomised (1:1:1) to monthly fremanezumab (Month 1: EM, 225 mg; CM, 675 mg; Months 2 and 3: 225 mg), quarterly fremanezumab (Month 1: 675 mg; Months 2 and 3: placebo), or matched monthly placebo for 12 weeks of double-blind treatment. Changes from baseline in monthly average number of migraine days over 12 weeks were evaluated by sex and age. Results: 838 patients were randomised. Reducions in monthly average migraine days were significantly greater with both fremanezumab dosing regimens vs placebo in subgroups of males, females, and ages 18–45 and > 45 years (all P < 0.0001; Table). Discussion: Fremanezumab was efficacious, based on statistically significant reductions in monthly average migraine days vs placebo, in males, females, and those aged ≤45 and > 45 years with inadequate response to 2–4 classes of migraine preventive treatments.
Early onset of response to fremanezumab in patients with migraine and a documented inadequate response to 2–4 classes of migraine preventive treatments: results of the international, multicentre, randomised, placebo-controlled FOCUS study

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The Journal of Headache and Pain 2020, 21(Suppl 1):A.59

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Background: Fremanezumab, a fully-humanised monoclonal antibody (lgG2Δα) that selectively targets calcitonin gene-related peptide (CGRP), has proven efficacy for migraine preventive treatment in adults. The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in adults with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive treatments. Patients were randomised (1:1:1) to monthly fremanezumab (Month 1: 225 mg; Months 2 and 3: 675 mg), or placebo, or matched monthly placebo for 12 weeks of double-blind treatment. Proportion of responders (≥50% and ≥75% reduction in migraine days) were significantly greater with fremanezumab vs placebo in migraine patients with documented inadequate response to 2–4 classes of migraine preventive treatments.

A.60 Efficacy and safety of fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive treatments: results of the international, multicentre, randomised, placebo-controlled FOCUS study

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Results: 838 patients were randomised. Reductions from baseline in monthly average migraine days over 12 weeks were greater with fremanezumab (LSM(SE) change: monthly, −4.1[0.34]; quarterly, −3.7[0.34]) vs placebo (−0.6[0.34]; both P < 0.0001). With monthly and quarterly fremanezumab, respectively, vs placebo, higher proportions of patients achieved >50% (>34% and 34% vs 9%) and >75% (12% and 8% vs 2%) reductions in migraine days over 12 weeks (all P < 0.0002). Reductions in monthly average days of acute headache medication use were greater with fremanezumab (LSM(SE) change: monthly, −3.9[0.32]; quarterly, −3.7[0.32]) vs placebo (−0.6[0.32]) over 12 weeks, as were reductions in monthly average days of migraine-specific acute headache medication use (all P < 0.0001).

Discussion: Reductions in monthly average migraine days and days of acute headache medication use and clinically meaningful response rates were significantly greater with fremanezumab vs placebo in migraine patients with documented inadequate response to 2–4 classes of migraine preventive treatments.

Table 1 (abstract A.57). Change from baseline in monthly average migraine days during 12-weeks of double-blind treatment by sex and age group*

|                  | Placebo | Monthly fremanezumab | Quarterly fremanezumab |
|------------------|---------|----------------------|------------------------|
| Males            | (n = 46) | (n = 45)             | (n = 47)               |
| LSM (SE) change  | −0.4 (0.74) | −4.6 (0.78) | −4.2 (0.73) |
| LSMD (SE) vs     | −4.2 (0.91)b | −3.8 (0.87)b | placebo       |
| Females          | (n = 232) | (n = 238)             | (n = 229)               |
| LSM (SE) change  | −0.6 (0.33) | −3.9 (0.34) | −3.6 (0.35) |
| LSMD (SE) vs     | −3.3 (0.39)b | −3.0 (0.39)b | placebo       |
| Age 18–45 years  | (n = 120) | (n = 128)             | (n = 125)               |
| LSM (SE) change  | −0.8 (0.47) | −4.6 (0.49) | −4.1 (0.48) |
| LSMD (SE) vs     | −3.8 (0.51)b | −3.2 (0.51)b | placebo       |
| Age > 45 years   | (n = 158) | (n = 155)             | (n = 151)               |
| LSM (SE) change  | −0.4 (0.48) | −3.8 (0.47) | −3.6 (0.49) |
| LSMD (SE) vs     | −3.4 (0.50)b | −3.2 (0.51)b | placebo       |

LSM least-squares mean; LSMD LSM difference
*aModified ITT population (n = 837)
bP < 0.0001 vs placebo

Discussion: Monthly and quarterly fremanezumab demonstrated early onset of efficacy, with significantly greater clinically meaningful response rates after 4 weeks of treatment and significantly greater reductions from baseline in weekly migraine days as early as Week 1 vs placebo, in patients with EM or CM and documented inadequate response to 2–4 classes of migraine preventive treatments.

A.59 Efficacy, clinically meaningful responses, and impact on acute headache medication use with fremanezumab in patients with migraine and documented inadequate response to 2–4 classes of migraine preventive treatments: results of the international, multicentre, randomised, placebo-controlled FOCUS study

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Results: 838 patients were randomised. Reductions from baseline in monthly average migraine days over 12 weeks were greater with fremanezumab (LSM(SE) change: monthly, −4.1[0.34]; quarterly, −3.7[0.34]) vs placebo (−0.6[0.34]; both P < 0.0001). With monthly and quarterly fremanezumab, respectively, vs placebo, higher proportions of patients achieved >50% (>34% and 34% vs 9%) and >75% (12% and 8% vs 2%) reductions in migraine days over 12 weeks (all P < 0.0002). Reductions in monthly average days of acute headache medication use were greater with fremanezumab (LSM(SE) change: monthly, −3.9[0.32]; quarterly, −3.7[0.32]) vs placebo (−0.6[0.32]) over 12 weeks, as were reductions in monthly average days of migraine-specific acute headache medication use (all P < 0.0001).

Discussion: Reductions in monthly average migraine days and days of acute headache medication use and clinically meaningful response rates were significantly greater with fremanezumab vs placebo in migraine patients with documented inadequate response to 2–4 classes of migraine preventive treatments.
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Background: Fremanezumab, a fully-humanised monoclonal antibody (IgG2Δα) that selectively targets calcitonin gene-related peptide (CGRP), is effective for the preventive treatment of migraine. The FOCUS study of fremanezumab was the first and largest study of a migraine preventive treatment in patients with both episodic and chronic migraine (EM and CM) and documented inadequate response to 2–4 classes of migraine preventive treatments.

Methods: For 12 weeks of double-blind treatment, patients were randomised (1:1:1) to monthly fremanezumab (Month 1: EM, 225 mg; CM, 675 mg; Months 2 and 3: 225 mg), quarterly fremanezumab (Month 1, 675 mg; Months 2 and 3, placebo), or matched monthly placebo. The primary efficacy endpoint was mean change from baseline in monthly average migraine days over 12 weeks and was compared using analysis of covariance.

Results: 838 patients were randomised. Reductions from baseline in monthly average migraine days over 12 weeks were significantly greater with monthly fremanezumab (least-squares mean[SE] change, −4.1[0.34]) and quarterly fremanezumab (−3.7[0.34]) versus placebo (−0.6[0.34]; both \( P < 0.0001 \)) in the overall population. In subgroups of patients with EM and CM, reductions from baseline in monthly average migraine days were also significantly greater with both fremanezumab regimens versus placebo (all \( P < 0.0001 \)). The incidence of AEs was similar in the placebo and combined fremanezumab groups, respectively, including overall AEs (48% and 50%), AEs leading to discontinuation (1% and < 1%), and SAEs (1% and 1%). None of the SAEs were considered treatment-related, and no safety signals were identified.

Discussion: Fremanezumab demonstrated significant improvements in efficacy, based on reductions in monthly average migraine days versus placebo, and was safe and well tolerated over 3 months in patients with EM or CM and documented inadequate response to multiple classes of migraine preventive treatments.

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