The Impact of Using Real-World Data on the Cost-Effectiveness of Fremanezumab for Migraine Prevention in a UK Healthcare Perspective Analysis

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Conclusions

- Improved incremental cost-effectiveness ratios (ICERs) were observed using models populated with real-world versus randomised clinical trial (RCT) data when comparing fremanezumab versus best supportive care (BSC) in a population with inadequate response to two or more classes of preventive migraine treatments
- Real-world data led to more patients remaining on treatment, but the additional costs of treatment were compensated by the QALY gains driven by reductions in monthly migraine days (MMD) and headache burden on patients
- Scenario analyses demonstrated the potential cost-effectiveness advantages to assessing response after 6 months of treatment rather than after 12 weeks, as per RCT data, as well as improved cost-effectiveness under a placebo dissipation scenario

Introduction

- Fremanezumab, a humanized monoclonal antibody that selectively targets the calcitonin gene-related peptide, is approved for migraine prevention in adults with ≥4 MMDs[1]
- Real-world evidence (RWE) for fremanezumab is growing
  - PEARL (EUPAS35111) is a 24-month, pan-European, prospective, observational study of adults with episodic migraine (EM) or chronic migraine (CM) who initiate fremanezumab treatment in real-world clinical practice[2,3]
- Economic modelling for fremanezumab has been conducted using RCT data from the FOCUS trial (NCT03308968)[4,5]

Objectives

- To investigate the use of RWE data in economic modeling for fremanezumab from a UK healthcare perspective

Methods

Model and Model Inputs

- A cost-economic model for fremanezumab,[5] used in several health technology assessment submissions, was updated
- The model compared fremanezumab treatment with BSC consisting of acute migraine treatment only
- Patients entered a decision tree with treatment response* assessed after 12 weeks
- Responders continuing treatment moved into a semi-Markov model which distributed patients across MMD states (0–28 MMDs)
- The main model health states were 'on-treatment' and 'off-treatment' with a death sink state
- Resource-use costs and utilities were applied based on overall health state and distribution across MMD states
- The patient population was those with failure on two or more other migraine preventive treatments
- MMD responder rates* at 3 and 6 months were estimated from FOCUS[4] or PEARL (2nd interim analysis),[3] as indicated
  - As 6-month estimates were not available from FOCUS (12-week double-blind treatment period), responder rates were assumed to be the same at 3 and 6 months for RCT data
  - FOCUS responder rates were 48.45% for EM and 48.96% for CM
  - PEARL responder rates were:
    - EM: 68.90% at 3 months and 69.44% at 6 months[3]
    - CM: 67.80% at 3 months and 71.37% at 6 months
- Other clinical patient characteristics and efficacy inputs were derived from FOCUS trial data[4†]
- Other main model assumptions: 3.5% discount for costs and quality-adjusted life years (QALYs) (UK standard assumption); 20% of on-treatment patients positively stop annually; UK NHS costs with medication list prices; patients revert to BSC MMDs after treatment stops; non-responders revert to baseline MMDs
- Results were reported from a healthcare system perspective as ICERs of costs per QALY gained over 10-year time horizon
- Sensitivity analyses were conducted on the base case, including one-way and probabilistic analyses

Methods (cont.)

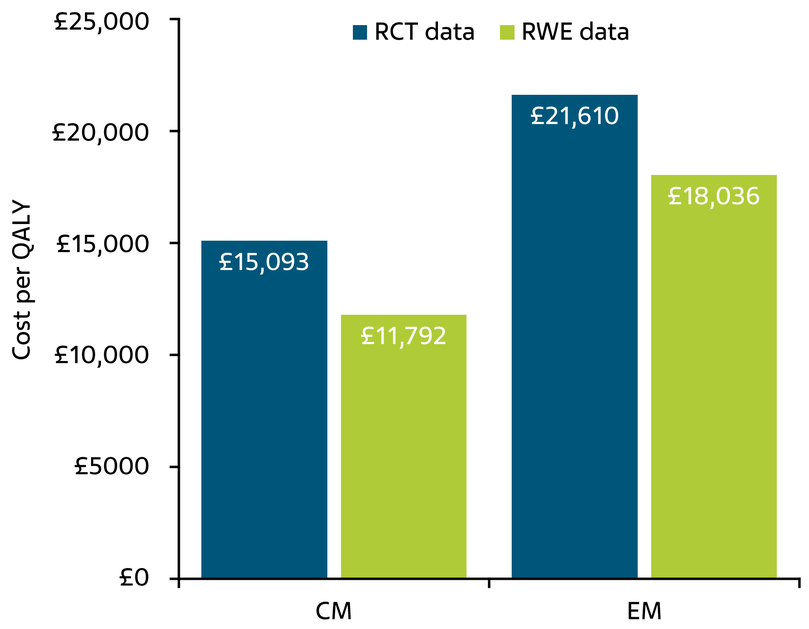
Model Scenarios

- Scenario analyses were conducted to investigate specific model assumptions
  - 6-month response assessment: model assumes a response assessment at 12 weeks; however, the PEARL primary endpoint is assessed at 6 months, so response assessment at 6 months was investigated
  - RWE discontinuation rate: US chart review showed a discontinuation rate of 1.2% per cycle (equivalent to base case)[6]; a scenario using a rate of 1.0% per cycle was run based on UK chart review data[7]
  - Placebo dissipation: an alternative set of long-term assumptions were utilized, which included a reversion to baseline MMDs after treatment cessation and the dissipation of the placebo effect over 1 year

Results

- ICERs were improved in real-world versus RCT settings, with an ~£3500 reduction (**Figure 1**; **Table 1**)

Figure 1. Base case cost-effectiveness results fremanezumab versus best supportive care.



CM, chronic migraine; EM, episodic migraine; QALY, quality-adjusted life year; RCT, randomized clinical trial; RWE, real-world evidence.

Table 1. Base Case Cost-Effectiveness Results

	Total costs	Total QALYs	Incr costs	Incr QALYs
CM				
RCT response data				
BSC	£9407	4.251	-	-
Frem	£16,856	4.744	£7450	0.494
RWE response data				
BSC	£9407	4.251	-	-
Frem	£18,830	5.050	£9423	0.799
EM				
RCT response data				
BSC	£7265	5.276	-	-
Frem	£14,862	5.627	£7597	0.352
RWE response data				
BSC	£7265	5.276	-	-
Frem	£17,222	5.828	£9957	0.552

BSC, best supportive care; CM, chronic migraine; EM, episodic migraine; Frem, fremanezumab; Incr, incremental; QALY, quality-adjusted life year; RCT, randomized clinical trial; RWE, real-world evidence.

Results (cont.)

- Improvements in cost-effectiveness were driven by reductions in headache burden, resulting in greater QALY gains when using RWE data (**Table 2**)
  - In CM, there was a 66.8% greater reduction in incremental MMDs using RWE (–664.2) versus RCT data (–398.2), resulting in a similar gain of 61.9% in incremental QALYs (0.799 [RWE] versus 0.494 [RCT])
  - Similar outcomes were observed in EM (63.4% improvement in incremental MMD reduction; 57.0% improvement in incremental QALYs)

Table 2. MMD and QALY Gains With Fremanezumab in Model

	RCT	RWE	% change
Chronic migraine			
Incremental MMD reduction[a]	–398.2	–664.2	66.8%
Incremental QALY gain[a]	0.494	0.799	61.9%
Episodic migraine			
Incremental MMD reduction[a]	–282.1	–460.9	63.4%
Incremental QALY gain[a]	0.352	0.552	57.0%

MMD, monthly migraine day; QALY, quality-adjusted life year; RCT, randomized clinical trial; RWE, real-world evidence.
[a]Incremental comparison of fremanezumab versus BSC.

- Results were robust to one-way sensitivity analysis adjusting variables by ±20%
- Probabilistic sensitivity analysis over 1000 replications at a threshold of £30,000 per QALY, showed that with RWE data there was a probability of 92.0% (CM) and 75.9% (EM) for fremanezumab to be cost-effective
- Scenario analyses showed that the model was stable to alternative assumption sets (**Table 3**)

Table 3. Results of Scenario Analyses

Scenario	Incr costs (£)	Incr QALYs	ICER versus BSC (£/QALY)
CM			
RCT response data			
Base case	£7450	0.494	**£15,093**
6-month response assessment	£8044	0.497	**£16,156**
Discontinuation rate of 1.0%	£7875	0.503	**£15,662**
Placebo dissipation scenario	£7476	0.615	**£12,163**
RWE response data			
Base case	£9423	0.799	**£11,792**
6-month response assessment	£10,131	0.860	**£11,787**
Discontinuation rate of 1.0%	£10,010	0.811	**£12,329**
Placebo dissipation scenario	£9614	0.908	**£10,587**
EM			
RCT response data			
Base case	£7597	0.352	**£21,610**
6-month response assessment	£8195	0.357	**£22,926**
Discontinuation rate of 1.0%	£8019	0.360	**£22,270**
Placebo dissipation scenario	£7806	0.362	**£21,546**
RWE response data			
Base case	£9957	0.552	**£18,036**
6-month response assessment	£10,374	0.561	**£18,496**
Discontinuation rate of 1.0%	£10,556	0.564	**£18,709**
Placebo dissipation scenario	£10,365	0.522	**£19,846**

BSC, best supportive care; CM, chronic migraine; EM, episodic migraine; ICER, incremental cost-effectiveness ratio; Incr, incremental; QALY, quality-adjusted life year; RCT, randomized clinical trial; RWE, real-world evidence

*Treatment response was defined as ≥30% (for CM) or ≥50% (for EM) reduction in MMDs; †Inputs included: patient baseline characteristics; MMD reductions; treatment discontinuation rate (1.2% per cycle); utilities (Migraine-Specific Quality-of-Life Questionnaire data was mapped to the EQ-5D-3L scale).

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