ONLINE SUPPLEMENT 2: DESCRIPTION OF ANALYSES
BAYESIAN EVALUATION OF INFORMATIVE HYPOTHESES

Effect of IVIg on pain.

The effect of pain after the infusions can be analysed using the regression model:

$$y_{1ti} = \alpha_{1t} + \beta_{1t}x_{1ti} + \epsilon_{1ti} \ , \quad (1)$$

where y_{1ti}, $t = 1, \dots, 7$ denotes the pain on a 14 point scale after 7 infusions, x_{1ti} denotes the number of days after the treatment, α_{1t} is the intercept, β_{1t} is the coefficient of the day number, and ϵ_{1ti} is the residual, which is normally distributed with mean 0 and unknown variance. We first tested the expectation that the decrease in pain in the first 7 days after IVIg infusions is greater than after placebo. This expectation can be translated into the following hypothesis H_1 among the coefficients of the day numbers:

$$H_1: \{\beta_{11}, \beta_{12}, \beta_{13}\} > \{\beta_{14}, \beta_{15}, \beta_{16}, \beta_{17}\} \ , \quad (2)$$

which was compared to the unconstrained hypothesis H_a:

$$H_a: \beta_{11}, \beta_{12}, \beta_{13}, \beta_{14}, \beta_{15}, \beta_{16}, \beta_{17}, \quad (3)$$

where β_{1t}, $t = 1, \dots, 3$ denote the coefficients after three placebo infusions, whereas β_{1t}, $t = 4, \dots, 7$ are those after four IVIg infusions. Note that the day numbers x_{1ti} for each infusion are 1, 4, 6, and 8, except the infusion $t = 6$ for which the day numbers are 0, 2, 5, and 7. Using SPSS, the estimate and squared standard error of each coefficient were obtained, which are displayed in Table 1 (see end of document). Hypothesis H_1 was then evaluated using BIG, which rendered a Bayes factor of 33.22 for H_1 against H_a, which implies that H_1 gains strong support from the data.

We then assessed whether IVIg produced a clinically relevant reduction in pain, which can be expressed by:

$$H_2: \beta_{14} < l_{14}, \ \beta_{15} < l_{15}, \ \beta_{16} < l_{16}, \ \beta_{17} < l_{17} \ , \quad (4)$$

where $l_{1t} = -30\% * y_{1t1}/7$, $t = 4, \dots, 7$ is the clinically relevant level for each treatment, and y_{1t1} is the pain on the day after each IVIg infusion is given. Using the results in Table 1 for β_{1t} and l_{1t}, $t = 4, \dots, 7$, we obtained a Bayes factor of 13.40 for H_2 against H_a, which implies strong evidence that IVIg produces a clinically meaningful reduction in pain in this patient.

We then proceeded to test the combined first and second expectations, i.e., in the first week after infusion, pain decreases more rapidly after IVIg than after placebo, and the pain after IVIg decreases beyond the clinically relevant level. This leads to the following hypothesis:

$$H_3: \{\beta_{11}, \beta_{12}, \beta_{13}\} > \{\beta_{14}, \beta_{15}, \beta_{16}, \beta_{17}\} ;$$

$$\beta_{14} < l_{14},\ \beta_{15} < l_{15},\ \beta_{16} < l_{16},\ \beta_{17} < l_{17}. \tag{5}$$

This hypothesis can be expressed as $H_3 : H_1 \& H_2$ because it contains the constraints both in H_1 and H_2. Evaluating this hypothesis rendered a Bayes factor of 63.74, which implies that there is strong evidence that IVIg decreases pain more than placebo, and that it decreases pain to a clinically meaningful extent in this patient.

Subjective muscle strength

A similar model was specified for the effect on subjective muscle strength:

$$y_{2ti} = \alpha_{2t} + \beta_{2t} x_{2ti} + \epsilon_{2ti} \tag{6}$$

where y_{2ti}, x_{2ti}, α_{2t}, β_{2t} and ϵ_{2ti} are the same notations but for muscle strength. Analogous to the effect on pain, we assessed whether the subjective increase in muscle strength in the first 7 days after IVIg infusion is greater than after placebo. This results in the following hypothesis:

$$H_4: \{\beta_{21}, \beta_{22}, \beta_{23}\} < \{\beta_{24}, \beta_{25}, \beta_{26}, \beta_{27}\} , \tag{7}$$

where β_{2t}, $t = 1, \ldots, 7$ again denote the coefficients after the treatments (see Table 1). Evaluating H_4 in BIG rendered a Bayes factor of 36.24, which implies strong evidence that IVIg increases muscle strength more than placebo in this patient.

Secondly, we assessed whether the increase in muscle strength was subjectively meaningful by evaluating the hypothesis:

$$H_5: \beta_{24} > l_{24},\ \beta_{25} > l_{25},\ \beta_{26} > l_{26},\ \beta_{27} > l_{27} , \tag{8}$$

where $l_{2t} = 30\% * y_{2t1}/7$, $t = 4, \ldots, 7$ is the subjectively relevant level for an increase in muscle strength, and y_{2t1} represents the muscle strength at the time of IVIg infusion. Using the results in Table 1 for β_{2t} and l_{2t}, $t = 4, \ldots, 7$, we obtained a Bayes factor of 15.05, which implies strong evidence that IVIg increases muscle strength to a meaningful extent in this patient.

Similar to pain, we then combined these hypotheses and tested whether in the first week after infusion muscle strength increased more rapidly after IVIg than after placebo and whether it increased beyond the clinically meaning level. This hypothesis can be expressed by:

$$H_6\colon \{\beta_{21}, \beta_{22}, \beta_{23}\} < \{\beta_{24}, \beta_{25}, \beta_{26}, \beta_{27}\}\ ;$$

$$\beta_{24} > l_{24},\ \beta_{25} > l_{25},\ \beta_{26} > l_{26},\ \beta_{27} > l_{27}. \tag{9}$$

where H_6 : H_4&H_5. Evaluating this hypothesis resulted in a Bayes factor of 61.51, meaning that there is strong evidence that IVIg increases subjective muscle strength more than placebo, and that it increases it to a clinically meaningful extent.

Course of pain and muscle strength following IVIg infusions

Finally, to assess the need for regular IVIg infusions, we tested the hypothesis that pain first decreases and then increases again in the three weeks following IVIg infusion. To investigate this expectation, a quadratic regression model was used:

$$y_{1ti} = \alpha_{1t} + \beta_{1t}x_{1ti} + \gamma_{1t}x_{1ti}^2 + \epsilon_{1ti}, \tag{10}$$

where γ_{1t}, $t = 1, \ldots, 4$ is the coefficient of the squared day number. If $\gamma_{1t} > 0$, this means the pain y_{1ti} decreased during the first several days after infusion and then increased again. For this reason we constructed the hypothesis:

$$H_7\colon \gamma_{11} > 0, \gamma_{12} > 0, \gamma_{13} > 0, \gamma_{14} > 0. \tag{11}$$

Running BIG with the estimates and variances of γ_{1t} shown in Table 1 rendered a Bayes factor of 13.78, which implies strong evidence that pain first decreases following IVIg, and then increases again as the effects of IVIg start to wear off. A similar quadratic model was used for subjective muscle strength:

$$y_{2ti} = \alpha_{2t} + \beta_{2t}x_{2ti} + \gamma_{2t}x_{2ti}^2 + \epsilon_{2ti}. \tag{12}$$

A negative γ_{2t} indicates that in the beginning days muscle strength y_{2ti} increases and thereafter it decreases again. Thus, hypothesis H_8 is as follows:

$$H_8\colon \gamma_{21} < 0, \gamma_{22} < 0, \gamma_{23} < 0, \gamma_{24} < 0. \tag{13}$$

The Bayes factor for this hypothesis was 15.67, indicating that there is strong support that subjective muscle strength increases in the first days after IVIg infusion, and then decreases again over the following weeks.

Table 1. Estimates and variances of the coefficients (l1t and l2t denote the relevant levels for the decrease of pain and increase of muscle strength, respectively, in the first week after IVIg).

	Pain					Muscle strength				
		n*	estimates	variance	l_{1t}		n*	estimates	variance	l_{2t}
placebo	β_{11}	4	0.416	0.187		β_{21}	4	-0.734	0.142	
	β_{12}	4	0.253	2.79E-2		β_{22}	4	-0.319	3.17E-2	
	β_{13}	4	0.824	2.76E-2		β_{23}	4	-0.234	5.04E-3	
IVIg (1 week)	β_{14}	4	-0.907	0.106	-0.27	β_{24}	4	0.823	3.39E-2	0
	β_{15}	4	-0.412	3.61E-2	-0.126	β_{25}	4	0.508	8.41E-4	0.216
	β_{16}	4	-0.753	1.04E-2	-0.294	β_{26}	4	0.321	4.10E-3	0.210
	β_{17}	4	-0.984	4.62E-3	-0.354	β_{27}	4	0.340	5.93E-3	0.246
IVIg (3 weeks)	γ_{11}	8	0.063	1.96E-4		γ_{21}	8	-0.041	4.9E-5	
	γ_{12}	9	0.016	1.69E-4		γ_{22}	9	-0.029	9.0E-6	
	γ_{13}	10	0.044	3.60E-5		γ_{23}	10	-0.022	9.0E-6	
	γ_{14}	9	0.056	2.89E-4		γ_{24}	9	-0.024	9.0E-6	

*This denotes the number of measurements upon which the estimates are based.