Supplement 3: Receiver Operating Characteristic (ROC) Curve

To explore factors affecting the normalization of serum VB12 concentration (yes/no) at 52 weeks, serum VB12 levels were studied at 8 weeks (at the end of the "charging period"). An ROC curve was built to determine the likelihood ratios for each cutpoint after the charging period to "predict" the normalization of levels (serum VB12 levels ≥211 pg/mL) at the end of the study.[1]

Table 1 shows the results of the likelihood ratios for the cutpoints at the main percentiles of the distribution of VB12 serum levels at week 8 ("charging period") to predict normalized VB12 serum levels at the end of the study. In Figure 1, the ROC curve is plotted. The level at the 5th percentile of the distribution was selected as the most useful value as it showed best classification ability and because when patients did not reach this level at week 8, they were almost twelve times more likely to not reach suitable VB12 levels at the end of the study than if they did reach levels over 281 pg at week 8 (12~1/negative likelihood ratio).

References

1. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology.* 1982;143(1):29-36.

Table 1. Exploring the value of several cutpoints of OB12 serum levels at week 8 to "predict" normalization of values of Vit B12 at the end of the study

Cutpoint	Sensitivity	Specificity	Correctly Classified	LR+	LR-	Percentil
≥ 281	0.977	0.273	94.30%	1.3435	0.0841	5
≥ 328	0.963	0.546	94.30%	2.1193	0.0673	10
≥ 353	0.931	0.636	91.70%	2.5608	0.1081	15
≥ 389	0.895	0.818	89.10%	4.9197	0.129	20
≥ 421	0.839	0.818	83.80%	4.617	0.1962	25

LR+: Positive Likelihood ratio. LR-: Negative Likelihood ratio

Figure 1. ROC curve