

M16-560 Primary Analyses of the Primary Endpoint

Two primary comparisons were performed between ABBV-3373 and adalimumab. The first was the comparison of ABBV-3373 to historical adalimumab reference value -2.13 based on a meta-analysis consisting of 242 subjects from 3 historical adalimumab studies in which the success criterion was 2-sided P value ≤ 0.1 .

Primary Comparison 1: Compare ABBV-3373 to a Historical Reference Value of Adalimumab

Change from Baseline in DAS28(CRP) at Week 12 (MMRM) (OC) (Full Analysis Set)											
----- Change from Baseline -----											
Parameter Treatment	N	Baseline Mean	Visit Mean	----- Within Group# -----			-- Compare to Historical Adalimumab Data@ --				
				LS Mean	[90% CI]	SE	LS Mean	[90% CI]	SE	P-value	
DISEASE ACTIVITY SCORE BASED ON CRP											
Adalimumab 80 mg SC EOW	16	5.60	2.88	-2.51	[-3.00, -2.02]	0.293					
ABBV-3373 100 mg IV EOW	29	5.49	2.78	-2.65	[-3.01, -2.29]	0.215	-0.52	[-0.89, -0.15]	0.215	0.022+	

Note: Baseline is defined as the last non-missing value prior to the first dose of study drug. Subjects with non-missing baseline and at least one post-baseline value is included in the analyses.

Within group least squares mean and 90% confidence interval are based on mixed effect model repeated measurement (MMRM) Analysis with unstructured variance-covariance matrix, including treatment, visit, stratification factors, and treatment-by-visit interaction as fixed factors and baseline value as covariate.

@ Single-arm comparison of LS mean of ABBV-3373 estimated from the MMRM model above with Historical mean of Adalimumab (-2.13).

The second comparison was ABBV-3373 to adalimumab with combined in-trial and borrowed historical adalimumab data using a Bayesian historical borrowing approach in which the success criterion was posterior probability of ABBV-3373 being better than adalimumab > 95%. When borrowing 30 historical adalimumab subjects, the combined mean change from Baseline in adalimumab was 2.29.

Primary Comparison 2: Compare ABBV-3373 to Adalimumab with Historical Data Borrowing

Change from Baseline in DAS28(CRP) at Week 12 Using Bayesian Historical Borrowing-Fixed Borrowing of 30 Historical Adalimumab Patients Borrowed (OC)
(Full Analysis Set)

Parameter Treatment / (Data Source)	N	Within Group		Between Groups Difference				
		- Change from Baseline -		----- Compared to Adalimumab (Posterior) -----				
		Mean	SE	Mean	[90% Credible Interval]	SE	P(Posterior Treatment Difference < 0)	Bayesian Success (>0.95)
DISEASE ACTIVITY SCORE BASED ON CRP								
Adalimumab 80 mg SC EOW (In trial)	16	-2.51	0.293					
Adalimumab 80 mg SC EOW (Prior/Historical)	30	-2.13	0.246					
Adalimumab 80 mg SC EOW (Posterior)		-2.29	0.189					
ABBV-3373 100 mg IV EOW (In trial)	29	-2.65	0.215	-0.37	[-0.84, 0.11]	0.286	0.899	N

Note: The mean within group for data source in trial is the least square mean from ABBV-3373 and Adalimumab estimated by MMRM model including up to week 12 data with unstructured variance-covariance matrix, including treatment, visit, stratification factors, and treatment-by-visit interaction as fixed factors and baseline value as covariate.
Baseline is defined as the last non-missing value prior to the first dose of study drug. Subjects with non-missing baseline and at least one post-baseline value is included in the analyses.