Supplemental Materials 1:

Improvement in Tender and Swollen Joints With or Without Dose Escalation

A summary of the improvement in tender and swollen joints at weeks 22 and 54 is provided in the table. The results in the table are separated into cohorts of patients who never required dose escalation and those who required dose escalation(s) at some time during the study. Patients who did not require dose escalation showed at least 20% improvement from baseline in tender and swollen joints at week 22 and did not meet the criteria for flare between weeks 22 and 54. Patients who received dose escalations did not show at least 20% improvement at week 22 or met the criteria for flare (at least 50% decrease in the improvement achieved) at some time point after responding at week 22.

The changes in swollen and tender joint counts from baseline provided in the table reflect the fact that patients who never received dose escalations were selected out as responders. Patients who never received dose escalation had greater improvement from baseline at weeks 22 and 54 in both tender and swollen joints. However, patients who did not require dose escalation achieved the majority of their improvement in tender and swollen joints by week 22 (median 70%), with a minimal improvement from week 22 to week 54 (median 9%). As a group, patients who required dose escalation had a median improvement in tender and swollen joints of 18% from baseline to week 22 and a median improvement of 22% from week 22 to 54 ($p = 0.0599$ compared with cohort that did not require dose escalation). The group that needed dose escalation had majority of their improvement after beginning dose escalation at week 22 (more than twice as much as the

group that didn't require dose escalation). In addition by week 54 the difference between the two groups' percent improvement in total joint counts from baseline had substantially reduced (from 58 % at week 22 to 30% at week 54). It appears that the patients benefited from dose escalation.

These results however, must be interpreted with caution. All patients who did not require dose escalations achieved response at week 22 and maintained it through week 54. In contrast, the dose-escalated group contains a mixture of patients who were responding at week 22 and week 54 as well as those who were not responding. Therefore, comparing week-54 improvements in joint counts between the groups is problematic. Moreover, patients not responding at week 22 or thereafter were not randomly assigned to receive or not receive dose escalation, and thus there was no appropriate control to compare the effect of dose escalation.

Although the results must be interpreted with caution, there issome evidence that patients who received dose escalation showed improvement in their total joint counts compared with baseline. These results may warrant further studies to evaluate if there is clinically meaningful improvement with dose escalation.

Supplemental Table 1: Percent improvement from baseline to weeks 22 and 54 and percent improvement from week 22 to 54 in tender and swollen joint counts for patients who received dose escalation and those who never received dose escalation.

Percent improvement in joint counts	Received dose escalation	No dose escalation at any time
Week 22		
Tender joints		
Mean ± standard deviation	14 ± 60	68 ± 26
Median (interquartile range)	17 (-16, 62)	71 (50, 90)
Swollen joints		
Mean ± standard deviation	34 ± 45	68 ± 25
Median (interquartile range)	39 (9, 69)	71 (53, 88)
Total joints		
Mean ± standard deviation	23 ± 47	67 ± 22
Median (interquartile range)	18 (-6, 64)	70 (52, 85)
Week 54		
Tender joints		
Mean ± standard deviation	34 ± 50	75 ± 27
Median (interquartile range)	47 (13, 68)	83 (63, 96)
Swollen joints		
Mean ± standard deviation	42 ± 53	75 ± 28
Median (interquartile range)	58 (16, 82)	84 (64, 100)
Total joints		
Mean ± standard deviation	38 ± 44	75 ± 24
Median (interquartile range)	50 (14, 67)	80 (63, 94)
Difference from week 22 to week 54		
Tender joints		
Mean ± standard deviation	21 ± 71	7 ± 30
Median (interquartile range)	17 (-24, 68)	6 (-7, 23)
p value		0.0267
Swollen joints		
Mean ± standard deviation	8 ± 63	7 ± 30
Median (interquartile range)	12 (-28, 53)	9 (8, 26)
p value		0.4167
Total joints		
Mean ± standard deviation	15 ± 59	8 ± 26.34
Median (interquartile range)	22 (-24, 55)	9 (-5, 23)
p value		0.0599*

*Based on an analysis of variance of the van der Waerden normal scores