

## Supplemental Online Content

Zhang Shenghong, Chen B, Wang B, et al. Effect of induction therapy with olamkicept vs placebo on clinical response in patients with active ulcerative colitis: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2023.1084

**eAppendix 1.** List of Participating Institutions

**eAppendix 2.** Supplementary Methods

**eAppendix 3.** Pharmacokinetics, Pharmacodynamics, And Immunogenicity

**eTable 1.** Efficacy Outcomes in Full Analysis Set

**eTable 2.** Summary of Biomarker Changes from Baseline in Each Dose Group

**eTable 3.** Summary of Pharmacokinetic Parameters of Olamkicept in Serum (PKS)

**eTable 4.** Summary of Development of Anti-Drug Antibodies in Patients Receiving Olamkicept

**eFigure 1.** Study Schema

**eFigure 2.** Efficacy of Olamkicept 600 mg and Placebo by Subgroups

**eFigure 3.** Change from Baseline in Biomarkers Over Time

**eFigure 4.** Lipid Profiles, Platelet and Neutrophil Count Over Time

**eFigure 5.** Olamkicept Plasma Concentrations Over Time

This supplemental material has been provided by the authors to give readers additional information about their work.

## **eAppendix 1. List of Participating Institutions**

Mackay Memorial Hospital

E-Da Hospital

Wanfang Hospital

Chang Gung Memorial Hospital-Linkou

National Taiwan University Hospital

The Catholic University of Korea Seoul St. Mary's Hospital

Inje University Haeundae Paik Hospital

CHA Bundang Medical Center, CHA University

Yeungnam University Medical Center

The First Affiliated Hospital of Sun Yat-sen University (leader institution)

West China Hospital of Sichuan University

Peking University First Hospital

Hebei General Hospital

The Sixth Affiliated Hospital of Sun Yat-sen University

Sir Run Run Shaw Hospital Zhejiang University, School of Medicine

Ruijin Hospital, Shanghai Jiaotong University School of Medicine

Renji Hospital, Shanghai Jiaotong University School of Medicine

Shanghai Changhai Hospital

Shengjing Hospital of China Medical University

The First Bethune Hospital of Jilin University

Second Hospital of Shanxi Medical University

Hainan General Hospital

Zhongda Hospital Southeast University

First Affiliated Hospital of Harbin Medical University

Beijing Friendship Hospital Affiliated to the Capital University of Medical Sciences

The Military General Hospital of Beijing PLA

Tianjin Medical University General Hospital

Xin Hua Hospital Affiliated to Shanghai Jiaotong University School of Medicine

Guangdong Provincial People's Hospital

Nanfang Hospital of Southern Medical University

Jiangsu Province Hospital

Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School

The First Affiliated Hospital of Nanchang University

## eAppendix 2. Supplementary Methods

### Other eligibility criteria

We excluded patients who had a history of enterostomy, colectomy or hemicolectomy or who were likely to receive surgery for UC within 1 month based on investigator's evaluation. Patients with a history of malignancy other than a successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma and/or localized carcinoma *in situ* of the cervix, or who had dysplasia or a malignancy on colonoscopy at screening were also ineligible. Patients with infections including active or latent tuberculosis were also excluded.

### Definitions

Clinical response was defined as a  $\geq 3$  and  $\geq 30\%$  decrease from baseline total Mayo score, including a  $\geq 1$  decrease from baseline in rectal bleeding subscore or  $\leq 1$  in rectal bleeding subscore. Clinical remission per total Mayo score was defined as a total Mayo score  $\leq 2$ , no individual subscore  $> 1$ , and rectal bleeding subscore = 0. Remission per modified Mayo score was defined as per modified Mayo score (total Mayo score excluding Physician's Global Assessment subscore), stool frequency subscore  $\leq 1$ , rectal bleeding subscore = 0, and endoscopy subscore = 0 or 1. Mucosal healing was defined as Mayo endoscopic subscore = 0 or 1. Clinical remission per partial Mayo score was defined as a stool frequency subscore = 0, rectal bleeding subscore = 0, and 9-point partial Mayo score (total Mayo score excluding endoscopy subscore)  $\leq 1$ . Clinical response per partial Mayo score was defined as decrease from baseline in 9-point partial Mayo score  $\geq 2$  and  $\geq 30\%$ , including decrease from baseline in rectal bleeding subscore  $\geq 1$  or rectal bleeding subscore  $\leq 1$

### eAppendix 3. Pharmacokinetics, Pharmacodynamics, And Immunogenicity

Other secondary outcomes included  $AUC_{inf}$ ,  $AUC_{0-t}$ ,  $AUC_{\tau}$ , maximum concentration ( $C_{max}$ ), time to  $C_{max}$  ( $T_{max}$ ), clearance (CL), apparent volume of distribution ( $V_z$ ), half-life ( $t_{1/2}$ ), and mean residence time (MRT) in pharmacokinetics subgroup and olamkicept trough concentration ( $C_{trough}$ ) in all subjects and change from baseline at Weeks 4, 8, and 12 in exploratory biomarkers (erythrocyte sedimentation rate, C-reactive protein, IL-6, s-IL6R, IL-6/sIL-6R complex, neutrophil and platelet count, fecal calprotectin).

Blood samples for the pharmacokinetics set were collected at the 1<sup>st</sup> dose (pre-dose and 0.5, 1, 2 (end of infusion), 6, 48, 144, and 240 h post-dose), 2<sup>nd</sup> to the 5<sup>th</sup> dose (pre-dose and at the end of infusion), and the 6<sup>th</sup> dose (pre-dose and 0.5, 1, 2, 6, 48, 144, 240, 336, 480, and 840 h post-dose). Pharmacokinetics parameters were calculated using a non-compartmental model (NCA) with the Phoenix WinNonlin 8.3.1 software. Single-dose pharmacokinetics parameters included,  $C_{max}$ ,  $T_{max}$ ,  $AUC_{0-14day}$ ,  $AUC_{0-t}$ ,  $AUC_{0-inf}$ , CL,  $V_z$ ,  $t_{1/2}$  and  $MRT_{inf}$  and multiple dose parameters included  $C_{max}$  at steady state ( $C_{max,ss}$ ), time to  $C_{max,s}$  ( $T_{max,ss}$ ),  $C_{trough}$ ,  $AUC_{\tau}$ ,  $AUC_{0-t}$ , CL,  $V_z$ ,  $t_{1/2}$ , accumulation ratio calculated from  $C_{max}$  ( $R_{ac,Cmax}$ ) and AUC ( $R_{ac,AUC}$ ) and  $MRT_{inf}$ . Multiple comparison based on the mixed model of  $C_{trough}$  was performed for the 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup>, and 6<sup>th</sup> consecutive doses of olamkicept in each dose group to evaluate whether olamkicept concentration had reached the steady state.

The pharmacokinetics/pharmacodynamics set included patients who received olamkicept and had at least one measurable post-dose blood sample. For pharmacokinetics analysis, single-dose and repeated-dose pharmacokinetics parameters were statistically summarized by dose group. Dose linearity was evaluated using the analysis of variance (ANOVA) after log-transformation of dose-corrected pharmacokinetics parameters (all doses were standardized to 100 mg), and plasma trough concentrations in each dose group were analyzed for olamkicept steady-state assessment using a mixed model with multiple comparisons for repeated measures.

In addition, blood samples were collected pre-dose within 1 h prior to dosing on days 0, 14, 28 and 56, and on days 84 and 105 for analysis of anti-olamkicept antibodies. The immunogenicity analysis set (IS) included all patients who underwent randomization and had received at least one dose of TJ301 and had measurable immunogenicity data after administration. Exploratory biomarkers as well as their changes in Week 4, 8 and 12 from baseline were summarized using descriptive statistics. A mixed-effects model for repeated measures (MMRM) was used for inter-group comparison. Anti-olamkicept antibody levels were also summarized using descriptive statistics.

In addition, there was no significant difference in changes from baseline in Physician's Global Assessment subscore at all visits among the groups ( $P > 0.10$ ).

**Supplement eTables:**

| <b>eTable 1. Efficacy Outcomes in Full Analysis Set<sup>a</sup></b> |                              |                              |                              |                                                                                      |                                                                                      |
|---------------------------------------------------------------------|------------------------------|------------------------------|------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
| <b>Outcomes</b>                                                     | <b>Olamkicept</b>            |                              | <b>Placebo<br/>(n=29)</b>    | <b>Difference vs Placebo</b>                                                         |                                                                                      |
|                                                                     | <b>600 mg Q2W<br/>(n=29)</b> | <b>300 mg Q2W<br/>(n=30)</b> |                              | <b>600 mg Q2W</b>                                                                    | <b>300 mg Q2W</b>                                                                    |
| <b>Primary outcome</b>                                              |                              |                              |                              |                                                                                      |                                                                                      |
| Clinical response at week 12                                        | 17 (58.6)                    | 13 (43.3)                    | 10 (34.5)                    | 26.6 (6.2, 47.1) <sup>c</sup><br>26.6 (2.3, 51.0) <sup>d</sup><br><i>P</i> = 0.032   | 8.3 (-12.6, 29.1) <sup>c</sup><br>8.3 (-16.7, 33.2) <sup>d</sup><br><i>P</i> = 0.516 |
| <b>Secondary Outcomes</b>                                           |                              |                              |                              |                                                                                      |                                                                                      |
| Clinical remission at week 12                                       | 6 (20.7)                     | 2 (6.7)                      | 0                            | 19.9 (12.5, 27.3) <sup>c</sup><br>19.9 (11.1, 28.7) <sup>d</sup><br><i>P</i> < 0.001 | 6.1 (-0.8, 12.9) <sup>c</sup><br>6.1 (-2.1, 14.3) <sup>d</sup><br><i>P</i> = 0.143   |
| Remission per modified Mayo score at week 12                        | 7 (24.1)                     | 3 (10.0)                     | 1 (3.4)                      | 21.2 (10.2, 32.2) <sup>c</sup><br>21.2 (8.1, 34.3) <sup>d</sup><br><i>P</i> = 0.002  | 5.7 (-4.6, 16.1) <sup>c</sup><br>5.7 (-6.6, 18.1) <sup>d</sup><br><i>P</i> = 0.363   |
| Mucosal healing at week 12                                          | 10 (34.5)                    | 3 (10.0)                     | 1 (3.4)                      | 33.1 (18.3, 47.9) <sup>c</sup><br>33.1 (15.4, 50.7) <sup>d</sup><br><i>P</i> < 0.001 | 6.0 (-4.4, 16.3) <sup>c</sup><br>6.0 (-6.4, 18.3) <sup>d</sup><br><i>P</i> = 0.343   |
| Total Mayo score change from baseline at week 12                    | -3.5 (2.2) [25] <sup>b</sup> | -2.3 (2.6) [27] <sup>b</sup> | -1.8 (2.6) [21] <sup>b</sup> | -1.6 (-2.9, -0.4) <sup>e</sup><br>-1.6 (-3.1, -0.1) <sup>f</sup><br><i>P</i> = 0.032 | -0.5 (-1.7, 0.7) <sup>e</sup><br>-0.5 (-1.9, 1.0) <sup>f</sup><br><i>P</i> = 0.514   |
| Modified Mayo score change from baseline at week 12                 | -2.8 (1.9) [25] <sup>b</sup> | -1.8 (2.0) [27] <sup>b</sup> | -1.3 (2.0) [21] <sup>b</sup> | -1.4 (-2.4, -0.4) <sup>e</sup><br>-1.4 (-2.6, -0.2) <sup>f</sup><br><i>P</i> = 0.021 | -0.5 (-1.5, 0.5) <sup>e</sup><br>-0.5 (-1.6, 0.7) <sup>f</sup><br><i>P</i> = 0.429   |
| Partial Mayo score change from baseline                             |                              |                              |                              |                                                                                      |                                                                                      |
| At week 4                                                           | -1.7 (1.9) [27] <sup>b</sup> | -1.6 (1.7) [29] <sup>b</sup> | -0.9 (1.7) [27] <sup>b</sup> | -0.7 (-1.5, 0.0) <sup>e</sup><br>-0.7 (-1.6, 0.2) <sup>f</sup><br><i>P</i> = 0.114   | -0.6 (-1.3, 0.2) <sup>e</sup><br>-0.6 (-1.5, 0.3) <sup>f</sup><br><i>P</i> = 0.198   |
| At week 6                                                           | -2.0 (1.7) [27] <sup>b</sup> | -2.1 (1.8) [29] <sup>b</sup> | -1.3 (2.0) [24] <sup>b</sup> | -0.6 (-1.4, 0.2) <sup>e</sup><br>-0.6 (-1.6, 0.4) <sup>f</sup><br><i>P</i> = 0.234   | -0.7 (-1.5, 0.1) <sup>e</sup><br>-0.7 (-1.7, 0.3) <sup>f</sup><br><i>P</i> = 0.156   |
| At week 8                                                           | -2.3 (1.9) [27] <sup>b</sup> | -2.6 (2.0) [29] <sup>b</sup> | -1.5 (2.2) [22] <sup>b</sup> | -1.0 (-1.9, -0.1) <sup>e</sup><br>-1.0 (-2.0, 0.1) <sup>f</sup><br><i>P</i> = 0.078  | -1.3 (-2.2, -0.4) <sup>e</sup><br>-1.3 (-2.3, -0.2) <sup>f</sup><br><i>P</i> = 0.018 |
| At week 10                                                          | -2.7 (1.7) [27] <sup>b</sup> | -2.5 (1.8) [29] <sup>b</sup> | -1.5 (2.4) [23] <sup>b</sup> | -1.2 (-2.0, -0.3) <sup>e</sup><br>-1.2 (-2.2, -0.2) <sup>f</sup><br><i>P</i> = 0.022 | -1.1 (-1.9, -0.2) <sup>e</sup><br>-1.1 (-2.1, -0.1) <sup>f</sup><br><i>P</i> = 0.036 |
| At week 12                                                          | -2.6 (1.8) [27] <sup>b</sup> | -2.1 (2.2) [28] <sup>b</sup> | -1.4 (2.1) [23] <sup>b</sup> | -1.2 (-2.1, -0.2) <sup>e</sup><br>-1.2 (-2.3, -0.1) <sup>f</sup><br><i>P</i> = 0.040 | -0.8 (-1.7, 0.2) <sup>e</sup><br>-0.8 (-1.9, 0.3) <sup>f</sup><br><i>P</i> = 0.173   |
| Clinical remission per partial Mayo score                           |                              |                              |                              |                                                                                      |                                                                                      |
| At week 4                                                           | 2 (6.9)                      | 2 (6.7)                      | 0                            | 6.9 (-0.8, 14.6) <sup>c</sup><br>6.9 (-2.3, 16.1) <sup>d</sup><br><i>P</i> = 0.140   | 6.6 (-0.8, 14.1) <sup>c</sup><br>6.6 (-2.2, 15.5) <sup>d</sup><br><i>P</i> = 0.141   |
| At week 6                                                           | 6 (20.7)                     | 3 (10.0)                     | 1 (3.4)                      | 16.9 (4.5, 29.2) <sup>c</sup><br>16.9 (2.1, 31.6) <sup>d</sup><br><i>P</i> = 0.025   | 7.9 (-1.4, 17.3) <sup>c</sup><br>7.9 (-3.2, 19.1) <sup>d</sup><br><i>P</i> = 0.164   |
| At week 8                                                           | 4 (13.8)                     | 3 (10.0)                     | 1 (3.4)                      | 13.4 (2.0, 24.8) <sup>c</sup>                                                        | 7.9 (-1.4, 17.3) <sup>c</sup>                                                        |

|                                          |                              |                              |                              |                                                                                      |                                                                                      |
|------------------------------------------|------------------------------|------------------------------|------------------------------|--------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|
|                                          |                              |                              |                              | 13.4 (-0.1, 27.0) <sup>d</sup><br><i>P</i> = 0.053                                   | 7.9 (-3.2, 19.1) <sup>d</sup><br><i>P</i> = 0.164                                    |
| At week 10                               | 5 (17.2)                     | 4 (13.3)                     | 2 (6.9)                      | 14.8 (2.3, 27.4) <sup>c</sup><br>14.8 (-0.1, 29.8) <sup>d</sup><br><i>P</i> = 0.052  | 9.2 (-1.4, 19.9) <sup>c</sup><br>9.2 (-3.5, 22.0) <sup>d</sup><br><i>P</i> = 0.155   |
| At week 12                               | 7 (24.1)                     | 5 (16.7)                     | 1 (3.4)                      | 23.8 (9.9, 37.6) <sup>c</sup><br>23.8 (7.3, 40.2) <sup>d</sup><br><i>P</i> = 0.005   | 14.6 (3.2, 26.0) <sup>c</sup><br>14.6 (1.0, 28.1) <sup>d</sup><br><i>P</i> = 0.035   |
| Clinical response per partial Mayo score |                              |                              |                              |                                                                                      |                                                                                      |
| At week 4                                | 12 (41.4)                    | 11 (36.7)                    | 7 (24.1)                     | 16.8 (-2.3, 35.8) <sup>c</sup><br>16.8 (-5.9, 39.4) <sup>d</sup><br><i>P</i> = 0.148 | 13.9 (-5.8, 33.6) <sup>c</sup><br>13.9 (-9.5, 37.4) <sup>d</sup><br><i>P</i> = 0.245 |
| At week 6                                | 14 (48.3)                    | 16 (53.3)                    | 6 (20.7)                     | 29.1 (10.7, 47.4) <sup>c</sup><br>29.1 (7.2, 51.0) <sup>d</sup><br><i>P</i> = 0.009  | 36.0 (16.9, 55.2) <sup>c</sup><br>36.0 (13.2, 58.8) <sup>d</sup><br><i>P</i> = 0.002 |
| At week 8                                | 17 (58.6)                    | 18 (60.0)                    | 8 (27.6)                     | 31.9 (12.4, 51.4) <sup>c</sup><br>31.9 (8.7, 55.2) <sup>d</sup><br><i>P</i> = 0.007  | 35.2 (15.1, 55.2) <sup>c</sup><br>35.2 (11.3, 59.0) <sup>d</sup><br><i>P</i> = 0.004 |
| At week 10                               | 18 (62.1)                    | 18 (60.0)                    | 6 (20.7)                     | 42.9 (24.6, 61.1) <sup>c</sup><br>42.9 (21.2, 64.6) <sup>d</sup><br><i>P</i> < 0.001 | 39.4 (20.3, 58.4) <sup>c</sup><br>39.4 (16.6, 62.1) <sup>d</sup><br><i>P</i> < 0.001 |
| At week 12                               | 18 (62.1)                    | 16 (53.3)                    | 10 (34.5)                    | 27.9 (7.8, 48.0) <sup>c</sup><br>27.9 (3.9, 51.8) <sup>d</sup><br><i>P</i> = 0.023   | 16.0 (-4.2, 36.1) <sup>c</sup><br>16.0 (-8.0, 39.9) <sup>d</sup><br><i>P</i> = 0.192 |
| PGA Change from baseline                 |                              |                              |                              |                                                                                      |                                                                                      |
| At week 4                                | -0.6 (0.8) [27] <sup>b</sup> | -0.4 (0.5) [29] <sup>b</sup> | -0.4 (0.6) [27] <sup>b</sup> | -0.2 (-0.4, 0.1) <sup>e</sup><br>-0.2 (-0.5, 0.1) <sup>f</sup><br><i>P</i> = 0.276   | -0.0 (-0.3, 0.2) <sup>e</sup><br>-0.0 (-0.3, 0.2) <sup>f</sup><br><i>P</i> = 0.763   |
| At week 6                                | -0.5 (0.6) [27] <sup>b</sup> | -0.7 (0.7) [29] <sup>b</sup> | -0.6 (0.9) [24] <sup>b</sup> | -0.0 (-0.3, 0.3) <sup>e</sup><br>-0.0 (-0.4, 0.3) <sup>f</sup><br><i>P</i> = 0.968   | -0.1 (-0.4, 0.2) <sup>e</sup><br>-0.1 (-0.5, 0.2) <sup>f</sup><br><i>P</i> = 0.488   |
| At week 8                                | -0.7 (0.7) [27] <sup>b</sup> | -0.7 (0.8) [29] <sup>b</sup> | -0.6 (0.9) [22] <sup>b</sup> | -0.2 (-0.5, 0.1) <sup>e</sup><br>-0.2 (-0.5, 0.2) <sup>f</sup><br><i>P</i> = 0.320   | -0.2 (-0.5, 0.1) <sup>e</sup><br>-0.2 (-0.6, 0.1) <sup>f</sup><br><i>P</i> = 0.177   |
| At week 10                               | -0.7 (0.7) [27] <sup>b</sup> | -0.7 (0.8) [29] <sup>b</sup> | -0.7 (0.9) [23] <sup>b</sup> | -0.1 (-0.4, 0.2) <sup>e</sup><br>-0.1 (-0.5, 0.2) <sup>f</sup><br><i>P</i> = 0.495   | -0.1 (-0.4, 0.2) <sup>e</sup><br>-0.1 (-0.4, 0.3) <sup>f</sup><br><i>P</i> = 0.656   |
| At week 12                               | -0.7 (0.5) [27] <sup>b</sup> | -0.5 (0.9) [28] <sup>b</sup> | -0.6 (0.7) [23] <sup>b</sup> | -0.2 (-0.5, 0.1) <sup>e</sup><br>-0.2 (-0.6, 0.2) <sup>f</sup><br><i>P</i> = 0.275   | -0.1 (-0.4, 0.3) <sup>e</sup><br>-0.1 (-0.4, 0.3) <sup>f</sup><br><i>P</i> = 0.780   |

<sup>a</sup> n (%), i.e. number and percentage of patients achieving the outcome unless otherwise noted.

<sup>b</sup> Mean (SD) [No. of patients].

<sup>c</sup> Adjusted percentage difference (90% CI).

<sup>d</sup> Adjusted percentage difference (95% CI).

<sup>e</sup> LS mean (90% CI).

<sup>f</sup> LS mean (95% CI).

| <b>eTable 2. Summary of Biomarker Changes From Baseline in Each Dose Group</b> |                                           |                           |                                 |                                 |                             |
|--------------------------------------------------------------------------------|-------------------------------------------|---------------------------|---------------------------------|---------------------------------|-----------------------------|
| <b>Biomarkers (units)</b>                                                      | <b>Visit cycle</b>                        | <b>Statistics</b>         | <b>600 mg olamkicept (N=29)</b> | <b>300 mg olamkicept (N=30)</b> | <b>Placebo group (N=29)</b> |
| Platelet count (*10 <sup>9</sup> /L)                                           | Baseline value                            | n                         | 29                              | 30                              | 29                          |
|                                                                                |                                           | Mean±SD                   | 304.79±131.83                   | 330.27±101.93                   | 256.62±76.76                |
|                                                                                | Changes from baseline at Week 4           | n                         | 27                              | 29                              | 26                          |
|                                                                                |                                           | Mean±SD                   | -9.26±62.94                     | -12.83±35.70                    | 5.23±40.54                  |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | -4.89 (-25.40, 15.62)           | -4.09 (-24.59, 16.41)           |                             |
|                                                                                |                                           | P value                   | 0.693                           | 0.741                           |                             |
|                                                                                | Changes from baseline at Week 8           | n                         | 27                              | 29                              | 22                          |
|                                                                                |                                           | Mean±SD                   | -18.48±55.53                    | -15.69±44.53                    | -3.64±46.46                 |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | -5.94 (-25.24, 13.35)           | 2.86 (-16.52, 22.24)            |                             |
|                                                                                |                                           | P value                   | 0.610                           | 0.807                           |                             |
|                                                                                | Changes from baseline at Week 12          | n                         | 25                              | 28                              | 21                          |
|                                                                                |                                           | Mean±SD                   | -5.16±52.42                     | 0.25±60.50                      | 4.19±48.32                  |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | -0.64 (-25.54, 24.27)           | 10.23 (-14.47, 34.93)           |                             |
|                                                                                |                                           | P value                   | 0.966                           | 0.493                           |                             |
| Neutrophil count (*10 <sup>9</sup> /L)                                         | Baseline value                            | n                         | 29                              | 30                              | 29                          |
|                                                                                |                                           | Mean±SD                   | 4.29±1.92                       | 4.56±2.16                       | 4.41±2.09                   |
|                                                                                | Changes from baseline at Week 4           | n                         | 27                              | 29                              | 26                          |
|                                                                                |                                           | Mean±SD                   | -0.03±1.66                      | -0.37±1.74                      | 0.04±1.54                   |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | -0.13 (-0.74, 0.48)             | -0.35 (-0.96, 0.25)             |                             |
|                                                                                |                                           | P value                   | 0.723                           | 0.331                           |                             |
|                                                                                | Changes from baseline at Week 8           | n                         | 27                              | 29                              | 22                          |
|                                                                                |                                           | Mean±SD                   | -0.22±1.56                      | -0.40±1.98                      | -0.04±1.69                  |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | -0.20 (-0.80, 0.39)             | -0.29 (-0.87, 0.30)             |                             |
|                                                                                |                                           | P value                   | 0.570                           | 0.417                           |                             |
|                                                                                | Changes from baseline at Week 12          | n                         | 25                              | 28                              | 21                          |
|                                                                                |                                           | Mean±SD                   | 1.50±11.11                      | 0.12±2.32                       | -0.51±1.44                  |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | 1.96 (-1.24, 5.16)              | 0.81 (-2.31, 3.93)              |                             |
|                                                                                |                                           | P value                   | 0.311                           | 0.667                           |                             |
| C-reactive protein (mg/L)                                                      | Baseline value                            | n                         | 27                              | 28                              | 24                          |
|                                                                                |                                           | Mean±SD                   | 12.54±23.00                     | 8.48±8.05                       | 8.19±12.28                  |
|                                                                                | Changes from baseline at Week 4           | n                         | 23                              | 24                              | 21                          |
|                                                                                |                                           | Mean±SD                   | -7.43±14.54                     | -0.08±6.50                      | -1.78±15.49                 |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | -3.80 (-7.75, 0.14)             | 0.88 (-2.92, 4.68)              |                             |
| P value                                                                        |                                           | 0.113                     | 0.700                           |                                 |                             |

| <b>eTable 2. Summary of Biomarker Changes From Baseline in Each Dose Group</b> |                                           |                           |                                 |                                 |                             |            |
|--------------------------------------------------------------------------------|-------------------------------------------|---------------------------|---------------------------------|---------------------------------|-----------------------------|------------|
| <b>Biomarkers (units)</b>                                                      | <b>Visit cycle</b>                        | <b>Statistics</b>         | <b>600 mg olamkicept (N=29)</b> | <b>300 mg olamkicept (N=30)</b> | <b>Placebo group (N=29)</b> |            |
|                                                                                | Changes from baseline at Week 8           | n                         | 24                              | 25                              | 18                          |            |
|                                                                                |                                           | Mean±SD                   | -5.93±14.14                     | -1.24±8.89                      | -0.82±16.63                 |            |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | -6.13 (-11.30, -0.97)           | -4.91 (-9.93, 0.10)             |                             |            |
|                                                                                |                                           | P value                   | 0.052                           | 0.107                           |                             |            |
|                                                                                | Changes from baseline at Week 12          | n                         | 20                              | 21                              | 16                          |            |
|                                                                                |                                           | Mean±SD                   | -4.04±15.23                     | 0.62±9.07                       | -1.13±9.59                  |            |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | -5.08 (-10.58, 0.42)            | -2.38 (-7.77, 3.01)             |                             |            |
|                                                                                |                                           | P value                   | 0.128                           | 0.464                           |                             |            |
|                                                                                | Erythrocyte sedimentation rate (mm/h)     | Baseline value            | n                               | 28                              | 29                          | 29         |
|                                                                                |                                           |                           | Mean±SD                         | 20.2±22.94                      | 30.2±24.47                  | 18.2±20.88 |
| Changes from baseline at Week 4                                                |                                           | n                         | 24                              | 28                              | 24                          |            |
|                                                                                |                                           | Mean±SD                   | -1.9±14.63                      | -2.3±14.99                      | 0.5±9.77                    |            |
| Changes as compared to placebo at Week 4                                       |                                           | LSMean Difference (90%CI) | -2.09 (-7.87, 3.69)             | 0.40 (-5.31, 6.10)              |                             |            |
|                                                                                |                                           | P value                   | 0.549                           | 0.909                           |                             |            |
| Changes from baseline at Week 8                                                |                                           | n                         | 25                              | 28                              | 22                          |            |
|                                                                                |                                           | Mean±SD                   | -2.3±24.25                      | -5.9±19.03                      | -1.3±14.36                  |            |
| Changes as compared to placebo at Week 8                                       |                                           | LSMean Difference (90%CI) | -1.51 (-8.80, 5.78)             | -2.32 (-9.56, 4.93)             |                             |            |
|                                                                                |                                           | P value                   | 0.731                           | 0.596                           |                             |            |
| Changes from baseline at Week 12                                               |                                           | n                         | 25                              | 27                              | 21                          |            |
|                                                                                |                                           | Mean±SD                   | -2.1±25.65                      | 0.6±24.49                       | 1.0±12.21                   |            |
| Changes as compared to placebo at Week 12                                      |                                           | LSMean Difference (90%CI) | -4.13 (-13.15, 4.88)            | 0.96 (-8.00, 9.92)              |                             |            |
|                                                                                |                                           | P value                   | 0.448                           | 0.859                           |                             |            |
| Fecal calprotectin (mg/kg)                                                     | Baseline value                            | n                         | 26                              | 30                              | 28                          |            |
|                                                                                |                                           | Mean±SD                   | 4139.03±4211.14                 | 4145.96±5477.21                 | 5680.05±9073.43             |            |
|                                                                                | Changes from baseline at Week 4           | n                         | 24                              | 29                              | 24                          |            |
|                                                                                |                                           | Mean±SD                   | 1327.66±7828.19                 | 1736.76±6717.39                 | -107.93±12784.03            |            |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | 320.18 (-3680.04, 4320.41)      | 623.73 (-3203.04, 4450.50)      |                             |            |
|                                                                                |                                           | P value                   | 0.894                           | 0.787                           |                             |            |
|                                                                                | Changes from baseline at Week 8           | n                         | 23                              | 29                              | 21                          |            |
|                                                                                |                                           | Mean±SD                   | -1137.36±5034.62                | 644.83±6387.06                  | 3234.91±17301.11            |            |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | -4786.54 (-9508.07, -65.00)     | -3156.07 (-7650.13, 1337.99)    |                             |            |
|                                                                                |                                           | P value                   | 0.095                           | 0.246                           |                             |            |
|                                                                                | n                                         | 22                        | 26                              | 19                              |                             |            |



| <b>eTable 2. Summary of Biomarker Changes From Baseline in Each Dose Group</b> |                                           |                           |                                 |                                 |                             |
|--------------------------------------------------------------------------------|-------------------------------------------|---------------------------|---------------------------------|---------------------------------|-----------------------------|
| <b>Biomarkers (units)</b>                                                      | <b>Visit cycle</b>                        | <b>Statistics</b>         | <b>600 mg olamkicept (N=29)</b> | <b>300 mg olamkicept (N=30)</b> | <b>Placebo group (N=29)</b> |
|                                                                                | Changes from baseline at Week 12          | Mean±SD                   | -1933.48±4685.84                | -112.96±7818.99                 | 4423.76±8673.50             |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | -7362.89 (-11138.25, -3587.53)  | -6070.70 (-9720.69, -2420.70)   |                             |
|                                                                                |                                           | P value                   | 0.002                           | 0.007                           |                             |
| IL-6 (pg/mL)                                                                   | Baseline value                            | n                         | 14                              | 19                              | 11                          |
|                                                                                |                                           | Mean±SD                   | 12.78±12.01                     | 7.27±4.07                       | 8.80±6.71                   |
|                                                                                | Changes from baseline at Week 4           | n                         | 12                              | 13                              | 9                           |
|                                                                                |                                           | Mean±SD                   | -5.30±9.57                      | 0.02±4.52                       | -1.52±4.46                  |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | -0.46 (-3.81, 2.89)             | 1.27 (-1.98, 4.51)              |                             |
|                                                                                |                                           | P value                   | 0.817                           | 0.513                           |                             |
|                                                                                | Changes from baseline at Week 8           | n                         | 11                              | 8                               | 3                           |
|                                                                                |                                           | Mean±SD                   | -4.91±9.41                      | 0.16±3.31                       | -8.45±2.75                  |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | 1.10 (-2.56, 4.75)              | 4.00 (0.08, 7.92)               |                             |
|                                                                                |                                           | P value                   | 0.614                           | 0.094                           |                             |
|                                                                                | Changes from baseline at Week 12          | n                         | 10                              | 9                               | 7                           |
|                                                                                |                                           | Mean±SD                   | -4.13±12.89                     | 1.34±7.31                       | -2.92±3.75                  |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | 0.20 (-3.87, 4.27)              | 4.07 (-0.06, 8.20)              |                             |
|                                                                                |                                           | P value                   | 0.934                           | 0.105                           |                             |
| IL-6/sIL-6R complex (pg/mL)                                                    | Baseline value                            | n                         | 2                               | 8                               | 3                           |
|                                                                                |                                           | Mean±SD                   | 364.63±24.49                    | 482.95±612.72                   | 226.93±16.56                |
|                                                                                | Changes from baseline at Week 4           | n                         | 2                               | 5                               | 2                           |
|                                                                                |                                           | Mean±SD                   | 68.21±100.94                    | -230.98±430.57                  | -23.89±49.96                |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | 246.79 (-273.37, 766.96)        | 201.70 (-234.01, 637.42)        |                             |
|                                                                                |                                           | P value                   | 0.414                           | 0.425                           |                             |
|                                                                                | Changes from baseline at Week 8           | n                         | 2                               | 5                               | 3                           |
|                                                                                |                                           | Mean±SD                   | -25.52±72.97                    | -316.82±738.31                  | -35.35±56.66                |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | 167.63 (36.61, 298.65)          | 144.55 (31.08, 258.02)          |                             |
|                                                                                |                                           | P value                   | 0.042                           | 0.042                           |                             |
|                                                                                | Changes from baseline at Week 12          | n                         | 2                               | 6                               | 3                           |
|                                                                                |                                           | Mean±SD                   | -59.57±104.75                   | -252.03±761.71                  | -34.74±36.91                |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | 132.97 (-118.87, 384.81)        | 127.95 (-70.52, 326.41)         |                             |
|                                                                                |                                           | P value                   | 0.365                           | 0.273                           |                             |
| Baseline value                                                                 | n                                         | 29                        | 30                              | 29                              |                             |

| <b>eTable 2. Summary of Biomarker Changes From Baseline in Each Dose Group</b> |                                           |                           |                                 |                                 |                             |
|--------------------------------------------------------------------------------|-------------------------------------------|---------------------------|---------------------------------|---------------------------------|-----------------------------|
| <b>Biomarkers (units)</b>                                                      | <b>Visit cycle</b>                        | <b>Statistics</b>         | <b>600 mg olamkicept (N=29)</b> | <b>300 mg olamkicept (N=30)</b> | <b>Placebo group (N=29)</b> |
| sIL-6R (pg/mL)                                                                 |                                           | Mean±SD                   | 34252.1±7633.93                 | 35531.9±10173.42                | 35406.9±9320.21             |
|                                                                                | Changes from baseline at Week 4           | n                         | 27                              | 28                              | 26                          |
|                                                                                |                                           | Mean±SD                   | 1817.3±3295.43                  | -858.4±3877.49                  | -604.9±4637.79              |
|                                                                                | Changes as compared to placebo at Week 4  | LSMean Difference (90%CI) | 2153.75 (507.35, 3800.14)       | -333.61 (-1961.75, 1294.53)     |                             |
|                                                                                |                                           | P value                   | 0.032                           | 0.734                           |                             |
|                                                                                | Changes from baseline at Week 8           | n                         | 27                              | 28                              | 22                          |
|                                                                                |                                           | Mean±SD                   | 960.3±3329.72                   | -1231.0±3141.48                 | 15.7±3783.23                |
|                                                                                | Changes as compared to placebo at Week 8  | LSMean Difference (90%CI) | 1175.58 (-272.26, 2623.42)      | -811.89 (-2246.15, 622.36)      |                             |
|                                                                                |                                           | P value                   | 0.180                           | 0.349                           |                             |
|                                                                                | Changes from baseline at Week 12          | n                         | 25                              | 28                              | 21                          |
|                                                                                |                                           | Mean±SD                   | 375.8±3395.95                   | 1684.0±3745.86                  | 455.3±3809.24               |
|                                                                                | Changes as compared to placebo at Week 12 | LSMean Difference (90%CI) | 49.31 (-1686.69, 1785.30)       | 1623.19 (-72.95, 3319.33)       |                             |
|                                                                                |                                           | P value                   | 0.962                           | 0.115                           |                             |

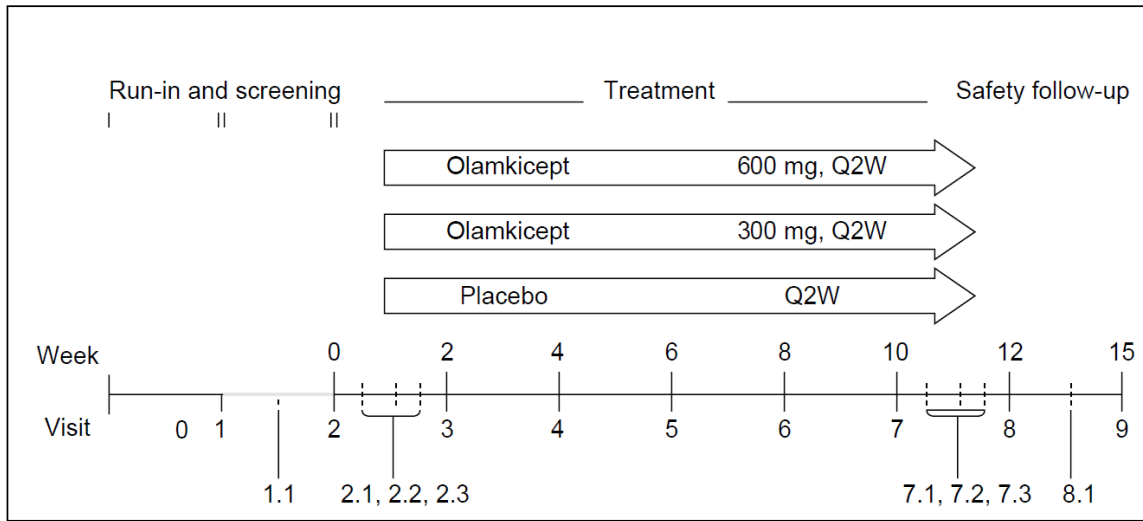
| eTable 3. Summary of Pharmacokinetic Parameters of Olamkicept in Serum (PKS) |                             |                 |              |                              |                             |                      |
|------------------------------------------------------------------------------|-----------------------------|-----------------|--------------|------------------------------|-----------------------------|----------------------|
| PK Parameters (Unit)                                                         | Statistics                  | First dose      |              | PK Parameters (Unit)         | Statistics                  | 6 <sup>th</sup> dose |
|                                                                              |                             | 600 mg (N=4)    | 300 mg (N=1) |                              |                             | 600 mg (N=3)         |
| T <sub>max</sub> (h)                                                         | Mean(SD)                    | 2.0 (0.0)       | 2.68         | T <sub>max,ss</sub> (h)      | Mean(SD)                    | 2.0 (0.1)            |
| C <sub>max</sub> (µg/mL)                                                     | Mean(SD)                    | 163.5 (43.1)    | 77.8         | C <sub>max,ss</sub> (µg/mL)  | Mean(SD)                    | 185.0 (59.0)         |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 159.7 (24.8)    | 77.8         |                              | GeoMean (%CV <sub>b</sub> ) | 178.4 (34.5)         |
| AUC <sub>0-t</sub> (µg*h/mL)                                                 | Mean(SD)                    | 4189.5 (1706.9) | 1487.3       | C <sub>trough</sub> (µg/mL)  | Mean(SD)                    | 1.1 (0.4)            |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 3973.4 (37.2)   | 1487.3       |                              | GeoMean (%CV <sub>b</sub> ) | 1.1(46.0)            |
| AUC <sub>0-inf</sub> (µg*h/mL)                                               | Mean(SD)                    | 4287.6 (1740.1) | 1556.9       | AUC <sub>τ</sub> (µg*h/mL)   | Mean(SD)                    | 4804.9 (921.8)       |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 4066.9 (37.2)   | 1556.9       |                              | GeoMean (%CV <sub>b</sub> ) | 4748.3 (18.9)        |
| CL (L/h)                                                                     | Mean(SD)                    | 0.2 (0.0)       | 0.2          | AUC <sub>0-t</sub> (µg*h/mL) | Mean(SD)                    | 4842.9 (985.1)       |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 0.1 (37.2)      | 0.2          |                              | GeoMean (%CV <sub>b</sub> ) | 4779.1 (20.0)        |
| V <sub>z</sub> (L)                                                           | Mean(SD)                    | 16.5 (4.4)      | 8.0          | CL <sub>ss</sub> (L/h)       | Mean(SD)                    | 0.1 (0.0)            |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 16.0 (32.6)     | 8.0          |                              | GeoMean (%CV <sub>b</sub> ) | 0.1 (18.9)           |
| t <sub>1/2</sub> (h)                                                         | Mean(SD)                    | 75.3 (6.8)      | 28.9         | V <sub>ss</sub> (L)          | Mean(SD)                    | 14.8 (2.5)           |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 75.1 (9.5)      | 28.9         |                              | GeoMean (%CV <sub>b</sub> ) | 14.7 (17.8)          |
| MRT <sub>inf</sub> (h)                                                       | Mean(SD)                    | 62.6 (8.6)      | 39.6         | t <sub>1/2</sub> (h)         | Mean(SD)                    | 82.2 (20.6)          |
|                                                                              | GeoMean (%CV <sub>b</sub> ) | 62.1 (15.0)     | 39.6         |                              | GeoMean (%CV <sub>b</sub> ) | 80.5 (25.4)          |
|                                                                              |                             |                 |              | R <sub>ac,Cmax</sub>         | Mean(SD)                    | 1.1 (0.2)            |
|                                                                              |                             |                 |              | R <sub>ac,AUC</sub>          | Mean(SD)                    | 1.2 (0.3)            |

Note: N represents the number of subjects in each group. In addition, since there was only 1 subject in the 300 mg dose group, SD and %CV<sub>b</sub> of the parameter statistics could not be calculated.

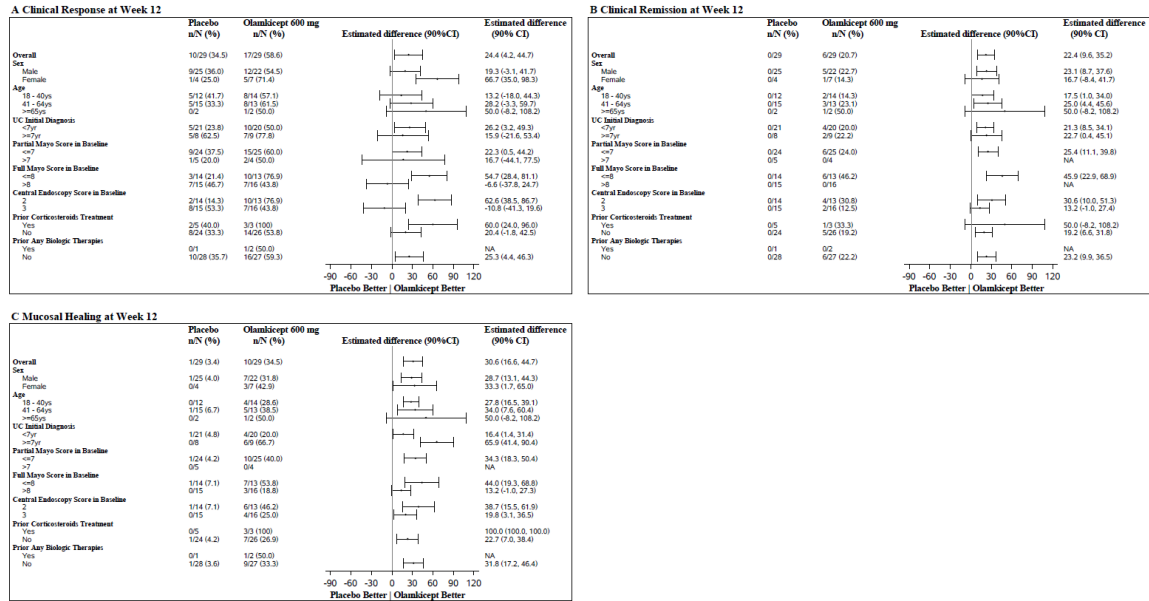
| <b>eTable 4. Summary of Development of Anti-Drug Antibodies in Patients Receiving Olamkicept</b> |                       |                                         |                                         |                                 |
|--------------------------------------------------------------------------------------------------|-----------------------|-----------------------------------------|-----------------------------------------|---------------------------------|
| <b>Test time</b>                                                                                 | <b>Classification</b> | <b>600 mg Olamkicept<br/>(N=30) (%)</b> | <b>300 mg Olamkicept<br/>(N=31) (%)</b> | <b>Overall<br/>(N = 61) (%)</b> |
| <b>Baseline</b>                                                                                  | Negative              | 30 (100)                                | 30 (97)                                 | 60 (98)                         |
|                                                                                                  | Positive              | 0                                       | 1 (3)                                   | 1 (2)                           |
|                                                                                                  | Total                 | 30 (100)                                | 31 (100)                                | 61 (100)                        |
| <b>Week 2</b>                                                                                    | Negative              | 26 (87)                                 | 30 (97)                                 | 56 (92)                         |
|                                                                                                  | Positive              | 0                                       | 0                                       | 0                               |
|                                                                                                  | Total                 | 26 (87)                                 | 30 (97)                                 | 56 (92)                         |
| <b>Week 4</b>                                                                                    | Negative              | 27 (90)                                 | 28 (90)                                 | 55 (90)                         |
|                                                                                                  | Positive              | 0                                       | 1 (3)                                   | 1 (2)                           |
|                                                                                                  | Total                 | 27 (90)                                 | 29 (94)                                 | 56 (92)                         |
| <b>Week 8</b>                                                                                    | Negative              | 27 (90)                                 | 29 (94)                                 | 56 (92)                         |
|                                                                                                  | Positive              | 0                                       | 0                                       | 0                               |
|                                                                                                  | Total                 | 27 (90)                                 | 29 (94)                                 | 56 (92)                         |
| <b>Week 12</b>                                                                                   | Negative              | 24 (80)                                 | 24 (77)                                 | 48 (79)                         |
|                                                                                                  | Positive              | 1 (3)                                   | 4 (13)                                  | 5 (8)                           |
|                                                                                                  | Total                 | 25 (83)                                 | 28 (90)                                 | 53 (87)                         |
| <b>Safety Follow-up Visit</b>                                                                    | Negative              | 28 (93)                                 | 26 (84)                                 | 54 (89)                         |
|                                                                                                  | Positive              | 1 (3)                                   | 1 (3)                                   | 2 (3)                           |
|                                                                                                  | Total                 | 29 (97)                                 | 27 (87)                                 | 56 (92)                         |
| <b>Overall</b>                                                                                   | Negative              | 29 (97)                                 | 26 (84)                                 | 55 (90)                         |
|                                                                                                  | Positive              | 1 (3)                                   | 5 (16)                                  | 6 (10)                          |
|                                                                                                  | Total                 | 30 (100)                                | 31 (100)                                | 61 (100)                        |

## Supplement eFigures

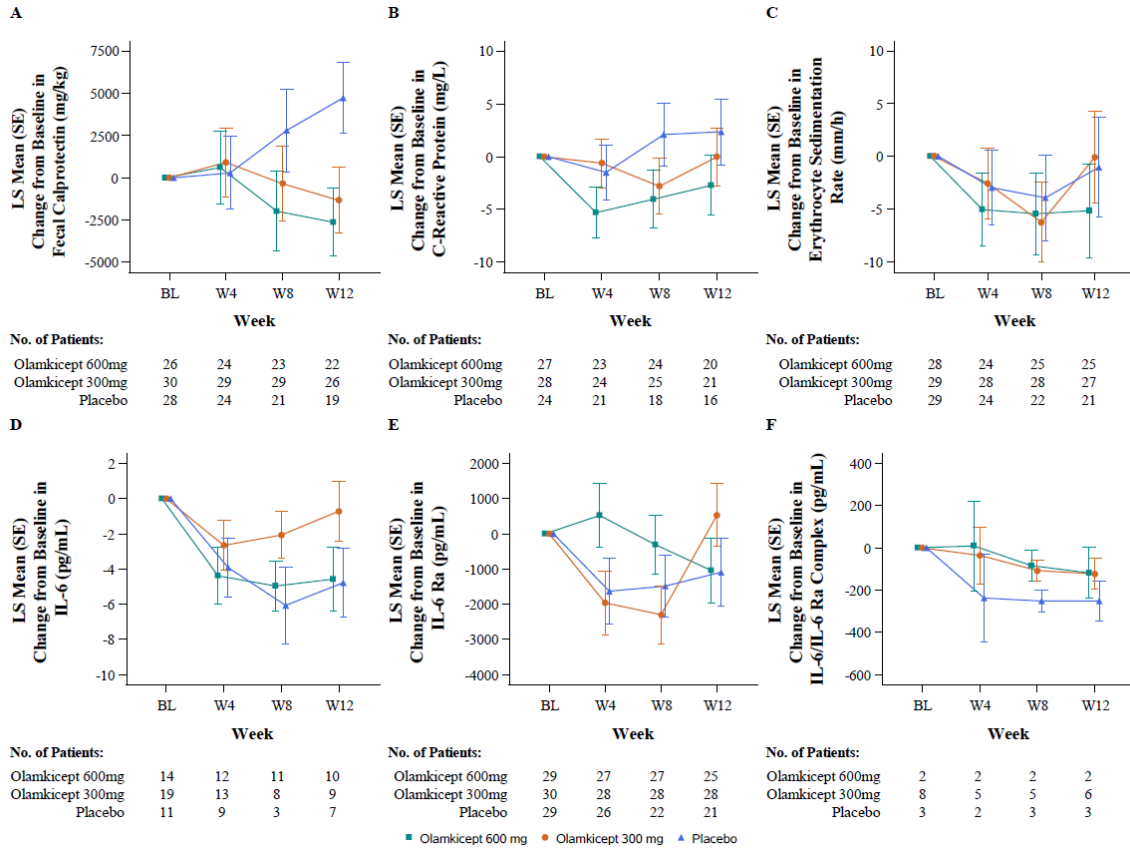
**eFigure 1. Study Schema**



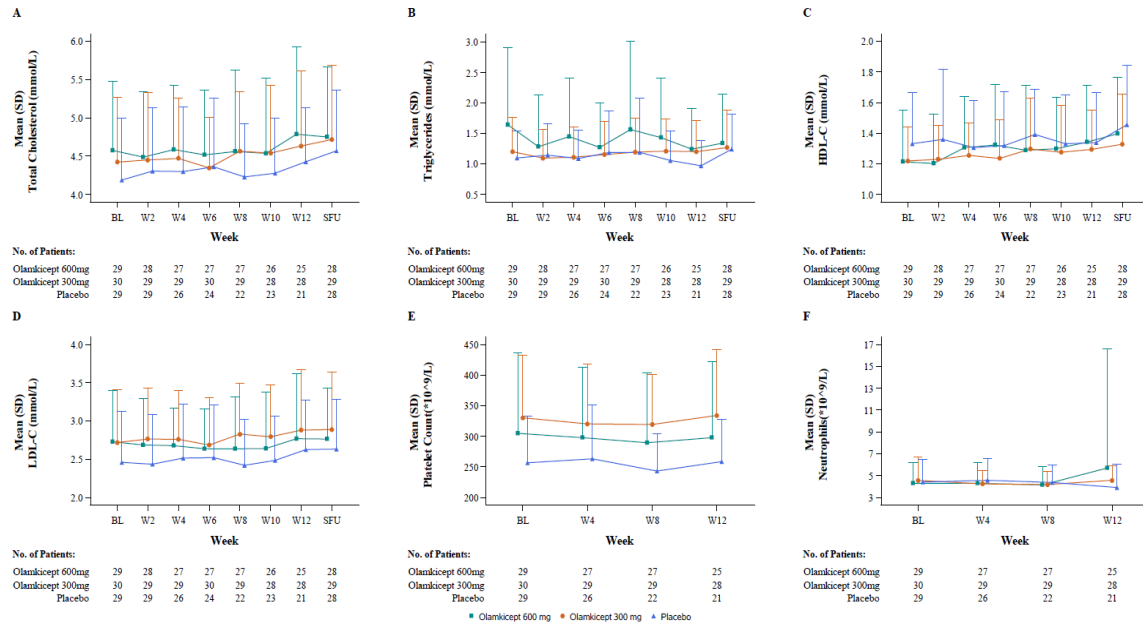
**eFigure 2. Efficacy of Olamkicept 600 mg and Placebo by Subgroups.**



**eFigure 3. Change from Baseline in Biomarkers Over Time**



**eFigure 4. Lipid Profiles, Platelet and Neutrophil Count Over Time**





**eFigure 5. Olamkicept Plasma Concentrations Over Time**

