# Effects of the Oral SYK Inhibitor, Fostamatinib (R788), on Health-Related Quality of Life in a Phase II Study of Active Rheumatoid Arthritis

Sunday, November 6, 2011: 9:00 AM-6:00 PM

Hall F2 - Poster Hall (McCormick Place West)

**Michael E. Weinblatt**[1], Arthur Kavanaugh[2], Mark C. Genovese[3], David A. Jones[4], Theresa K. Musser[5], Elliott B. Grossbard[5] and Daniel B. Magilavy[5], [1]Department of Medicine, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, MA, [2]University of California San Diego, San Diego, CA, [3]Stanford University, Palo Alto, CA, [4]AstraZeneca, Macclesfield, United Kingdom, [5]Rigel Pharmaceuticals, South San Francisco, CA

**Presentation Number:** 420

Background/Purpose: Fostamatinib (R788), an oral spleen tyrosine kinase inhibitor, met its primary signs and symptoms efficacy endpoint in a 6-mo, phase II, multicenter, randomized, double-blind, placebo (pbo)-controlled study in patients with rheumatoid arthritis (RA) who failed to respond to methotrexate (MTX) (NCT00665925).[1] This current analysis assessed the impact of fostamatinib on health-related quality of life (HRQL) measures in this phase II study.

Method: RA patients with prior long-term MTX treatment (n=457) were randomized to receive fostamatinib (150 mg qd [n=152]/100 mg bid [n=152]) or pbo (n=153), and background MTX. Patients self-administered the American College of Rheumatology (ACR) patient-reported outcomes (PRO) core set: pain (visual analog scale [VAS]); patient's global assessment (PtGA) of disease activity [VAS]; and physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]) at baseline, Week (Wk) 1, 2, 4, 6, 8, 12, and 24. HRQL (Short Form-36 [SF-36]) was assessed at baseline and Wk24, and fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-Fatigue]) was assessed at baseline, Wk12, and 24. The main analyses compared the mean changes from baseline between the treatment groups using a generalized linear model. A responder analysis of the proportion of patients achieving a minimum clinically important difference (MCID) in each treatment group used the Cochran Mantel-Haenszel test. All tests of statistical significance were 2-sided; $\alpha=0.05$.

Result: The study population had a duration of RA in excess of 8 years.[1] ACR responder rates were significant with fostamatinib 100 mg bid vs pbo (ACR20: 67% vs 35%; ACR50: 43% vs 19%; $p\leq0.001$). Fostamatinib 100 mg bid significantly improved pain, PtGA, and physical function at Wk1 vs pbo ($p\leq0.001$), and was sustained throughout the trial (24 wks) (Table). Also, by Wk24, a significantly greater proportion of patients receiving fostamatinib 100 mg bid achieved MCID for pain, PtGA, and physical function vs pbo (73.3% vs 62.0% [$p<0.05$] for pain; 74.0% vs 55.4% [$p\leq0.01$] for PtGA; 74.8% vs 55.8% [$p\leq0.01$]) for physical function). A significant improvement in the SF-36 physical component summary (PCS) was seen with fostamatinib 100 mg bid vs pbo at Wk24 ($p\leq0.001$, including for each SF-36 physical domain), as well as for fatigue ($p<0.05$) but not for the SF-36 mental component summary (Table). Moreover, at Wk24, a significantly greater proportion of patients (achieved the SF-36 PCS MCID with fostamatinib 100 mg bid vs pbo (72.9% vs 57.6%; $p\leq0.01$) and a numerically greater percentage for fatigue (59.8% vs 48.6%; $p\geq0.05$).

**Table. Results of the main PRO analyses**

| | | Mean change from baseline | | |
|---|---|---|---|---|
| | | Pbo | Fostamatinib | |
| | | | 150 mg qd | 100 mg bid |
| Pain | Wk 1 | 4.5 (20.7) | 10.3 (19.4)* | 15.4 (22.0)** |
| | Wk 24 | 17.8 (27.0) | 23.0 (24.1) | 31.3 (28.1)** |
| PtGA | Wk1 | 4.4 (20.2) | 8.3 (19.4) | 14.6 (23.3)** |
| | Wk24 | 16.7 (26.6) | 20.3 (25.3) | 29.1 (25.9)** |
| Physical Function | Wk1 | 0.06 (0.41) | 0.24 (0.43)** | 0.22 (0.39)** |
| | Wk24 | 0.34 (0.67) | 0.54 (0.66)* | 0.65 (0.74)** |
| **Other PROs** | | | | |
| SF-36 physical component summary | Wk24 | 4.9 (8.5) | 5.9 (9.0) | 8.5 (8.7)** |
| SF-36 mental component summary | Wk24 | 3.7 (10.7) | 2.0 (10.7) | 4.0 (10.5) |
| FACIT-Fatigue | Wk24 | 4.5 (9.8) | 5.7 (10.3) | 7.4 (10.9)* |

Data are mean (SD). Difference from pbo: *p<0.05; **p≤0.001.

PRO, patient-reported outcome; ACR, American College of Rheumatology; PtGA, patient's global assessment; HAQ-DI, Health Assessment Questionnaire-Disability Index; SF-36, Short Form-36; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; SD, standard deviation; pbo, placebo.

Conclusion: In this phase II study, 100 mg bid fostamatinib significantly improved HRQL outcomes including physical function, pain, fatigue, and overall physical health status. Phase III clinical trials of fostamatinib in RA are in progress.

**Reference**

1. Weinblatt ME, et al. *N Engl J Med.* 2010;363:1303–1312.

**Keywords:** Health Assessment Questionnaire, kinase and rheumatoid arthritis (RA)

**Disclosure: M. E. Weinblatt**, Rigel Pharmaceuticals, 5, AstraZeneca, 5 ; **A. Kavanaugh**, Rigel Pharma, 5 ; **M. C. Genovese**, Rigel Pharma, 2, Rigel Pharma, 5, AstraZeneca, 2, AstraZeneca, 5 ; **D. A. Jones**, AstraZeneca, 1, AstraZeneca, 3 ; **T. K. Musser**, Rigel Pharma, 3 ; **E. B. Grossbard**, Rigel Pharma, 1, Rigel Pharma, 3 ; **D. B. Magilavy**, Rigel Pharma, 3 .