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SAT0187 SAFETY, PHARMACOKINETICS AND EFFICACY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN A FIRST-IN-PATIENT PHASE 1/2 STUDY IN RHEUMATOID ARTHRITIS; ADDTIONAL DATA OF 400 MG COHORT

Y. Tanaka[1], T. Takeuchi[2], H. Umehara[3], T. Nanki[4], N. Yasuda[5], F. Tago[6], Y. Kitahara[6], M. Kawakubo[6], S. Hojo[6], T. Kawano[5], T. Imai[5]. *[1]University of Occupational and Environmental Health, Japan, Kitakyushu; [2]Keio University, Tokyo; [3]Division of Rheumatology and Immunology, Nagahama City Hospital, Shiga; [4]School of Medicine, Faculty of Medicine, Toho University, Tokyo; [5]KAN Research Institute, Inc., Kobe; [6]EISAI Co. Ltd., Tokyo, Japan*

Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. Accumulating evidence is telling that FKN-CX3CR1 axis plays a pivotal role in leukocyte/lymphocyte accumulation in inflamed tissues in RA[1]. Last year, we presented an interim report (up to 200 mg cohort) of Phase 1/2 study of E6011, a novel humanized anti-FKN monoclonal antibody, for active Japanese RA patients[2].

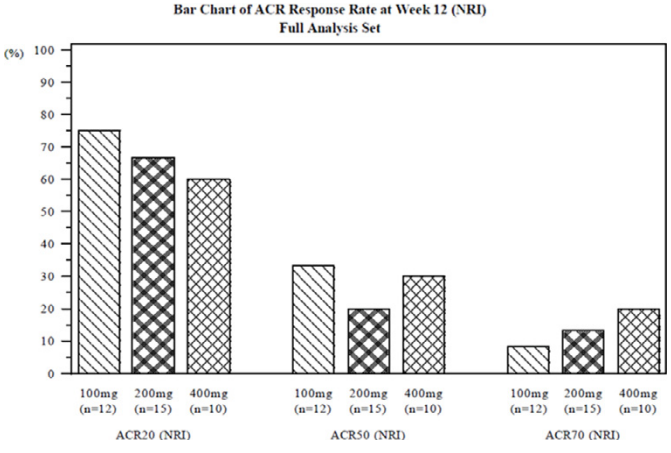
Objectives: To evaluate safety, pharmacokinetics and efficacy of E6011 with the dosage up to 400 mg in a Phase 1/2, open-label, multiple ascending dose study in RA patients (NCT02196558).

Methods: Active RA patients with inadequate response (IR) to MTX or TNF inhibitors (TNFi) were received 7 consecutive doses (subcutaneous) of E6011 at week 0, 1, 2 and thereafter every 2 weeks up to week 10. The safety, pharmacokinetics and efficacy up to week 12 were evaluated.

Results: Twelve, 15 and 10 subjects were enrolled in the cohort of 100, 200 and 400 mg dosage, respectively, in total 37 subjects received repeated subcutaneous (SC) administrations of E6011. As a result, repeated dose of E6011 was found safe and well tolerated. The incidence of adverse event (AE), treatment-related AE and serious AE were 56.8%, 29.7% and 5.4%, respectively. AEs occurring in ≥2 subjects were nasopharyngitis, Injection site erythema, headache and oropharyngeal pain, among which there were no severe AEs, serious infections and deaths. No significant differences were observed in the incidence or severity of AEs across the cohorts.

After starting multiple SC injection of E6011, serum E6011 concentration reached steady-state at week 2, and its level was maintained up to week 12 in all cohorts. Clinical outcome was also available in the study in which response rates of ACR20, 50 and 70 at week 12 calculated using the non-responder imputation (NRI) were 75.0%, 33.3%, 8.3% in 100 mg cohort, 66.7%, 20.0%, 13.3% in 200 mg cohort and 60.0%, 30.0%, 20.0% in 400 mg cohort, respectively. The percentage of patients categorized "good response" with the EULAR response criteria at week 12 (NRI) were 16.7% in 100 mg cohort, 20% in 200 mg cohort and 40% in 400 mg cohort.

Conclusions: E6011 was safe and well tolerated, and the study demonstrated a promising efficacy of E6011 in active RA patients with MTX- or TNFi-IR. The results obtained suggest that a novel approach to target FKN/CX3CR1 interaction will be clinically beneficial for RA, and support to conduct phase 2 clinical trials in which the efficacy and safety should be confirmed in a placebo controled double-blind manner.



References:

[1] Nanki T. Arthritis Rheum. 2002; 46(11):2878–83.
[2] Tanaka Y, et al., EULAR Congress 2016, Poster Number FRI0236.

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SAT0188 FIRST-LINE TREATMENT PATTERNS OF PATIENTS WITH RHEUMATOID ARTHRITIS WHO ARE ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY POSITIVE VERSUS NEGATIVE

K. Price[1], Y. Doleh[1], M. Eaddy[2], A. Ogbonnaya[2], H.-C. Shih[2], H. Ahmad[1], L. Lamerato[3], A. Szymialis[1]. *[1]Bristol-Myers Squibb, Princeton; [2]Xcenda, LLC, Palm Harbor; [3]Henry Ford Health System, Detroit, United States*

Background: Patients with RA who are at a higher risk for progressive and destructive arthritis could be identified using anti-cyclic citrullinated peptide (anti-CCP) levels.[1] Treatment guidelines recommend the use of non-biologic DMARDs as initial treatment in RA; but, if warranted, biologic (b)DMARDs could be considered in early treatment of RA.[2] Real-world data describing treatment patterns based on anti-CCP designations are limited.

Objectives: This study evaluated treatment patterns of patients with RA who are anti-CCP positive (+) or negative (–).

Methods: This retrospective study was based on electronic medical record (EMR) data with a supplemental chart review from a large integrated delivery system. Patients newly diagnosed with RA (International Classification of Diseases, Ninth Revision, Clinical Modification diagnosis code 714.0x) were identified between 1 January 2009 and 31 December 2014. The first RA diagnosis date was designated as the index date. Patients were required to have 12 months of continuous activity in the EMR (6 months pre- and 6 months post-index). Based on the baseline anti-CCP test results, patients were categorized as anti-CCP+ (≥7.0 U) or anti-CCP– (<7.0 U). First-line therapy (time to treatment initiation, treatment regimen, treatment changes and response to treatment) was evaluated in the post-index period. Response to treatment was determined based on physicians' notes.

Results: Overall, 217 anti-CCP+ and 191 anti-CCP– patients with RA were included in this study. A higher proportion of anti-CCP+ (153, 70.5%) than anti-CCP– patients (44, 23.0%; p<0.0001) initiated treatment, generally within 1 month after diagnosis (anti-CCP+, mean [SD]: 31.1 [42.1] days and anti-CCP–, 28.1 [37.4] days; p=0.6538). MTX was most commonly used as first-line therapy. More anti-CCP+ than anti-CCP– patients received MTX (73.2 vs 56.8%; p=0.0374), while more anti-CCP– than anti-CCP+ patients received hydroxychloroquine (31.8 vs 13.1%; p=0.0037). Only three anti-CCP+ and no anti-CCP– patients were treated with a bDMARD. Response to treatment was similar between the cohorts (p=0.2444); 22.9% of anti-CCP+ and 18.2% of anti-CCP– patients had a complete response to the first-line therapy, and 33.3% of anti-CCP+ and 25.0% of anti-CCP– patients had a partial response to the first-line therapy. Treatment change, however, significantly differed between the two cohorts (p=0.0058); 11.1 and 9.1% of patients discontinued, 9.8 and 9.1% of patients switched, and 3.9 and 9.1% of patients augmented in the anti-CCP+ and anti-CCP– cohorts, respectively. Treatment changes occurred approximately 3 months after treatment initiation (anti-CCP+, 82.0 [49.7] days and anti-CCP–, 83.8 [52.7] days; p=0.9178).

Conclusions: After diagnosis of RA, patients who are anti-CCP+ were more likely to start therapy, indicating that physicians were more aggressive in treating this cohort. Patients were treated according to guidelines with non-biologic DMARDs, predominantly MTX. Patterns of treatment change differed between the cohorts; however, treatment response was similar with a complete response rate of 20%.

References:

[1] Singh JA, et al. Arthritis Rheumatol 2016;68:1–26.
[2] Niewold TB, et al. QJM 2007;100:193–201.