SAT0088

COMPARISON OF THE INITIAL DIAGNOSTIC FINDINGS AND ONSET FACTORS OF RHEUMATOID ARTHRITIS (RA) IN ELDERLY ONSET RA AND ADULT ONSET RA BY MULTICENTER COHORT – ARE THERE ANY DIFFERENCES OF ONSET FACTORS? –

Keiko Funahashi¹, Tsukasa Matsubara², Esuke Shono³, Motohiro Oribe⁴, Keisuke Hashimoto⁵, Akira Sagawa⁶, Tamami Yoshitama⁷, Takeshi Mitsuka⁸, Tomohiko Yoshida⁹, Atsuko Imai¹⁰, Nobuaki Miyake¹¹, Kazuyasu Ushio¹², Izumihara Tomomaro¹³, Tsuru Tomomi¹⁴, Yosuke Nishioka¹⁵, Shigeto Kiyokawa¹⁶, Norihiro Nishimoto¹⁷. ¹Matsubara Mayflower Hospital, Clinical research, Kato, Japan; ²Matsubara Mayflower Hospital, Rheumatology, Kato, Japan; ³Shono Rheumatism clinic, Fukuoka, Japan; ⁴Oribe Rheumatology clinic, Oita, Japan; ⁵Hashimoto Rheumatology clinic, Kobe, Japan; ⁶Sagawa Akira Rheumatic clinic, Sapporo, Japan; ⁷Yoshitama rheumatology clinic, Kirishima, Japan; ⁸Mitsuka clinic, Narashino, Japan; ⁹Yoshida clinic, Setagaya-ku, Japan; ¹⁰Ichibancho Rheumatology clinic, Matsuyama, Japan; ¹¹Miyake clinic, Shizuoka, Japan; ¹²Ushio clinic, Osaka, Japan; ¹³Izumihara rheumatology clinic, Kagoshima, Japan; ¹⁴PS clinic, Fukuoka, Japan; ¹⁵Nishioka memorial central clinic, Shima, Japan; ¹⁶Fujimori clinic, Hachioji, Japan; ¹⁷Osaka Rheumatology clinic, Osaka, Japan

Background: In recent years, it has been reported that elderly onset RA (EORA) is a pathology different from that adult RA (AORA) ¹⁾. It has been reported that RA is due to genetic background, and many other factors. However it is not clear whether EORA and AORA share onset factors.

Objectives: We compared the initial diagnostic finding of EORA and AORA patients who were diagnosed by RA specialist at their own hospital. We also compared the presence or absence of the onset factors between EORA and AORA.

Methods: 1185 patients at 18 facilities who were initially diagnosed with RA were included. EORA (n=398) was defined by disease onset at over 60 years and AORA (n=732) was defined by disease onset from 16 to 59 years. We compared blood examination, clinical findings, presence of bone erosion, gender, age, and background factors pre-onset (family history, history of smoking/operation, presence of periodontal disease/gynecological diseases/digestive system diseases) between EORA and AORA. Clinical findings were analyzed with Mann-Whitney U-test and frequency of pre-onset history were analyzed by 2 × 2 Chi square test.

Results: The average age of EORA and AORA were 72 years and 54 years old. The ratio of female was 75% in EORA, but 84% in AORA, a significant difference (P<0.01). The average values of CRP (ug/ml) were 2.0 in EORA, but it is 1.3 in AORA, significantly lower (P<0.001). Also ESR (mm/h) and MMP-3 (ng/ml) of EORA were 46 and 83, whereas those of AORA were 36 and 29 significant as CRP. On the other hand, TJC, SJC, PaGA and PhGA were not significantly different.

We also compared the prevalence of onset factors between EORA and AORA. There was no clinical significant difference in smoking history and gynecological conditions. The presence rate of stress and family history in AORA were 71% and 38%, whereas that in EORA was 54% and 26%, significantly lower (P<0.001). On the other hand, the presence rate of history of gastrointestinal disease, periodontal disease and operation history in AORA were 43%, 36% and 40%, but those in EORA were 49%, 46% and 52%, significantly higher (P<0.01).

As in previous reports²⁾, the ratio of men and the inflammation values in EORA were significantly higher, but there was no difference in SJC, PaGA, and PhGA. This study verified in Japanese EORA as the other reports. There were differences in the presence rate of onset factors between the two groups, while EORA had many external factors such as surgical history, whereas AORA had genetic factors and stress in their backgrounds. Regarding the presence of bone erosion, it was caused by the period from the appearance of the symptoms until the diagnosis and was unrelated to age at onset.

Conclusion: This study suggests that the onset of EORA is more likely to be attributed to external factors than genetic factors.

REFERENCES

- 1) G.Bajocchi et.al, Clin Exp Rheumatol 2000; 18(suppl.20), S49-50
- 2) DeJaco.C et.al., Arthritis Care & Res 2013; 65, 304-308

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SAT0089

SAFETY AND EFFICACY OF LY3337641, A BRUTON'S TYROSINE KINASE INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 2-PART PHASE 2 STUDY

Mark C. Genovese¹, Alberto Spindler², Akira Sagawa³, Won Park⁴, Anna Dudek⁵, Alan Kivitz⁶, Jeannie Chao⁷, Lai Shan (Melanie) Chan⁷, William Barchuk⁷, Ajay Nirula⁷. ¹Stanford Univ Medical Center, Palo Alto, United States of America; ²Centro Medico Privado de Reumatologia, Tucuman, Argentina; ³Sagawa Akira Rheumatology Clinic, Sapporo, Japan; ⁴Inha University Hospital, Incheon, Korea, Rep. of (South Korea); ⁵AMED Medical Center, Kalisz, Poland; ⁶Altoona Center for Clinical Research, Uncansville, United States of America; ⁷Eli Lilly and Company, Indianapolis, United States of America

Background: LY3337641 is an irreversible covalent inhibitor of Bruton's tyrosine kinase (BTK), a key signaling molecule in the B-cell-receptor and Fc-receptor pathways and mediator of B-cell- and myeloid-cell-dependent inflammatory arthritis.^{1,2} RA-JUVENATE was a multicenter, randomized, double-blind, placebo-controlled, 2-part Phase 2 trial with long-term extension (LTE) in adult patients (pts) with rheumatoid arthritis (RA).

Objectives: The objective of this analysis is to present the primary results from Part B of the study.

Methods: In Part A, 36 pts with at least mildly active RA were randomized 1:1:1:1 to receive oral LY3337641 5, 10, or 30 mg or placebo (PBO) once daily (QD) for 4 weeks (wks) with the primary objective of safety and tolerability. There were no safety signals to preclude moving to Part B; pts in Part A were not eligible to participate in Part B. In Part B, 250 pts with active moderate to severe RA were randomized 1:1:1:1 receive oral LY3337641 5 (N=63), 10 (N=62), or 30 mg (N=63) or PBO (N=62) QD for 12 wks. The primary endpoint of Part B was the proportion of pts achieving ≥20% improvement in American College of Rheumatology criteria (ACR20) at Wk 12. A logistic regression model was used to compare each LY3337641 dose to PBO for primary and secondary endpoints. Nonresponder imputation was used to impute missing data. After an interim analysis showed a low likelihood of demonstrating significant efficacy at the conclusion of the trial, the sponsor discontinued Part B of the study, including the LTE. Efficacy results (except analysis of low disease activity and remission) included pts who completed through Wk 12 at the time of study discontinuation; safety was results included all pts who received ≥1 dose of study drug.

Results: Of the 250 pts (mean age 51.0 years; 86.4% female; mean disease duration 11.2 years) randomized in Part B, 189 (75.6%) completed 12 weeks and 180 entered the LTE (72.0%); 61 discontinued study treatment in Part B.. The most common reasons for discontinuation were study terminated by sponsor (27 [10.8%]), withdrawal by subject (8 [3.2%]), adverse event (8 [3.2%]), and lack of efficacy (4 [1.6%]). There was no statistically significant difference in the ACR20 response between any treatment group of LY3337641 and PBO at Wk 12 (p>0.05 for all comparisons; Table); a high placebo rate was noted, but no underlying reason was identified in post hoc analyses. There were 5 serious adverse events: 2 in PBO pts (joint dislocation and cholecystitis acute) and 3 in 30-mg pts (foot fracture, multiple injuries, and venous thrombosis). There was 1 death (30-mg pt, multiple injuries after 4-story fall down elevator shaft). There were no safety findings that precluded continuation of the study.

Conclusion: Although there were no safety findings that precluded continuation of the study, the study sponsor determined that the observed benefit-risk profile of LY3337641 in the study did not warrant its continuation.