

Selection of Abatacept for Patients with Rheumatoid Arthritis Aged 70 Years or Older

Hiraku Kikuchi^{1*}, Wataru Shimada¹, Sei Mihira¹, Jin Nakajima¹ and Taeko Yumoto²

¹Department of Orthopaedic Surgery, Sakai Sakibana Hospital, Japan

²Department of Internal medicine, Sakai Sakibana Hospital, Japan

***Corresponding Author:** Hiraku Kikuchi, Department of Orthopedic Surgery, Sakai Sakibana Hospital, Osaka, Japan.

Received: July 12, 2019; **Published:** July 18, 2019

Abstract

Aim: We prospectively selected abatacept for elderly patients with Japanese rheumatoid arthritis and investigated adverse effects that occurred during treatment.

Subject and Methods: Selection of abatacept for 54 patients with Japanese rheumatoid arthritis aged ≥ 70 years who had various complications.

Results and Discussions: After six months of this trial, the treatment duration was extended or on the dose was reduced because the treatment was effective in 32/54 (59.3%), continued without change in 15 (27.8%) patients, ineffective in seven (13.0%). Two severe rheumatoid arthritis were received anti-biotics for reversible pneumonia. No serious adverse reactions were observed. An important reason why abatacept exerted a good clinical effect and the duration of ABT treatment could be extended or the dose could be reduced is that Japanese people are thin.

Conclusion: To select of abatacept for elder Japanese rheumatoid arthritis were considerable treatment.

Keywords: Elderly Rheumatoid Arthritis; Abatacept; Body Mass Index; Methotrexate

Abbreviations

ERA: Elderly Rheumatoid Arthritis; ABT: Abatacept; BMI: Body Mass Index; MTX: Methotrexate; RA: Rheumatoid Arthritis

Introduction

Infection is a serious complication in Japanese patients with rheumatoid arthritis (RA), which is characterized by high frequencies of a thin body (decreased body mass index [BMI]), poor oral care, anemia, renal impairment, and pulmonary complications [1]. Moreover, for patients with RA with hepatitis B, etc. biological products are difficult to use, particularly methotrexate (MTX) [2]. In post-marketing surveillance, patients receiving abatacept (ABT; Orencia, Bristol-Myers Squibb Company) displayed fewer serious infections than those receiving other biological products, and the continuation rate of ABT was high in reports from actual clinical practice in Japan [3]. Among biological products, the efficacy of ABT without the concomitant use of MTX has been confirmed, and its dose can be reduced. Therefore, ABT is suitable for administration to elderly Japanese patients with RA with decreased renal function. Furthermore, according to its package insert, ABT can be used in patients with heart failure. We previously reported that there was no difference in the efficacy of ABT between elderly patients aged ≥ 75 years and those aged 65 - 74 years [4]. We also reported its efficacy in two patients with RA receiving

hemodialysis due to renal failure [5]. The Japanese insurance system allows the treatment of patients aged > 90 years for osteoporosis and other diseases and maintains the greatest healthy longevity in the world [6]. In this study, we prospectively selected ABT for elderly patients with RA and investigated infections that occurred during treatment.

Subjects and Methods

In 2018, treatment with ABT was selected for patients with RA aged ≥ 70 years in our hospital. Priority was given to the patient's understanding and willingness to undergo treatment. Those who provided consent were enrolled. During the study period, 72 patients with RA received ABT (1st line: 49 patients, 2nd line or later: 23 patients) and 54 subjects were aged ≥ 70 years (72 - 94 years old, four men and 50 women; 1st line: 46 patients; 2nd line or later: 8 patients). ABT was used alone in 37 patients, with MTX (dose: 2 - 8 mg/week) in nine patients, and with other disease-modifying antirheumatic drugs (leflunomide and so on) in eight patients, and it was administered intravenously or subcutaneously in 43 and 11 patients, respectively. Clinical evaluation was performed with regular blood biochemistry tests (for patients who continued receiving treatment for at least 6 months). However, because these patients were elderly, patient satisfaction was prioritized over disease activity, and the goal was to treat patients without causing complications. If a patient was satisfied more than once, the duration of ABT treatment was extended, the dose was reduced, or the concomitant drugs were adjusted.

Results and Discussion

Patient characteristics and treatment results

In the 54 patients with RA aged ≥ 70 years, the mean disease duration was 28 (1 - 60) years and the mean BMI was 21.1 (15.6 - 28.8) kg/m². There were two, four, eight and 40 patients in RA Stage 1, 2, 3 and 4, respectively. There were 10 patients in Class 1, 31 in Class 2, 11 in Class 3 and two in Class 4. Nineteen patients had previously undergone surgery. There were various complications, including renal dysfunction, hypertension, diabetes mellitus, and a history of pneumonia, and all patients received treatment for osteoporosis. Because ABT was preferentially selected, the proportion of patients who received it as the first-line drug was high (46/54, 85.2%). After ≥ 6 months of ABT administration in the 54 patients, the treatment duration was extended or the dose was reduced because the treatment was effective in 32 (59.3%) patients, treatment was continued without change in 15 (27.8%) patients, and treatment was discontinued because the treatment was ineffective in seven (13.0%) patients. Notably, discontinuation due to serious adverse reactions was not observed. During the study period, ABT administration was postponed for 1 - 2 weeks due to cold symptoms (if a patient had a fever of $\geq 38^\circ\text{C}$, abnormal respiratory sounds, or unusual cough or sputum, they came to the hospital and were reexamined) or other reasons in 8 (14.8%) patients, two of whom received treatment for pneumonia. After the pneumonia was cured, ABT treatment resumed as per the patients' requests.

Pneumonia cases

Case 1 involved a 74-year-old woman with RA, Stage 4 Class 2. Her BMI was 19.6 kg/m². The patient underwent total knee arthroplasty and bipolar hip prosthesis. She had interstitial pneumonia + goiter. Antibiotics had been used concomitantly, and ABT had been administered every 6 - 8 weeks and sometimes at longer intervals.

Case 2 involved a 78-year-old man with RA, Stage 4 Class 2. His BMI was 16.8 kg/m² and he was a smoker. After undergoing spinal instrumentation, ABT was administered every 6 weeks. He developed pneumonia and was hospitalized for treatment with antibiotics. Three months later, ABT was resumed at the patient's request.

A high proportion of Japanese patients with RA and patients aged ≥ 70 years who undergo surgery have poor renal function and nephrogenic anemia [1]. Low body weight and anemia increase the postoperative infection rate and accelerate the onset of complications [7]. In elderly patients, surgical intervention, such as artificial joint surgery and spinal surgery, is a major treatment method for RA and exerts a temporary systemic anti-inflammatory effect when damaged components are removed. The elderly patients are also vulnerable to pain. When undergoing surgery, they must have a good general condition during the perioperative period. Therefore, autologous blood

transfusion, which is immunologically excellent and safe, is accepted in Japan [8]. The patient's motivation is an important positive factor in preventing frailty. When ABT was selected for elderly patients with RA aged ≥ 70 years, the treatment duration was extended or the dose was reduced because of patient satisfaction in 59.3% of the patients. In 13.0% of the patients, ABT treatment was discontinued. In our previous report of Japanese patients with RA aged ≥ 65 years (BMI: 14.6 - 32.0 kg/m²; mean, 21.7 kg/m²), the ABT dose was halved in 32 of the 47 patients (68.1%) a year later, correlating with the results in this study [4]. Data from multicenter studies in actual clinical practice in Japan revealed that the continuation rates of tocilizumab (mean age when administered: 56.5 \pm 15.6 years) and ABT (mean age when administered: 63.1 \pm 13.4 years) were high, and ABT tended to be consciously selected for elderly patients [9]. Unlike patients with early RA or working patients for whom controlling disease activity is essential, the treatment of elderly patients with ABT emphasizes patient satisfaction. ABT treatment was also beneficial in terms of medical economics and was readily accepted by both patients and their families. An important reason why ABT exerted a good clinical effect and the duration of ABT treatment could be extended or the dose could be reduced is that Japanese people are thin [4,5]. Being thin helps maintain the effective concentration of ABT. ABT has a longer half-life (approximately 10 days) compared with other biological products, making it easier to extend its administration intervals [4]. ABT is not contraindicated in patients on dialysis or with heart failure, which is advantageous to elderly patients with complications [5].

Conclusion

When ABT was selected for patients with RA aged ≥ 70 years, the treatment duration was extended or the dose was reduced because of patient satisfaction in 59.3% of cases. No serious adverse reactions were observed.

Acknowledgements

Special thanks for the director general Dr. Keiji Inoue (Keijin group).

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Bibliography

1. Hiroaki Kasuga, *et al.* "Surgical status of patients with orthopedic disease based on the estimated glomerular filtration rate". *EC Orthopaedics* 4.1 (2016):450-452.
2. Japanese collage of Rheumatoid Arthritis. Guideline: Methotrexate treatment in Japan (2016).
3. Masayoshi Harigai, *et al.* "Postmarketing surveillance of the safety and effectiveness of abatacept in japanese patients with rheumatoid arthritis". *Modern Rheumatology* 26.4 (2016): 491-498.
4. Yasunori Itoh, *et al.* "Clinical effects of half-and full-dose abatacept are equivalent". *Journal of Indian Orthopaedic Rheumatology Association* 2.1 (2016): 33-40.
5. Jin Nakajima, *et al.* "Two cases of abatacept treatment for patients with rheumatoid arthritis on hemodialysis". *EC Orthopaedics* 6.1 (2017): 40-44.
6. Hiraku Kikuchi, *et al.* "A real-world pilot study on zoledronate-based treatment of osteoporosis in japanese women aged over 65 years including very advanced age". *EC Orthopaedics* 10.3 (2019): 153-156.
7. Jarge Manrique, *et al.* "Surgical site infection and transfusion rates are higher in underweight total knee arthroplasty patients". *Arthroplasty Today* 3.1 (2017): 57-60.

8. Hiraku Kikuchi, *et al.* "Erythropoietin administration for preoperative autologous blood donation from patients scheduled for orthopedic surgery". *Japanese Journal of Rheumatology* 8.2 (1998): 139-145.
9. Kousuke Ebina, *et al.* "Drug tolerability and reasons for discontinuation of seven biologics in elderly patients with rheumatoid arthritis -The ANSWER cohort study". *PLoS One* 15 (2018): e0194130.

Volume 10 Issue 8 August 2019

©All rights reserved by Hiraku Kikuchi, *et al.*