Effectiveness and safety of secukinumab in Chinese patients with plaque psoriasis in a clinical practice setting: a pilot study

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To the Editor: Psoriasis is a chronic, recurrent, systemic, immune-mediated inflammatory disease that mainly affects the skin, nails, and joints. Plaque psoriasis is the most common type of psoriasis, accounting for more than 80% to 90% of all cases. Secukinumab, a human IgG monoclonal antibody that antagonizes interleukin 17A (IL-17A), was approved by the US Food and Drug Administration in 2015 to treat moderate-to-severe plaque psoriasis. A Chinese multicenter, double-blind, placebo-controlled phase III randomized clinical trial (RCT) demonstrated excellent efficacy and safety.[1] Secukinumab has been available on the Chinese market since May 2019, with a recommended dose of 300 mg. It is well-known that RCTs, due to their rigorous, normalized design schemes, cannot fully reflect what happens in clinical practice settings. The concept of the “efficacy-effectiveness gap” was also introduced,[3] which supports the importance of real-world study. Here, we retrospectively summarized all the inpatients with plaque psoriasis who were treated with secukinumab at Peking University Third Hospital from June to December 2019. General information (sex, age, weight, body mass index, etc.) and clinical features (disease duration, family history, comorbidities, laboratory tests, previous treatments, concomitant treatments, etc.) were collected from clinical records. The psoriasis area severity index (PASI), body surface area (BSA), dermatology life quality index (DLQI), psoriasis scalp severity index (PSSI), nail psoriasis severity index (NAPSI), and palmoplantar psoriasis area and severity index (ppPASI) were also recorded. Safety was assessed by adverse events, and special cases that met the exclusion criteria of clinical trials were monitored accordingly. Statistical analysis was performed with SPSS 26.0 software (IBM Corp, Armonk, NY, USA). This study was approved by the Ethical Committee of Peking University Third Hospital (No. 329-01).

Twenty inpatients started secukinumab treatment during the half-year study period. Twelve (60.0%) did not meet the eligibility criteria for the phase III RCT: ten patients (10/20) did not meet the inclusion criteria, one patient had concurrent hepatitis B virus (HBV)/hepatitis C virus (HCV) infection, and one patient had pre-existing idiopathic thrombocytopenia. General patient characteristics were summarized and compared with those in the phase III RCT,[1] and a lower severity was noted in our patients [Supplementary Table 1, http://links.lww.com/CM9/A403]. All patients followed the standard regimen with secukinumab (300 mg) administered subcutaneously once weekly for four weeks and then once every four weeks. During the treatment, four patients used concomitant topical treatments intermittently; two used calcipotriol, and two used calcipotriol betamethasone ointment.

The percentages of PASI 75/90/100 responders, BSA involvement ≤3%, and BSA involvement ≤1% responders, and DLQI ≤5 and DLQI 0/1 responders are shown in Figure 1A–C. The PASI scores were 8.40 (3.25–11.85), 3.65 (1.38–5.75), and 0.50 (0.0–1.50) at weeks 2, 4, and 12, respectively. All reached statistical significance compared with the baseline PASI of 11.10 (6.00–17.03) (Zweek 2 = –3.622, P < 0.001; Zweek 4 = –2.803, P = 0.005; Zweek 12 = –3.464, P = 0.001). At week 2, the PASI 75/90/100 responses were 11.8%/5.9%/0%. At week 12, they reached 87.5%, 68.8%, and 43.8%, respectively. The median time to achieve a PASI 75 response was 8 weeks. Considering all patients, 87.5% achieved an absolute PASI ≤3, and the PASI score improvement was 95.74% (84.63–100.00%) at week 12.

There was no data available concerning BSA or DLQI in the Chinese phase III RCT. An acceptable response of BSA ≤3% or a target response of BSA ≤1% was considered to be a more practical instrument for real-world application. In our study, the BSA values were 21.5% (6.3%–32.8%), 10.3% (6.1%–17.1%), and 1.0% (0.0%–2.8%) at weeks 2, 4, and 12, respectively. BSA slightly improved at week 2 but did not reach statistical significance (Zweek 2 = –1.663, P = 0.096);
however, at weeks 4 and 12, BSA was significantly reduced compared with the baseline BSA of 20.3% (7.6–31.3%) ($Z_{week\ 4} = -2.810, P = 0.005; \ Z_{week\ 12} = -3.408, P = 0.001$). At week 2, the BSA ≤ 3%/BSA ≤ 1% responses were 11.8%/5.9%. At week 12, they reached 81.3%, and 62.5%, respectively.

Achieving an improvement of 4 points or more in the DLQI was proposed as an assessment criterion in the British guidelines. A DLQI score of less than 5 (DLQI < 5) was one of the parameters in the decision algorithms for treatment in the French guidelines, and a DLQI of 0/1 was considered to indicate that there was no impact of psoriasis on quality of life. In our study, the DLQI scores were 7.0 (4.3–10.8), 4.0 (2.0–9.0), and 0 (0–4.0) at weeks 2, 4, and 12, respectively. All improved significantly compared with the baseline DLQI of 11.0 (8.0–21.0) ($Z_{week\ 2} = -2.692, P = 0.007; \ Z_{week\ 4} = -2.032, P = 0.042; \ Z_{week\ 12} = -2.913, P = 0.004$). At week 2, 50% of patients had a reduction of ≥ 4 points compared to the baseline DLQI scores, and 25% and 12.5% of patients achieved a DLQI < 5 and DLQI 0/1, respectively. At week 12, a reduction of ≥ 4 points, DLQI < 5, and DLQI 0/1 were achieved in 60%, 80%, and 66.7% of patients, respectively.

The results were comparable to those of the phase III RCT in China.[1] In addition, in line with the superior efficacy demonstrated in Chinese patients in clinical trials, our data also supported superior effectiveness in a real-life clinical setting (PASI 75/90/100: 87.5%/68.8%/43.8% vs. 72%/50%/36%, DLQI 0/1: 66.7% vs. 57%, compared with the results of a meta-analysis including 43 studies conducted in other countries and regions[13]). In the Chinese results, the lower proportion of overweight or obese patients and the higher proportion of biologic-naïve patients might be the reasons for the superior efficacy and effectiveness.

The efficacy of secukinumab in difficult-to-treat locations, such as the scalp, nail, and palmoplantar regions, was not reported in the Chinese phase III RCT. In our study, 13 patients had scalp psoriasis. The PSSI scores were 1.5 (0–8.0), 2.0 (0–21.0), and 0 (0–3.3) at weeks 2, 4, and 12, respectively. All reached statistical significance compared with the baseline PSSI of 5.0 (3.0, 12.5) ($Z_{week\ 2} = -2.692, P = 0.007; \ Z_{week\ 4} = -2.032, P = 0.042; \ Z_{week\ 12} = -2.913, P = 0.004$). At week 12, the PSSI 75/90/100 responses were 83.3%, 75.0%, and 66.7%, respectively [Figure 1D and 1G]. In three patients with fingernail psoriasis, NAPSI improved by 100.0%, 53.3%, and 28.6% [Figure 1E and 1H]. Only one patient had toenail psoriasis, and achieved a 45.0% improvement in NAPSI. Only one patient had hyperkeratotic palmoplantar psoriasis, with a baseline ppPASI of 16.6, and this was completely cleared at week 8 (ppPASI 100).

During the 12-week secukinumab treatment schedule, nine patients (45.0%) had at least one adverse event. The most common adverse events were upper respiratory tract infections (four cases), tinea pedis (two cases), and facial dermatitis (two cases). No serious adverse events occurred, and no patient had to discontinue drug treatment due to adverse events.

One special case was a patient with a concurrent HBV/HCV infection. He was positive for hepatitis C virus antibody (HCV-IgM) and hepatitis B virus core antibody (HBcAb) at baseline, and HBsAg, HBV-DNA, and HCV-RNA were negative. He did not show virus reactivation during the 48 weeks of secukinumab treatment without antiviral
prophylaxis. Although virus reactivation was not found in our patient, it has been reported that without antiviral prophylaxis, 1 of 11 HBsAg-negative/HBeAb-positive/HBsAb-negative patients, and one of nine patients with HCV infection developed HBV reactivation and enhanced replication of HCV with hepatitis after three months of secukinumab therapy, and both were clinically asymptomatic at the time of reactivation.[4] The viral load and transaminase should be closely monitored.

Another special case was a patient with idiopathic thrombocytopenia. The platelet counts increased from $52 \times 10^9/L$ at baseline to $84 \times 10^9/L$ at week 12, and remained at $82 \times 10^9/L$ at week 32 [Figure 1F]. To our knowledge, there have been no previous reports concerning secukinumab (or any other biologic) treatment in patients with psoriasis and pre-existing idiopathic thrombocytopenia. Other occurrences of transient thrombocytopenia during biologic treatment with normal platelet count at baseline were reported,[5] with adalimumab as the probable cause. In this case, considering that the face and nails were affected, and taking into account obesity (body mass index = 30 kg/m²), hypertension, and the patient’s intentions and expectations, the decision to initiate secukinumab treatment was made after discussion with the patient and consultation with hematologists. PASI 100 was achieved at week 8 and was sustained during the 32-week follow-up. A slightly increasing platelet count over time even suggested a possible co-benefit. Fully understanding the effect of secukinumab on platelet count in patients with idiopathic thrombocytopenia requires long-term follow-up studies with larger sample sizes.

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**Conflicts of interest**

None.

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