Janus Kinase Inhibitors against Other Biological Treatments in Alopecia Areata

To the Editor:

Because of complicated cells interactions between activated T cells and hair follicles in patients with alopecia areata (AA), the treatment of this disease still remained a controversial issue. Despite the high global rate of AA, there is no U.S. food and drug administration (FDA) approved biological drug for treating this disease. Several studies were shown the dominancy of T helper (Th1) cells responses, especially interferon-gamma (IFN-γ). At the first seen, this disease is thought to be a Th1 dominant one and inhibition of Th1 cells should be a possible treatment. However, several other cell responses could be confused with Th1 responses. For example, IFN-γ or interleukin (IL)-12, which are critical players in Th1 responses could be secreted via different pathways and several cell types. Thus, two things should be considered. Firstly, inducing the similar responses to the Th1 cells via other known and unknown cells may be occurred. Secondly, Th1 cells may be promoted with other cells responses, but increased number of Th1 cells does not necessarily mean involvement of these cells in AA development. These possible occurrences could lead to the Th1 phenotype in AA patients. Thus, inhibition of Th1 cells differentiation may not necessarily result in disease remission. It was reported that multiple sclerosis (MS) patients, who show the Th1 and Th17 phenotypes, did not benefit from targeting differentiation of these cells via ustekinumab, which is known as the anti-IL-12/23p40 monoclonal antibody [1]. That study boosts the idea that targeting the dominant cells may not to improve the disease.

Different antitumour necrosis factor (TNF) inhibitors, such as etanercept and infliximab, anti-CD11a agent (efalizumab) and anti-CD2 agent (alefacept) have been tested in patients with AA. However, the majority of them did not demonstrate the favourable outcomes. Additionally, there are some studies associated with the AA development, followed by etanercept and infliximab therapies [2, 3]. Despite the ability of ustekinumab to impairment of Th1 and Th17 responses via inhibition of IL-12 and IL-23, AA could be developed parallel to improvement of psoriasis during ustekinumab therapy [4]. Thus, the idea of Th1 involvement in pathogenesis of AA could be revised. It is also possible that those conditions are only similar to the AA, but are considered as the AA, mistakenly.

Recently, Xing et al. [5] found that cytotoxic CD8(+) NKG2D(+) T cells are responsible for AA development. Thus, the elevated level of IFN-γ could be associated with these cells, instead of Th1 cells. Indeed, IFN-γ is produced by the CD8(+)NKG2D(+) T cells, which could explain the lack of ustekinumab efficiency to treating AA disease. It was also shown that the use of Janus kinase (JAK) inhibitors could reverse symptoms of the AA in mice as well as three patients, who were treated with ruxolitinib, an JAK1/2 inhibitor [5]. Considering the blockage of several signalling pathways, which are critical for immune responses by JAK inhibitors, this new emerged therapy in AA caused a hope to treating this disease. As the other attempts, it was reported that JAK inhibitors, including ruxolitinib and tofacitinib, which are JAK1/2 and JAK1/3, respectively, reversed alopecia universalis [6, 7]. Followed by these studies, baricitinib, a JAK1/2 inhibitor was introduced as the effective treatment of AA [8]. These results are implying to the high potential of JAK inhibitors to treating AA disease. Although there is no study on safety of these drugs in AA patients, no serious safety concern associated with the use of baricitinib was reported in rheumatoid arthritis and psoriasis patients [9, 10]. In addition to JAK inhibitors, fotolizumab, an anti-IFN-γ may be another novel biological treatment of AA, which needs for further studies, associated with its efficiency and safety in patients with AA.

References