DOI: 10.4274/turkderm.galenos.2022.83797
Turkderm-Turk Arch Dermatol Venereol 2022;56(Suppl 1):45-7

Certolizumab

Sertolizumab

Savaş Yaylı

Karadeniz Technical University Faculty of Medicine, Department of Dermatology and Venereology, Trabzon, Turkey

Abstract

Certolizumab is a Fab fragment of a humanized monoclonal antibody against tumor necrosis factor-alpha (TNF-α). Differing from the other TNF-α inhibitors due to the absence of Fc fragment and pegylation, it binds to both the soluble and transmembrane forms of TNF-α, creating a strong TNF-α blockage. Previously approved for psoriatic arthritis, certolizumab received another approval from FDA in 2018 for the treatment of moderate to severe chronic plaque psoriasis that does not respond to conventional systemic treatments or for which these treatments are contraindicated. Administered via subcutaneous injections, certolizumab also has a low-dose option for patients weighing less than 90 kg. Certolizumab is considered a safe biological drug that can be preferred during pregnancy and lactation.
Keywords: Certolizumab, TNF-α, psoriasis, pregnancy, lactation

Öz

Sertolizumab, tümör nekroz faktörü-alfa'ya (TNF-α) karşı humanize bir monoklonal antikorun Fab kısmından oluşur. Fc kısmının olmaması ve pegile oluşu ile diğer TNF-α inhibitörlerinden farklı olarak TNF-α'nın hem çözünür, hem de membrana bağlı formlarını bağlayarak kuvvetli bir TNF-α blokajı yapar. Daha öncesinde psoriatik artrit için onayı bulunan sertolizumab, 2018 yılında konvansiyonel sistemik tedavilere yanıt vermeyen veya bu tedavilerin kontrendike olduğu orta şiddette veya şiddetli kronik plak psoriasis tedavisi için FDA onayı almıştır. Subkütan enjeksiyon ile uygulanan sertolizumabın kilosu 90 kg altında olan hastalar için düşük doz seçeneği de bulunmaktadır. Sertolizumab gebelik süreci ve laktasyonda öncelikle tercih edilebilecek güvenli bir biyolojik ilaç olarak konumlandırılmaktadır.
Anahtar Kelimeler: Sertolizumab, TNF-α, psoriasis, gebelik, laktasyon

General information

Certolizumab is indicated for the treatment of moderate to severe chronic plaque psoriasis that does not respond to conventional systemic therapies or for which these therapies are contraindicated. Previously approved for psoriatic arthritis, certolizumab received in 2018 another approval for the treatment of psoriasis from the American Food and Drug Administration. Certolizumab is a Fab fragment of a humanized monoclonal antibody that is pegylated with polyethylene glycol to act against TNF-α.

Mechanism of action

Differing from the other TNF-α inhibitors due to the absence of Fc fragment and pegylation, certolizumab, in its monoclonal antibody structure, binds to both the soluble and transmembrane forms of TNF-α, which is a major proinflammatory cytokine in the pathogenesis of psoriasis, and creates a strong TNF-α blockage. The absence of Fc fragment prevents complement-mediated cytotoxicity and antibody-dependent cellular cytotoxicity reactions, and the fact that it does not bind to the Fc receptor renders placental transmission negligible. Pegylation, on the other hand,

Address for Correspondence/Yazışma Adresi: Savaş Yaylı MD, Karadeniz Technical University Faculty of Medicine, Department of Dermatology and Venereology, Trabzon, Turkey
E-mail: savasyayli@gmail.com **Received/Geliş Tarihi:** 07.02.2022 **Accepted/Kabul Tarihi:** 11.02.2022
ORCID: orcid.org/0000-0001-9402-940X

Cite this article as: Yaylı S. Certolizumab. Turkderm-Turk Arch Dermatol Venereol 2022;56(Suppl 1):45-7

Turkderm - Turk Arch Dermatol Venereol
2022;56(Suppl 1):45-7

prolongs the half-life of certolizumab in circulation to approximately 14 days[1,2].

Dosage/treatment scheme

Administered via subcutaneous injections, the recommended dose of certolizumab in patients with moderate to severe psoriasis is 400 mg every two weeks, which can be given in two 200 mg injections. Another option for patients weighing less than 90 kg is 400 mg at weeks 0, 2 and 4 and then 200 mg every other week.

Efficacy

The randomized, double-blind, placebo-controlled Phase 3 studies made on the efficacy and safety of certolizumab in chronic plaque psoriasis (CIMPASI1 and 2, CIMPACT) have found certolizumab superior to both placebo and etanercept[3,4].

In the study of Gottlieb et al.[3] reporting the common results of CIMPASI1 and 2, which included a total of 461 patients, certolizumab 200 mg and 400 mg administered every two weeks had statistically significantly higher efficacy than placebo and showed no new safety signal. In the combined analysis of this study, the PASI75 and PASI90 results of the certolizumab 400 mg every two weeks and 200 mg every two weeks arms and the placebo arm at week 16 are as follows respectively: PASI75: 82.0%, 76.7% and 9.9%; PASI90: 52.2%, 45.9% and 2.5%.

The week 48 results of the remaining part of the study which was conducted only with certolizumab 400 mg and 200 mg turned out to be 83.6% and 70.7% for PASI75 and 61.6% and 50.0% for PASI90, respectively[3].

In the CIMPACT study made with 559 patients, Lebwohl et al.[4] compared 400 mg and 200 mg doses of cerolizumab with the usual dose of etanercept and placebo. At week 12, the PASI75 responses were found to be 66.7%, 61.3%, 53.3% and 5.0% respectively and the PASI90 responses 34.0%, 31.2%, 27.1% and 0.2%. In the arms that used only certolizumab 400 mg and 200 mg after week12, PASI90 responses were 49.1% and 39.8% respectively at week 16. Both doses of certolizumab were found superior to both etanercept and placebo with a more apparent difference in the higher dose[4].

Follow-up

Achieving a PASI90 response at weeks 12-16 of a certolizumab therapy is the major indicator of efficacy and the therapy may be continued in patients who exhibit such a response as long as the response is maintained and no safety issue develops. In line with the follow-up scheme of TNF-α inhibitors, the tests that were done at the beginning of the treatment including whole blood count, metabolic profile, chest X-ray, and infection-related parameters (tuberculosis, hepatitis B and C, HIV) should be repeated as scheduled based on the patient's clinical findings[5].

Safety/side effects

In the CIMPASI1 and CIMPACT studies and the recently published study of Blauvelt et al.[6] giving the long-term results, certolizumab did not produce a new safety signal compared to placebo and etanercept[3,4].

The most common side effects were nasopharyngitis and upper respiratory tract infections, which did not differ from placebo in the CIMPASI1 and 2 studies and from etanercept in the CIMPACT study in a statistically significant way[3,4]. Blauvelt et al.[6] who reported a long-term follow-up that extended to 144 weeks and recorded 2231.3 patient years of exposure found the risk of severe infection to be 3.2% and did not define a new safety signal in relation to long-term or high-dose use.

Contraindications

A history of allergic reaction to the drug is a definite contraindication. It is also not suitable for use in the presence of tuberculosis and other active bacterial infections, untreated hepatitis B infection, congestive heart failure (New York class 3-4), a history of malignancy, and multiple sclerosis. In the case of infections that are not complicated but require an antibiotic therapy, a decision may be made based on the individual status of the patient. When the signs of infection disappear and the related treatment is discontinued, the treatment for psoriasis may resume from the point where it stopped[5].

Drug interactions

Due to increased risk of infection when used concurrently with TNF-α inhibitors, certolizumab should also not be used in combination with anakinra, abatacept, rituximab or natalizumab. Live vaccines should not be used concurrently.

Special cases

a. Pregnancy and lactation

In their CRIB pharmacokinetic study investigating the use of certolizumab in pregnancy and placental transmission, Mariette et al.[7] found immeasurable amounts of certolizumab in 13 of 14 infants born to the mothers who received certolizumab therapy after week 30 of their pregnancy and a minimal amount of certolizumab in 1 of them at birth, and no measurable amounts of certolizumab in any of the babies at weeks 4 and 8 of their birth. Clowse et al.[8] also found immeasurable or minimal certolizumab values in the milk samples taken from 17 mothers who were being treated with certolizumab. These results place certolizumab in the position of a first choice biological drug to be used during pregnancy and lactation.

b. COVID-19

There are no drug-specific data on the use of certolizumab in the period of COVID-19 pandemic. Although a moderate degree of COVID-19 infection risk has been attached to it due to its characteristics specific to the group of anti-TNF drugs[9], sufficient data to reach a general opinion is not available.

As in all patients with psoriasis who are on a systemic immunosuppressive therapy, the treatment should be suspended also in certolizumab using patients who are diagnosed with COVID-19 unless the negative effects of these drugs can be completely ruled out. Restarting the drug after recovery from infection should be evaluated on the basis of patient-specific risks[10].

EVIDENCE-BASED TREATMENT SUGGESTIONS

- It is one of the biological treatment options in moderate to severe psoriasis.
- It is in the form of subcutaneously administered injection and its standard dose is 400 mg every two weeks. In patients <90 kg, it can be used in a dose of 200 mg every two weeks after the first 3 injections (at weeks 0, 2 and 4).
- Its efficacy can be evaluated at week 12-16. Its PASI75 and PASI90 responses are satisfactory and the therapy will be continued without break in patients who has shown a response.
- Its pregnancy plan shows that it can be chosen as one of the first systemic treatment options in pregnancy and lactation.

References

1. Tracey D, Klareskog L, Sasso EH, Salfeld JG, Tak PP: Tumor necrosis factor antagonist mechanisms of action: A comprehensive review. Pharmacol Ther 2008;117:244-79.
2. Delgado Frías E, Díaz González JF: Certolizumab pegol. Reumatol Clin 2011;6S3:7-11.
3. Gottlieb AB, Blauvelt A, Thaçi D, et al.: Certolizumab pegol for the treatment of chronic plaque psoriasis: Results through 48 weeks from 2 phase 3, multicenter, randomized, double-blinded, placebo-controlled studies (CIMPASI-1 and CIMPASI-2). J Am Acad Dermatol 2018;79:302-14.
4. Lebwohl M, Blauvelt A, Paul C, et al.: Certolizumab pegol for the treatment of chronic plaque psoriasis: results through 48 weeks of a phase 3, multicenter, randomized, double-blind, etanercept- and placebo-controlled study (CIMPACT). J Am Acad Dermatol 2018;79:266-76.
5. Menter A, Strober BE, Kaplan DH, et al.: Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol 2019;80:1029-72.
6. Blauvelt A, Paul C, Van de Kerkhof P, et al.: Long-term safety of certolizumab pegol in plaque psoriasis: pooled analysis over 3 years from three phase 3, randomised, placebo-controlled studies. Br J Dermatol 2020;12. DOI: https://doi.org/10.1111/bjd.19314
7. Mariette X, Förger F, Abraham B, et al.: Lack of placental transfer of certolizumab pegol during pregnancy: results from CRIB, a prospective, postmarketing, pharmacokinetic study. Ann Rheum Dis 2018;77:228-33.
8. Clowse MEB, Förger F, Hwang C, et al.: Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study Ann Rheum Dis 2017;76:1890-16.
9. Price KN, Frew JW, Hsiao JL, Shi VY: COVID-19 and immunomodulator/immunosuppressant use in dermatology. J Am Acad Dermatol 2020;82:e173-5.
10. Nast A, Smith C, Spuls PI, et al.: Euroguiderm Guideline for the systemic treatment of Psoriasis Vulgaris. J Eur Acad Dermatol Venereol 2020;34:2461-98.