Anifrolumab

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Approved indication: systemic lupus erythematosus

Saphnelo (AstraZeneca)
vials containing 300 mg concentrated solution for dilution

Type I interferons are cytokines that are implicated in the pathogenesis of systemic lupus erythematosus. Anifrolumab is a fully human immunoglobulin G1 kappa monoclonal antibody that inhibits the signalling of type I interferon receptor subunit 1, thereby inhibiting the activity of all type I interferons. Anifrolumab is indicated as add-on treatment for moderate to severe active systemic lupus erythematosus.

The recommended dose of anifrolumab is 300 mg given as an intravenous infusion over 30 minutes every four weeks. Treatment may be discontinued if there is no improvement in disease control after six months. Anifrolumab is metabolised into small peptides and amino acids by proteolytic enzymes and is unlikely to be metabolised by hepatic enzymes. There have been no studies of anifrolumab in patients with renal or hepatic impairment. No drug–drug interaction studies have been conducted. Concurrent use with biologic therapies has not been studied.

Two randomised, placebo-controlled, phase III trials enrolled patients 18–70 years of age with moderate to severe active systemic lupus erythematosus who were receiving stable treatment consisting of at least one of either prednisone or equivalent, an antimalarial, azathioprine, mizoribine, mycophenolate mofetil or mycophenolic acid, or methotrexate. In the Treatment of Uncontrolled Lupus via the Interferon Pathway (TULIP)-1 trial, patients received either anifrolumab 300 mg, anifrolumab 150 mg or placebo every four weeks for 48 weeks. The primary end point was the difference between the proportion of patients who achieved a systemic lupus erythematosus responder index-4 (SRI-4) response at week 52 with anifrolumab 300 mg versus placebo.[1] In the TULIP-2 trial, patients received either anifrolumab 300 mg or placebo every four weeks for 48 weeks. The primary end point of this trial was a response at week 52 defined by the British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA).[2]

In the TULIP-1 trial, the primary end point was not reached, as the proportion of patients with an SRI-4 response was similar between the anifrolumab 300 mg (36%, 65/180 patients) and placebo (40%, 74/184 patients) arms. This response was also similar in the anifrolumab 150 mg arm (38%, 35/93 patients), suggesting a lack of efficacy at the lower dose.[1] In the TULIP-2 trial, a BICLA response was noted in 48% of patients in the anifrolumab arm (86/180) and in 32% of patients in the placebo arm (57/182) at week 52. In patients who were taking high-dose prednisone or equivalent at baseline, there was a dose reduction (to 7.5 mg/day or less) from week 40 to week 52 by 52% of patients in the anifrolumab arm (45/87) compared with 30% of patients in the placebo arm (25/83). Among patients with at least moderate cutaneous activity at baseline, a reduction of at least 50% in the Cutaneous Lupus Erythematosus Disease Area and Severity Index was observed in 49% of patients in the anifrolumab arm (24/49) and in 25% of patients in the placebo arm (10/40) at week 12. The annualised rate of flares (defined as worsening in any of nine organ systems in the BILAG index) at week 52 was 0.43 in the anifrolumab arm and 0.64 in the placebo arm.[2]

The most common adverse events in the anifrolumab of the TULIP-2 trial were upper respiratory tract infection (22% vs 10% in the placebo arm), nasopharyngitis (16% vs 11%), infusion-related reactions (14% vs 8%), bronchitis (12% vs 4%) and cutaneous herpes zoster infection (7% vs 1%, resolved without stopping treatment in all cases). These adverse events were serious in 8% of the anifrolumab arm (15/180 patients) and 17% of the placebo arm (31/182 patients). No anaphylactic reactions were reported.[2] Infusions may be stopped or the infusion rate may be reduced to manage infusion reactions. Adverse events led to discontinuation of anifrolumab in 11/180 patients in the TULIP-1 trial and 5/180 patients in the TULIP-2 trial, and one death occurred in each trial due to pneumonia.[1,2]

The safety and efficacy of anifrolumab have not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Malignant neoplasms were reported in 2% of patients in the anifrolumab 300 mg arm of the TULIP-1 trial.[1] As with all therapeutic proteins, immunogenicity may occur. One patient in the anifrolumab arm of the TULIP-2 trial tested positive for antidrug antibodies.[2] It is not recommended to receive live or attenuated vaccines during treatment.

There are limited data in patients 65 years of age and older. There are no data on the effects of anifrolumab on fertility. The safety and efficacy of anifrolumab have not been established in children and pregnant or breastfeeding women.

A monthly dose of anifrolumab in conjunction with usual treatment led to a clinical response in a greater proportion of patients than with placebo in the TULIP-2 trial. The drug is well tolerated with mild to moderate adverse events in most patients that

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can be managed appropriately. The durability of the drug's modest effect and safety beyond 52 weeks are unknown.

T manufacturer provided the product information

REFERENCES

1. Furie RA, Morand EF, Bruce IN, Manzi S, Kalunian KC, Vital EM, et al. Type I interferon inhibitor anifrolumab in active systemic lupus erythematosus (TULIP-1): a randomised, controlled, phase 3 trial. Lancet Rheumatol 2019;1:e208-19. https://doi.org/10.1016/S2665-9913(19)30076-1
2. Morand EF, Furie R, Tanaka Y, Bruce IN, Askanase AD, Richez C, et al. Trial of anifrolumab in active systemic lupus erythematosus. N Engl J Med 2020;382:211-21. https://doi.org/10.1056/NEJMoa1912196

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.