New drugs

Aust Prescr 2019;42:207–8
https://doi.org/10.18773/austprescr.2019.071
First published 10 October 2019

Dupilumab

Approved indication: atopic dermatitis

Dupixent (Sanofi-aventis)
Pre-filled syringe containing 300 mg/2 mL solution

Dupilumab is a subcutaneously injected monoclonal antibody for people with moderate–severe atopic dermatitis who require systemic therapy. It is intended for long-term rather than episodic use and can be given with or without topical corticosteroids. Currently, oral immunosuppressants such as ciclosporin, azathioprine or methotrexate are used in severe atopic dermatitis.

People with atopic dermatitis produce increased amounts of interleukin-4 and interleukin-13. Dupilumab inhibits signalling mediated by these cytokines by blocking their receptors.

The safety and efficacy of dupilumab has been investigated in three main placebo-controlled phase III trials. SOLO-1 and SOLO-2 assessed dupilumab monotherapy for 16 weeks and LIBERTY AD CHRONOS assessed dupilumab with concomitant topical corticosteroids for 52 weeks.[1,2] Efficacy in all three trials was measured at 16 weeks.

In total, 2119 people with moderate–severe atopic dermatitis (minimum of 10% body surface area involvement) were enrolled in the three trials. All patients used emollient twice a day. Patients were randomised to one of three treatments:

- an initial loading dose of dupilumab 600 mg subcutaneously as two injections, followed by a 300 mg dose every two weeks
- initial 600 mg dupilumab dose, followed by 300 mg each week
- matching placebo.

A primary outcome of the trials was the proportion of patients with an Investigator's Global Assessment (IGA) score of 0 or 1 (clear or almost clear skin) and a reduction of at least 2 points in their IGA score from baseline, after 16 weeks of treatment.

At baseline, 46–50% of patients had an IGA score of 4. After 16 weeks of treatment, 36–38% of people given dupilumab in the SOLO trials and 39% in the LIBERTY AD CHRONOS trial had reached the primary outcome. This was compared to 8–12% in the corresponding placebo groups (see Table). More improvement of pruritus was also reported with dupilumab compared to placebo.[1,2] Efficacy was maintained at 52 weeks in the LIBERTY AD CHRONOS trial.[2]

The most common adverse events with dupilumab included injection-site reactions (9.6–15.9%), allergic conjunctivitis (3–7%), bacterial conjunctivitis (0.9–1.9%), blepharitis (0.4–4.5%), oral herpes (2.5–3.8%), eye pruritus (0.4–2.9%) and dry eye (0.2–1.8%). These were less common in the placebo groups. In the LIBERTY AD CHRONOS trial, keratitis

Table **Efficacy of dupilumab in moderate–severe atopic dermatitis**

Trial (treatment duration)	Response to treatment after 16 weeks*		
	Placebo	Dupilumab 300 mg fortnightly	Dupilumab 300 mg weekly
SOLO-1 (16 weeks)	10% (23/2224)	38% (85/224)	37% (83/223)
SOLO-2 (16 weeks)	8% (20/236)	36% (84/233)	36% (87/239)
LIBERTY AD CHRONOS (52 weeks)†	12% (39/315)	39% (41/106)	39% (125/319)

* Efficacy defined as the proportion of patients with an Investigator's Global Assessment (IGA) score of 0 or 1 (clear or almost clear skin) and a reduction of at least 2 points in their IGA score from baseline following 16 weeks of treatment.

† Patients received concomitant topical corticosteroids in the LIBERTY AD CHRONOS trial but not in the SOLO trials.

Source: references 1–2

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

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occurred in 4% of patients treated with dupilumab and topical corticosteroid compared to none of the patients treated with placebo and topical corticosteroid. There were occasional elevations in eosinophils with dupilumab but these were usually transient. There were two cases of serum sickness in people with high titres of anti-drug antibody.

There are no data on dupilumab in pregnancy. However, studies in animals did not indicate toxicity. As dupilumab is an IgG antibody, it is expected to cross the placenta and also be excreted in human breast milk.

In theory, dupilumab could affect the immune response to helminth infections. Pre-existing infections should be treated before dupilumab is started. If a patient develops an infection during therapy and does not respond to anti-helminth treatment, dupilumab should be stopped.

It is not known if live vaccines are safe to use in people receiving dupilumab. There are also no data on the concomitant use of other medicines that modulate the immune system.

An initial loading dose of dupilumab 600 mg is recommended, given subcutaneously as two 300 mg injections at different sites. This is followed by a 300 mg dose given every two weeks. Maximum serum concentrations are reached within 3–7 days of injection.

In the trials, 36–39% of patients with moderate to severe dermatitis had clear or almost clear skin after 16 weeks of dupilumab treatment. There appeared to be little extra benefit of adding topical corticosteroids to dupilumab treatment. Injection-site reactions were very common with dupilumab. It is not known how dupilumab will compare to other treatments for severe disease as there were no active comparators in the trials. This drug is not currently approved for children but trials are ongoing. Dupilumab is also being investigated in asthma.

T T manufacturer provided additional useful information

REFERENCES

1. Simpson EL, Bieber T, Guttman-Yassky E, Beck LA, Blauvelt A, Cork MJ, et al.; SOLO 1 and SOLO 2 Investigators. Two phase 3 trials of dupilumab versus placebo in atopic dermatitis. N Engl J Med 2016;375:2335-48.https://doi.org/10.1056/NEJMoa1610020
2. Blauvelt A, de Bruin-Weller M, Gooderham M, Cather JC, Weisman J, Pariser D, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): a 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet 2017;389:2287-303. https://doi.org/10.1016/S0140-6736(17)31191-1

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.