Introduction to systemic treatment

The area of systemic therapy of AE has flourished during the last few years, as many new substances are marketed, licensed, or in the last step of clinical development. The licensing programs of the various new biologics and small molecules are providing much better levels of evidence than what is available for the longer existing drugs due to more robust RCT evidence.

Systemic therapy of AE is deemed necessary if the signs and symptoms of AE cannot be controlled sufficiently with appropriate topical treatments and UV-light therapy. Systemic therapy can also be useful to reduce the total amount of topical corticosteroids (TCS) in patients who need large amounts of potent TCS over prolonged periods to control their AE.

Candidates for systemic treatment may be either patients with a high composite score such as a SCORAD above 50 (scale definition), or patients clinically failing to respond to an appropriately conducted topical therapy (functional definition), or patients unable to participate in normal daily life activities whilst following an adequate treatment regimen (social definition).

Local regulations may necessitate the use of scores such as physician-reported scores (e.g. EASI) in combination with patient reported outcomes (e.g. DLQI). Many other scores exist summarized and assessed by the HOME initiative that may also serve as a basis to classify disease severity.[7]

It must be highlighted that the indication to systemic treatment is a patient individual decision, and that a signs-only score, such as EASI, is not a sufficient tool to make a final decision on commencing systemic therapy to an individual patient.

100 % agreement

Before starting systemic treatment, it is important to rule out relevant differential diagnoses such as cutaneous T-cell lymphoma and in selected cases primary immunodeficiency syndromes[8], and to ascertain that potential trigger factors such as allergic contact dermatitis have been excluded, and behavioural as well as educational reasons for poor responses have been adequately addressed.

Conventional systemic immunosuppressants, such as systemic corticosteroids (SCS), ciclosporin, azathioprine (AZA), mycophenolate mofetil (MMF), enteric-coated mycophenolate sodium (EC-MPS) and methotrexate (MTX) were used traditionally for difficult-to-treat AE. Most were not licensed for this indication. These drugs may roughly be divided in two groups: SCS and ciclosporin have a rapid onset of action and can be used to treat flares of AE or to bridge the time until onset of action of slower acting systemic immunosuppressants such as MTX, AZA and MMF/EC-MPS. The kinetics of the novel janus kinase inhibitors baricitinib (Bari), abrocitinib (Abro) and upadacitinib (Upa) place these agents in the fast-acting group, whereas the Th2-blocking agents (like IL13 or IL13/IL4 inhibitors) dupilumab (Dupi), tralokinumab (Tralo) and lebrikizumab (Lebri), as well as the IL31-receptor blocking agent nemolizumab (Nemo) need some weeks to reach full efficacy.

The following recommendations for systemic drugs are based on the living systematic review by Drucker et al[2,3], other published literature and medical considerations as well as expert opinion, and may differ from the legal licensing status and access routes, which are not uniform in European countries.

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