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Review

European Organisation for Research and Treatment of Cancer consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome – Update 2017

Franz Trautinger [a,b,*], Johanna Eder [a,b], Chalid Assaf [c], Martine Bagot [d], Antonio Cozzio [e], Reinhard Dummer [f], Robert Gniadecki [g,h], Claus-Detlev Klemke [i], Pablo L. Ortiz-Romero [j], Evangelia Papadavid [k], Nicola Pimpinelli [l], Pietro Quaglino [m], Annamari Ranki [n], Julia Scarisbrick [o], Rudolf Stadler [p], Liisa Väkevä [n], Maarten H. Vermeer [q], Sean Whittaker [r], Rein Willemze [q], Robert Knobler [s]

[a] *Department of Dermatology and Venereology, University Hospital of St. Pölten, Karl Landsteiner University of Health Sciences, St. Pölten, Austria*
[b] *Karl Landsteiner Institute of Dermatological Research, St. Pölten, Austria*
[c] *Department of Dermatology, HELIOS Klinikum Krefeld, Krefeld, Germany*
[d] *Department of Dermatology, Hôpital Saint Louis, Université Paris 7, INSERM U976, Paris, France*
[e] *Department of Dermatology and Allergology, Kantonsspital St. Gallen, St. Gallen, Switzerland*
[f] *Department of Dermatology, University of Zurich, Zurich, Switzerland*
[g] *Department of Dermatology, University of Copenhagen, Copenhagen, Denmark*
[h] *Division of Dermatology, Department of Medicine, University of Alberta, Edmonton, Alberta, Canada*
[i] *Hautklinik, Städtisches Klinikum Karlsruhe, Karlsruhe, Germany*
[j] *Department of Dermatology, Hospital Universitaria 12 de Octubre, Madrid, Spain*
[k] *2nd Department of Dermatology and Venereology, Attikon General Hospital, University of Athens, Chaidari, Greece*
[l] *Department of Surgery and Translational Medicine, Division of Dermatology, University of Florence, Florence, Italy*
[m] *Department of Medical Sciences, Section of Dermatology, University of Turin, Turin, Italy*
[n] *Department of Dermatology and Allergology, Inflammation Center, Helsinki University Central Hospital, Helsinki, Finland*
[o] *Department of Dermatology, University Hospital Birmingham, Birmingham, United Kingdom*
[p] *Department of Dermatology, Johannes Wesling Medical Centre, Minden, Germany*
[q] *Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands*
[r] *St. John's Institute of Dermatology, Division of Genetics and Molecular Medicine, Faculty of Life Sciences and Medicine, King's College London, London, United Kingdom*
[s] *Department of Dermatology, Medical University of Vienna, Vienna, Austria*

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* *Corresponding author*: Department of Dermatology and Venereology, University Hospital of St. Pölten, Propst Führer-Straße 4, A-3100 St. Pölten, Austria. Fax: +43 2742 9004 11919.
E-mail address: franz.trautinger@klpu.eu (F. Trautinger).

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Abstract In order to provide a common standard for the treatment of mycosis fungoides (MF) and Sézary syndrome (SS), the European Organisation for Research and Treatment of Cancer–Cutaneous Lymphoma Task Force (EORTC-CLTF) published in 2006 its consensus recommendations for the stage-adapted selection of management options for these neoplasms. Since then, the understanding of the pathophysiology and epidemiology of MF/SS has advanced, the staging system has been revised, new outcome data have been published and novel treatment options have been introduced. The purpose of the present document is to update the original recommendations bearing in mind that there are still only a limited number of controlled studies to support treatment decisions for MF/SS and that often treatment is determined by institutional experience and availability.

This consensus on treatment recommendations was established among the authors through a series of consecutive consultations in writing and a round of discussion. Recommended treatment options are presented according to disease stage, whenever possible categorised into first- and second-line options and supported with levels of evidence as devised by the Oxford Centre for Evidence-Based Medicine (OCEBM).

Skin-directed therapies are still the most appropriate option for early-stage MF, and most patients can look forward to a normal life expectancy. For patients with advanced disease, prognosis is still grim, and only for a highly selected subset of patients, prolonged survival can be achieved with allogeneic stem cell transplantation (alloSCT). There is a high need for the development and investigation in controlled clinical trials of treatment options that are based on our increasing understanding of the molecular pathology of MF/SS.

1. Introduction

Cutaneous T-cell lymphomas (CTCLs) are a group of rare non-Hodgkin lymphomas (NHLs) characterised by initial localisation of malignant T-lymphocytes to the skin. Current definition of these neoplasms follows the 2016 revision of the World Health Organisation (WHO) classification of tumours of haematopoietic and lymphoid tissues that largely incorporates the WHO-EORTC classification for cutaneous lymphomas published in 2005 (Table 1) [1,2]. The most common form among CTCLs is mycosis fungoides (MF), accounting for around 55% of cases. Sézary syndrome (SS) is much rarer making up only approximately 5%. A recent analysis by the Surveillance, Epidemiology and End Results (SEER) program of the United States National Cancer Institute (NCI) demonstrated an incidence rate of MF of about 5.6 per million persons, which has remained stable since 1995 after an increase in prior years; this may be attributed to improvement in diagnostic accuracy [3].

The clinical presentation of MF is manifold with early stages presenting with limited patches and plaques suspicious only to the experienced physician and late stages characterised by severe disease presenting with tumours, ulceration, systemic involvement and death. A number of clinical variants of MF have been described of which folliculotropic MF, pagetoid reticulosis, and granulomatous slack skin are separately mentioned in the WHO-EORTC classification due to distinctive clinicopathological features and biological behaviour [1]. SS is pathologically and clinically closely related to MF and defined by the occurrence of erythroderma, lymphadenopathy and leukaemic involvement. Since the initial description of MF ascribed to Jean-Louis Alibert in 1806 and of SS to Albert Sézary in 1938, both from the Hôpital Saint Louis in Paris, a number of therapeutic options have been introduced ranging from topical steroids to cytostatic chemotherapy and more recently also molecular targeted approaches [4–7]. However, due to the fact that in MF/SS the majority of available treatments are rarely able to induce long-term remissions, and according to the results of an early seminal study it is still a paradigm that treatment of patients with MF/SS is palliative and should follow a stepwise, stage-adapted approach [8]. The rare exceptions to this are allogeneic stem cell transplantation (alloSCT) in advanced disease and the anecdotal patient with long-term remission after skin-directed therapy (SDT) in early stages. These facts together with the want of evidence from larger prospective trials in an orphan disease has supported a need for the development of consensus statements by various national and international groups in which published evidence is integrated with expert opinion to provide the best available support for decision making in clinical practice [6,7,9–12]. It was with this intention that in 2004 the Cutaneous Lymphoma Task Force of the EORTC (EORTC-CLTF) embarked on an international attempt to establish consensus recommendations for the treatment of MF/SS with a special emphasis on treatment availability and access in Europe that were eventually published in 2006 [9]. As, in the meantime,