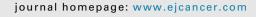


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Review

Blood classification and blood response criteria in mycosis fungoides and Sézary syndrome using flow cytometry: recommendations from the EORTC cutaneous lymphoma task force



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KEYWORDS

Cutaneous T-cell lymphoma; CD26; CD7; Staging; Classification; Blood; Erythroderma **Abstract** Our current mycosis fungoides (MF) and Sézary Syndrome (SS) staging system includes blood-classification from B0-B2 for patch/plaque/tumour or erythroderma based on manual Sézary counts but results from our EORTC survey confirm these are rarely performed in patch/plaque/tumour MF, and there is a trend towards using flow cytometry to measure blood-class. Accurately assigning blood-class effects overall stage and the 'global response' used to measure treatment responses in MF/SS and hence impacts management. The EORTC Cutaneous Lymphoma Task Force Committee have reviewed the literature and held a Workshop (June 2017) to agree a definition of blood-class according to flow cytometry.

No large study comparing blood-class as defined by Sézary count with flow cytometry has been performed in MF/SS. The definition of blood-class by flow cytometry varies between publications. Low-level blood involvement occurs in patch/plaque/tumour much less than

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erythroderma (p < 0.001). The prognostic relevance of blood involvement (B1 or B2) in patch/ plaque/tumour is not known. Studies have not shown a statistically worse difference in prognosis in erythrodermic MF patients with low-level blood involvement (IIIB) versus those without (IIIA), but Sezary patients who by definition have a leukaemic blood picture (staged IVA1 or higher) have a worse prognosis.

For consistency flow, definition for blood-class must be an objective measurement. We propose absolute counts of either CD4+CD7-or CD4+CD26-where $B0<250/\mu$ L, $B1 = 250/\mu$ L $-<1000/\mu$ L and $B2\geq1000/\mu$ L plus a T-cell blood clone. Fluctuations between B0 and B1 should not be considered in the treatment response criteria until further prognostic information is known.

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1. Introduction

Blood-classification was introduced into the TNM classification of mycosis fungoides (MF) and Sezary syndrome (SS) in the 2007 revision [1]. Blood-class from B0-B2 was defined using manual Sézary counts based on morphology, but these are highly subjective and have never been validated in a multicentre prospective international study. B2 was defined as $\geq 1000/$ µL Sézary cells and, in those with erythroderma and a positive blood T-cell clone identical to skin, were the diagnostic criteria for SS. B1 was defined as greater than 5% circulating Sézary cells (as a percentage of circulating lymphocytes) using a manual Sézary count (on a peripheral blood smear) to differentiate those patients with low-level blood involvement from B0; thereby defining B0 as $\leq 5\%$ circulating Sézary cells [1]. Blood involvement may occur in MF and SS especially in advanced stages of disease notably erythroderma (defined as >80% of skin involved), but blood involvement may also occur in patch/plaque or tumour MF. In erythroderma, blood-class defines the patients who do not reach the criteria for SS stage (IVA1) as stage IIIA (blood-class; B0) or stage IIIB (blood-class; B1). Blood-class is similarly recorded for patch/plaque or tumour MF, but B0-1 does not change stage, whereas B2 is designated IVA1 independent of the level of skin involvement. Circulating Sezary cells have recently been shown to have a diverse phenotype from skin Sezary cells despite demonstrating clonality with skin-derived Sezary cells showing a more advanced maturation pattern with differences in cytokine/chemokine receptor expression [2]. CD4+CD7- and CD4+CD26-subsets are the most commonly used to identify the neoplastic population in MF/SS. However, partial loss of these markers may occur on benign Tlymphocytes with ageing, in inflammatory dermatoses or following therapy [1-5]. Other aberrant phenotypes may also occur but are less common.

As there is no objective definition of blood-class using flow cytometry, centres have adopted different definitions for publications. The EORTC is leading a Prospective Cutaneous Lymphoma International Prognostic Index study (PROCLIPI study) in early-stage MF which collects staging, survival and treatment data. For the TNMB stage to be comparative and consistent in future publications, an agreement for the definition of blood-class is required. Furthermore, as response in blood is considered as part of treatment response used for clinical trials in MF/SS, it is essential that there is a universal objective definition. Here, we review the literature and report on our EORTC Workshop defining blood-class in MF/SS.

2. Material and methods

We reviewed the literature of blood involvement in MF/ SS using flow cytometry, through an internet search of relevant medical databases (e.g. PUBMED, MEDLINE) as well as a targeted search of relevant professional bodies and their guidelines (e.g. EORTC, ISCL (International Society for Cutaneous Lymphoma), UK-CLG (UK-Cutaneous Lymphoma Group). We performed an EORTC survey of centres detailing their current practice for measuring blood involvement by flow cytometry and reviewed preliminary PROCLIPI data.

Following discussions at the EORTC Annual General Meeting (April, 2017), an EORTC Blood Classification Workshop to review the literature and define blood-class using flow cytometry was held (June 2017).

3. Results

3.1. Workshop discussion and interpretation of current staging and response criteria

A comprehensive literature review confirms that there is no objective universal definition of blood-class in MF/ SS according to flow cytometry. The adoption of CD26cells in the assessment of blood involvement in MF/SS followed the work by Bernengo *et al.* [3] which compared the percentage of CD4+CD26-% in 103 MF/ SS patients with blood-class defined by Sézary counts. Of 151 MF patients, 14 (9%) had B1 (>5% Sézary cells Download English Version:

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