To the editor:

Minimal residual disease testing in multiple myeloma by flow cytometry: major heterogeneity

As more effective therapies become routinely used to treat multiple myeloma, standardized methods (such as flow cytometry) to determine the presence/absence of minimal residual disease (MRD) will likely play an increasingly important role in the clinical, research, and regulatory settings. Indeed, prior studies show that among patients who obtain a complete response, those who are MRD negative in their bone marrow by flow cytometry have better survival than those who are MRD negative. At this time, there are no established consensus criteria for MRD by flow cytometry of the bone marrow in multiple myeloma. To improve our understanding of MRD assessment practices, we conducted a survey of 30 major medical institutions in the United States. Directors of flow cytometry at each institution were sent an e-mail with 14 questions regarding their measurement of MRD by flow cytometry of the bone marrow in multiple myeloma patients.

Twenty-six institutions responded; 11 (42%) said they perform MRD testing (Table 1). The number of events acquired for MRD testing by flow cytometry varied from 100,000 to 4,000,000, with most institutions (6/11; 55%) obtaining 100,000 to 500,000 events. The number of abnormal plasma cells needed to define MRD positivity ranged from 20 to 50. In 2008, the European Myeloma Network organized 2 flow cytometry workshops to identify specific indications for flow cytometry in patients with monoclonal gammopathies and to facilitate the development of consensus technical approaches. In our survey, we found the definition of abnormal plasma cells to differ substantially between institutions (Table 1), with some relying on CD19 and CD45 negativity with or without CD56 positivity to determine the extent of MRD despite previous studies showing that normal plasma cell subpopulations can be negative for CD19 and CD45(+) and CD8(+) T-cell responses with concurrent molecular remission in acute myeloid leukemia with NPM1 mutation. J Clin Oncol. 2013;31(3):e44-e47.

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References


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multiple myeloma. At the current time, to our knowledge, most centers assess MRD status at the time of complete response. Collaborative efforts are needed to develop standardized criteria for MRD testing in multiple myeloma.

**To the editor:**

**Detection of an NRAS mutation in Erdheim-Chester disease**

In a recent paper in *Blood*, Haroche et al reported dramatic efficacy of vemurafenib in 3 cases of multisystem and refractory Erdheim-Chester disease (ECD) and Langerhans cell histiocytosis harboring the *BRAF* V600E mutation.1 The findings of an ~50% prevalence of *BRAF* mutations in this disease and effective treatment with vemurafenib suggest that Ras/Raf/MEK/ERK pathway activation is central to the biology of these histiocytic diseases.2,3

We report a 66-year-old man who presented with several months of progressive cognitive impairment, deterioration of gait, fatigue, and urinary incontinence. A gadolinium-enhanced magnetic resonance imaging scan demonstrated multifocal contrast-enhancing lesions of the cerebral meninges (Figure 1A). Computed tomography and then positron emission tomography imaging of the chest, abdomen, and pelvis revealed paravertebral, pleural, presacral, and renal masses,
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