

## CORRESPONDENCE



## Deletion of *IKZF1* and Prognosis in Acute Lymphoblastic Leukemia

**TO THE EDITOR:** Mullighan et al. (Jan. 29 issue)<sup>1</sup> report on the prognostic significance of *IKZF1* alterations in pediatric patients with acute lymphoblastic leukemia (ALL). The authors also find that the gene-expression signature in patients with *BCR-ABL*-negative ALL, which is associated with a poor outcome (as predicted by *IKZF1* alterations), is similar to the gene-expression profile in patients with *BCR-ABL*-positive ALL. Given that approximately 85% of children with *BCR-ABL*-positive ALL also have a deletion of *IKZF1*,<sup>2</sup> two questions with potential clinical and prognostic implications come to mind.

First, could a supervised analysis detect significant differences in the gene-expression signatures between patients with *BCR-ABL*-positive ALL who also have an alteration in *IKZF1* and those who have wild-type *IKZF1*?

Second, since *IKZF1* alterations confer a poor prognosis in patients with standard-risk ALL and patients with high-risk B-cell ALL, is the poor outcome for children with *BCR-ABL*-positive ALL simply a reflection of the high incidence of *IKZF1* alterations in this population? In other words, do patients with *BCR-ABL*-positive ALL and wild-type *IKZF1* have a better outcome than patients with *BCR-ABL*-positive ALL who have a deletion of *IKZF1*?

Bruno C. Medeiros, M.D.

Stanford University School of Medicine  
Stanford, CA 94305  
brnom@stanford.edu

1. Mullighan CG, Su X, Zhang J, et al. Deletion of *IKZF1* and prognosis in acute lymphoblastic leukemia. *N Engl J Med* 2009; 360:470-80.
2. Mullighan CG, Miller CB, Radtke I, et al. *BCR-ABL1* lymphoblastic leukaemia is characterized by the deletion of *Ikaros*. *Nature* 2008;453:110-4.

**THE AUTHORS REPLY:** Medeiros raises two interesting questions related to the clinical and prognostic implications of *IKZF1* mutations in pediatric ALL. Both questions concern the very small subgroup of patients with *BCR-ABL1*-positive ALL who do not have an alteration of *IKZF1*. Specifically, Medeiros asks whether patients with *BCR-ABL1*-positive ALL who have wild-type *IKZF1* have a distinct gene-expression profile or outcome as compared with patients with *BCR-ABL1*-positive ALL who have an *IKZF1* mutation. Unfortunately, neither our original ALL cohort<sup>1</sup> nor an expanded cohort<sup>2</sup> had a sufficient number of patients with *BCR-ABL1*-positive ALL who did not have an *IKZF1* alteration to enable us to perform statistically sound analyses of differences in the gene-expression profile and outcome. Only 5 of 21 patients with *BCR-ABL1*-positive ALL did not have an *IKZF1* mutation. The analysis of a much larger number of pediatric and adult patients with *BCR-ABL1*-positive ALL will be required to definitively answer these important questions.

James R. Downing, M.D.  
Charles G. Mullighan, M.D.  
St. Jude Children's Research Hospital  
Memphis, TN 38105  
james.downing@stjude.org

### THIS WEEK'S LETTERS

- 1787 **Deletion of *IKZF1* and Prognosis in Acute Lymphoblastic Leukemia**
- 1788 **Vitiligo**
- 1789 **More on Reports of Esophageal Cancer with Oral Bisphosphonate Use**
- 1792 **Mutations in a Thiamine-Transporter Gene and Wernicke's-like Encephalopathy**

1. Mullighan CG, Goorha S, Radtke I, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukemia. *Nature* 2007;446:758-64.

2. Mullighan CG, Miller CB, Radtke I, et al. BCR-ABL1 lymphoblastic leukaemia is characterized by the deletion of Ikaros. *Nature* 2008;453:110-4.

## Vitiligo

**TO THE EDITOR:** In their Clinical Practice article on vitiligo, Taïeb and Picardo (Jan. 8 issue)<sup>1</sup> do not include data to provide support for the use of some combination therapies. Recent evidence suggests that the combination of erbium:yttrium–aluminum–garnet (YAG) laser skin ablation with fluorouracil application before narrow-band ultraviolet B (UVB) phototherapy confers a benefit as compared with phototherapy alone.<sup>2</sup> In addition, the authors state that it is unclear whether topical corticosteroid treatment with UVB radiation is superior to UVB radiation alone. However, we have reported a significant benefit of the combination of excimer laser UVB phototherapy and topical hydrocortisone 17-butyrate cream (applied twice daily in 3-week cycles, with a corticosteroid-free interval of 1 week), as compared with excimer laser therapy alone, in a randomized, parallel-group trial. This trial involved 84 consecutive patients with vitiligo who had lesions on the face, neck, or both that were unresponsive to previous conventional UVB phototherapy. At 12 weeks, the rates of the primary outcome — at least a 75% reduction from baseline in overall lesional areas, based on an automated analysis of reflected ultraviolet photographs — were 43% with the combination of corticosteroid treatment and UVB phototherapy versus 17% with phototherapy alone ( $P=0.01$ ).<sup>3</sup> No skin atrophy or hypertrichosis was reported in patients who received corticosteroid therapy. Combination treatments for vitiligo warrant further investigation in randomized trials.

Luigi Naldi, M.D.

Fabrizia Sassi, M.D.

Ospedali Riuniti  
24100 Bergamo, Italy  
luigi.naldi@gised.it

1. Taïeb A, Picardo M. Vitiligo. *N Engl J Med* 2009;360:160-9.
2. Anbar TS, Westerhof W, Abdel-Rahman AT, Ewis AA, El-Khayyat MA. Effect of one session of ER:YAG laser ablation plus topical 5-Fluorouracil on the outcome of short-term NB-UVB phototherapy in the treatment of non-segmental vitiligo: a left-right comparative study. *Photodermatol Photoimmunol Photomed* 2008;24:322-9.
3. Sassi F, Cazzaniga S, Tessari G, et al. Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone

or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck. *Br J Dermatol* 2008;159:1186-91.

**THE AUTHORS REPLY:** We did not cite the recent articles by Anbar et al.<sup>1</sup> and Sassi et al.<sup>2</sup> in our review article because they were published after our article was accepted for publication. In the study reported by Sassi et al.,<sup>2</sup> the excimer laser was used as a source of UVB radiation; treatment with this device is more potent than conventional narrow-band UVB treatment. Indeed, their patients were selected because they did not have a response to conventional ultraviolet treatment, topical corticosteroids, or both. The results suggest that this new combination may be a valuable addition to possible treatments for vitiligo in patients with limited disease, although more data are needed to better inform its role.

The report by Anbar et al.<sup>1</sup> raises promise for the treatment of vitiligo in difficult-to-treat areas such as the dorsum of the hands. However, experience with the use of fluorouracil in vitiligo is limited, and its use cannot be considered to be conventional. Its mechanism of action in vitiligo has not been clarified, although a photosensitizing capacity of the drug has been reported, as well as repigmentation after systemic administration in isolated cases.

Alain Taïeb, M.D.

Centre Hospitalier Universitaire de Bordeaux  
33075 Bordeaux, France  
alain.taieb@chu-bordeaux.fr

Mauro Picardo, M.D.

San Gallicano Dermatological Institute  
00144 Rome, Italy

1. Anbar TS, Westerhof W, Abdel-Rahman AT, Ewis AA, El-Khayyat MA. Effect of one session of ER:YAG laser ablation plus topical 5-Fluorouracil on the outcome of short-term NB-UVB phototherapy in the treatment of non-segmental vitiligo: a left-right comparative study. *Photodermatol Photoimmunol Photomed* 2008;24:322-9.
2. Sassi F, Cazzaniga S, Tessari G, et al. Randomized controlled trial comparing the effectiveness of 308-nm excimer laser alone or in combination with topical hydrocortisone 17-butyrate cream in the treatment of vitiligo of the face and neck. *Br J Dermatol* 2008;159:1186-91.