To the editor:

**T-cell homeostasis: the dark(ened) side of common variable immunodeficiency**

We have read with interest the paper by Wehr et al., recently published in *Blood*, which defines subgroups in common variable immunodeficiency (CVID). CVID is a heterogeneous immunodeficiency syndrome characterized by hypogammaglobulinemia, recurrent bacterial infections and a variety of immunologic abnormalities. The authors stated that the aims of their study were “to determine the clinical and immunologic phenotype of CVID patients in Europe and to test and possibly improve and unify the current classification schemes.” In fact, the vast heterogeneity of this immunodeficiency has so far hindered the fulfillment of a commonly accepted approach to classify subgroups of patients. Therefore, any attempts to improve the classification of this disease are welcome news. The article by Wehr et al. was no exception.

A severe reduction of switched memory B cells, associated with splenomegaly and granulomatous disease, was shown in most of the patients, while an expansion of CD21<sup>+</sup> B cells marked the patients with splenomegaly. Finally, lymphadenopathy was significantly linked with alterations in the T-cell compartment will be of additional value to the harvested clinical data, being solely restricted to the compartment appears inadequate to the complexity and importance of the harvested clinical data, being solely restricted to the evaluation of the peripheral distribution of CD4<sup>+</sup> and CD8<sup>+</sup> T lymphocytes. We should hereby like to raise the issue of T-cell homeostasis: the dark(ened) side of common variable immunodeficiency. Particularly, CD4<sup>+</sup>-naive T cells were strongly associated with clinical severity. This was quantified on the basis of several criteria evaluated within the last 5 years of the patients’ history and included, among others, severe respiratory tract infections. A detailed comparison between the CD4<sup>+</sup>-naive T cell–based classification and the Freiburg classification allowed us to reveal the limits of a “pure” B cell–based classification. A similar comparison was not performed by Wehr et al., who nonetheless stated that their proposed classification “is superior to previous models in the differentiation of clinical phenomena.”

Therefore, while the data presented in the above mentioned papers are not disputed, we would like to remark here that both reports would have been more meaningful if the deep alteration of the T-cell compartment (firstly the loss of CD4<sup>+</sup>-naive T cells) had been considered somehow. Such information is not only of cursory interest but also may have therapeutic implications. In fact, current therapy for CVID includes regular infusions of intravenous immunoglobulin and antibiotics as needed, but significant morbidity and mortality remain. CVID patients might be likely to benefit from therapies which can enhance T-cell functions and reverse T-cell anergy.

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**References**


**Response**

**Improving classification in CVID**

We thank A. Giovannetti and coauthors for shedding some light on the T-cell side of common variable immunodeficiency (CVID). We absolutely agree, as already stated in our review, that the analysis of alterations in the T-cell compartment will be of additional value for the classification of CVID. This has been nicely proven by the same group in their 2007 paper.

However, when we initialized the EUROclass trial in 2004 “in order to test and possibly improve and unify the current classifica-
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