

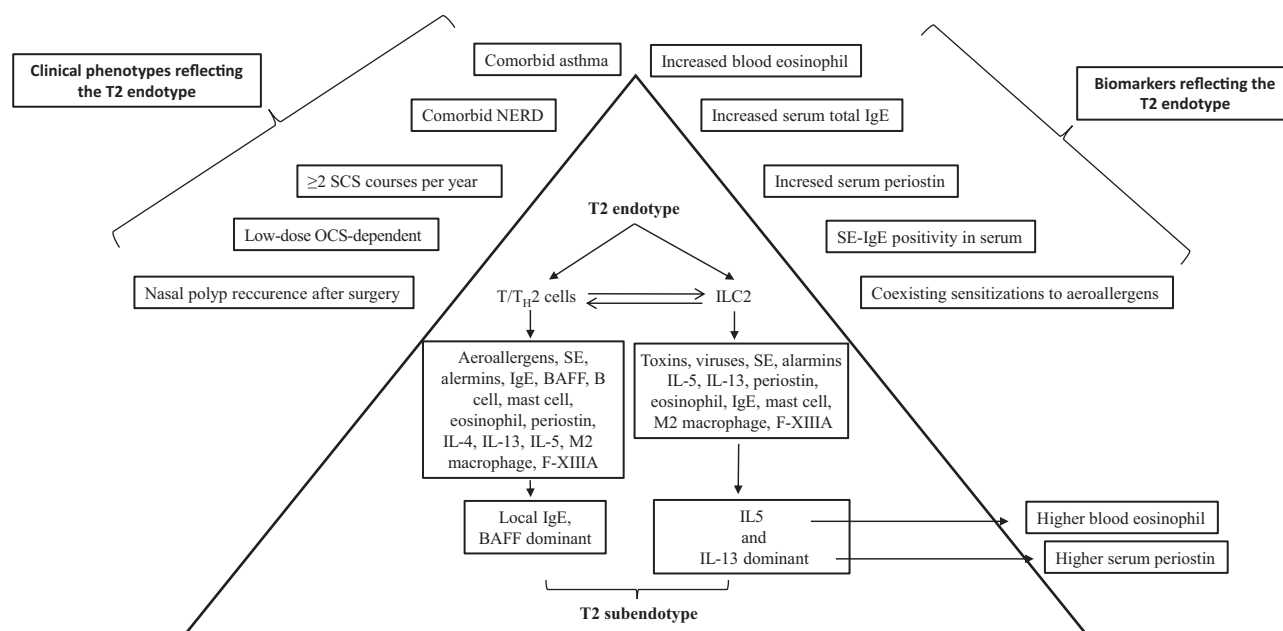


FIGURE 1. Phenotypes and endotypes of T2 CRSwNP. *BAFF* cytokine, B-cell activating factor; *NERD*, nonsteroidal anti-inflammatory drug–exacerbated respiratory disease; *OCS*, oral corticosteroid; *SCS*, systemic corticosteroid; *SE*, *Staphylococcus aureus* enterotoxins; *T*, type.

In conclusion, the ILC2 pathway and IL-5/IL-13 cytokines seem to be one of the dominant endotypes in the T2 CRSwNP phenotype. Therefore, higher blood eosinophil levels and higher serum periostin levels might be considered as biological markers reflecting the ILC2 subendotype. At this point, it is necessary to reduce the levels of eosinophils and periostin in sinonasal mucosa. Anti-IL-4Rα (dupilumab) therapy seems to be a bit more effective in the subendotype.⁷ In the future, treatment regimens using combined biological agents, in which all pathways are suppressed, will be used to obtain better clinical results in this phenotype. We can think of this combined biologic agents concept (such as anti-IgE + anti-IL-4Rα + anti-IL-5/anti-IL-5R) as using systemic corticosteroids with minimal side effects because systemic corticosteroids suppress type 2 endotype regardless of their subgroups in the T2 CRSwNP phenotype.

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Reply to “Type 2 chronic rhinosinusitis with nasal polyps: From phenotype to endotype”



To the Editor:

I appreciate the comment by Yılmaz¹ on our publication on type 2 chronic rhinosinusitis with nasal polyps (CRSwNP)² and for supporting our view on the need of endotyping chronic rhinosinusitis for the selection of the most adequate treatment approach for an individual patient. We have recently further illustrated the currently available biomarkers for endotypes in uncontrolled severe CRSwNP in a patient group in whom the selection of adequate treatment is of utmost importance and in whom predictors for treatment approaches are particularly needed.³

In fact, although we are in a position to differentiate type 2 from non-type 2 CRSwNP with reasonable accuracy, we are not yet able to predict the response of an individual patient to a specific biologic approach, for example, anti-IL-4 receptor alpha,

anti-IgE, or anti-IL-5/IL-5R alpha. Phase 3 trials have been published only for fuplumab and omalizumab.^{4,5} So far, no studies have delivered biomarker data allowing for a solid analysis of response to treatment in relation to specific biomarkers; thus, we are still far away from a differentiation of biologics for treatment based on biomarkers, or even specific cell populations such as the group 2 innate lymphoid cells, and this still might take considerable time. For the moment we should, however, do our best to differentiate type 2 from non-type 2 immune reactions, using as simple and practical methods as possible,³ and select suitable patients for biologics among those using clinical markers.

Finally, the use of combined biological agents—double or even triple combinations—seems at least questionable at the current moment. The phase 3 trials in CRSwNP mentioned above have already suggested—in the absence of head-to-head studies—different levels of efficacy, which may help to select one biologic over another as first choice. No knowledge exists today on the success of a second biologic after the failure of a first drug, nor of the efficacy of a combination of biologics versus a single compound in CRSwNP. Although costs should not be our first concern as medical doctors dealing with uncontrolled severe patients, combining of several biologics would certainly increase the financial burden and needs to be justified.

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