

TABLE 1. (Continued)

OA questionnaire	Item selection and pretesting	Item reduction	Responsiveness	MID	Validity	Reliability
QUICK (2007)	Items were generated through: 1. A review of the literature on QOL and OA; 2. A panel of ophthalmologists and immunologists to assess for VKC; 3. Ten children with VKC in the active phase; 4. Two psychologists with experience in the process of development and validation in QOL questionnaires.	Items that were redundant, ambiguous, difficult to understand, or expressed negatively were removed. Further to this, the remaining items were administered to patients who had to indicate which item they had experienced in the last 2 wk on a scale whereby the highest scoring items were used for the QUICK questionnaire.	NA	NA	Construct validity, specifically convergent validity, was assessed using the Pearson correlation coefficient to evaluate the relationship between another questionnaire and the QUICK questionnaire. Further to this, factorial analysis was performed on the preliminary QUICK questionnaire to identify potential subscales.	Assessed by internal consistency reliability method.

AdoRQLQ, Adolescent Rhinoconjunctivitis Quality of Life Questionnaire; *DEDIQ*, Dry Eye Disease Impact Questionnaire; *EAPIQ*, Eye Allergy Patient Impact Questionnaire; *MiniRQLQ*, Mini Rhinoconjunctivitis Quality of Life Questionnaire; *NA*, not applicable/not assessed; *N/RQLQ*, Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire; *PAQLQ*, Paediatric Asthma Quality of Life Questionnaire; *PROLQ*, Paediatric Rhinoconjunctivitis Quality of Life Questionnaire; *QOL*, quality of life; *QUICK*, Quality of Life in Children with Vernal Keratoconjunctivitis Questionnaire; *RQLQ*, Rhinoconjunctivitis Quality of Life Questionnaire; *RQLQ(S)*, Standardised Rhinoconjunctivitis Quality of Life Questionnaire; *VKC*, Vernal Keratoconjunctivitis.

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



To the Editor:

I read with great interest the report by Bachert et al.¹ The authors reported current knowledge and personal opinions on the efficacy of therapeutic options, such as reboot surgery and biologics targeting type 2 (T2) cytokines in chronic rhinosinusitis with nasal polyps (CRSwNP). Another point the authors mentioned is that CRSwNP endotypes should be defined by clinical signs and/or biomarkers.¹ We thank Bachert et al for their contribution to literature with such a valuable review. We would like to share our opinions on this subject.

We share the same view as the authors. It is very important to associate T2 CRSwNP subendotypes with T2 CRSwNP phenotypes (Figure 1). This will provide cost-effective use of biologics in T2 CRSwNP phenotypes. At this point, because there are no 1-to-1 comparative studies with these biologics, “What should be the most effective biological treatment for the T2 CRSwNP phenotype?” and “Which clinical and biological markers would be useful to select the appropriate biologics for this phenotype?” are remaining questions. To answer these questions, we need to know the subendotype (the dominant pathway of the T2 endotype) of the T2 endotype underlying the T2 CRSwNP phenotype.

T2 CRSwNP endotype presents as T2-biased inflammation. T2 immune responses in CRSwNP are mediated mainly by T_H2 cells, group 2 innate lymphoid cells (ILC2s), local IgE, and profound tissue eosinophilia. ILC2s are known to produce type 2 cytokines, especially IL-5 and IL-13, and T_H2 cells secrete IL-4, IL-5, and IL-13. Both IL-4 and IL-13 induce IgE switching and IgE synthesis by B cells. Although IL-5 is the important driver of blood eosinophilia, IL-13 is strongly associated with airway eosinophilia and periostin. Periostin is a downstream molecule of IL-4 and IL-13, which potentially passes the IL-4 receptor α.²⁻⁴ IL-5 and IL-13 drive many features of the inflammation and eosinophil recruitment that is characteristic of the T2 CRSwNP.²⁻⁵ Patients with a T2 CRSwNP phenotype have higher levels of serum periostin and blood eosinophils.²⁻⁶

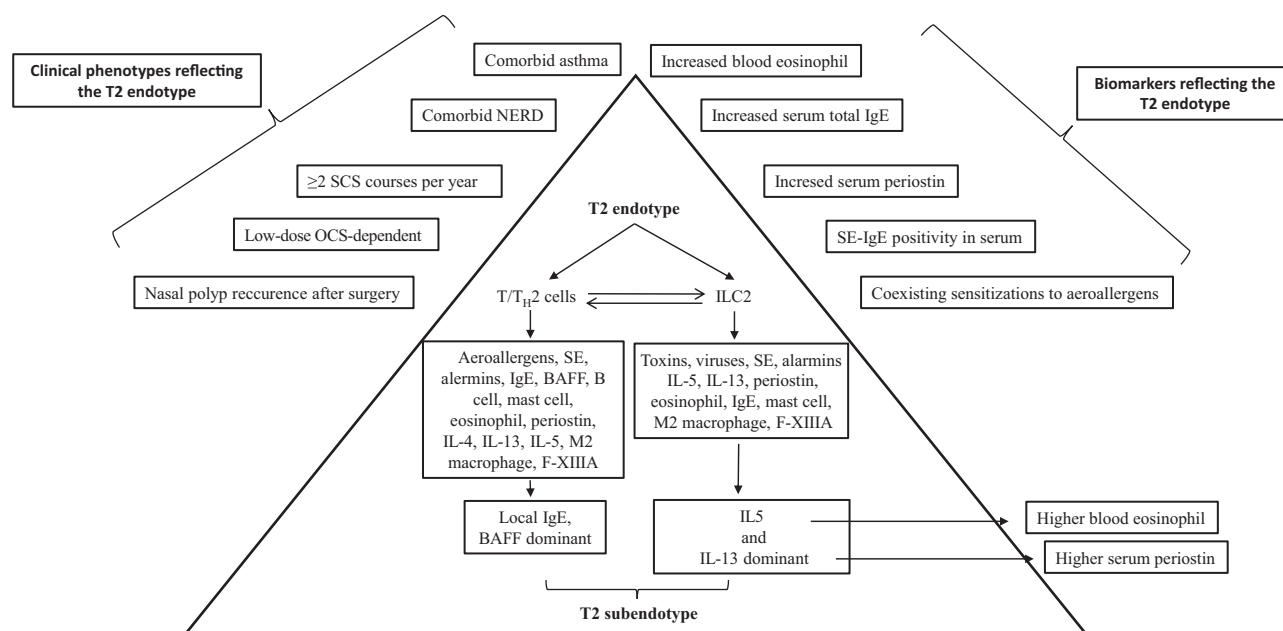


FIGURE 1. Phenotypes and endotypes of T2 CRSwNP. *BAFF* cytokine, B-cell activating factor; *NERD*, nonsteroidal anti-inflammatory drug–exacerbated respiratory disease; *OCS*, oral corticosteroid; *SCS*, systemic corticosteroid; *SE*, *Staphylococcus aureus* enterotoxins; *T*, type.

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-4R α (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-4R α + 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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Conflicts of interest: The author reports no relevant conflicts of interest.

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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,