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Correspondence

Author's reply: "Anti-parietal cell antibodies are more prevalent and clinically relevant in autoimmune endocrine diseases: Comment on the ARIOSO position paper"

Dear Editor,

We appreciate the letter to the editor written by Kundzina-Steinberga L. and colleagues [1] on our position paper on autoimmune gastritis (AIG) [2] and we thank the authors for their genuine interest in our work and for sharing their real-world clinical experience with AIG.

We fully agree with Dr Kundzina-Steinberga L. and colleagues that the timely diagnosis of AIG is key to prevent potentially negative consequences of undiagnosed AIG, such as gastric neoplasms and deficiencies of micronutrients [2]. The association between AIG and other autoimmune conditions, in particular autoimmune thyroid disease, has been observed since the early 1960s, giving rise to the term "thyrogastric syndrome" [3]. In 40 % of histologically diagnosed patients with AIG, an associated autoimmune thyroid disease was observed, as documented by serology and thyroid ultrasound, and risk factors for this association included parietal cell autoantibody (PCA) positivity (OR 2.5), along with female sex and metaplastic atrophy [4]. Dr Kundzina-Steinberga L. and colleagues showed a 34 %, 60 %, and 52 % PCA positivity in Graves' disease, Hashimoto thyroiditis, and type 1 diabetes, respectively [1], which was significantly higher than in controls without autoimmune diseases (16 %) [1], but also higher as previously reported: PCA positivity was observed in up to 40 % of patients with autoimmune thyroid disease [5] and in up to 15–20 % of patients with type 1 diabetes [6]. These data again strongly confirm that both disorders occur in a closely linked fashion with AIG, strengthening the benefits of proactive screening for AIG in other autoimmune diseases. As stated in the ARIOSO position paper [2], proactive screening should focus on high-risk populations, including besides patients with autoimmune thyroid disease and type 1 diabetes, those with autoimmune polyendocrine syndromes, uninvestigated dyspepsia, micronutrient deficiency anaemia, and fertility issues, where the prevalence of AIG is significantly higher [2], thus resulting in an efficient and cost-effective approach [7,8].

Unfortunately, there is no single, absolutely accurate, non-invasive test for diagnosing AIG. The combination of serum autoantibodies (PCA, intrinsic factor autoantibodies, IFA) and markers of corpus oxyntic mucosa damage (pepsinogens, gastrin) has shown the best overall accuracy for diagnosing AIG, which must, in all cases, be confirmed by histology [2,8]. PCA are considered a hallmark of AIG, showing an overall high sensitivity (80–100 %) and specificity (90–99 %) [2], but they may test positive also in *Helicobacter pylori*-related gastritis (up to 20 %) and in healthy people (up to 9 %) [9]; on the other hand, they may represent a very early marker of AIG, even before corpus atrophy occurs [10]. Thus, it is likely that among the PCA-positives with autoimmune thyroid disease or type 1 diabetes reported by Dr Kundzina-Steinberga L. and colleagues, a proportion of *H. pylori*-positive individuals without AIG were included, as well as individuals with a healthy stomach or corpus mucosa inflammation without atrophy, potentially evolving into overt AIG over time. Only histological assessment of gastric biopsies can provide a precise estimate of the prevalence of the association between thyroid and gastric autoimmunity and type 1 diabetes.

However, it should be noted that in about 20 % of patients with AIG, PCA test is negative [11], albeit in seronegative AIG, the association with other autoimmune diseases is less common [12]. Anyhow, proactive screening for AIG should not rely solely on PCA [2,8], but should include at least another marker.

Dr Kundzina-Steinberga L. and colleagues reported higher gastrin levels in autoimmune atrophic gastritis and type 1 gastric neuroendocrine neoplasms than in controls [1], as expected, given the stimulating effect on antral gastrin-producing G cells of reduced gastric acid secretion resulting from the inflammatory destruction of corpus parietal cells. We fully agree that high gastrin levels are useful predictors of type 1 gastric neuroendocrine neoplasms [13,14], and high gastrin levels have been shown to be a decisional marker indicating the progression from potential to overt AIG [10], with a further steady increase as the disease progresses [15]. Unfortunately, gastrin levels are influenced by proton pump inhibitor use and *H. pylori* infection, giving pepsinogens an advantage because their serum levels are not influenced by these factors [8].

Thus, in conclusion, we thank the authors for their contribution, emphasising that AIG should be timely recognised and actively sought, particularly in high-risk populations, including, first of all, the whole spectrum of autoimmune diseases, with autoimmune thyroid disease and type 1 diabetes among the most common. The proactive screening approach, PCA and/or IFA together with gastrin or pepsinogens, will ultimately depend on local availability and individual patient features and, in any case, requires histological confirmation.

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Declaration of competing interest

None.

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