

ACTIVITY A.T3.2 IMPLEMENTATION OF PILOT PROJECT

D.T3.2.8 Improvement of diagnostic of atypical CD
patients Pilot project Final Report





1. RESULTS ACHIEVED ACCORDINGLY TO OBJECTIVES

- Please review the objectives you have set up in your D.T3.1.1 description, in the Status report Phase 1 and describe activities and results achieved by your pilot. Give an overview of the processes that are part of your pilot project.

Our Pilot project “Improvement of diagnostic of atypical CD patients” comprises 3 topics:

1) Application and verification of new immunological technique in the diagnosis of celiac disease (CD) in all its clinical presentation forms in our clinical practice.

- Activity: we investigated whether histological analysis of the duodenal biopsies combined with intestinal IgA anti-transglutaminase deposits immunoassay makes CD diagnosis possible in at-risk children with low concentrations of serum anti-transglutaminase antibodies and normal intestinal mucosa.

- Results: Two hundred forty-five symptomatic children positive for serum anti-tTG (>7 U/mL) were enrolled and divided into 3 groups: extensive duodenal atrophy (n=209), with IgA anti-tTG deposits throughout the duodenum and high serum anti-tTG concentrations (157±178 U/mL); bulb duodenal atrophy (n=22), with widespread IgA anti-tTG deposits in 9 and in the bulb alone in 13 and low serum anti-tTG concentrations (13.9±8.7 U/mL); and normal duodenum (n=14), with widespread IgA anti-tTG deposits in 8 and in the bulb alone in 6 and low serum anti-tTG concentrations (10.6±6.2 U/mL). All patients in the first 2 groups were diagnosed with CD and 8 from the third group. All improved after 1 year of gluten-free diet. Bulb duodenal analysis led to a 12% (30/245) increase in CD diagnosis. No CD-related lesions were observed in the 30 control subjects.

- Conclusions: In children at risk for CD, bulb duodenum biopsy sampling is essential to identify villous atrophy and detect IgA anti-tTG deposits even in absence of intestinal lesions. These mucosal autoantibodies could well represent a new standard for diagnosing CD.

We have shared these results with the gastroenterologists of our region in two meetings and promoted a stable collaboration for the diagnosis of the patients described above. We have also published these original data (Gastrointest Endosc 2018;88:521) and declared the support of the Interreg Central Europe “Focus in CD” project.

2) Transferability of these innovative immunological techniques to other partners of the Focus in CD project.

- Activity: in order to spread this diagnostic technique among the partners of the present project we have made available our activity to analyze intestinal biopsy specimens and teach this immunological technique to people belonging to the other partners.

- Results: We received 100 intestinal biopsies from the pediatric gastroenterology of Maribor University Medical Center (PP2) and assessed the level of sensitivity and diagnostic specificity of the test which was 100%. At our laboratory, Petra Rižnik MD. (PP2’s resident of pediatrics) spent a month where she followed a training to look for anti-ttg antibodies on 10 intestinal biopsies of subjects with celiac disease, learning all the operative steps of the immunological test. In this way this technique has been successfully transferred to the PP2’s pediatric gastroenterology.



3) Sharing of these diagnostic techniques among pediatric gastroenterology centers in northeastern Italy.

- Activities: involve pediatricians and adult gastroenterologists in the existence of different clinical and biological forms of CD and the possibility of recognizing all these forms with immunological techniques now available. Promote the formation of stakeholders groups in the care of these CD subjects.

- Results: we have organized several scientific meetings where we have illustrated the new clinical forms of CD and the new immunological techniques able to identify these conditions. In addition, with the support of the Italian Celiac Association (AIC), we have established a stable working group of pediatricians and adult gastroenterologists from our region and of the north-east Italy (gastroenterological units of Trieste, Udine, Aviano, Pordenone, Gorizia, Treviso, Padova, Vicenza, Monza) to share all the "difficult" cases of CD. Recently, a study project entitled "Use of intestinal anti-transglutaminase antibodies in the diagnosis of celiac disease in pediatric age and in the adult: multicentric prospective study" was carried out and funded by our Institute to give continuity to this collaboration.

2. ADDED VALUE OF THE DEVELOPED & TESTED PILOT SOLUTION IN YOUR REGIONAL ENVIRONMENT

- Please describe shortly, what is the gained added value for the end-user of pilot service solution

ADDED VALUE for END-USER

Short term effects	Long-term effects
1. We have identified some clinical forms of celiac disease and above all verified a specific CD diagnostic pathway. We have shared this knowledge with pediatricians and gastroenterologists now able to recognize and manage these new CD-clinical conditions.	1. Repeat of the meetings in our institution and alerting HCPs and stakeholders to share CD-diagnostic guidelines will strengthen the level of CD-medical care.
2. The interaction with other partners has led to the dissemination of immunological techniques for the best medical practice in the CD-diagnosis.	2. This collaboration, inaugurated by the present project, will allow an effective collaboration on CD and the drafting of other bilateral projects.
3. Increased knowledge on the presence of different CD-clinical forms, their recognition with an appropriate diagnostic path, and the medical care in daily clinical practice.	3. The stable presence of stakeholder groups on this specific field will allow the continuity of the knowledge acquired during this project.



3. DEVIATION AND PROBLEMS ENCONTERED

- In case your outcomes are different from the planned, please give an explanation of the reasons and formulate your modified results achieved. Was your planned model working or did you had to make modifications, if yes, describe ? Did you had any problems in you pilot implementation? If yes, which was the solution adopted?

We have no particular problems in the implementation of our pilot project. This is due to the high interest of pediatricians and gastroenterologists involved in the project but also from the association of patients and their families that keep alive the interest on this disease both to ensure an early diagnosis and a good medical care.



4. LESSON LEARNED RELATED TO CO-CREATION OF PILOT SOLUTIONS WITH ENGAGED STAKEHOLDERS

- Please describe what were the benefits and setbacks related to co-creation of pilot project with stakeholders.

LESSONS LEARNED

Benefits	Setbacks
1. Collaboration with pediatricians and adult gastroenterologists has been extremely productive and useful in daily clinical practice and has generated a stable collaboration never before experienced.	1. There were no setbacks in bringing our project to a successful conclusion.
2.	2.
3.	3.

5. FURTHER ACTION PLAN (ACTIVITIES FOR THE FUTURE)

- What are your further activities of the pilot project development,
On the local level ? We intend to maintain a constant interaction with the groups of pediatricians and adult gastroenterologists who have been trained in this project with two annual meetings with the discussion of clinical cases and sharing innovative CD-diagnostic methods.
On transnational level ? we intend to extend this pilot project model to other working groups on celiac disease, which are present in European scientific societies.
- How did you plan to ensure sustainability to your pilot? Have you plan any action for the maintenance/follow up/development of the actions implemented, after the project ends?
- Working groups: the presence of working groups (pediatricians and adult gastroenterologists) born during the project will ensure the continuity of the new clinical and diagnostic features acquired. The acquisition of diagnostic techniques and the knowledge of the various clinical forms of celiac disease will allow some groups of this project to extend this knowledge to other Italian regions and work groups.
- Guidelines: the acquired clinical and diagnostic experience will allow to formulate and apply innovative guidelines for CD treatment by the various working groups.