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Efficacy and safety of Adalimumab in Very Early-onset IBD- A Multicentre Study from the Paediatric IBD Porto Group of ESPGHAN

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Background: Patients with very early onset inflammatory bowel disease (VEOIBD) often present with severe disease course and require escalation to biologics. Exclusion of pediatric patients from clinical trials lead to scarcity of efficacy and safety data on TNFa antagonists therapy in VEOIBD. We aimed to assess safety and efficacy of adalimumab (ADM) induction and maintenance therapy in patients with VEOIBD.

Methods: This was a retrospective study involving 31 sites affiliated with the IBD Porto Group and IBD Interest Group of ESPGHAN, as well as centers in North America. Demographic, clinical and laboratory data were collected from patients diagnosed with VEOIBD who commenced ADM therapy before 6 years of age between 2014 to 2023.

Results: We identified 77 VEOIBD patients with a median age at diagnosis of 2.6 years (interquartile range [IQR] 1.3–4.1), of whom 29 (38%) were diagnosed at age <2 years (infantile-onset IBD). Thirty-seven (48%) patients were diagnosed with Crohn's disease, 25 (32%) with ulcerative colitis and 15 (20%) with IBD-unclassified. Five (9%) from those genetically tested were diagnosed with monogenic disease. Median age at initiation of ADM was 4.2 (IQR 2.8-5.1) years. Forty-four patients (57%) were Infliximab experienced, discontinued mainly due to pharmacokinetic (20 [45%]) and pharmacodynamic (13 [30%]) failures. At initiation of ADM, concomitant corticosteroids and immunomodulators were given in

37 (48%) and 29 (37%) patients, respectively. The median wPCDAI and PUCAI scores at baseline were 45 [37.5-60] and 45 [27.5-57.5], respectively. Median follow-up time was 85.4 (IQR 40.4-139.2) weeks. While patients with CD showed significant clinical improvement after 26 and 52 weeks (PCDAI decreased to 10 [0-33.4], $p<0.001$, and 10 [0-25], $p<0.05$, respectively), No significant improvement in PUCAI score was observed among patients with UC (Figure 1). Inflammatory markers and calprotectin showed a gradual decrease over time (Figure 1). Weight and Height Z scores did not differ significantly throughout the follow-up period. ADM discontinuation rates after 1 and 3 years were 40% and 65%, respectively, mainly due to primary non-response (14, 29.8%) and loss of response (19, 40.4%). Drug discontinuation rates were not dependent on concomitant immunomodulator treatment or ADM initiation or on age (less or above 3 years). Four patients (5.2%) developed severe infections, including a patient with TTC7A mutation who died following septic shock.

Conclusion: Adalimumab therapy was relatively safe and seemed more effective in young patients with Crohn's disease, but not in those with ulcerative colitis. Durability was relatively low due to high rates of primary non-response and secondary loss of response.