



P-59 - EFFECT OF THE HLA-DQA1*05 ALLELE ON THE EFFICACY OF USTEKINUMAB IN PATIENTS WITH CROHN'S DISEASE. MULTICENTER STUDY BASED ON THE ENEIDA REGISTRY OF GETECCU

Jordi Guardiola¹, Katja Serra¹, Marisa Iborra², Ariadna Padró²¹, Luisa de la Peña¹, Agnes Fernandez³, Francisco Mesonero⁴, Carlos González-Muñoz⁵, Rocio Ferreiro-Iglesias⁶, Pablo Navarro⁷, Montserrat Rivero⁸, Albert Martin-Cardona⁹, Beatriz Sicilia¹⁰, Monica Sierra-Ausin¹¹, Xavier Calvet¹², Joaquin Hinojosa¹³, Eva Iglesias-Flores¹⁴, Lucia Marquez¹⁵, Maria Dolores Martin-Arranz¹⁶, Ruth de Francisco¹⁷, Fiorela Cañete¹⁸, Ana Gutiérrez¹⁹, Santiago Garcia-López²⁰, Eugèni Domènech¹⁸, Pilar Nos², Sabino Riestra¹⁷, Maia Bosca-Watts⁷, Yamile Zabana⁹, Beatriz Castro²², Manuel Barreiro⁶, Esther Garcia-Planella⁵, Elena Ricart³, Gerard Surís¹, Alexandra Ruiz-Cerulla¹, Lorena Rodríguez-Alonso¹, Judit Orobitg¹ and Francisco Rodríguez-Moranta¹

¹Hospital Universitari de Bellvitge, Gastroenterologia, Hospitalet de Llobregat. ²Hospital Universitario y Politécnico La Fe, Valencia. ³Hospital Clínic de Barcelona. ⁴Hospital Ramón y Cajal, Madrid. ⁵Hospital Santa Creu i Sant Pau, Barcelona. ⁶Hospital Clínico Universitario de Santiago de Compostela. ⁷Hospital Clínico Universitario de Valencia. ⁸Hospital Universitario Marqués de Valdecilla, Santander. ⁹Hospital Mutua de Terrassa. ¹⁰Hospital Universitario de Burgos. ¹¹Complejo Asistencial Universitario de León. ¹²Corporació Sanitaria Parc Taulí de Sabadell. ¹³Hospital de Manises. ¹⁴Hospital Universitario Reina Sofía, Córdoba. ¹⁵Hospital Parc de Salut Mar, Barcelona. ¹⁶Hospital Universitario La Paz, Madrid. ¹⁷Hospital Central de Asturias, Oviedo. ¹⁸Hospital Germans Trias i Pujol, Badalona. ¹⁹Hospital General de Alicante. ²⁰Hospital Miguel Servet, Zaragoza. ²¹Hospital Universitari de Bellvitge, Genética molecular Laboratori clínic, Hospitalet de Llobregat. ²²Hospital Marques de Valdecilla, Santander.

Resumen

Introduction: HLA-DQA1*05 carriage is associated with the development of anti-drug antibodies and loss of response (LOR) to tumor necrosis factor antagonists (anti-TNF) in patients with inflammatory bowel diseases (IBD) (Sazonovs *et al.* Gastroenterology 2020). Ustekinumab has shown very low rates of immunogenicity and presumably will not be affected by this risk. Identifying patients at high risk of treatment failure would be important when selecting therapy for IBD.

Objectives: AIM: The objective of this analysis was to investigate the relationship between the HLA-DQA1*05 allele and ustekinumab on development of LOR and drug persistency.

Methods: This is a retrospective cohort study from a prospectively maintained ENEIDA registry. LOR was defined as recurrence or worsening of IBD related symptoms that required a change or intensification in treatment, hospitalization or surgery. Independent predictors of LOR were identified using univariate and multivariable Cox proportional hazard regression. The HLA-DQA1*05 allele was determined from a saliva sample (kit OGD-600 de DNA Genotek Oragene) and DNA extraction with the Maxwell[®] RSC-Stabilized Saliva DNA kits.

Results: 204 patients with Crohn's disease were included. Previous exposure to biological drugs was 96% (61% ≥ 2 biological drugs). Basal fecal calprotectin levels were 907 ± 970 μg/g and

PCR levels 16.2 ± 25 mg/dL. The median follow-up was 417 ± 154 days. During this period, 25%, 16% and 13% of the patients required drug intensification, hospitalization or surgery, respectively. 43% of the patients included were carriers of one or two copies of the HLA-DQA1*05 allele. The presence/absence of this allele was not associated with LOR to ustekinumab (20 vs. 16%, $p = \text{ns}$) nor with drug withdrawal (11 vs. 6%, $p = \text{ns}$). In the multivariate analysis (Cox regression), only the number of previous biological drugs was associated with ustekinumab persistency.

Conclusions: The presence of the HLA-DQA1*05 allele is not related to LOR or persistency of ustekinumab treatment. First-line treatment with ustekinumab rather than anti-TNF agents may be considered in HLA-DQA1*05-positive patients, particularly when the use of a concomitant immunosuppressant is contraindicated.