strategies deeply changed when Ivacaftor (2015) and the combination therapy Ivacaftor/Tezacaftor/Elexacaftor (ETI) (2021) were marketed. At this moment ETI therapy is licensed to treat CF's patients>6 years with at least one F508del mutation, the most common one; however, patients with rarer CFTR's mutations don't have access to this therapy.

Aim and Objectives With this work we would like to report the use of the combination therapy Ivacaftor-ETI in two young patients with rare CFTR's mutations: the N1303K/2183AA>G and the W1282X/N1303K.

Material and Methods Starting from the off-label authorisations from January-2015 to June-2022 by our Hospital Committee (composed with a Clinician, a Pharmacologist and a Hospital Pharmacyst) in accord to Law 94/98, we identified patients that required off-label CFTR modulators' combination therapy due to their CFTR's rare mutations and in vitro response to ETI therapy. For these we analysed: age at the beginning of the therapy, gender, type of mutation, clinical manifestations, period of therapy, Adverse Drug Reactions (ADRs) notified.

Results Only in 2022 two patients were authorised to use off-label CFTR modulators' combination therapy due to their rare CFTR's mutations. The first patient (P1) was a female, 20 years, W1282X/N1303K mutations; her clinical history showed meconium ileus, serious pneumopaty and she often required antibiotic therapy due to her lungs infections. The second patient (P2) was a female, 19 years, N1303K/2183AA>G mutations; her clinical history showed pancreatic and lungs insufficiency, BMI<14, infections induced by multi-drug resistant Pseudomonas and Mycobacterium Abscessus, D hypovitaminosis. At first, Hospital Committee authorised 3 cycles of therapy for P1 and 4 cycles (28 days for each cycle) for P2; both of them were authorised to prolonge their therapy due to clinical evident efficacy. No significant ADRs related to treatment were notified.

Conclusion and Relevance CFTR modulators are small molecules that directly impact and achieve the function of CFTR channel. They give long-term improvements in clinical outcomes and we hope more research on their efficacy in patients with rarer CFTR's mutations.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of Interest No conflict of interest

4CPS-218 TNF GENE POLYMORPHISMS PREDICTORS OF RESPONSE TO ANTI-TNF DRUGS IN PATIENTS DIAGNOSED WITH MODERATE-SEVERE PSORIASIS

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Background and Importance Psoriasis is a chronic inflammatory skin disease. Biological treatments against tumour necrosis factor (anti-TNF) are effective in treating this disease, however, not all patients respond to this treatment, and it can cause serious side effects. Biomarkers involved in the TNF cytokine may be implicated in the response to the anti-TNF drug.

Aim and Objectives To determine the utility of Single Nucleotide Polymorphisms of HLA-B and TNF-238, TNF857, TNF-308, TNF-1031, TNFRSF1B as prognostic and predictive markers in patients diagnosed with moderate-severe psoriasis treated with adalimumab, etanercept or infliximab. As well as, to evaluate the efficacy of anti-TNF treatment in the induction phase.

Material and Methods A prospective cohort study was performed. Data and DNA were obtained from saliva samples of 103 patients residing in the province of Granada with moderate and severe psoriasis who had been treated with anti-TNF. The genotypes were determined by Taqman PCR Real Time.

Results Patients' mean age was 54.19 ± 13.65 years; 54 male (54/103); 100 had plaque psoriasis (100/103), 90 located in trunk and extremities, and 89 on scalp and face, 42 with psoriatic arthritis (42/103), 33 smokers (33/103), 36 drinkers (36/103), 62 had psoriasis family history (62/103). These 103 patients have been treated with 135 anti-TNF (adalimumab, ADA=80; etanercept, ETN=39; infliximab, INF=16). Also 20 received oral administration of the concomitant methotrexate (20/135).

In reference to efficacy, 74 patients had a response to anti-TNF (74/135), and 61 do not show the expected response in the induction phase (61/135). Concerning PASI75 values, 55 patients treated with ADA achieved PASI75 at 3-6 months (55/80), 12 patients treated with ETN (12/39), and 7 patients treated with INF (7/16).

Furthermore, patients carrying TNFRSF1B-rs1061622-G allele an association with ADA response at 3 months (p=0.0026) and patients carrying TNFα-1031-rs1799964-T an association with ETN response at 6 months (p=0.0047), also patients carrying TNFα-238- rs361525-G treated with INF have a response at 6 months (p=0.045).

Conclusion and Relevance In conclusion, response to anti-TNF drugs was associated with different single nucleotide allelic polymorphisms of the TNF gene. Nonetheless, further studies with large cohorts of patients have to be performed to confirm these data in order to apply for this personalised medicine in routine clinical practice.

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Conflict of Interest No conflict of interest

4CPS-219 AGAMENON-SEOM MODEL FOR THE PREDICTION OF SURVIVAL IN PATIENTS WITH HER2-POSITIVE ADVANCED OESOPHAGOGASTRIC ADENOCARCINOMA RECEIVING TRASTUZUMAB-BASED FIRST-LINE TREATMENT

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