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.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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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Background and Importance Trastuzumab associated with chemotherapy (platinum and fluoropyrimidine) is the standard first-line treatment in HER2-positive advanced oesophagogastric adenocarcinoma (AGA); however, its benefits are heterogeneous.
Aim and Objectives To develop and validate a predictive model for overall survival (OS) and progression-free survival (PFS) in patients with AGA treated with trastuzumab.
Material and Methods Patients from the Spanish Society of Medical Oncology (SEOM)-AGAMENON registry with HER2-positive AGA treated in first-line with chemotherapy and trastuzumab between 2008 and 2021 were selected for this study. An accelerated time-to-event model was developed to predict survival and represented as a nomogram and an online calculator. The nomogram was externally validated in an independent series from The Christie NHS Foundation Trust hospital in Manchester, England.
Results 737 patients were recruited (AGAMENON-SEOM, n= 654; Manchester, n= 83). In the referral cohort the median PFS and OS were 7.76 (95% CI, 7.13-8.25) and 14.0 months (95% CI, 13.0-14.9), respectively. Patients received a median of six cycles of platinum, eight cycles of fluoropyrimidine and trastuzumab for a median of 7.6 months (95% CI, 7.10-8.30).

In the validation cohort, the median PFS and OS were 8.1 (95% CI, 7.1-11.3) and 12.8 months (95% CI, 10.3-20.4), respectively. Patients received chemotherapy for a median of five cycles and trastuzumab for a median of 6.3 months.

Six covariates were significantly associated with OS and were used to construct the nomogram: neutrophil-lymphocyte ratio (time ratio (TR):0.73; 95% CI: 0.63-0.83), ECOG status (TR:0.59; 95% CI 0.48-0.73), Lauren histologic subtype (TR:0.73; 95% CI 0.57-0.94), HER2 expression (TR:0.85; 95% CI 0.73-1), histologic grade (TR:0.87; 95% CI 0.72-1.07), and tumour burden (TR:1.69; 95% CI 1.34-2.13). The AGAMENON-HER2 model demonstrated adequate calibration and fair discriminatory ability with a c-index for PFS and OS of 0.606 (95% CI 0.58-0.64) and 0.623 (95% CI 0.59-0.66), respectively. In the Manchester validation cohort, the model is well calibrated, with a c-index of 0.65 and 0.68 for PFS and OS, respectively.
Conclusion and Relevance HER2-positive AGA patients receiving trastuzumab and chemotherapy can be stratified according to their estimated survival endpoints using the AGAMENON-HER2 prognostic tool. This nomogram could be a valuable tool for making treatment decisions in daily clinical practice.

REFERENCES AND/OR ACKNOWLEDGEMENTS
Conflict of Interest No conflict of interest

4CPS-222 HAPLOIDENTICAL HAEMATOPOIETIC CELL TRANSPLANTATION IN PATIENTS AGED > 55 YEARS WITH ACUTE MYELOID LEUKAEMIA

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Background and Importance In the elderly patients with AML, both the development of reduced-intensity conditioning (RIC) regimens and the use of haploidentical donors have improved their accessibility to allo-HCT.
Aim and Objectives To analyse the clinical characteristics and results of haploidentical family donor allo-HCT, performed in our hospital during the years 2014 to 2021, in patients with AML >55 years.
Material and Methods
Retrospective observational study. Data collected: age, sex, HCT status, time from diagnosis to transplant, ECOG Performance Status, comorbidity indexes (HCT-CI, EBMTs, DRindex), haematopoietic progenitor source (HPS), CMV-mismatch, conditioning regimen, graft-versus-host disease (GVHD) prophylaxis, and post-HCT complications. Overall survival (OS) and progression free survival (PFS) were analysed using Kaplan-Meier.
Results Thirty patients were included. Median (range): 64 (56–71) years, 57% women. 70.3% in first complete remission. Median (range) time from diagnosis was 6.5 (3.47-52.37) months.74% ECOG 0. 33% DR index high and very high 15% patients. The EBMTs >4 in 26% and the HCT-CI ≥3 in 56% patients. HPS was peripheral blood in 52% and bone marrow in 48%. 56% CMV-mismatch (donor -/patient +). All patients received a RIC regimen and post-HCT cyclophosphamide and 89% tacrolimus as the only immunosuppressant.

Major non-haematological toxicities included mucositis, gastrointestinal and liver toxicity in 26%, 19% and 7% of patients, respectively. 19% patients developed haemorrhagic cystitis, one patient underwent thrombotic microangiopathy, 41% developed acute GVHD and 37% patients presented chronic GVHD cmv infection occurred in 78% of patients.

Median (range) follow-up was 21.55 (1.67-89.80) months, OS at 1 year was 65% (95% CI, 46-83%), at 2 years 56% (95% CI, 36-75%). PFS at 1 year was 61% (95% CI, 42-80%), at 2 years 48% (95% CI, 28-68%). 48% are still alive and all in complete remission.
Conclusion and Relevance The small sample prevents numerous affirmations from being emphatically extracted, but the results obtained, which are very comparable to the published experiences, support the use of this type of donor in this patient population. Currently, we should not delay transplantation in elderly patients with AML trying to find an HLA-identical donor. If the experience of the Centre is extensive, performing a transplant from a haploidentical donor should be considered in the algorithm of the Allo-HSCT procedure.

REFERENCES AND/OR ACKNOWLEDGEMENTS
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4CPS-223 BOTULINUM TOXIN TYPE A: THE NON-INVASIVE SUCCESS FOR OVERACTIVE BLADDERS

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Background and Importance Intradetrusor injections of botulinum toxin type A (TBA) have significantly changed the management of overactive bladder (OAB), allowing the acquisition of urinary continence and control of renal risks. This technique makes it possible to avoid bladder replacement surgery by