**Materials and Methods** We present data from the ENESTnd study. In ENESTnd, a phase 3, multicentre, open-label, randomised study, patients treated with nilotinib demonstrated higher and faster rates of major molecular response (MMR), more profound molecular response (MR), and complete cytogenetic responses (CCyR) compared with imatinib by 12 and 24 months. 282 adult patients were randomly assigned to receive nilotinib 300 mg twice daily, 281 to receive nilotinib 400 mg twice daily and 283 to receive imatinib. Patients were eligible if they had been diagnosed with chronic phase, Philadelphia chromosome-positive CML within the previous 6 months.

**Results** By 24 months after the start of treatment, significantly more patients had a MMR with nilotinib than with imatinib (201 with nilotinib 300 mg twice daily, 187 with nilotinib 400 mg twice daily and 124 with imatinib; $p < 0.0001$ for both comparisons). Significantly more patients in the nilotinib groups achieved a complete molecular response at any time than did those in the imatinib group (74 with nilotinib 300 mg twice daily, 59 with nilotinib 400 mg twice daily and 29 with imatinib; $p < 0{\cdot}0001$ for nilotinib 300 mg twice daily vs. imatinib, $p = 0.0004$ for nilotinib 400 mg twice daily vs. imatinib).

**Conclusions** Nilotinib continues to demonstrate superiority vs. imatinib with faster and more profound molecular responses. These results support nilotinib as a first-line treatment option for patients with newly diagnosed Philadelphia chromosome-positive and chronic myeloid leukaemia.

No conflict of interest.

## PHC-017 PHARMACOGENETIC STUDY ABOUT INFLUENCE OF A POLYMORPHISM IN GENE TRAILR1 IN RESPONSE TO INLFIXIMAB IN PATIENTS WITH CROHN'S DISEASE (CD)

doi:10.1136/ejhpharm-2013-000276.362

[1]M de Andrés Bautista, [1]D Lacruz Guzmán, [2]V Dominguez Leñero, [1]P Pérez Cañadas, [1]M Martinez Penella, [1]H Garcia Lagunar, [1]E Ferris Villanueva, [1]R Guerrero Bautista. *[1]Hospital Universitario Santa Lucia, Farmacia, Murcia, Spain; [2]Hospital Perpetuo Socorro, Farmacia, Murcia, Spain*

**Background** Anti-TNF drugs show high inter-individual variability in efficacy and toxicity.

Currently there are no genetic, biochemical or environmental markers to predict response to treatment.

**Purpose** To assess the influence of gene polymorphism rs2230229 TRAILR1 as a genetic marker in response to treatment with infliximab in patients diagnosed with Crohn's disease (CD). Will it enable us to predict response and improve the effectiveness of the drug?

**Materials and Methods** Prospective observational study of all patients diagnosed with CD treated with infliximab at our hospital. The assessment of response to infliximab was performed using as criteria of clinical response a decreased questionnaire score CDAI (Crohn Disease Activity Index) at the 4th dose. Subsequently patients were considered to have responded if their CDAI decreased by 70 points or more with respect the baseline and at least 25% on the total score and clinical remission was achieved by a CDAI of less than 150 points. Biological response criteria were defined such as patient responders, partial responders or non-responders according to variation in levels of C-reactive protein (CRP) with regard to baseline at 3, 6 and 12 months. To detect polymorphism KASPAR probes were used in a PCR-based allele-specific competitive FRET technology using a computer and a real time PCR of Aplied Biosystems 7500F in 96-well plate. All patients included in the study received a starting dose of infliximab 5 mg/kg at 0, 2 and 6 weeks after the start and then a maintenance dose every 8 weeks. Statistical analyses were performed with Epidat 3.1 and the level of significance was indicated by a p value of less than 0.05.

**Results** The study included a total of 40 patients. The mean age of the patients was 38.66 ± 13.98 years and 61.1% were female. The distribution for genotypes was 81.6% AA, 15.8% GA and 2.6% GG. Significant correlation wasn't found between genotypes or alleles of this polymorphism and clinical response to infliximab. Instead, statistically significant differences were shown for approximately 6 months of treatment when comparing patients with genotypes GG and GA/AA and a positive response ($p = 0.047$) when considering the biological response. Similarly patients with a G allele had a more frequent negative response than those with the A allele ($p = 0.043$). On the other hand, significant correlation was found between patients carrying the A allele and the positive response, at 3, 6 and 12 months based on biological response distribution.

**Conclusions** The results of our study show an association of this polymorphism with response to infliximab. Worst response rates are observed in patients carrying allele G diagnosed with CD. We need more studies on this polymorphism and with a larger sample size to confirm these findings.

No conflict of interest.

## PHC-018 PHARMACOGENETIC STUDY AS A PREDICTOR OF EFFICACY AND TOXICITY IN PATIENTS WITH ADVANCED RENAL CELL CARCINOMA TREATED WITH SUNITINIB

doi:10.1136/ejhpharm-2013-000276.363

[1]I Cañamares-Orbis, [2]JM Sepúlveda-Sánchez, [3]C Rodríguez-Antona, [2]CA Farfan, [1]C García-Muñoz, [1]S Cortijo-Cascajares, [1]M Goyache-Goñi, [1]I Escribano-Valenciano. *[1]University Hospital 12 Octubre, Pharmacy, Madrid, Spain; [2]University Hospital 12 Octubre, Medical Oncology, Madrid, Spain; [3]Spanish National Cancer Research Centre, CNIO Cancer Center, Madrid, Spain*

**Background** Sunitinib (SU) is an oral, small-molecule, multitargeted tyrosine kinase receptor inhibitor that is approved for the treatment of renal cell carcinoma (RCC). However, several patients either do not respond to treatment, or they do, but they experience significant toxicity.

**Purpose** To find genetic markers of toxicity and efficacy using a commercially available DNA microarray genotyping system.

**Materials and Methods** 25 patients with newly-diagnosed metastatic RCC were evaluated prospectively from January 2010 to May 2011. Patients received SU in repeated 6-week cycles of 50 mg/day orally for 4 weeks, followed by 2 weeks off treatment. A total of 92 single nucleotide polymorphisms (SNPs) in 34 genes in the pharmacokinetic and pharmacodynamic pathways of drugs were analysed using the Drug inCode pharmacogenetic service. This test is performed from a saliva sample and uses a DNA microarray system. Polymorphisms in candidate genes, together with clinical characteristics, were tested by univariate analysis for association with the number of days of sunitinib treatment until the first reduction of dose, progression free survival (PFS) and overall survival (OS).

**Results** Patients with CYP1A2*1/*1, a low-metabolising genotype, needed dose reduction due to an increased risk of toxicity vs. *1F/*1F or 1F/1F*(Median time to dose reduction: 2.33 months vs. not reached during study period; $p < 0.006$). Patients with CYP2C19*1/*1, wild type genotype, had an increased risk of dose reductions due to toxicity versus other genotypes (Median time to dose reduction: 2.8 months vs. 9.73 months; $P < 0.021$). No statistically significant associations were observed among drug metabolising genes and PFS or OS.

Val(158)Met Catechol-O-methyltransferase (COMT) gene polymorphisms have been associated with PFS and OS. We found that Met/Met carriers, low metabolising allele, had longer PFS and OS compared to those with Met/Val (PFS not reached vs. 15 months; OS not reached Vs17.2 months) and Val/Val (PFS = 3.3 months; OS = 4.4 months) phenotypes ($P = 0.005$ for PFS and $P = 0.003$ for OS).