eahp european association of hospital pharmacists
18th Congress
making the difference in medication
PHC-025

Single nucleotide polymorphisms associated with adverse events in taxane-treated breast cancer patients

V. Bosó-Ribelles[1], M.J. Herrero-Cervera[1], A. Santaballa-Beltran[2], L. Palomar-Abad[2], H. de la Cueva-Sapiña[2], J. Montalar-Salcedo[2], S.F. Aliño-Pellicer[3], J.L. Poveda-Andrés[1].

[1] Pharmacy Department, Hospital Universitari i Politècnic La Fe (HUPLF), Valencia (Spain). [2] Medical Oncology, HUPLF, Valencia (Spain). [3] Pharmacology Department, Facultad de Medicina, Universidad de Valencia.

Background

Inter-individual differences in drug efficacy and toxicity are linked, in many cases, to single nucleotide polymorphisms (SNPs) in genes coding for drug metabolizing enzymes and transporters. Taxanes are active for several tumour types, including breast cancer. But this is limited by adverse events such as neurotoxicity and haematological toxicity.

Purpose

To evaluate the associations between a panel of 92 SNPs in 33 genes and adverse events developed by breast cancer patients treated with taxanes.

Materials and Methods

Between June 2011 and May 2012 breast cancer patients treated with taxanes who gave informed consent were genotyped for 92 SNPs in 33 genes. Genomic DNA was analysed by a genetic analysis platform (MassArray, Sequenom). Hardy-Weinberg equilibrium was assessed. Clinical data were recorded. The association between genotypes and adverse reactions was assessed with Fisher's exact test and X2-test.

Results

Sixty-seven Caucasian women were genotyped. All genotype frequencies were in Hardy-Weinberg equilibrium.

Patient's characteristics

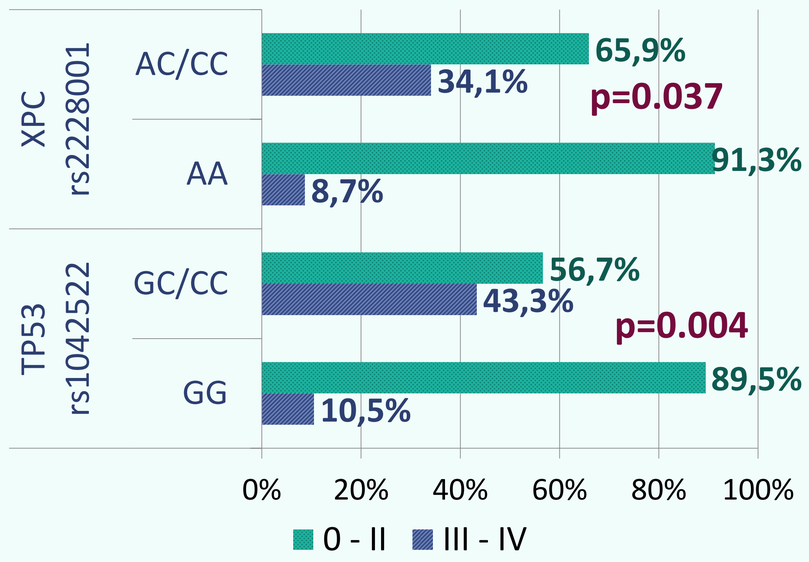
Age (mean, 95%CI)	53 years (49 - 56)
Drug (%, n)	
- **Docetaxel**	53.7% (n=36)
- **Paclitaxel**	46.3% (n=31)
Histotypes (%, n)	
- **Ductal**	88.1% (n=59)
- **Lobular**	7.5% (n=5)
- **Other**	4.5% (n=3

Genotype frequencies

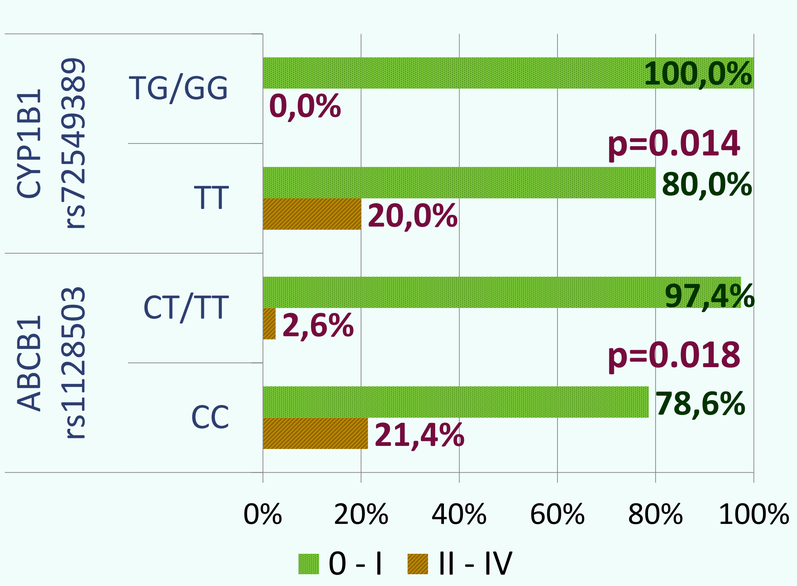
Gene/SNP		n	%
ABCB1 rs1128503	CC	27	40,3%
	CT/TT	40	59,7%
CYP1B1 rs72549389	TT	36	56,3%
	TG/GG	28	43,8%
CYP2C8 rs1341164	TT	31	46,3%
	TC/CC	36	53,7%
ERCC2 rs1799793	GG	28	41,8%
	GA/AA	39	58,2%
XPC rs2228001	AA	23	34,3%
	AC/CC	44	65,7%
TP53 rs1042522	GG	37	55,2%
	GC/CC	30	44,8%

(Due to the limited space, among the 92 SNPs, only those for which associations were found are shown)

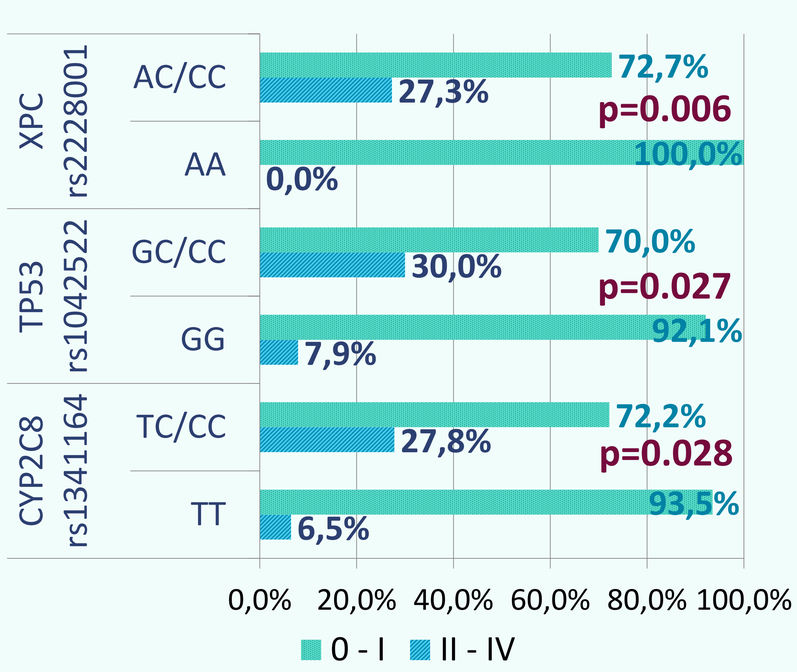
Overall grade III-IV toxicity



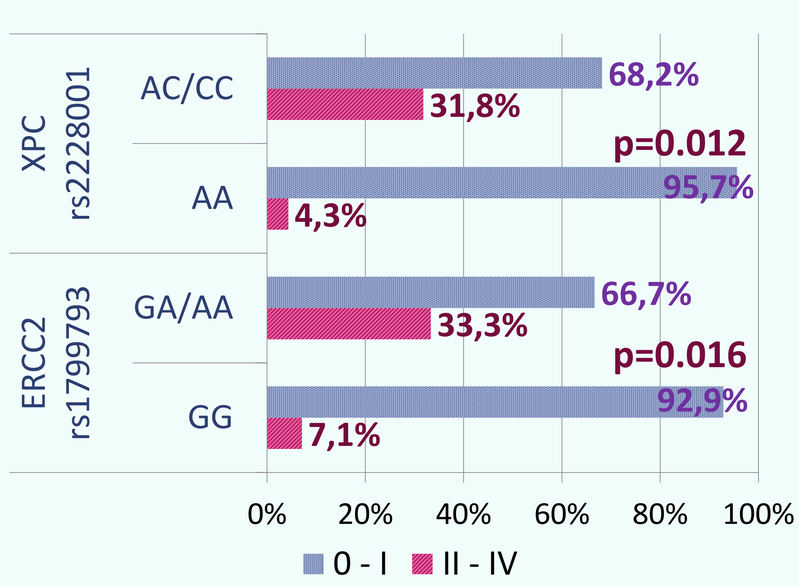
Diarrhoea grade II-IV



Neutropenia grade II-IV



Anaemia grade II-IV



Conclusions

Studying genetic variations can help to identify patients at higher risk of suffering adverse events and provides useful information to individualize therapy.

Contact: Virginia Bosó. Servicio de Farmacia, Hospital Universitari i Politècnic La Fe. Edificio C Planta S. Bulevar Sur, s/n 46026 Valencia (Spain).
E-mail: boso_vir@gva.es