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Title: The pharmacogenetic effect of ADRB2 polymorphisms on therapeutic response in COPD

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Body: Background Most pharmacogenetics studies of COPD have focused on the role of variants in the b2-adrenergic receptor gene on bronchodilator response, but the findings have been inconclusive. Objective To investigate lung function responses following a 24-week treatment with a long-acting b2 agonist combined with a steroid inhaler in patients with COPD with various ADRB2 genotypes. Methods In 73 patients with stable COPD, polymorphisms in the amino acid position 16 (Arg16/Gly16) and 27 (Gln27/Glu27) of the ADRB2 gene were assessed by allele-specific polymerase chain reaction. Long-term response was evaluated using observed change in spirometric values before and after the treatment with formoterol (12 ug) combined with budesonide (400 ug) inhalation twice daily for 24-week. Results In terms of codon 16 variants, the FEV1 changes following the 24-week treatment were $5.64 \pm 1.49\%$ predicted in Gly/Gly patients, $-3.40 \pm 0.85\%$ predicted in Arg/Gly patients, and $-7.00 \pm 1.38\%$ predicted in Arg/Arg patients (p < 0.1). In terms of codon 27 variants the FEV1 changes after 24-week treatment was $3.32 \pm 0.89\%$ predicted in Gln/Glu patients, $2.01 \pm 0.97\%$ predicted in Gln/Glu patients, and $-1.36 \pm 0.42\%$ predicted in Gln/Gln patients (p < 0.1). Conclusion Arg16-Gln27 haplotype was associated with decreased lung function after 24-week treatment with long-acting β2-agonists plus inhaled corticosteroids in a Russian population.