Introduction: The most frequent psychiatric disorder is depression. Half of patients treated by tianeptine present a positive response. In fact, tianeptine response, as well as, other antidepressants is modulated by genetic factors. This molecule was shown acting on glutamate and serotonin pathways.

Objectives: We analyzed polymorphisms of 12 candidate genes involved in glutamate and serotonin pathways in 3536 outpatients treated with tianeptine for a major depressive episode (MDE) to find an association to a positive treatment response.

Aims: The aim of this study was to identify the pharmacogenetic response to tianeptine treatment in MDE.

Methods: A total of 3536 outpatients with a MDE were treated with tianeptine. The criteria for a MDE were characterized by clinicians according to the DSM-IV diagnosis and, the duration and intensity of each symptom was recorded during the inclusion at 4 to 8 weeks of treatment. The Hospital Anxiety and Depression Scale (HAD) was evaluated at the two visits. DNA was extract from saliva samples and genotyping of 49 single nucleotide polymorphisms (SNPs) in 12 genes was performed by Taqman assay.

Results: All clinical and genotype data were collected for 3536 tianeptine-treated patients. A total of 7 SNPs, located in 4 different genes, were found associated to a positive treatment response, corresponding to a reduction of 50% of the HAD. This was confirmed in the Caucasians subgroup of 3040 patients.

Conclusions: We detected pharmacogenetic associations between glutamate and serotonin genes and the response to tianeptine in major depressive episode.