The treatment of early Parkinson's disease with dopaminergic agents remains the mainstay of symptomatic therapy for this incurable neurodegenerative disorder. However, clinical responses to dopaminergic drugs vary substantially from person to person due to individual-, drug- and disease-related factors that may in part be genetically determined. Using clinical data and DNA samples ascertained through the ADAGIO clinical trial of the monoamine oxidase B inhibitor, rasagiline (ClinicalTrials.gov number, NCT00256204), we examined how polymorphisms in candidate genes associate with the clinical response to rasagiline in early Parkinson's disease. Variants in genes that express proteins involved in the pharmacokinetics and pharmacodynamics of rasagiline, and genes previously associated with the risk to develop Parkinson's disease were genotyped. The LifeTechnologies OpenArray NT genotyping platform and polymerase chain reaction-based methods were used to analyse 204 single nucleotide polymorphisms and five variable number tandem repeats from 30 candidate genes in 692 available DNA samples from this clinical trial. The peak symptomatic response to rasagiline, the rate of symptom progression, and their relation to genetic variation were examined controlling for placebo effects using general linear worsening in Parkinson symptoms from Weeks 12 to 36 after correction for multiple testing. The results indicate a clinically meaningful benefit to rasagiline in terms of the magnitude of improvement in parkinsonian symptoms for those with the favourable response genotypes. Future work is needed to elucidate the specific mechanisms through which these DRD2 variants operate in modulating the function of the nigrostriatal dopaminergic system.