Evaluation of six CTLA-4 polymorphisms in high-risk melanoma patients receiving adjuvant interferon therapy in the He13A/98 multicenter trial.

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Source

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Abstract

PURPOSE:

Interferon is approved for adjuvant treatment of patients with stage IIb/III melanoma. The toxicity and uncertainty regarding survival benefits of interferon have qualified its acceptance, despite significant durable relapse prevention in a fraction of patients. Predictive biomarkers that would enable selection of patients for therapy would have a large impact upon clinical practice. Specific CTLA-4 polymorphisms have previously shown an association with response to CTLA-4 blockade in patients with metastatic melanoma and the development of autoimmunity.

EXPERIMENTAL DESIGN:

286 melanoma patients and 288 healthy controls were genotyped for six CTLA-4 polymorphisms previously suggested to be important (AG 49, CT 318, CT 60, JO 27, JO30 and JO 31). Specific allele frequencies were compared between the healthy and patient populations, as well as presence or absence of these in relation to recurrence. Alleles related to autoimmune disease were also investigated.

RESULTS:

No significant differences were found between the distributions of CTLA-4 polymorphisms in the melanoma population compared with healthy controls. Relapse free survival (RFS) and overall survival (OS) did not differ significantly between patients with the alleles represented by these polymorphisms. No correlation between autoimmunity and specific alleles was shown. The six polymorphisms evaluated where strongly associated (Fisher's exact p-values < 0.001 for all associations) and significant linkage disequilibrium among these was indicated.

CONCLUSION:

No polymorphisms of CTLA-4 defined by the SNPs studied were correlated with improved RFS, OS, or autoimmunity in this high-risk group of melanoma patients.