The Effects of IFN-α + 13-CRA on Patients with Squamous Cell Carcinoma

Robert Collins, M.A.[1], Scott Lippman, M.D.[2], Christina Meyers, Ph.D.[3]

[1]Dept. of Psychology, University of Houston, [2]Dept. of Neuro-Oncology, MD Anderson Cancer Center

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Abstract

Combination treatment with interferon-α (IFN-α) and 13-cis-retinoic acid (13-CRA) has shown promise in reducing the recurrence of primary skin cancers; however, the IFN- α component of the treatment is associated with depression and cognitive dysfunction. The present study assessed differences in BDI-II (BDI) scores, quality of life (QOL), and verbal fluency in patients diagnosed with squamous cell carcinoma. Patients were assessed prior to randomization to IFN-α and 13-CRA treatment, or surveillance, and again following 3-months on treatment, or surveillance. The initial sample was screened for outliers, and missing data, and all multivariate assumptions were met. The final sample (N=36) was predominantly male, with an average age of 63 and 12 years of education (no group differences, p>0.05). A doubly multivariate analysis, with age and education as covariates, revealed a treatment by time interaction at the first assessment. At 3 months, patients treated with IFN-α and 13-CRA evidenced an increase in BDI scores and a decrease in QOL, whereas patients under surveillance evidenced a decrease in BDI scores and an increase in QOL. Only BDI scores were significant in the stepdown analysis of the treatment by time interaction (p<0.05). Treatment with IFN- α and 13-CRA appeared to have little effect on verbal fluency.

Introduction

Squamous cell carcinoma of the head and neck is relatively common and associated with disfigurement, increased risk for recurrence, and significant morbidity. Interferon-α (IFN-α) and 13-cis-retinoic-acid (13-CRA) are used as a combination treatment for squamous cell carcinoma (Lippman et al, 1992). Patients treated with IFN-α frequently evidence increases in depression and develop significant cognitive dysfunction (Meyers et al, 1995). Impairments are typically restricted to the treatment period (i.e., a 3-6 month period), but some patients may experience impairments long after treatment cessation. As such, treatment related declines in mood and cognitive functioning must be considered against the clinical benefit of the therapy.

The purpose of the present study was to assess BDI-II scores (BDI), quality of life (QOL), and verbal fluency in patients with squamous cell carcinoma prior to, and during, randomization to treatment with IFN-α + 13-CRA or surveillance (SURV). It was predicted that patients randomized to the treatment arm of the study would evidence increases in reported BDI-II scores, decreases in reported quality of life, and decreases in verbal fluency at 3 months treatment relative to patients randomized to the SURV arm. Moreover, it was predicted that the pattern of scores for patients in the SURV arm would remain unchanged over time, whereas patients receiving treatment would evidence a pattern of scores that would change from baseline to 3 months treatment.

Method

Data were obtained from 66 patients diagnosed with squamous cell carcinoma of the head and neck and participating in an IFN-α + 13-CRA protocol at MD Anderson Cancer Center, Houston, Texas. Patients underwent baseline neuropsychological testing and then while on treatment at 3-months. The Beck Depression Inventory-II used to assess depression, while verbal fluency was assessed with the Controlled Oral Word Association. Quality of life was assessed with the Functional Assessment of Cancer Therapy (FACT). This Includes subscales for physical, social/family, emotional, and functional well-being, with higher scores indicating better QOL (D'Antonio et al., 1998). The data were screened for outliers and missing data and all multivariate assumptions were met.

Results

Demographic information can be seen in Table 1. Figures 1-3 summarize the group means for each of the DV's at baseline and 3 months treatment. A doubly-multivariate analysis was performed on INF-α and SURV treatment groups completing BDI-II, FACT, and COWA measures prior to treatment and at 3-months treatment. Age and education were used as covariates. The between-subjects measure was treatment arm and the within-subjects measure were the 3 DV's at baseline and 3 months treatment.

The composite dependent variable scores varied by treatment group across baseline to the 3 month assessment (deviation from parallelism; see Table 2). Tests for differences among levels, and deviation from flatness, were not assessed (group and time main effects not significant, p>0.05). With experiment-wise error of 5% (α = .016), only BDI-II scores were significant in a stepdown analysis for the treatment by time interaction [$F(1,33)=16.42$, $p<0.001$, partial $\eta^2 = .333$].

Table 1. Mean Age and Education for Patients treated with Interferon-α and 13-cis-retinoic-acid (IFN-α) and those under surveillance (SURV)

	Age	Ed	t-test
IFN-α			
n	18	18	
M (SD)	60.5 (12.1)	12.4 (2.5)	NS
SURV			
n	18	18	
M (SD)	66.4 (13.3)	12.9 (3.6)	NS

Table 2. Multivariate tests of significance

	F	DF	Sig	η^2
Treatment	1.79	(3,31)	NS	
Time	1.21	(3,31)	NS	
Tx × Time	5.39	(3,31)	.004	.343

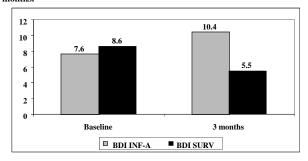Figure 1. Average BDI-II scores for treatment groups at baseline and 3 months.

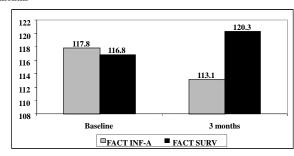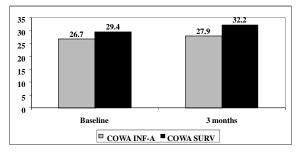Figure 2. Average FACT scores for treatment groups at baseline and 3 months

Figure 3. Average COWA scores for treatment groups at baseline and 3 months

Discussion

In the present study it was predicted that composite BDI-II, QOL, and COWA scores would 1) differ between patients treated with IFN-α and patients under surveillance and 2) that the difference would also vary from the baseline assessment to 3-months treatment. It appears as though patients entered the study with slightly elevated BDI-II scores and reduced QOL, which is not inconsistent with having a recent diagnosis of squamous cell carcinoma. In this study it is likely that the reduction in BDI-II scores, and increases on measures of QOL in the SURV group, may actually represent a return to pre-illness levels. In contrast, the increased BDI-II scores and decreased measures of QOL among the patients treated with IFN-α likely represent the unpleasant physical side effects from the treatment. It is interesting that IFN-α treatment had little impact on verbal fluency, as IFN-α treatment likely has an impact on subcortical white matter. However, it should also be noted that the present sample was older, with an average age of 63, and that it is possible that patients entered the study with age-related declines in verbal fluency. This sample should be assessed after additional treatment, and then shortly after cessation of treatment, to more fully characterize the effect IFN-α treatment on mood and cognitive functioning.

For Correspondence:
rcollins4@uh.edu