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Intravenous high-dose interferon with or without maintenance treatment in melanoma at high risk of recurrence: meta-analysis of three trials.

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Abstract

Resected stage IIB-IIIC malignant melanoma has a poor prognosis with a high risk of relapse and death. Treatment with adjuvant interferon alfa-2b (IFN-α-2b) is associated with improved relapse-free and overall survivals (OS), but the most appropriate dose and duration of treatment are unknown. In this article, we present an individual patient data random effects meta-analysis of melanoma patients from the U.K., Greek, and Chinese randomized trials. All patients were randomized either to IFN-α-2b 15-20 MIU/m^2 IV daily 5 days per week for 4 weeks (IV) or to the same regimen followed by IFN-α-2b 9-10 MIU/m^2 administered three times per week for 48 weeks (IV and SC). Allowing for dose interruptions and reductions, an equivalent total dose of IFN-α-2b was delivered in all three studies. We assessed whether IV was noninferior to IV and SC in terms of relapse-free survival (RFS) and investigated tumor and patient characteristics that impacted on outcomes. Median follow-up of 716 stage IIB-IIIC patients was 5.4 years. Noninferiority of IV compared to IV and SC could not be conferred for RFS (hazard ratio [HR] 1.16, 95% confidence interval [CI] 0.89-1.52; noninferior $P = 0.17$). Stage ($P < 0.0001$), site (acral vs. other, $P < 0.0001$), and Breslow thickness ($P = 0.02$) were significant predictors of RFS. The HR for death was 1.13 for IV compared to IV and SC, (95% CI 0.91-1.39). Stage ($P < 0.0001$) and Breslow thickness ($P = 0.001$) were significant independent predictors of OS. The available data suggest that where adjuvant high-dose interferon is being considered there is no evidence to deviate from the year long regimen described in the Eastern Cooperative Oncology Group and Intergroup studies.