4LB Late Breaking

Results of the Nordic randomised adjuvant trial of intermediate-dose interferon alfa-2b in high-risk melanoma

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Background: The trial was designed to investigate the effects of adjuvant post-operative therapy with intermediate-dose interferon alfa-2b (IFN) in patients with stage IIB-C/III cutaneous melanoma. The outcome of maintenance treatment with IFN for 1 versus 2 years following a 4 week induction period was studied.

Materials and Methods: Between November 1996 and August 2004 a total of 855 patients were entered into the study. Patients were randomized in equal proportions to three study arms: Arm A: Observation only. Arm B: induction: IFN 10 MU S.C. 5 days/week for 4 weeks; maintenance: IFN 10 MU S.C. 3 days/week for 12 months. Arm C: induction as arm B; maintenance: IFN 10 MU S.C. 3 days/week for 24 months.

Recurrence-free survival (RFS) and overall survival (OS) were analysed using life table techniques, taking censored observations into account. Univariate analyses were performed with Kaplan-Meier and Log-Rank tests. Multivariate analyses were performed with Cox regression analysis.

Results: Adjuvant IFN therapy significantly improved RFS. Median RFS for Arm A: 20.5 months: Arm B: 37.7 months; Arm C: 24.0 months. Hazard ratio (HR) for recurrence for IFN treated patients (Arms B + C combined) was 0.82 ($p = 0.045$) compared to Arm A. HR for Arm B vs. Arm A: 0.76 ($p = 0.019$) and for Arm C vs. Arm A: 0.88 ($p = 0.217$). Adjuvant IFN therapy had no significant effect on OS. Median OS for Arm A: 54.6 months: Arm B: 69.6 months; Arm C: 55.4 months. Hazard ratio (HR) for death for IFN treated patients (Arms B + C combined) was 0.93 ($p = 0.515$) compared to Arm A. HR for Arm B vs. Arm A: 0.92 ($p = 0.484$) and for Arm C vs. Arm A: 0.95 ($p = 0.679$).

Conclusions: Adjuvant treatment with intermediate-dose IFN in high-risk melanoma patients significantly improved RFS without significantly increasing OS. There was no indication that prolonging the maintenance treatment with IFN from 1 to 2 years improved the outcome in these patients. Further translational research is ongoing to better define the subgroup of patients who benefit from adjuvant IFN therapy.