5LB Late Breaking

Prognostic value of autoantibodies in melanoma stage III patients in the EORTC 18991 phase III randomized trial comparing adjuvant pegylated interferon α2b vs observation

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Background: Appearance of autoantibodies during IFN-adjuvant therapy is a prognostic factor and potentially a predictive factor in melanoma patients (pts). We evaluated this in the pivotal randomized controlled EORTC 18991 trial.

Methods: 1256 stage III pts were randomized to receive either long-term therapy with pegylated interferon (PEG-IFN) for a 5 yr period or no adjuvant therapy (Observation). Serum samples were collected pre-treatment and every 6 months for a maximum period of 5 years. Anti-cardiolipin (C) anti-thyreoglobulin (T) and anti-nuclear (N) antibody levels of serial samples were assessed centrally. Prognostic impact of CTN on relapse-free survival (RFS) was assessed by 3 methods: (1) usual Cox model (lead-time bias); (2) Cox Time dependent model using the latest *positive* CTN value; (3) Classical Cox Time dependent model using the latest *any* CTN value.

Initial CTN status = NEGATIVE

Endpoint	Any positive CTN (usual Cox model)		Latest *positive* CTN (Time-Dependent Cox model)		Latest *any* CTN (Time-Dependent Cox model)	
RFS	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
All patients (N = 220, O = 100)						
CTN + vs –	0.82 (0.54–1.23)	0.33	1.27 (0.80–2.00)	0.32	1.21 (0.75–1.95)	0.43
# of LN	1.91 (1.46–2.49)	<0.0001	1.85 (1.42–2.41)	<0.0001	1.85 (1.42–2.41)	<0.0001
PEG-IFN-pts (N = 107, O = 50)						
CTN + vs –	0.69 (0.40–1.20)	0.19	1.37 (0.74–2.53)	0.31	1.44 (0.79–2.64)	0.24
# of LN	1.67 (1.16–2.41)	0.006	1.68 (1.17–2.43)	0.006	1.69 (1.17–2.44)	0.006
Obs pts only (N = 113, O = 50)						
CTN + vs –	1.00 (0.50–1.97)	0.99	1.34 (0.59–3.07)	0.49	1.01 (0.35–2.90)	0.98
# of LN	1.99 (1.34–2.98)	0.0007	1.96 (1.34–2.88)	0.0006	1.99 (1.35–2.94)	0.0005

Results: The presence of autoantibodies at any time was determined in 361 pts. Among them, 296 pts [170 stage III N1 (microscopic involvement only), 126 stage III N2 (macroscopic involvement only)], Obs (149) or PEG-IFN (147), had their initial CTN status assessed. 76 (26%) were CTN-positive (pos) (similar in both arms) and 220 (74%) were CTN-negative (neg). Of these CTN-neg pts the following became CTN-pos (at least once) during the study: 23/113 (20%) Obs and 60/107 (56%) PEG-IFN. 1-yr conversion rate was 33%, 58% and 2-yr rate was 38%, 76% (Obs, PEG-IFN resp.) Median follow-up = 3.6 years. Relapse occurred in 139/296 pts. Median RFS = 4.3 years. In the 220 pts with *negative* initial CTN status, according to the usual Cox model, HR for CTN-pos vs CTN-neg was 0.82. To adjust for Lead Time Bias, the Cox time dependent models were used; CTN status was not a significant prognostic factor in these analyzes (HR: 1.27 Latest *positive* CTN, HR: 1.21 Latest *any* CTN).

All analyses were adjusted for # of pos nodes, which was a strong independent prognostic factor. These results were similar when only IFN or Obs pts were considered. Analyses for different cut off points, regarding only strong positive CTN, will be carried out shortly for both the EORTC 18991 and the previous 18952 study.

Conclusion: Presence or appearance of autoantibodies was not associated with improved outcome in melanoma patients.