NSCLC, metastatic

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SMOKING HISTORY AND RESPONSE TO NIVOLUMAB IN PATIENTS WITH ADVANCED NSCLCS

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Aim: Robust responses to nivolumab (Nivo, anti-PD1 antibody) are seen in both melanomas and NSCLCs. Both of these cancers are characterized by high somatic mutation burden, suggesting a potential link between mutational burden and immunogenicity. Since smoking-related NSCLCs have significantly greater mutation burden compared to never smokers, we hypothesized that smoking history may be associated with response to nivolumab in pts with NSCLCs.

Methods: Smoking status, histology, and EGFR/KRAS genotype were recorded from 88 of 129 pretreated, advanced NSCLCs treated with Nivo monotherapy at 5 of 11 centers that participated in a previously reported study (NCT00730639, Topalian et al, NEJM 2012). Self-reported smoking history was categorized as never (<100 cigarettes), minimal (≤5 pk-yrs), former (>5 pk-yrs, quit > 1 yr prior), or current smokers. In smokers, time-since-quitting was also recorded. Response was assessed every 8 wks by RECIST v1.0. Associations between smoking, histology, genotype, and response were assessed using the Fisher’s exact, unpaired T-, log-rank tests.

Results: The response rate was significantly higher in former/current smokers (20/75, 27%, 95% CI 17-38%) vs minimal/never smokers (0/13, 0%, 95% CI 0-25%) (p = 0.034). Responders had significantly more tobacco exposure than non-responders (median 50 pk-yrs [range 15-150] vs 36 pk-yrs [range 0-100], p = 0.036). Among smokers, there was no association between response and time-since-quitting (Current smokers ORR 27%; Quit 1-15 yrs ago 24%; Quit >15 yrs ago 24%, p = 0.18). There was no significant difference in response rate in adeno vs squamous histology (16 vs 21%, p = 0.58). In adenos, response rates in EGFR muts vs KRAS muts vs all others were 1/9 vs 3/13 vs 4/27; the one EGFR mut responder was a 40 pk-yr current smoker.

Conclusions: In advanced NSCLCs, the response rate to Nivo was significantly higher in former/current smokers compared to never/minimal smokers. There were no objective responses in never or minimal smokers in this subset of pts. Smoking history should be considered as a stratification factor for trials of PD-1 pathway inhibitors in lung cancer. Further work is needed to identify the underlying basis of this differential response rate.

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