were developed to predict time-to-event outcomes based on patient-level data from pooled CheckMate-067 &-069 trials. Risk equations were inserted into a discrete event simulation to estimate the average life-years (LYs) and quality-adjusted life-years (QALYs) that can be gained with various treatment sequences over a lifetime horizon. Treatment sequences and corresponding efficacy data sources are presented below (table 1). Utility weights for quality-adjustment of LYs were obtained from published literature.

Results Treatment sequences starting with IO followed by BRAF+MEK were associated with 2.9–4.3 years of additional survival and 2.2–3.3 years of quality-adjusted survival versus sequences starting with BRAF+MEK followed by anti-PD-1. After 1L IO, the time spent in the treatment-free interval (TFI) is 3.3–5.0 years. LYs, QALYs, and time spent in TFI were higher with sequences starting with anti-PD-1+anti-CTLA-4 vs. anti-PD-1 alone.

Conclusions In this sequencing model with 5-year data from randomized clinical trials, initiating 1L treatment with IO provided prolonged survival compared to initiating 1L treatment with BRAF+MEK. Time spent in TFI represents a significant proportion of survival time for patients on IO initiating sequences. Limitations of the study are the reliance on published information for BRAF+MEK, which could lead to biases due to unmeasured differences in the patient populations or trial conduct and the absence of data on 2L combinations. Anti-PD-1+anti-CTLA-4 as second line option has been included because of a lack of clinical evidence. Findings or trial conduct and the absence of data on 2L combinations. Limitations of the study are the reliance on published information for BRAF+MEK, which could lead to biases due to unmeasured differences in the patient populations or trial conduct and the absence of data on 2L combinations. Anti-PD-1+anti-CTLA-4 as second line option has been included because of a lack of clinical evidence.

References


Background Nivolumab is approved in the US and EU for the adjuvant treatment of resected stage III-IV melanoma based on results from the CheckMate-238 clinical trial.1,2 However, the trial did not enroll any patients with Stage IIIA disease per the American Joint Committee on Cancer (AJCC) 7th edition criteria and included a limited number of patients with stage IIIA disease per the AJCC 8th edition.1,3 Recognizing the need for real-world data to assess outcomes of patients with resected stage IIIA melanoma treated with adjuvant nivolumab, a non-interventional study was conducted to investigate treatment patterns and outcomes among patients receiving adjuvant nivolumab within the US community practice setting.

Methods A retrospective analysis of the US Oncology Network’s iKnowMed medical data was conducted to examine patients with resected stage II melanoma treated with adjuvant nivolumab between 01-Jan-2018 and 31-Dec-2019 with a follow-up period through 31-Mar-2020. Patients were followed for up to 27 months after their sentinel lymph node biopsy. Baseline demographic/clinical characteristics and treatment patterns were examined descriptively. Duration of treatment (DOT) and overall survival were analyzed using the Kaplan-Meier method.

Results A total of 58 patients with stage II melanoma treated with adjuvant nivolumab were identified. Median age was 57.8 years (range 21.5–93.5), 62.1% were male, and 75.9% were Caucasian. Among patients with a documented Eastern Cooperative Oncology Group (ECOG) performance status (51.7%), all had an ECOG score of 0 or 1. Median follow-up time was 12.6 months (range 0.3–25.1). Median DOT was 10.6 months (range 6.8–12.0). Overall survival rates at 12 and 24 months were 97.7% (95% CI 84.6–99.7) and 92.2% (95% CI 69.6–98.2), respectively.

Conclusions This real-world analysis of patients with stage II melanoma treated with adjuvant nivolumab showed that a large proportion of patients were alive at the end of the study period, suggesting these patients have a favorable prognosis. Further investigation and follow-up is warranted to assess clinically relevant outcomes among patients with resected stage II melanoma.

Ethics Approval The study was approved by US Oncology Inc’s Institutional Review Board, approval number 20-020E-2020-0224-01.

221 POOR PERFORMANCE STATUS NEGATIVELY AFFECTS SURVIVAL BENEFIT OF IMMUNOTHERAPY IN NON–SMALL CELL LUNG CANCER

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Background Immunotherapy has shown survival benefit as both frontline and subsequent therapy in multiple cancers. However, its efficacy in patients with poor performance status is unknown since they are excluded from the clinical trials. We conducted a retrospective study to investigate the effect of poor performance status (PS) on survival in patients with non–small cell lung cancer (NSCLC) who received immunotherapy as a subsequent line of treatment.
Methods We reviewed the medical records of 341 patients with NSCLC receiving immunotherapy as between July 2013 and June 2018. Progression-free survival and overall survival was calculated using Kaplan-Meier curve.

Results The average age of patients was 66 years (range: 39–90 years), with a male predominance (57%). Majority of the patients were Caucasian (87%), followed by African-American (12%), and Asian (1%). Most of the patients were former smoker (72%), followed by current smoker (19%) and never smoker (7%). Adenocarcinoma and squamous cell carcinoma was diagnosed in 206 (60%) patients and 112 (33%) patients, respectively. The ECOG-PS was 0, 1, 2 and 3 in 46 (13%), 175 (51%), 86 (25%) and 34 (10%), respectively. Four different immunotherapies were used, namely atezolizumab in 10 (3%), durvalumab in 34 (10%), nivolumab in 152 (44%) and pembrolizumab in 144 (42%) patients. Average number of cycles of atezolizumab received by the patient was 6 (range 2–22 cycles), durvalumab 15 (range 1–29 cycles), nivolumab 11 (range 1–112 cycles), and pembrolizumab 12 (range 1–52 cycles). Patients were grouped in good performance status (ECOG 0–1) and poor performance status (ECOG ≥2). The median progression free survival (PFS) was 7 months (95% CI 6.3–8.2) in patients with good PS and 3 months (95% CI 1.8–4.6) in patients with poor performance status (p<0.001). The median overall survival (OS) for patients with good performance status was 30 months (95% CI 16.6–42.3) and 4 months (95% CI 3.2–8.1) in patients with poor PS (figure 1). Adverse effects were recorded in a total of 83 (24%) patients, 18 (5%) patients had ECOG-PS 0, 50 (14%) patients had ECOG-PS 1, 18 (4%) patients had ECOG-PS 2 and 3 (1%) patients had ECOG-PS of 3. Most common adverse effects were pneumonitis (28%), diarrhea (8%) and hyperthyroidism (8%).

Conclusions Our data suggests that while the patients with poor PS tolerated the immunotherapy. However, poor PS was associated with significantly lower PFS and OS. Further studies are required to evaluate the effect of PS on survival in frontline immunotherapy.

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Trial Registration N/A

Ethics Approval The study was approved by the Institution Review Board at KUMC, #CR00009003.

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222 INCREASED PD-L1 TUMOR EXPRESSION CORRELATES WITH HIGH RATE OF RESPONSE TO PD-1 INHIBITORS IN PATIENTS WITH UNRESECTABLE, RECURRENT, AND METASTATIC CUTANEOUS SQUAMOUS CELL CARCINOMA

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Background PD-1 inhibitors were approved for locally advanced and metastatic cutaneous squamous cell carcinoma (CSCC) in 2019.1 The identification of tumor characteristics that predict potential responders to immune checkpoint inhibitors (ICI) is an area of ongoing research. Here we present a series of consecutive patients with locally advanced, recurrent, or metastatic CSCC treated with PD-1 inhibitors and analyze tumor and blood genomics as well as PD-L1 expression with the aim of correlating with treatment response.

Methods We analyzed cases of CSCC treated with single agent PD-1 inhibitors in the last 2 years at Wake Forest. Demographic and outcome data were collected. Tumor tissue, whenever available, was tested for PD-L1, TMB, MSI, and genetic mutations. Blood was tested for circulating tumor at the beginning of treatment and at the time of maximum response.

Results Fourteen patients with CSCC treated with PD-1 ICI were included in this study. Six had locally advanced disease, seven had recurrent locally advanced disease, and one had metastatic disease. Four patients received treatment for >12 months and all had complete response (CR). Five patients had 6–12 months of treatment and all had near CR (pending imaging studies and ctDNA to confirm). Three patients had <6 months of treatment and had partial response (PR). Two of the patients had progressive disease, although one with possible pseudoprogression based on review of post-treatment surgical pathology specimen. Treatment was well tolerated with no immune related side-effects except one case of grade I hypothyroidism. Eleven patients had sufficient tumor tissue for genomic and PD-L1 testing. Initial blood genomic testing was performed in 12 of 13 patients and in follow up in patients who achieved maximum response. Patients with CR had PD-L1 of at least 30%. The additional tested patients had PD-L1 above 10%. The most frequently mutated gene was TP53 present in tumor in all tested patients and in blood in 6 patients, followed by NOTCH1/2 detected in the tumor of 10 of 11 patients tested. TMB was intermediate/high in tested patients except in the only patient who presented clear tumor progression.

Conclusions Treatment of locally advanced, recurrent, and metastatic CSCC with ICI led to a dramatic change in the management and prognosis of CSCC. Our series of patients with CSCC had a higher than reported rate of response. This corresponded with high TP53 alterations, NOTCH 1/2 alterations, high/intermediate TMB, and high level of expression of PD-L1. PD-L1 rates were higher than previously published.1 2