Racial Differences in Outcomes for Metastatic Renal Cell Carcinoma (mRCC) Patients Managed on Immune-Checkpoint Inhibitor (ICI) Therapy

Background
Immune checkpoint inhibitors (ICIs) have increased in prevalence for the treatment of metastatic clear-cell renal cell carcinoma (mccRCC) in recent years given their efficacy and favorable toxicity profile. However, there has been insufficient investigation in the literature of how clinical outcomes differ on the basis of race. In this paper, we investigated differences in clinical outcomes between African American (AA) and Caucasian mRCC patients treated with ICI therapy.

Methods
We performed a retrospective study of 198 patients with mRCC who received ICI at the Emory Winship Cancer Institute from 2015–2020. Clinical outcomes were measured by overall survival (OS), progression-free survival (PFS), and clinical benefit (CB). OS and PFS were calculated from ICI initiation to date of death and radiographic or clinical progression, respectively. CB was defined as a best radiographic response of complete response, partial response, or stable disease maintained for at least 6 months per response evaluation criteria in solid tumors version 1.1. The association of self-identified race with OS and PFS was generally modeled by Cox proportional hazards model. Univariable and multivariable criteria in solid tumors version 1.1. The association of self-identified race with OS and PFS was generally modeled by Cox proportional hazards model. Univariable and multivariable logistic regression models were used for binary outcomes of CB. The univariate association of immune-related adverse events (irAEs) and non-clear-cell RCC (ncRC) with race was assessed using Chi-square test.

Results
Our cohort was made up of 38 AA (19%) and 160 Caucasian (81%) patients. Most of the patients were diagnosed with cCRCC (78%) and more than half received PD-1 monotherapy (57%). Most patients were international mRCC database consortium (IMDC) intermediate (57%) or poor-risk (25%) groups. AA patients displayed significantly shorter PHR (HR=1.52, 95% CI: 1.01–2.3, p=0.045) and trended towards decreased CB (OR=0.51, 95% CI: 0.22–1.17, p=0.111) in MVA (table 1). There was no difference in OS (HR=1.09, 95% CI: 0.61–1.95, p=0.778) between the two racial groups in MVA (table 1). On Kaplan-Meier method, AA patients had shorter median OS (17 vs 25 months, p=0.3676) and median PFS (3.1 vs 4.4 months, p=0.0676) relative to Caucasian patients (figure 1). Additionally, AA patients more commonly had ncRCC compared to Caucasian patients (41.7% vs 17.5% ncRCC, p=0.002). AA patients also trended towards a lower incidence of irAEs compared to Caucasian patients in UVA (23.7% vs 35.8%, p=0.153).

Conclusions
In this group of mRCC patients treated with ICI, African American patients had significantly shorter PFS compared to Caucasian patients. These findings suggest race could play a role in the management of late-stage mRCC. Larger, prospective studies are needed to validate these findings.

Acknowledgements
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Trial Registration
Not applicable.

Ethics Approval
This retrospective study was approved by the Emory University Institutional Review Board.

Consent
Not applicable.

REFERENCES
Not applicable.
Abstract 224 Figure 1  OS in patients with melanoma treated with IO

Among patients who received IO, 2-year OS significantly improved by 2015 (40% [95%CI, 37–42%] for both 2004–2010 and 2011–2014 vs. 48% [95%CI, 44–51%] in 2015; p=0.01) (figure 1). In the overall cohort, younger patients (<60 years), female gender, private insurance, no comorbidities, and treatment at academic/research centers were associated with better OS (p<0.0001 for all). Receipt of radiation therapy and lack of surgery were both associated with worse OS (p<0.0001 for both). Race and area of residence (metro/rural/urban) were not associated with differences in OS (p=0.09 and p=0.07, respectively). In 2015–2016, receipt of IO was associated with younger age (<60 years), lack of comorbidities, private insurance, higher median income (= $38,000), residence in metro area, and treatment at academic/research centers (p<0.0001 for all) (table 1).

Conclusions Survival was improved in stage IV patients with melanoma receiving IO, especially in 2015, with the approvals of pembrolizumab and nivolumab. Our findings are consistent with recent trials, like KEYNOTE 006 and CheckMate 067 where 2-year OS for anti-PD-1 therapy was 55% and 60%, respectively. Significant socioeconomic factors may impact receipt of IO and survival.

REFERENCES

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Abstract 224 Table 1  Factors associated with receipt of IO for patients diagnosed in 2015

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Background It is incompletely understood which populations of tumor-infiltrating lymphocytes (TIL) respond to checkpoint blockade (CB) and when. Recent studies in murine MC-38 colon carcinoma demonstrate CD4+ T cells are among the most prominent responders, but these studies were undertaken late in tumor growth, weeks after CB blockade was initiated. Here, we profile how the landscape of CB-responding TIL change between early and late MC-38 tumor growth, and uncover a novel switch that occurs between natural killer T (NKT) and conventional CD4/CDD T cell responses.

Methods We treated C57BL/6 mice bearing subcutaneous MC-38 tumors with anti-PD-1 and/or anti-CTLA-4 antibodies, and analyzed TIL 11 or 21 days later using a 23-paramenter flow cytometry panel that includes three markers of effector function: TNFalpha, IFN-gamma, and CD107a. We then investigated major populations, including NKT TIL, and in vivo cytotoxicity assays and in vivo tumor growth studies using CD11d overexpressin MC-38 cells.

Results Our analysis identified 37 TIL populations in MC-38 tumors, representing CD4+ or CD8+ T cells, natural killer (NK), and NKT cells. The distribution and effector function among TIL shift dramatically between early and late MC-38 growth. At 11 days, the immune response is dominated by...