Experience of Immune-Related Adverse Events Associated with Ipilimumab and Nivolumab in a Single Center

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Background
Immune-related adverse events
• Immune checkpoint inhibitors have been approved for use in a many different cancers including metastatic melanoma, advanced renal cell and lung cancers, colorectal and other gastrointestinal, urological and head and neck cancers.
• Immune-related adverse events (irAEs) have been reported to occur in the majority of patients treated with immune checkpoint inhibitors, with rates of up to 60% if a high dose is used.
• These events are often managed in an outpatient setting and are usually manageable. irAEs are generally related to a strong immune response to the tumor.
• The most common irAEs are dermatological, gastrointestinal and endocrinological.

Methods
Inclusion Criteria
NIVOLUMAB
- The patient has histologically or cytologically documented locally advanced or metastatic NSCLC.
- The patient has progressed on or after treatment with a minimum of 1 prior systemic treatment for stage IIIB or IV NSCLC.
- The patient has histologically confirmed advanced or metastatic RCC with a clear cell component.
- The patient has histologically confirmed advanced or metastatic dCRC with KRAS wild-type.

MALIGNANT MELANOMA
- The patient has histologically documented stage IV (unresectable or stage IV (translocatable) cutaneous, ocular or mucosal melanoma.
- The patient has advanced melanoma at least 1 prior systemic treatment; aged ≥ 18 years of age.
- The patient has performance status of ≤ 2.

Exclusion Criteria
NIVOLUMAB
- Known allergy or intolerance to ipilimumab, nivolumab or any other biologic agents.
- The patient has active or uncontrolled autoimmune disease unless treated and in stable condition.
- The patient has any known active chronic liver disease.
- The patient has known medical condition (e.g., a condition associated with diarrhea or acute diverticulitis).
- The patient has a medical condition requiring systemic treatment with either corticosteroids (>10 mg/day prednisone or equivalent).
- The patient has not recovered from major surgery.

Data Collection
- Data were collected at the time of enrollment in the SA-EAP and courses of treatment.
- Treatment-related irAEs included history of concurrent drug use, details of irAEs and follow-up for patients with severe irAEs.
- Treatment-related irAEs were recorded in the adverse events database for each patient. irAEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0.

Statistical Analysis
- All statistical data were analyzed in this study will be normally distributed. All collected data and subject variables were summarized using descriptive statistics in addition to statistical modeling.

Conclusions
- A higher percentage of patients are treated with anti-PD-1 and anti-PD-L1 antibodies. Cancers are more common with anti-PD-1 antibodies than with anti-PD-L1 antibodies. Pemetrexed alone in NSCLC is less effective with irAEs resulting in increased morbidity and mortality.

Results
- A total of 29 patients (20 males, 9 females) were analyzed.
- The median age was 64 years.
- The median performance status was 1.

Ipilimumab Group
- NIVOLUMAB: 15 patients
- REC-2 patients
- HD: 2 patients
- Nivolumab: 167 cycles of niv (median = 4, range 1 - 16)

Other Inclusion Criteria
- Age ≥ 18 years of age.
- ECOG performance status of ≤ 2.
- Histologically verified stage IV (unresectable or stage IV (translocatable) cutaneous, ocular or mucosal melanoma.
- The patient had received prior therapy with an anti-PD-1 or an anti-PD-L1 antibody.
- The patient had any known active chronic liver disease.
- The patient had a known medical condition (e.g., a condition associated with diarrhea or acute diverticulitis).
- The patient had to sign informed consent.
- The patient has histologically or cytologically documented locally advanced squamous or non-squamous NSCLC: 18 patients
- The patient has previously treated unresectable stage III or stage IV melanoma and has progressed on or after treatment with a minimum of 1 prior systemic treatment for stage IIIB or IV NSCLC: 19 patients
- The patient has histologically confirmed advanced or metastatic RCC with a clear cell component.
- The patient has histologically confirmed advanced or metastatic dCRC with KRAS wild-type.

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- NIVOLUMAB: 15 patients
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Immune-Related AEs With Immunotherapy

HD
- The patient is ineligible for or has received prior high-dose conditioning chemotherapy followed by ASCT, and needs immediate allogeneic transplantation as a part of their treatment history for HM.
- The patient had a known medical condition (e.g., a condition associated with diarrhea or acute diverticulitis).
- The patient had documented failure to achieve at least PR.

Other Inclusion Criteria
- Age ≥ 18 years of age.
- ECOG performance status of ≤ 2.
- Histologically verified stage IV (unresectable or stage IV (translocatable) cutaneous, ocular or mucosal melanoma.
- The patient had received prior therapy with an anti-PD-1 or an anti-PD-L1 antibody.
- The patient had any known active chronic liver disease.
- The patient has histologically or cytologically documented locally advanced squamous or non-squamous NSCLC: 18 patients
- The patient has previously participated in a nivolumab clinical study.
- The patient is ineligible for or has received prior high-dose conditioning chemotherapy followed by ASCT, and needs immediate allogeneic transplantation

Other Exclusion Criteria
- Known allergy or intolerance to ipilimumab, nivolumab or any other biologic agents.
- The patient has active or uncontrolled autoimmune disease unless treated and in stable condition.
- The patient has any known active chronic liver disease.
- The patient has a medical condition requiring systemic treatment with either corticosteroids (>10 mg/day prednisone or equivalent).
- The patient has not recovered from major surgery.
- The analyses of data collected in this study will be mainly descriptive. All collected data and endpoint variables were summarized using descriptive statistics in addition to statistical modeling.