Background Autoimmunity is associated with increased risk of malignancy. However, patients with pre-existing autoimmune diseases (AIDs) were excluded from immune checkpoint inhibitor (ICI) trials as these agents can cause immune-related adverse events (irAEs). Data are limited on the safety and efficacy of combination immunotherapy in this at-risk population.

Methods We conducted a multi-center retrospective study to evaluate the safety and efficacy of ICI therapy in patients with pre-existing AID treated at NYU and at MD Anderson Cancer Center. Primary endpoints were occurrence of irAEs and AID flares. Secondary endpoints were time to treatment failure (TTF) and overall survival (OS).

Results Of 121 patients identified from our institutional databases, 53% received single-agent anti-PD-1 therapy, and 47% received ICI combination. Over half of malignancies were lung cancer (34%) and melanoma (20%). Preexisting AIDs included: rheumatologic (58%), gastrointestinal (12%), endocrine (16%) and neurologic (4%). Overall, 94% had asymptomatic AID, and 21% were receiving systemic immunomodulatory drugs at ICI initiation. Median duration of follow up after ICI initiation was 9 (0.4–41.9) months in patients receiving ICI combination and 8 (0.2–47.3) months in patients receiving anti-PD-1 monotherapy. Combination therapy was associated with higher rates of irAEs compared with anti-PD-1 monotherapy (56% versus 28%). Grade 3/4 irAEs were equivalent in both groups: combination (38%) and anti-PD-1 group (39%). Treatment related deaths were not observed in any group. AID flares occurred in 36% of the anti-PD-1 group versus 29% of combination group. Adverse events (irAEs and/or flares) required systemic immunomodulatory therapies more frequently in the combination group (84%) versus the anti-PD-1 group (59%), and permanent ICI discontinuation was reported in 19% of patients in the combination group versus 11% in the anti-PD-1 group. Tumor progression was observed in 49% of patients on combination ICI and TTF was 14.5 months (95% CI 0.000–31.5), while progression was observed in 64% of patients on anti-PD-1 monotherapy and TTF was 6.4 months (95% CI 4.01–8.9) (p=0.019). Median OS in the combination therapy group was not reached whereas it was 27.3 months in the anti-PD-1 monotherapy group.

Conclusions Our novel findings suggest that high rates of adverse events were observed in patients with pre-existing AIDs treated with ICI combination therapy. However, they were manageable and rarely required permanent ICI discontinuation. Taken together, these data show that ICIs should be offered, albeit with caution in patients with AIDs, to achieve durable cancer remission. Prospective clinical data are needed to guide these complex decisions.

Ethics Approval The study was approved by NYU Langone’s Ethics Board, approval number I18-01657 and MD Anderson’s Ethics Board, approval number PA19-0089.

Background The novel coronavirus, known as SARS-CoV-2, or COVID-19 became a pandemic in early 2020, causing significant human suffering and economic woes globally. The pathophysiology of acute respiratory failure may be related to a robust immune reaction against the virally infected cells (figure 1). This mechanism is molecularly similar to that of cytokine release syndrome, which is mediated by cytokine IL-1 and can be seen as a complication of immunotherapy.

Methods Clinical data from cancer patients treated for cytokine release syndrome were collected from an interventional oncology practice and retrospective analysis was performed.

Results Five patients were treated for cytokine release syndrome related to administration of immunotherapy agents. Symptoms included hypotension, loss of consciousness, fever, headache, and respiratory failure. Three of these patients were treated with anakinra, with abrogation of symptoms of cytokine release syndrome (table 1). The remaining two patients...
Abstract 659 Table 2  Glucocorticoids cohort

Two patients who experienced clinical signs and symptoms of cytokine release syndrome after administration of immunotherapy. These patients were treated with glucocorticoids, vasopressors, and supportive measures, and subsequently died.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>68</td>
<td>59</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>Underlying malignancy</td>
<td>Stage 4 GIST*</td>
<td>Stage 4 colorectal cancer</td>
</tr>
<tr>
<td>Treatment administered</td>
<td>IPILimumab, nivolumab, carboplatin</td>
<td>Ipilimumab, nivolumab, ipilimumab, Gp100</td>
</tr>
<tr>
<td>Symptoms of cytokine release syndrome</td>
<td>Hypotension, loss of consciousness, renal failure, respiratory failure</td>
<td>Hypotension, loss of consciousness, respiratory failure, myocardial failure</td>
</tr>
<tr>
<td>Treatment for cytokine release syndrome</td>
<td>Prednisone 1000 mg daily, tacrolimus, vasopressors, dialysis, intubation and mechanical ventilation</td>
<td>Prednisone 1000 mg daily, tacrolimus, vasopressors, intubation and mechanical ventilation</td>
</tr>
<tr>
<td>Outcome</td>
<td>Non responsive to treatment</td>
<td>Progressive symptoms of CRS</td>
</tr>
</tbody>
</table>

Here, we present a segmentation approach to adapt knowledge learned from source data of one cancer type to unlabelled target data of another organ cancer type via unsupervised domain adaptation (UDA) frameworks. This research will help build deep learning models that significantly reduce the need for expert manual annotations.

Methods Annotated colorectal cancer (CRC)* (target domain) and prostate cancer (source domain) were used for tumor tissue segmentation model development, containing image tiles from 38 and 20 whole slide images, respectively. We compared the performance and robustness of four approaches. First, we implemented two output-space domain-adversarial based UDAs. We then implemented a self-training-based approach. Additionally, we designed a two-stage UDA approach by first conducting self-training and then further aligning target domain features with category-anchors generated from source data after a first stage of self-training.

Results Directly applying a tumor tissue segmentation model trained on prostate cancer images (source) to CRC images (target) resulted in an intersection-over-union (IOU) score of 62.5%, which was 19% IOU lower (domain gap) than using a model trained on target data. Methods based on output-space domain adversarial training reduced the domain gap by up to 8% IOU, a performance result which was better than with self-training-based methods, which only reduced the domain gap by 4%. Both sets of approaches improved precision by 10%.

Conclusions We demonstrate the feasibility of designing tumor segmentation models that are robust and generalizable to multiple indications. The UDA approaches have the potential to speed our understanding of factors influencing immunotherapy efficacy through automated annotation of tissue regions required.

REFERENCES

Machine learning, artificial intelligence, and computational modeling

660 DEVELOPING GENERALIZABLE DEEP LEARNING MODELS FOR TUMOR SEGMENTATION IN PATHOLOGY IMAGES TO ENABLE THE IDENTIFICATION OF PREDICTIVE BIOMARKERS FOR IMMUNOTHERAPIES

Qiile Ba*, Peng Yang, Jennifer Yearley, Merck, Kenilworth, CA, USA

Background Despite recent advances in cancer immunotherapies, their efficacies vary significantly among patients. To better understand the mechanisms of drug resistance, it is essential to characterize immune responses to immunotherapies in the tumor immune microenvironment (TME) from intact patient tissues. To this end, quantitative spatial immune profiling of pathology images has been the focus for many recent studies. Such analysis often depends critically on the automated image segmentation of tumor and stromal compartments. However, current segmentation approaches, even these based on deep learning, often fail to perform well when given datasets to segment, which differ from the data on which they were trained. Specifically, tissue segmentation models trained for one type of organ (source) face challenges in performance when applied directly to images of another organ type (target), even when the targeted regions to segment are highly similar in morphology between the source and target.

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