Luminex. To identify biomarkers of checkpoint inhibition, mice transferred with a defined population of ovalbumin (OVA)-specific T cells were challenged with OVA antigen or EG7 tumour. Activation and proliferation of antigen-specific T cells was determined and Nanostring gene expression analysis performed. Flow cytometry staining panels for human immune markers including CD4, CD14, CD25 and FOXP3 were established pre-clinically. As part of the assay validation process for a clinical trial, whole blood SEB activation was performed in normal donors, with Luminex analysis of IL-2, IL-17, IFNgamma and TNFalpha.

Results Immune checkpoint inhibitors resulted in increased IL-2 and IFNgamma secretion in human PBMC stimulated with SEB. In the murine PD model, anti-PD-L1 caused upregulation of CD25, IFNgamma and granzyme B by antigen-specific CD8 T cells. Gene expression analysis of murine tumours elucidated changes in response to a vaccine. Flow cytometry panel staining determined the frequencies of human Treg and monocytes, which are common targets of immune-modulating therapies. For-purpose validation was performed for a human SEB activation assay resulting in robust changes in cytokine production.

Conclusions The experiments here show the flow of experiments that can be performed to identify a PD biomarker for use in first in man trials; the pre-clinical human PBMC SEB screening assay provides a simple assay demonstrating that a therapy can enhance T cell function and would be translatable to the clinic. The murine PD model provides a platform to screen for biomarkers of T cell function and monitor gene expression modulation. Biomarkers identified in the murine setting provide a good starting point for exploratory assessment in early phase clinical trials, where inclusion of exploratory PD biomarker endpoints can confirm proof of mechanism and improve study success rates.

Ethics Approval Human tissues used in this study were collected with ethical approval from UK Research Ethics Committee South West, Bristol (UK), approval number 15/SW/0029.

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7 PROGNOSTIC FACTORS FOR OVERALL SURVIVAL IN PATIENTS WITH ADVANCED MELANOMA TREATED WITH ANTI-PD-1 THERAPY – THE MELIMMUNE SCORE

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Background Immune checkpoint inhibitors (ICI) have changed the paradigm of advanced malignant melanoma (MM). Several prognostic factors, mostly linked to inflammation, have been under scope to better select patients for such therapies. We aimed to build and apply a prognostic score in this setting.

Methods Baseline characteristics and outcomes on 147 patients with advanced MM treated with an anti-PD1 (nivolumab or pembrolizumab) in monotherapy, between Jan-2016 and Oct-2019, in the 1st, 2nd or 3rd line setting were collected from two centres in Portugal. Data cut-off for follow-up was May-2020. Cox proportional hazards regression was used to identify independent prognostic factors for OS.

Results With a median FU of 28.93 months (95% CI [22.52–33.54]), mOS for the whole cohort was 14.75 months (95% CI, [10.80–18.71]). Overall, 43 and 104 patients were treated with nivolumab and pembrolizumab, respectively. We identified four adverse prognostic factors that were independent predictors of bad prognosis: number of metastatic sites >2 (p<0.001), baseline PS-ECOG =1 (p<0.001), presence of baseline lymphopenia (over lower limit of normal) (p=0.002) or very high baseline LDH (>2x upper limit of normal) (p<0.001). Patients were separated into three risk categories according to the number of risk factors present: favourable prognosis (no risk factors; n=34), intermediate prognosis (one risk factor; n=65) and poor prognosis (two or more risk factors; n=48). mOS was 43.41 (95% CI [32.13–54.69], 14.39 (95% CI [6.78–22.01]) and 6.53 months (95% CI [3.61–9.44]), for favourable, intermediate, and poor prognosis group, respectively (p<0.001; figure 1). AUC of ROC curve for OS was 0.737 (95% CI [0.654–0.819], p<0.001).

Conclusions Using easily accessible parameters from our daily practice, we propose the MELImmune prognostic score for advanced MM patients treated with anti-PD1 in monotherapy that could be incorporated to the daily clinical practice and clinical trials. We further aim to validate this score in an independent larger sample.

Ethics Approval The study was approved by both institutions’ Ethics Committee.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0007

8 IMMUNE CORRELATES ASSOCIATED WITH CLINICAL OUTCOMES IN PATIENTS WITH ADVANCED MALIGNANCIES TREATED WITH AVELUMAB AND OX40 AGONIST

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Background We evaluated immune correlates of avelumab in combination with PF-04518600 (OX40 agonist) in a phase I/II study (NCT03217747) in patients with advanced malignancies.
Methods Eligible patients received intravenous avelumab 10 mg/kg and PF04518600 100 mg every 2 weeks in a 4-week cycle. Initially, patients received avelumab from cycle 3 day 1 (C3D1), later from cycle 1 day 15 (C1D15). Response was assessed per RECIST 1.1 and irRECIST. Peripheral blood and tumor tissue were obtained from patients at pre-treatment, post-OX40, and post-combo for correlative studies. Translational assays include immunohistochemistry (IHC: PD-L1, OX40 and CD139), multiplex immunofluorescence (mIF: PD-L1/P-1 axis and T-cell activation/regulatory panels), and Nanostring (panCancer Immune Panel) for tumor tissues, and flow cytometry performed on peripheral blood. Fisher’s exact test was used to compare response between the two treatment schedules. Log-rank test was performed to test the difference in overall survival (OS) and progression-free survival (PFS) between groups. Linear mixed-effect model was used to estimate the effect of schedule and treatment (time) effects on flow and IHC mIF biomarkers.

Results Twenty-eight patients were treated, 12 received avelumab from C3D1 and 16 from C1D15. Patient characteristics are summarized in table 1 and response data in table 2. The median follow-up time was 17.8 months. The median OS was 7.9 months and PFS was 3.2 months. Patients on C3D1 schedule had superior PFS than patients on C1D15 schedule (4.6 months vs 2.5 months; P=0.032). The biomarkers associated with survival were investigated in the C3D1 group. Patients with following baseline biomarker characteristics had superior PFS (table 3): lower density of total cells expressing CD137 (6.0 vs 3.2 months, P=0.047) and lower percentage of malignant cells expressing OX40+ (5.8 vs 3.2 months, P=0.024). Patients with superior OS had higher frequencies of CD86+HLA-DR+CD141 dendritic cells and CD3+ cells in circulation at baseline (17.2 vs 7.9 months, P=0.012) (table 4). This combination was not found to expand circulating T regulatory cells. Early data suggests that while higher neutrophil score correlates with PD, higher exhausted CD8+ T cell score correlates with SD. More translational data will be presented at the conference.

Conclusions With limited data, there is evidence that patients receiving avelumab from C3D1 in combination with PF-04518600 have better response. Antigen presentation machinery showed changes but remained overall intact within the tumor with baseline circulating CD141+CD86+HLA-DR+ DCs positively correlating with OS. Additional studies to evaluate the effect of T-cell agonist on their receptors on malignant cells are needed.

Trial Registration NCT03217747

Abstract 8 Table 2 Best response per irRECIST and RECIST 1.1

<table>
<thead>
<tr>
<th>RECIST criteria</th>
<th>Group</th>
<th>Overall*</th>
<th>Stable Disease (SD)</th>
<th>Progressive Disease (PD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>irRECIST</td>
<td>C1D15</td>
<td>12</td>
<td>4 (33)</td>
<td>8 (67)</td>
<td>0.666</td>
</tr>
<tr>
<td></td>
<td>C3D1</td>
<td>10</td>
<td>5 (50)</td>
<td>5 (50)</td>
<td></td>
</tr>
<tr>
<td>RECIST v 1-1</td>
<td>C1D15</td>
<td>12</td>
<td>2 (17)</td>
<td>10 (83)</td>
<td>0.172</td>
</tr>
<tr>
<td></td>
<td>C3D1</td>
<td>10</td>
<td>5 (50)</td>
<td>5 (50)</td>
<td></td>
</tr>
</tbody>
</table>

* 4 patients in C1D15 group and 2 patients in C3D1 group were not evaluable for response per PRECIST/RECIST v 1.1

Abstract 8 Table 3 Progression-free survival in C3D1 group in relation to the biomarkers at baseline and change from baseline to second collection

<table>
<thead>
<tr>
<th>p-value</th>
<th>Median PFS (95% CI) (months)</th>
<th>Median PFS (95% CI) (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; median</td>
<td>&gt; median</td>
</tr>
</tbody>
</table>

HCMIF/Flow at baseline
- Density of total cells expressing CD137 (number of cell/mm³) (median=2.9)
  - Median=3.0 (2.0, 8.6)
  - Median=2.4 (5.5)
  - 0.047
- Percentage of malignant cells expressing OX40+ (CincteCT-35 M) (median=20.0)
  - Median=8.0 (2.9, 3.5)
  - Median=2.9 (2.9, 3.5)
  - 0.024

HCMIF/Flow change from baseline to second collection
- Malignant cells expressing OX40+ (number of cell/mm³) (median=2.23)
  - Median=4.9 (2.1, 6.9)
  - Median=1.4 (1.4, 2.1)
  - 0.035
- Percentage of malignant cells expressing OX40+ (CinccteCT-35 M) (median=9.1)
  - Median=4.5 (2.1, 6.9)
  - Median=1.4 (1.4, 2.1)
  - 0.002

Abstract 8 Table 4 Overall survival in C3D1 group in relation to the biomarkers at baseline and change from baseline to second collection

<table>
<thead>
<tr>
<th>p-value</th>
<th>Median OS (95% CI) (months)</th>
<th>Median OS (95% CI) (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; median</td>
<td>&gt; median</td>
</tr>
</tbody>
</table>

HCMIF/Flow at baseline
- CD3+ (median=91.4)
  - Median=7.9 (3.0, 15.7)
  - Median=17.2 (16.0, 20.4)
  - 0.012
- Immature myeloid CD68 on CD141 (median=97.9)
  - Median=7.9 (3.0, 15.7)
  - Median=16.6 (9.2, 20.4)
  - 0.030
- Mature myeloid CD68 on CD141 (median=66.4)
  - Median=7.9 (3.0, 15.7)
  - Median=17.2 (16.0, 20.4)
  - 0.012

HCMIF/Flow change from baseline to second collection
- Immature myeloid CD68 on CD123 (median=67.0)
  - Median=15.0 (8.1, 19.3)
  - Median=6.4 (1.5, 6.0)
  - 0.011
- Mature myeloid CD68 on CD141 (median=68.6)
  - Median=15.5 (13.8, 19.3)
  - Median=6.4 (1.6, 8.1)
  - 0.004

Ethics Approval The study was approved by The University of Texas MD Anderson Cancer Center Institutional Review Board (FWA #: 00000363).


9 MESENCHYMAL FEATURES OF A NOVEL 27-GENE ALGORITHM ASSOCIATE WITH CANONICAL TUMOR PROMOTING SIGNALING PATHWAYS WHICH MAY IDENTIFY THERAPEUTIC OPTIONS FOR IMMUNOTHERAPY RESISTANT PATIENTS

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Background Immune checkpoint inhibitors have emerged as a front-line treatment for cancer in multiple indications. Unfortunately, a majority of patients do not realize durable response as a result of primary resistance to the