Background The landscape for clinician education in immuno-oncology (IO) has changed dramatically since the first approval of an immune checkpoint inhibitor (ICI) in 2011. Educational initiatives have had to evolve with the multitude of new IO approvals and indications, as well as continuous integration of these therapies in patient care. As such, an IO census survey was administered and analyzed to better assess the current knowledge and educational needs of the oncology care team at the start of a new decade in IO.

Methods In June 2020, the Association of Community Cancer Centers launched an online survey to its membership of multidisciplinary oncology providers. The survey included questions related to demographic information, current IO practices, and top priorities and challenges in IO. In August 2020, an interim, descriptive analysis was conducted on complete survey responses (n=38).

Results At the time of interim analysis, survey respondents represented the full multidisciplinary cancer care team (e.g., advanced practice providers [18%], pharmacists [16%], medical and surgical oncologists [14%]), as well as diverse practice settings (e.g., community cancer program [28%], physician practice [20%]). In addition, the majority (67%) of respondents treated more than 20 patients per week with immunotherapies across most cancer types. When assessing familiarity with IO agents, most respondents were 'moderately familiar' or 'extremely familiar' with ICIs (26% and 53%, respectively). However, many respondents were 'not at all familiar' or only 'slightly familiar' with chimeric antigen receptor (CAR) T-cell therapy (5% and 42%, respectively) and bispecific antibody therapies (16% and 42%, respectively). The top challenges (i.e., 'very challenging' or 'extremely challenging') for respondents included the expansion of indications for IO agents (45% and 11%, respectively), coordinating care with non-oncology providers (29% and 18%, respectively), and financial toxicity (32% and 26%, respectively). Regarding future education topics, respondents expressed most interest (i.e., 'very interested' or 'extremely interested') in biomarker and molecular testing (71% and 18%, respectively), patient access, advocacy, and financial impact (61% and 24%, respectively), and evidence, data, and publication updates (55% and 26%, respectively).

Conclusions These interim results from a representative cohort strongly indicate that clinicians desire more clinical and operational support on use of IO agents and associated testing, easing patients' and programs' associated financial strain, and coordinating care across specialties. Additional analysis will focus on if/how respondents' specific disciplines or practice settings influence the results.

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491 DEVELOPING EDUCATIONAL MATERIALS ABOUT IMMUNOTHERAPY FOR PATIENTS AND THEIR CAREGIVERS

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Background As the use of immunotherapy as treatment for cancer patients continues to expand, it is important that patients and caregivers have access to relevant educational and community resources to support them in making informed decisions and receiving optimal care.[1] To help meet these needs, the Cancer Support Community (CSC) designed Frankly Speaking About Cancer (FSAC): Immunotherapy. The intent of FSAC: Immunotherapy is to act as a patient education resource that offers information about immunotherapy, side effects, psychosocial impacts, and patient-provider communication. It is critical to gather stakeholder feedback when developing such programs to ensure all information and resources are appropriate and useful to the target audience. To achieve this, CSC worked with patients and caregivers to get feedback and refine the FSAC: Immunotherapy educational materials.

Methods In June 2020, CSC facilitated a virtual discussion board with cancer patients that have received immunotherapy (N = 8) and their caregivers (N = 2). Participants were asked to talk through and provide feedback on two booklets: FSAC: Immunotherapy and FSAC: Immunotherapy & Lung Cancer. Participants reviewed the booklets and answered open-ended questions about clarity and completeness of information. Sample points of discussion focused on their comprehension and perception of information regarding immunotherapy, immunotherapy options, side effects, and decision-making.

Results Qualitative analysis of discussion board responses revealed that while participants judged most of the content to be clear and informative, they desired more information about differences between immunotherapy types, technical terms, and cost. Specific requests included: Explain how types of immunotherapies differ from one another.Provide information on oncolytic vaccines and how they work.Clarify if immunotherapy can be used in adjuvant treatment or just in metastatic disease.Add information about costs associated with immunotherapy treatment and common practices in health insurance reimbursement. Add information about how is immunotherapy administered.

Conclusions Patients and caregivers provide valuable perspectives to those creating educational resources. Incorporating these stakeholder voices can increase the effectiveness of materials and should continue throughout the resource development processes. Regarding implementation, CSC distributes the booklets at no charge to cancer patients and caregivers via its internal network of almost 50 Cancer Support Communities and Gilda's Clubs worldwide, the CancerSupportCommunity.org webpage, and partner patient advocacy groups. We also promote these materials to the medical community and allow them to order/download it, at no charge, to help patients undergoing immunotherapy treatment and their caregivers.

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Ethics Approval This study was conducted under IRB-exempt protocols [category 45 CFR 46.101(b) 2].

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Immune cell biology

492 INTEGRATION OF HIGH DIMENSIONAL DATASETS IN AN IMMUNOCOMPETENT MAMMARY MOUSE MODEL REVEALS PATHWAYS OF TOLERANCE AND RESISTANCE TO IMMUNE CHECKPOINT BLOCKADE

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Background Checkpoint inhibitors can induce robust and durable responses in a subset of patients. Extending this benefit to more patients could be facilitated by better understanding of how interacts with immune cells with the tumor microenvironment, which is a critical barrier to control both local and systemic disease. The composition and pattern of the immune infiltrate associates with the likelihood of response to immunotherapy. Inflamed tumors that exhibit a brisk immune cell infiltrate are responsive, while those in which immune cells are completely or partially excluded are not. Transforming growth factor β (TGFβ) is immunosuppressive and associated with the immune excluded phenotype.

Methods Using an immune competent mammary tumor derived transplant (mTDT) model recently developed in our lab, exhibits inflamed, excluded or deserts immune infiltrate phenotypes based on localization of CD8 lymphocytes. Using whole transcriptome deep sequencing, cytof, and PET-CT imaging, we evaluated the tumor, microenvironment, and immune pathway activation among immune infiltrate phenotypes.

Results Three distinct inflamed tumors phenotypes were identified: 'classically' inflamed characterized by pathway evidence of increased CD8+ T cells and decreased PD-L1 expression, inflamed tumors with pathways indicative of neovascularization and STAT3 signaling and reduced T cell mobilization, and an inflamed tumor with increased immunosuppressive myeloid phenotypes. Excluded tumors were characterized by TGFβ gene expression and pro-inflammatory cytokine signaling (e.g. TNFα, IL1β), associated with decreased leukocytes homing and increased immune cell death of cells. We visualized and quantified TGFβ activity using PET-CT imaging of 89Zr-fresolimumab, a TGFβ neutralizing antibody. TGFβ activity was significantly increased in excluded tumors compared to inflamed or desert tumors, which was supported by quantitative pathology (Perkin Elmer) of its canonical signaling target, phosphorylated SMAD2 (pSMAD2). pSMAD2 was positively correlated with PD-L1 expression in the stroma of excluded tumors. In contrast, in inflamed tumors, TGFβ activity positively correlated with increased F4/80 positive macrophages and negatively correlated with expression of PD-L1. CyTOF analysis of tumor and spleen immune phenotypes revealed increased trafficking of myeloid cells in mice bearing inflamed tumors compared to excluded and deserts.

Conclusions The immunocompetent mTDT provides a model that bridges the gap between the immune landscape and tumor microenvironment. Integration of these high-dimensional data with further studies of response to immunotherapies will help to identify tumor features that favor response to treatment or the means to convert those that are unresponsive.

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493 TIRED AND HUNGRY: A POTENTIAL ROLE FOR CD47 IN T CELL EXHAUSTION

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Background Multiple suppressive mechanisms within the tumor microenvironment are capable of blunting anti-tumor T cell responses, including the engagement of inhibitory receptors expressed in tumor-associated, exhausted CD8+ T cells, such as programmed cell death protein 1 (PD-1), T-cell immunoglobulin and mucin-domain containing-3 (TIM-3), lymphocyte-activation gene 3 (LAG-3), 2B4 (also known as CD244), and T cell immunoreceptor with Ig and ITIM domains (TIGIT).[1 2] While immune checkpoint blockade therapies aimed at reinvigorating T cell effector function have demonstrated their clinical effectiveness,[3 4] not all patients demonstrate long-term disease control.[5] The refractory nature of terminally differentiated, exhausted CD8+ T cells to be reinvigorated by PD-1 blockade is one potential cause.[6–8] This limitation warrants the need to explore modulatory pathways that potentially program T cells toward exhaustion.

Methods Single cell-RNA sequencing (scRNA-seq) data derived from the tumor-infiltrating lymphocytes (TILs) of melanoma patients[9] were used for transcriptomic analysis and flow cytometry results were used to quantify protein levels in TILs. Murine B16-F10 (B16) melanoma model was used for both in vitro and in vivo studies. TCR-transgenic Pmel-1 and OT-1 transgenic mice, as well as CD47-/- (knockout, KO) mice were purchased from the Jackson Laboratory to generate CD47+/+ (wild-type, WT), CD47± (heterozygote, HET) mice with Pmel-1 or OT-1 background. For T cell co-transfer studies, Rag-deficient mice or C57BL/6j mice with sub-lethal irradiation (600cGy) were used as recipients. Naïve TCR-transgenic CD47-WT and CD47-HET CD8+ T cells were labelled, mixed in a 1:1 ratio for co-transfer experiments.

Results Flow cytometry analysis of human melanoma TILs found a strong upregulation of CD47 expression in tumor-associated, exhausted CD8+ T cells. We confirmed that CD47 transcription is significantly elevated among CD8+ T cells with a phenotype consistent with exhaustion using scRNA-seq results of TILs derived from melanoma patients.[9] Our study in murine B16 melanoma model confirms our finding in melanoma patients. To specifically address the role of CD47 in anti-tumor CD8 effector function, we conducted T cell co-transfer studies and found that CD8+ T cells with lower copy number of CD47 (CD47-HET) significantly outnumber the co-transferred CD47-WT CD8+ T cells within the tumor, exhibiting an enhanced effector function and less exhausted phenotype. Our study demonstrates a potentially novel role for CD47 in mediating CD8+ T cell exhaustion.

Conclusions CD47 expression in CD8+ T cells programs T cells toward exhaustion.

Ethics Approval All mice were maintained in microisolator cages and treated in accordance with the NIH and American Association of Laboratory Animal Care regulations. All mouse procedures and experiments for this study were approved by the MSKCC Institutional Animal Care and Use Committee (IACUC).

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