site as serious AEs and had more detailed clinical information available. Ocular AEs occurred within several months of initiating the study treatment (all ocular AEs: median 6 weeks, IQR 0–18, ocular AEs reported as serious: median 12 weeks, IQR 6–20). CTCAE grade for ocular AEs was generally mild to moderate (all ocular AEs: grade 1, IQR 1–2, ocular AEs reported as serious: grade 2, IQR 2–3). Clinical workup and treatment varied for the ocular AEs reported as serious. 30/47 patients (64%) receiving ophthalmologic evaluation. 16/47 (34%) of patients with serious ocular AEs had to delay or discontinue study drug treatment. However, 14/47 (30%) had improvement in their ocular AE and 16/47 patients (34%) had resolution of their ocular AE. The most common ocular AE treatments in our dataset were steroids (intraocular, oral, and steroid eye drops).

Conclusions Ocular adverse events are rare complications of PD-1/PD-L1 inhibitor therapy, can be severe enough to cause PD-1/PD-L1 treatment discontinuation or delay, but patients may not always be referred to eye specialists. Future PD-1/ PD-L1 inhibitor studies would benefit from standardized plans for ophthalmologic evaluation of ocular toxicities.

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http://dx.doi.org/10.1136/jitc-2020-SITC2020.0644

PRECLINICAL DEVELOPMENT OF A NOVEL COLON-TARGETED THERAPEUTIC FOR THE TREATMENT OF IMMUNE CHECKPOINT INHIBITOR (ICI)-COLITIS

Background Immune Checkpoint Inhibitor (ICI) therapies have significantly improved overall survival in numerous cancers, but colitis has emerged as the most frequent dose-limiting toxicity associated with these therapies. Patients experiencing colitis side effects have to discontinue their cancer therapy to treat the colitis, which repositions life-threatening cancer. An ideal therapeutic would offer a colon-restricted approach to treating colitis side effects, while allowing patients to stay on their ICI therapy, an approach unavailable with currently approved therapies.

Methods To test this localized approach for the treatment of ICI-mediated colitis, we have developed a new chemical entity as a next-generation candidate therapeutic designed for oral administration. Permeability was tested in predictive epithelial monolayers and confirmed in rodent pharmacokinetic studies. We tested the drug in the preclinical adoptive transfer model for colitis. In this model, immunodeficient mice are hosts for adoptive transfer of naïve CD4+ T cells. In the absence of regulatory T cells, the transferred cells drive systemic inflammation and migrate to the colon, causing disease. Without treatment, these mice develop signs of colitis including weight loss, altered crypt architecture and infiltration of the lamina propria by week four. Furthermore, we developed a live biopsy culture system to test drug effects on ICI-colitis patient biopsies obtained via colonoscopy.

Results In-vitro studies demonstrate that the drug has minimal toxicity and that it potently suppresses T cell proliferation and cytokine secretion. Permeability studies show a limited ability to cross the colonic mucosa restricting anti-inflammatory effects to sites of ulceration and active colitis. When colitis mice were given drug by oral gavage after colitis had developed, treated mice showed a significant increase in weight over controls and improved histological scores. Importantly, markers of systemic inflammation remained unchanged, and the cancer-killing ability of the primary ICI therapy was preserved. Results of the live biopsy culture studies will be presented.

Conclusions These preliminary studies demonstrate that the candidate therapeutic has potential to become a novel next-generation oral therapy for ICI-colitis because it effectively limits leukocyte function in-vitro and in-vivo with minimal systemic absorption and minimal expected side effects. Given the favorable drug profile and the rapid growth of ICI therapies, our colon-restricted colitis therapeutic has the potential to improve outcomes in a large number of cancer patients. We anticipate commencing first-in-human studies in Q4 of 2021.

Acknowledgements None

Evaluating a Preclinical Model of Contact Hypersensitivity for Skin Immune Checkpoint Toxicity

Background Immune checkpoint inhibitors (ICIs) are limited by the high incidence of immune-related adverse events (irAEs) occurring in up to 40% of solid tumor patients on anti-PD-1 monotherapy and 72% in anti-CTLA-4/anti-PD-1 combination. These toxicities can cause treatment cessation, hospitalization and even death. IrAEs are variable in severity, timing, onset, and remain poorly understood. Amongst the different toxicities, skin irAEs are most frequent, occur the earliest, and are correlated with a positive prognosis. However, there is a lack of preclinical models to study checkpoint toxicity. We evaluated a murine model of allergic contact dermatitis (contact hypersensitivity to 2,4-dinitrofluorobenzene) that is mediated by CD8+ T cells to gain a mechanistic understanding of skin checkpoint toxicity.

Methods C37BL/6 mice (n = 5 per group) were sensitized epicutaneously on shaved flank with hapten 0.3% DNFB on day -5 and elicited on their ears with DNFB on day 0. Starting four weeks later, mice were treated with either anti-programmed cell death protein (PD-1) or isotype. At the time of the first recall challenge only, mice were given either anti-PD-1 or isotype. Mice received subsequent rechallenges with DNFB to the ears and ear swelling was measured at various time points. Mice were depleted of circulating or skin CD8+...