activity in mouse models. The combination of SEA-CD40 and chemotherapeutic agents with a T cell targeted anti-PD1 antibody could deepen and extend these anti-tumor responses.

Conclusions These data support continued clinical evaluation of SEA-CD40 in combination with chemotherapeutic agents and potentially in the future MMAE based ADCs. A phase 1 clinical trial is actively enrolling (NCT02376699) and includes a cohort in pancreatic cancer assessing the combination of SEA-CD40, gemcitabine, nab-paclitaxel, and pembrolizumab.

Ethics Approval Studies with human samples were performed according to institutional ethics standards. Animals studies were approved by and conducted in accordance with Seattle Genetics Institutional Care and Use Committee protocol #SGE-029.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0438

439 DUAL MODES OF ACTION FOR ANTI-TIM-3 ANTIBODY MBG453 IN MYELODYSPLASTIC SYNDROMES (MDS) AND ACUTE MYELOID LEUKEMIA (AML): PRECLINICAL EVIDENCE FOR IMMUNE-MEDIATED AND ANTI-LEUKEMIC ACTIVITY

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Background TIM-3 is expressed on leukemic stem cells (LSCs) and blasts in AML,[1 2] and TIM-3 expression on MDS blasts correlates with disease progression.[3] Functional evidence for TIM-3 in AML was established with an anti-TIM-3 antibody which inhibited engraftment and development of human AML in immuno-deficient murine hosts.[1] TIM-3 promotes an autocrine stimulatory loop via the TIM-3/Galectin-9 interaction, supporting LSC self-renewal.[4] In addition to its cell-autonomous role on LSCs/blasts, TIM-3 also has a critical role in immune system regulation, in adaptive (CD4+ and CD8+ T effector cells, regulatory T cells) and innate (macrophages, dendritic cells, NK cells) immune responses.[5] MBG453 is a high-affinity, humanized anti-TIM-3 IgG4 antibody (Ab) (stabilized hinge, S228P), which blocks the binding of TIM-3 to phosphatidylserine (PtdSer). Recent results from a multi-center, open label phase Ib dose-escalation study (NCT03066648) in patients with high-risk MDS and no prior hypomethylating agent therapy evaluating MBG453 in combination with decitabine demonstrated encouraging preliminary efficacy with an overall response rate of 58%,[6] and MBG453 combined with azacitidine also showed encouraging response rates.[7] Preclinical experiments were undertaken to define the mechanism of action of the hypomethylating agent and anti-TIM-3 combination.

Methods THP-1 cells (a human monocytic AML cell line) were pre-treated with decitabine and co-cultured with anti-CD3 activated healthy human donor peripheral blood mononuclear cells (PBMCs) in an Incucyte-based assay to measure cell killing. The ability of MBG453 to mediate antibody-dependent cellular phagocytosis (ADCP) was measured by determining the phagocytic uptake of an engineered TIM-3-overexpressing Raji cell line in the presence of MBG453 by phorbol 12-myristate 13-acetate (PMA)-activated THP-1 cells. Patient-derived AML xenograft studies were undertaken in immune-deficient murine hosts to evaluate the combination of decitabine and MBG453.

Results MBG453 was determined to partially block the TIM-3/Galectin-9 interaction in a plate-based MSD (Meso Scale Discovery) assay, supported by a crystal structure of human TIM-3.[8] Pre-treatment of THP-1 cells with decitabine enhanced sensitivity to immune-mediated killing in the presence of MBG453. MBG453 was determined to mediate modest ADCP, relative to controls. MBG453 did not enhance the anti-leukemic activity of decitabine in patient-derived xenograft studies in immuno-deficient hosts.

Conclusions Taken together, these results support both direct anti-leukemic effects and immune-mediated modulation by MBG453. Further studies are ongoing to determine: (1) whether MBG453 can mediate physiologically relevant ADCP of TIM-3-expressing leukemic cells; and (2) the potential of MBG453 to impact the autocrine feedback loop of TIM-3/Galectin-9.

Ethics Approval The human tissue used in these studies was under the Novartis Institutes of BioMedical Research Ethics Board IRB, Approval Number 201252867.

REFERENCES

1. Kikushige Y, Shima T, Takayanagi S, *et al*. TIM-3 is a promising target to selectively kill acute myeloid leukemia stem cells. *Cell Stem Cell* 2010;**7**(6):708–717.
2. Jan M, Chao MP, Cha AC, *et al*. Prospective separation of normal and leukemic stem cells based on differential expression of TIM3, a human acute myeloid leukemia stem cell marker. *Proc Natl Acad Sci USA* 2011; **108**(12): 5009–5014.
3. Asayama T, Tamura H, Ishibashi M, *et al*. Functional expression of Tim-3 on blasts and clinical impact of its ligand galectin-9 in myelodysplastic syndromes. *Oncotarget* 2017;**8**(51): 88904–88917.
4. Kikushige Y, Miyamoto T, Yuda J, *et al*. A TIM-3/Gal-9 autocrine stimulatory loop drives self-renewal of human myeloid leukemia stem cells and leukemic progression. *Cell Stem Cell* 2015; **17**(3):341–352.
5. Acharya N, Sabatos-Peyton C, Anderson AC. Tim-3 finds its place in the cancer immunotherapy landscape. *J Immunother Cancer* 2020; **8**(1):e000911.
6. Borate U, Esteve J, Porkka K, *et al*. Phase Ib Study of the Anti-TIM-3 Antibody MBG453 in combination with decitabine in patients with high-risk myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). *Blood* 2019;134 (Supplement_1):570.
7. Borate U, Esteve J, Porkka K, *et al*. Abstract S185: Anti-TIM-3 antibody MBG453 in combination with hypomethylating agents (HMAs) in patients (pts) with high-risk myelodysplastic syndrome (HR-MDS) and acute myeloid leukemia (AML): a Phase 1 study. EHA 2020.
8. Sabatos-Peyton C. MBG453: A high affinity, ligand-blocking anti-TIM-3 monoclonal Ab. *AACR* 2016.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0439

440 ACTIVITY AND SAFETY OF CAMRELIZUMAB, AN ANTI-PD-1 IMMUNE CHECKPOINT INHIBITOR, FOR PATIENTS WITH ADVANCED NON-SMALL-CELL LUNG CANCER

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Background Effective options are limited for patients with non–small-cell lung cancer (NSCLC) whose disease progresses after first-line chemotherapy. Camrelizumab is a potent anti-PD-1 monoclonal antibody and has shown promising activity in NSCLC. We assessed the activity and safety of camrelizumab for patients with previously treated, advanced NSCLC patients with negative oncogenic drivers.

Methods Patients who progressed during or following platinum-based doublet chemotherapy were enrolled. All patients received camrelizumab(200 mg)every 3 weeks or in combination with chemotherapy until loss of clinical benefit. The primary endpoint was objective response rate (ORR), other

endpoints included disease control rate (DCR), progression-free survival (PFS) and safety.

Results Between Aug 5, 2019, and Jun 19, 2020, we enrolled 29 patients, 25 patients were available evaluated, ORR and DCR was 36% (9/25) and 92% (23/25), respectively. 25 of 29 patients were still receiving the treatment, the median PFS was not yet achieved. Compared with those without reactive cutaneous capillary endothelial proliferation (RCCEP), patients with RCCEP had higher ORR (60% vs. 28.6%). Treatment-related adverse events (AEs) occurred in 69.0% of patients (all Grade), and the most common were RCCEP (37.9%), pneumonitis (6.9%), and chest congestion (6.9%). Treatment-related grade 3 to 4 adverse events occurred in 10.3% of patients.

Conclusions In patients with previously treated advanced NSCLC, camrelizumab demonstrated improved ORR and DCR, compared with historical data of the 2nd line chemotherapy, with a manageable safety profile. While patients with RCCEP derived greater benefit from camrelizumab. Further studies are needed in large sample size trials.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0440

441 OUTCOMES OF PATIENTS WITH METASTATIC RENAL CELL CARCINOMA WITH INTERMEDIATE- OR POOR-RISK SYMPTOMATIC DISEASE WHO RECEIVED THEIR FIRST CYCLE OF NIVOLUMAB AND IPILIMUMAB WHILE BEING HOSPITALIZED

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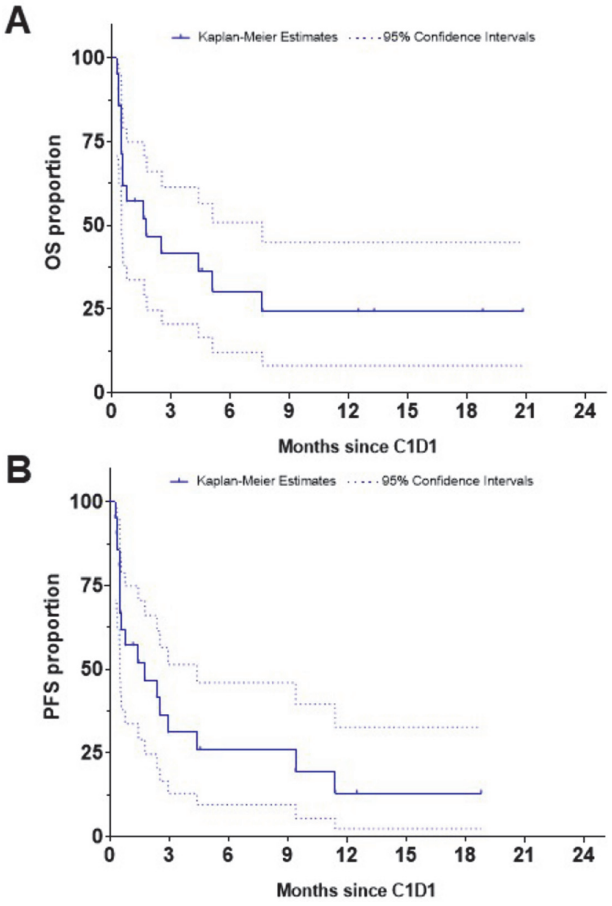
Background Nivolumab plus ipilimumab (nivo/ipi) is an approved therapy for patients with metastatic renal cell carcinoma (mRCC) who have intermediate- or poor-risk disease.[1] Clinical factors that guide the selection of this regimen for patients with mRCC are urgently needed.

Methods We retrospectively analyzed medical records of patients with mRCC who were hospitalized because of cancer-related symptoms and received their first cycle of nivo/ipi in the inpatient setting. Clinical parameters including demographics, histology, clinical history, response and survival were collected. The 4-month survival probability, progression-free survival (PFS) and overall survival (OS) were calculated using Kaplan-Meier methods.

Results Between November 2017 and June 2020, 21 patients were identified that fit the search: 19 patients (91%) had poor-risk disease based on the International metastatic Renal Cell Carcinoma Database Consortium (IMDC) risk score; 17 patients (81%) had ≥4 risk factors; 9 patients (43%) had sarcomatoid features on histology. Shortness of breath (28%) and abdominal pain (19%) were the two most common reasons for hospitalization. Partial response was achieved in 14% (3/21) of patients. Median PFS for all patients was 1.7 months (95% CI 0 - 3.9); median OS for all patients was 1.7 months (95% CI 0 – 4.2); the 4-month survival probability was 36% (95% CI 25% - 47%) (figure 1).

Conclusions In this retrospective study, patients with mRCC who have intermediate- or poor-risk disease and are hospitalized for cancer-related symptoms derive little clinical benefit from nivo/ipi when started in the inpatient setting. Alternative more effective systemic therapies should be considered for these patients.



Abstract 441 Figure 1 Overall and progression-free survival. Panels A and B depict overall survival (OS) and progression-free survival, with 95% confidence intervals using Kaplan-Meier methods, respectively

Acknowledgements We would like to thank the software developers at the Department of Genitourinary Medical Oncology at MD Anderson Cancer Center and the informatics analysts from the Department of Pharmacy Quality Improvement and Analytics at MD Anderson Cancer Center.

Trial Registration N/A

Ethics Approval This study was approved by the Institutional Review Board of MD Anderson Cancer Center, approval number PA16-0736.

Consent N/A

REFERENCE

1. Motzer RJ, Tannir NM, McDermott DF, Aren Frontera O, Melichar B, Choueiri TK, *et al*. Nivolumab plus Ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Engl J Med*. 2018;**378**:1277–90.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0441

442 ICT01, AN ANTI-BTN3A MAB THAT ACTIVATES VG9VD2 T CELLS, PLUS INTERLEUKIN-2: A POTENT AND PROMISING COMBINATION FOR CANCER IMMUNOTHERAPY

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Background gdT-cells are attractive targets for cancer immunotherapy given their strong cytolytic and pro-inflammatory