differences across treatment classes in the association between tumor regrowth and OS.

Conclusions Our results suggest that not all reductions in tumor size are equal. A patient with a certain degree of tumor shrinkage on the PD-1/PD-L1 inhibitor will have lower mortality risk than a patient with a similar degree of shrinkage on the other regimens evaluated. More research is needed to determine whether the result is unique to this particular PD-1/PD-L1 inhibitor, to determine what mechanisms of action mediate these treatment-specific effects, and to develop improved surrogate measures of treatment efficacy.

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277 COMBINED NEOADJUVANT CHEMO-IMMUNOTHERAPY THERAPY ACHIEVES SUPERIOR DOWNSTAGING OF RESECTABLE NON-SMALL CELL LUNG CANCER AS COMPARED TO CHEMOTHERAPY, MONO OR DUAL IMMUNOTHERAPY

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Background Tumor and nodal downstaging following neoadjuvant therapy in resectable non-small cell lung cancer (NSCLC) are important markers of therapeutic response associated with favorable prognosis. We studied the impact of four different systemic neoadjuvant therapies on tumor, nodal and overall pathological downstaging of surgically resectable I-IIIA NSCLC (AJCC 7th edition).

Methods Our study cohorts consisted of NSCLC patients treated with three cycles of neoadjuvant platinum doublet chemotherapy from 2001–2012 (N=302, 84%), and patients treated on the NEOSTAR study (NCT03158129) who received neoadjuvant nivolumab (N=21,6%), nivolumab plus ipilimumab (N=16, 4%), or platinum doublet chemotherapy plus nivolumab (N=22, 6%). Clinical and pathological (yp) T and N staging were evaluated for downstaging and upstaging; differences were assessed using Fisher's exact test.

Results Following neoadjuvant platinum doublet chemotherapy, nivolumab, nivolumab plus ipilimumab and platinum doublet chemotherapy plus nivolumab, the rates of clinical-to-pathological ypT downstaging were 26% (N=79), 29% (N=6), 38% (N=6) and 59% (N=13), respectively, p =0.012 (table 1). The rates of clinical-to-pathological ypN downstaging in patients with clinical N1 or N2 disease with each therapy were 55% (N=96), 50% (N=3), 50% (N=2), and 42% (N=5) respectively, p =0.862. Overall clinical-to-pathological (ypT and/or ypN) downstaging rates were 38% (N=114), 38% (N=8), 38% (N=6), and 68% (N=15) respectively, p=0.048. The proportions of patients being overall upstaged following each therapy were 28% (N=85), 38% (N=8), 38% (N=6) and 14% (N=3), respectively, p=0.251. These results suggest superior downstaging effect and clinically meaningful lower upstaging probability of combined platinum doublet chemotherapy plus nivolumab as compared to other neoadjuvant regimens.

Abstract 277 Table 1 Response to Chemotherapy, Immunotherapy, and Combination Therapy

TABLE: Response to Chemotherapy, Immunotherapy, and Combination Therapy

	Chemotherapy N=302	Single-agent ICI N=21	Dual-agent ICI N=16	Chemotherapy+ ICI N=22	p
ypT downstaged vs. stable/upstaged	26% (79)	29% (6)	38% (6)	59% (13)	0.012
ypN downstaged vs. stable/upstaged*	55% (96)	50% (3)	50% (2)	42% (5)	0.862
Overall yp downstaged vs. stable/upstaged	38% (114)	38% (8)	38% (6)	68% (15)	0.048

*Among those with cN1 disease

ICI: immune checkpoint inhibitor

Conclusions The combination of neoadjuvant platinum doublet chemotherapy with nivolumab achieves the most robust tumor and overall pathological downstaging and decreases the probability of upstaging at surgery. Whether the overall downstaging effect results in improved survival will be determined with longer follow-up, in conjunction with results from ongoing phase III neoadjuvant chemo-immunotherapy trials.

Trial Registration NCT03158129

Ethics Approval This study was approved by the University of Texas MD Anderson Institutional Review Board with a waiver of informed consent, protocol 2020-0337.

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278 PHASE I CLINICAL TRIAL EVALUATING THE SAFETY OF ADP-A2M10 SPEAR T-CELLS IN PATIENTS WITH MAGE-A10$^+$ ADVANCED NON-SMALL CELL LUNG CANCER

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Background ADP-A2M10 SPEAR T-cells are genetically engineered autologous T-cells that express a high affinity MAGE-A10-specific T-cell receptor targeting MAGE-A10$^+$tumors in the context of HLA-A*02. This trial is now complete (NCT02592577).

Methods This first-in-human dose escalation trial utilized a modified 3+3 design to evaluate safety and antitumor activity. Eligible patients (pts) were HLA-A*02$^+$ with advanced non-small cell lung cancer (NSCLC) expressing MAGE-A10. Pts underwent apheresis; T-cells were isolated, transduced with a lentiviral vector containing the TCR targeting MAGE-A10, and expanded. Pts underwent lymphodepletion (LD) with varying doses/schedules of fludarabine (Flu) and cyclophosphamide (Cy) prior to receiving ADP-A2M10. ADP-A2M10 was

administered at Dose Level (DL) 1= 0.1×10^9, DL2 0.5–1.2×10^9, and DL3/Expansion= 1.2–15×10^9 transduced cells.

Results As of Jan 10, 2020, 11 pts (6 male/5 female) with NSCLC (3 squamous cell, 7 adenocarcinoma, 1 adenosquamous) were treated. Five, 3 and 3 pts received cells at DL1, DL2, and DL3/Expansion, respectively. The most frequently reported adverse events ≥ Grade 3 were lymphopenia (11), leukopenia (9), neutropenia (8), anemia (6), thrombocytopenia (5), and hyponatremia (5). Three pts reported CRS (Grades 1, 2, and 4, respectively). One pt received the highest dose of LD (Flu 30 mg/m^2 Day 1 4 and Cy 1800 mg/m^2 Day 1–2) prior to a second infusion and had a partial response (PR). This pt subsequently developed aplastic anemia and died. Responses included: 1 pt – PR, 3 pts - stable disease, 2 pts – progressive disease, 1 pt - too early to determine, 4 pts - off-study prior to tumor assessment. SPEAR T-cells were detectable in peripheral blood from pts at each dose level, and in tumor tissue from pts at DL1 and DL3.

Conclusions ADP-A2M10 SPEAR T-cells have shown acceptable safety and no evidence of toxicity related to off-target binding or alloreactivity. Given the minimal antitumor activity and the discovery that MAGE-A10 expression frequently overlaps with MAGE-A4 expression, the clinical program has closed. Several trials with SPEAR T-cells targeting MAGE-A4 are ongoing (https://bit.ly/35htsZK).

Trial Registration NCT02592577

Ethics Approval The trial was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines and was approved by local authorities. An independent ethics committee or institutional review board approved the clinical protocol at each participating center. All the patients provided written informed consent before study entry.

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279 DURVALUMAB AFTER CHEMORADIOTHERAPY FOR PD-L1 EXPRESSING INOPERABLE STAGE III NSCLC IMPACTS LOCAL-REGIONAL CONTROL AND OVERALL SURVIVAL

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Background Chemoradiotherapy (CRT) followed by maintenance treatment with the PD-L1 inhibitor durvalumab is a new standard of care for inoperable stage III NSCLC. The present study aims to evaluate the oncological outcome of patients treated with CRT alone to those treated with CRT and durvalumab (CRT-IO) in the real-world setting.

Methods Retro- and prospectively collected data of 133 consecutive inoperable stage III NSCLC patients treated between 2011–2019 were evaluated. Local-regional-recurrence-free-survival (LRPFS - defined as progression in the mediastinum, hilum and/or supraclavicular region at both sides and the involved lung), progression-free survival (PFS) and overall survival (OS) were evaluated from last day of thoracic radiotherapy (TRT).

Results Median age at diagnosis was 68.5 years; 44 (33%) were female; 58 (44%) were diagnosed with adenocarcinoma. All patients were irradiated to a total dose of at least 60 Gy (EQD2). Median PTV was 709.8 cc (range: 181–1958 cc). 113 (85%) patients were treated with CRT and 20 (15%) PD-L1 expressing patients with CRT-IO. 83% of patients received two cycles of concomitant platinum-based chemotherapy. Median time to initiation of durvalumab after CRT was 0.8 months (range: 0.4–2.1). Median follow-up for entire cohort was 33.3 months (range: 4.8–111.8) and median overall survival (OS) was 24.7 (95% CI: 18.9–30.4) months. In the CRT-IO cohort after a median follow-up of 15.5 (range: 5.1–20.2) months, no deaths were reported at the time of evaluation (August 2020). Improved LRPFS (p=0.013), PFS (p=0.033) and OS (p=0.002) were correlated with CRT-IO compared to the historical cohort of conventional CRT patients.After propensity-score matching (PSM) analysis with age, gender, histology, tumor volume and treatment mode and exact matching for T-and N-stage, 18 CRT-IO patients were matched 1:2 to 36 CRT patients. 12-month LRPFS, PFS and OS rates in the CRT-IO vs CRT cohort were 80% vs 38.8% (p=0.001), 50% vs 22% (p=0.013) and 100% vs 75% (p=0.002), respectively. Also regarding intracranial failure, 6-month brain metastases rates were 0% vs. 6% in the CRT-IO vs CRT cohort (p=0.290).

Conclusions This real-world analysis demonstrates that durvalumab after CRT has led to significant improvement of local-regional control, PFS and OS in PD-L1 expressing inoperable stage III NSCLC patients compared to a historical cohort.

Acknowledgements The study was partly presented at 2020 Annual Meeting of the American Society of Clinical Oncology (ASCO).

Trial Registration N/A

Ethics Approval The study was approved by Ludwig-Maximilians-University (LMU), Munich, Germany: Institution's Ethics Board, approval number 17-230.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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280 BOTH TUMOR INTRINSIC AND EXTRINSIC FACTORS CONTRIBUTE TO TIL RESISTANCE IN LUNG CANCER PATIENTS

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Background Although cancer immunotherapies have achieved great success, many patients either do not respond or initially respond but later relapse. Several resistance mechanisms have been proposed from trials using immune checkpoint inhibitors or CAR-T therapy,[1,2] but few studies have been conducted on resistance mechanisms to TIL therapy. In our trial, anti-PD1 refractory lung cancer patients were treated using TIL therapy. Several patients responded while others did not. We hypothesize that both tumor intrinsic and extrinsic factors may contribute to TIL resistance in lung cancer patients.

Methods We performed whole exome sequencing on resected baseline tumors and predicted neoantigens using the netMHCpan algorithm. Neoantigen-reactive TIL were screened using IFN-gamma ELISpot assays in a T-DC-neoantigen co-culture system. We also did the same co-culture for TCRVβ sequencing to identify neoantigen-specific TCR clonotypes.[3] Therefore, we have been able to track tumor antigen-specific T cells over