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, respectively). Three pts reported adverse events Grade 3 were lymphopenia (11), 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, respectively). 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/35hnsZK).

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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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.

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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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279 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 TCRVs sequencing to identify neoantigen-specific TCR clonotypes. Therefore, we have been able to track tumor antigen-specific T cells over...