engineered to eliminate FcγR binding, consequently eliminating ADCC, ADCP and ADCR effects. This AK105-203 trial (NCT04172571) aimed to explore the efficacy and safety of penpulimab plus anlotinib in patients (pts) with histologically or cytologically confirmed uHCC.

Methods: In this single-arm, multicenter phase Ib/II trial, pts with uHCC and no prior systemic treatment were eligible if they were 18-75 years, and classified as BCLC stage B (not amenable for locoregional therapy) or C, Child-Pugh score ≤7 and ECOG PS of 0-1. Pts received anlotinib (8 mg, p.o., qd, d1-14, q3w) plus penpulimab (200mg, iv, d1, q3w). The primary endpoint was ORR (RECIST v1.1). Secondary endpoints were safety, DCR, DoR, TTP, PFS and OS.

Results: 31 pts (median age 56 years [23-74], ECOG 0/1 [64%/36%], BCLC B/C [23%/77%], HBV/HCV [61%/7%]) received combined therapy. As of August 5, 2022, median follow-up time was 23.0 months (range 3.7-31.9). The ORR was 31.0% (95% CI, 15.3-50.8%), and DCR was 82.8% (95% CI, 64.2-94.2%). The median PFS and TTP for 31 patients were 8.8 months (95% CI, 4.0-12.3) and 8.8 months (95% CI, 4.0-14) respectively. OS events were observed in 16 patients (51.6%), and the median OS was 23.0 months with 12-months OS rate was 67.9%. Treatment-related adverse events (TRAEs) occurred in 90.3% of pts (≥G3 in 25.8% [8/31]). No G5 AE occurred. Most common TRAEs (≥25%) were increased AST (41.9%) and ALT (35.5%), general disorders and administration site conditions (35.5%), skin and subcutaneous tissue disorders (32.3%), platelet count decreased (25.8%), asthenia (25.8%).

Conclusions: Anlotinib combined with penpulimab showed encouraging efficacy and acceptable safety in pts with uHCC. The further randomized, phase 3 study of penpulimab plus anlotinib at a higher dose (10 mg) in this setting is ongoing (NCT04344158).

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81P Is PD-1 inhibitor based treatment better than chemotherapy for metastatic NSCLC patients with PD-L1≥50% who develop EGFR-TKI resistance? A real-world investigation

Y. Li[1], H. Jiang[1], F. Qian[2], Y. Cheng[3], Y. Zhang[2], J. Lu[2], Y. Lou[4], B. Han[4], W. Zhang[2]

[1]Pulmonary Medicine, Shanghai Chest Hospital, Shanghai, China; [2]Pulmonary Medicine Dept., Shanghai Chest Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, China; [3]Department of Radiation Oncology, Shanghai Chest Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, China; [4]Respiratory Dept., Shanghai Chest Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, China

Background: Platinum-based chemotherapy is still the standard of care for Epidermal growth factor receptor (EGFR) mutated non-small cell lung cancer (NSCLC) patients after developing EGFR-TKI resistance. However, no study focusing on the role of PD-1 inhibitor based treatments for EGFR mutated NSCLC patients who carried PD-L1 TPS ≥ 50% progressed after EGFR-TKI therapy. Thus, we aimed to investigate the outcomes of PD-1 inhibitor based treatments for these patients and to explore the population that may benefited from PD-1 inhibitor based therapies.

Methods: We retrospectively collected data of EGFR mutated advanced NSCLC patients with PD-L1 TPS≥50% who have failed prior EGFR-TKI therapies without T790M mutation at Shanghai Chest Hospital between January 2018 and June 2021. Progression-free survival (PFS) and overall survival (OS) were utilized to evaluate the outcomes.

Results: A total of 146 patients were included. The median follow-up was 36.7 months (IQR, 12.5-44.2 months). Among the population, 66 patients (45.2%) received chemotherapy, the remaning (54.8%) received PD-1 inhibitor based therapies, including 56 patients(70.0%) received PD-1 inhibitor combined with chemotherapy (PC) and 24 patients (30.0%) received PD-1 inhibitor monotherapy (PM). Survival analysis shown that patients who received PD-1 inhibitor based therapies had better PFS and OS compared with those treated with other therapy (median PFS, 4.0 vs. 10.0 months, P < 0.001; median OS, 39.5 vs. 24.2 months, P < 0.001). What's more, patients who treated with PC treatment had a superior survival time than those received PM treatment (median PFS, 10.3 vs. 7.0 months, P < 0.001; median OS, 32.4 vs. 41.6 months, P < 0.001). Subgroup analysis found that the PFS and OS benefit of PC was evident in all subgroups.

Conclusions: For advanced NSCLC patients with EGFR mutations and PD-L1 TPS≥50% who have failed prior EGFR-TKI therapies without T790M mutation, PD-1 inhibitor based treatment could provide a more favorable survival than classical chemotherapy. What's more, compared with PD-1 inhibitor monotherapy, PD-1 inhibitor combined with chemotherapy seems to be the preferred treatment.

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82P Preliminary analysis of tislelizumab (TIS) and chemotherapy as neoadjuvant therapy for potentially resectable stage IIIA/IIIB non-small cell lung cancer (NSCLC)

T. Wang[1], L. Li[1], L. Huang[1], J. Liu[1], D.D. Zhu[1], C. Qin[1], J. Dong[1], H. Deng[1], X. Zheng[1], L. Tian[1], L. Jiang[2], W. Wang[2], P. Zhou[2], M. Su[3], D. Pu[1], X. Cai[4], M. Feng[5], X. Ou[5], Y. Wang[5], Q. Zhou[1]

[1]Lung Cancer Center, West China Hospital of Sichuan University, Chengdu, China; [2]Pathologic Department, West China Hospital of Sichuan University, Chengdu, China; [3]Department of Nuclear Medicine, West China Hospital of Sichuan University, Chengdu, China; [4]Molecular Network, West China Hospital of Sichuan University, Chengdu, China; [5]Thoracic Oncology Ward, Cancer Center, West China Hospital of Sichuan University, Chengdu, China

Background: The benefit of neoadjuvant immunotherapy and chemotherapy in resectable NSCLC indicated that this combination therapy may provide more surgical opportunities and survival benefits to potentially resectable locally advanced NSCLC. Herein, we initiated a phase II study to evaluate the feasibility of immunotherapy plus chemotherapy in stage IIIA/IIIB NSCLC.

Methods: We planned to recruit 33 patients (pts) with stage IIIA/IIIB EGFR/ALK/ROS wild-type NSCLC. Eligible pts received 2 cycles of neoadjuvant chemoimmunotherapy (PD-1 inhibitor TIS, nab-paclitaxel, and cisplatin/carboplatin) and were reassessed for surgery. Thereafter, pts underwent surgery within 6 weeks and continued 2 cycles of TIS plus chemotherapy, followed by up to 15 cycles of TIS monotherapy. The primary endpoint was the R0 resection rate. Secondary endpoints were major pathologic response (MPR), pathologic complete response (pCR), disease-free survival, and overall survival.

Results: From Jan 2021 to Sep 2022, 18 of 33 enrolled pts (54.5%) completed neoadjuvant therapy and underwent resection (13 with IIIA and 5 with IIIB disease). No treatment-related surgical delay occurred. 17 of 18 pts (94.4%) underwent successful R0 resection (Table). Of 18 pts who underwent resection,6 (33.3%) achieved pCR and 4 (22.2%) achieved MPR, resulting in an overall pathologic response rate of 55.6%. Of the 4 pts who achieved MPR, 3 had only 1% viable tumor cells in the resection specimen. The overall response rate (ORR) and disease control rate (DCR) were 88.9% (16/18) and 100 % (18/18), respectively. Both the clinical and pathological downstaging occurred in 16 of 18 pts (88.9%).

Table: 82P

Outcomes	Results, n (%, 95%CI); n = 18
Radiological response	
PR	16 (88.9, 65.29-98.62)
SD	2 (11.1, 1.38-34.71)
ORR	16 (88.9, 65.29-98.62)
DCR	18 (100, 81.5-100.0)
Surgical resection	
R0	17 (94.4, 72.71-99.86)
R1	1 (5.6, 0.14-27.29)
Downstaging rate	
clinical	16 (88.9, 65.29-98.62)
pathologic	16 (88.9, 65.29-98.62)
Pathologic response	10 (55.6, 30.76-78.47)
MPR	4 (22.2, 6.41-47.64)
pCR	6 (33.3, 13.34-59.01)

Conclusions: Neoadjuvant TIS plus chemotherapy increased surgical opportunities in potentially resectable locally advanced stage IIIA/IIIB NSCLC. The encouraging R0 resection rate observed in this study supports further investigation.

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83P The Immune-related adverse event (IRAE) Likelihood Score (ILS) identifies "pure" IRAEs strongly associated with outcome in a phase I-II trial population

L. Mazzarella[1], E. Nicolo[1], A. Esposito[1], E. Crimini[1], G. Tini[2], J. Uliano[1], C. Corti[1], P.M. Trillo Aliaga[3], C. Valenza[1], M. Repetto[1], G. Antonarelli[1], I. Minchella[1], C. Belli[1], M.A. Locatelli[1], C. Criscitiello[1], G. Curigliano[4]

[1]New Drug Development, Experimental Oncology, IEO - Istituto Europeo di Oncologia, Milan, Italy; [2]Laboratory of Translational Oncology, Dept of Experimental Oncology, IEO - Istituto Europeo di Oncologia IRCCS, Milan, Italy; [3]Division of Thoracic Oncology,

IEO - Istituto Europeo di Oncologia IRCCS, Milan, Italy; [4]Early Drug Development for Innovative Therapies Division, IEO - Istituto Europeo di Oncologia, Milan, Italy

Background: Immune-related adverse events (IRAE) pose a significant diagnostic and therapeutic challenge in patients treated with immuno-oncology (IO) drugs. IRAEs have been found to correlate with better outcome, but studies are conflicting on the magnitude and significance of this correlation. Estimating the true incidence of IRAEs is particularly difficult in the early phase 1/2 trial setting, with factors contributing to both over- and under-estimation. A key issue is the lack of IRAE diagnostic criteria, necessary to discriminate "pure" IRAEs from other treatment-related adverse events not sustained by an autoimmune process. We present the definitive analysis of a retrospective study conducted on patients treated with IO drugs within phase 1-2 trials at our institute.

Methods: We extensively reviewed clinical characteristics and temporal dynamics of IRAEs and empirically developed an IRAE Likelihood Score (ILS) based on availability of invasive or highly specific tests, response to immune suppression, temporal correlation with IO drug initiation, evidence ruling out alternative cause, known relationship with IO. We defined High Confidence (HC) or Low Confidence (LC) IRAEs by clinical consensus and estimated correlation with survival of treatment-related events by multivariate Cox analysis. To mitigate immortal time-bias, we also analysed data at 2-month landmark and modeling IRAEs as time-dependent covariate.

Results: 29.2% of 202 patients developed $\geq$ 1 treatment-related adverse event. ILS $\geq$ 5 discriminated between HC and LC IRAEs with >93% specificity and sensitivity. HC IRAE patients (n=24) had significantly improved outcome for PFS and OS, irrespective of the model used (landmark, time-dependent or uncorrected, HR for PFS ranging 0.24-0.44, for OS 0.18-0.23, all p values <0.01), whereas LC IRAE patients (n=35) showed no statistically significant correlation.

Conclusions: ILS provides a simple system to identify bona fide IRAEs, pruning for other treatment-related events likely due to different pathophysiology. Applying stringent criteria leads to lower and more reliable estimates of IRAE incidence and identifies events with significant impact on survival.

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84P Ambulatory management of ICI-induced hepatitis: A safe and effective management approach

A.C. Olsson-Brown[1], N. Garbutt[2], F. Dulson[2], T. Guinan[2]

[1]Medical Oncology Department, The Clatterbridge Cancer Centre - Liverpool, Liverpool, UK; [2]Immunotherapy, The Clatterbridge Cancer Centre - Liverpool, Liverpool, UK

Background: The incidence of immune related adverse events (irAEs) secondary to oncological immune checkpoint inhibitors (ICIs) are treated as standard with high dose corticosteroids (CST). Grade 3-4 hepatitis is managed with intravenous methylprednisolone (IVMP) as per international protocols. CST treatment is effective but if administered in the inpatient setting can lead to long hospital stays, psychological distress and increased risk of hospital related illness. Clatterbridge Cancer Centre (CCC), a UK tertiary cancer centre, has an established regional pan-tumour immunotherapy (IO) service to support all patients with irAEs and delivers a ambulatory IVMP pathway as part of that service.

Methods: A retrospective review of the ambulatory IVMP service since its introduction in 2018 was undertaken. The proportion of patients treated in an ambulatory setting was compared the situation prior to 2018. Additionally the responsiveness of the service and impact on admission, length of stay (LOS) and bed days (BD) was evaluated.

Results: Between 2018 and 2021 2017 patients were treated with checkpoint inhibitors regionally. 1027 patients experienced CST requiring irAEs of which 95 experienced grade 3/4 hepatitis requiring IVMP. Prior to the introduction of the service 100% (17/17) of patients required inpatient admission for IVMP associated with a median LOS of 12.5 days and accounting for 137.5 BD per annum. Following the introduction of the ambulatory service 15% (15/95) required admission for the introduction of IVMP, with 60% (9/15) of them completing their IVMP as an outpatient in the ambulatory setting. 75% (71/95) of patients had treatment commenced as a day case and there was an ambulatory to inpatient conversion of 9.9% (7/71), all of whom displayed CST insensitivity and required additional immunosuppresion. The median LOS was reduced to 4.75 days. Given the average number of patients requiring IVMP between 2020-22 was 34.5 (range 33-36) per year this is a saving of 268 bed days per annum resulting in a cost saving of £123,280 per annum.

Conclusions: The introduction of an ambulatory IVMP service for the management of immunotherapy induced hepatitis has been illustrated to be safe, effective, responsive to CST resistance and result in care provision efficiencies.

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85P Tislelizumab combined with apatinib and oxaliplatin plus S1 as neoadjuvant therapy for Borrmann IV large Borrmann III type and bulky N positive advanced gastric cancer: A single-arm multicenter trial (TAOS-3B-Trial)

L. Chen[1], Z. Ye[2], G. Liu[3], Q. Lin[4], Y. Chi[5], J. Wang[6], S. Wei[2], C. Wei[2], S. Liu[2], Y. Zeng[2], S. Chen[2], Y. Wang[2]

[1]Gastrointestinal Surgical Oncology, Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China; [2]Gastrointestinal Surgical Oncology, Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China; [3]Gastrointestinal Surgery, Putian University Affiliated Hospital, Putian, China; [4]Gastrointestinal Surgical Oncology, Sanming Second Hospital, Sanming, China; [5]Gastrointestinal Surgical Oncology, Fujian Medical University Sanming First Hospital, Sanming, China; [6]Gastrointestinal Surgical Oncology, Xiapu General Hospital, Fuzhou, China

Background: We aimed to investigate the efficacy and safety of S1 plus oxaliplatin in combination with tislelizumab, a novel engineered anti-PD-1 monoclonal antibody, and apatinib, an inhibitor of VEGFR-2, as neoadjuvant therapy for Borrmann IV、large Borrmann III type(tumor size>5cm) and Bulky N positive advanced gastric cancer (GC).

Methods: This was a single-arm, multicenter, open-label phase II trial (NCT05223088). Eligible patients (pts) had histologically proven advanced HER-2 negativeGC with Borrmann IV, large Borrmann III type(tumor size>5cm) and Bulky N positive. The surgery was performed after 4 cycles of drug treatment (S1+oxaliplatin+tislelizumab+apatinib).

Results: Baseline Patient Characteristics: Among the 25 pts eligible which have been already postoperative efficacy evaluation in 40 pts, the median age was 57 years. The histological types were mainly poorly differentiated adenocarcinoma.

Table: 85P

Characteristics	N (%)
Age, years	
Median	57
Mean	55.12±10.08
Range	39-73
Sex	
Male	19 (76.0)
Female	6 (24.0)
Enrollment factors	
Borrmann IV	3 (12.0)
Borrmann III	20 (80.0)
Bulky N positive	2 (8.0)
Histological classification	
Moderately differentiated adenocarcinoma	2 (8.0)
Poorly differentiated adenocarcinoma	23 (92.0)
MSI status	
MSS	25 (100.0)
MSI-H	0 (0.0)
PD-L1 (28-8) CPS score	
<1	5 (20.0)
1-5	13 (52.0)
>5	7 (28.0)
Tumor location	