Abstract 258 Figure 3 Tumor and peripheral immune repertoire diversity. A-D: In tumor RNA-Seq, higher IGH chain abundance and richness was associated with both clinical benefit (A, C) and response (B, D) (n=31). E-F: Inter-group comparisons showed fewer TRB chain similarities between patients who derived clinical benefit (E) or response (F) versus those who did not, in pre-treatment PBMC samples. G-I: Univariate Cox proportional hazards models for PFS showing immune diversity measures derived from pre-treatment tumor RNA-Seq (G), PBMC-derived amplicon sequencing pre-pembrolizumab (H), and PBMC-derived amplicon sequencing pre-pembrolizumab (I)
Methods MORPHEUS-PDAC, MORPHEUS-TNBC and MORPHEUS-CRC enrolled 1L metastatic (m) PDAC, 2L locally advanced or mTNBC or 3L mCRC patients, respectively. Experimental arm patients received atezo (840 mg IV q2w) and seli (16 mg SC on D1 every 28-day cycle for C1-4 and every third cycle thereafter). Patients also received gem (1000 mg/m²) and nabP (1000 mg/m², 125 mg/m² respectively, IV on D1, 8, 15 every 28-day cycle) in PDAC or bev (10 mg/kg IV q2w) in TNBC and CRC. Control treatments were gem+nabP in PDAC, capetibatin in TNBC, and regorafenib in CRC. Primary endpoints were safety and objective response rate (ORR; investigator-assessed RECIST 1.1). PD-L1 and CD8/panCK IHC were tested in all biopsies.

Results All treated patients were safety evaluable. MORPHEUS-PDAC (20-week interim analysis): 9 patients received atezo+seli+gem+nabP and 4 received control. Treatment-related adverse events (TRAEs) were seen in all. Treatment-related serious AEs (SAEs) occurred in 6 patients (67%) receiving atezo+seli+gem+nabP and 1 (25%) receiving control. Confirmed ORRs: 44% (95%CI:14-79) and 25% (95%CI:6-81), respectively. MORPHEUS-TNBC (27-week interim analysis): 6 patients received atezo+seli+bev and 24 received control. TRAEs were seen in 5 patients (83%) receiving atezo+seli+bev and 18 (75%) receiving control. Treatment-related SAEs occurred in 1 patient in each arm (17% and 4%, respectively). Confirmed ORRs: 17% (95% CI:0.4-64) and 21% (95%CI:7-42), respectively. All 6 patients receiving atezo+seli+bev were PD-L1 negative (SP142 IHC assay) at baseline; the only patient with partial response (PR) showed upregulation of PD-L1 expression at week 3. MORPHEUS-CRC (18-week interim analysis): 6 patients received atezo+seli+bev and 13 received control. TRAEs were seen in all patients receiving atezo+seli+bev and 12 (92%) receiving control. Treatment-related SAEs occurred in 3 patients (50%) receiving atezo+seli+bev and 1 (8%) receiving control. No responses occurred in either study arm. Paired biopsies for 3 patients (60%) receiving atezo+seli+bev suggest on-treatment increases in CD8 T-cell infiltration into tumors.

Conclusions Toxicities related to the atezo+seli combinations were consistent with individual study treatments. Preliminary efficacy was observed for atezo+seli+gem+nabP in PDAC. Together with preliminary evidence of on-treatment pharmacodynamic effects in CRC and TNBC tumor samples, CD40 agonist strategies warrant further investigation.

Trial Registration MORPHEUS-PDAC: NCT03193190; MORPHEUS-TNBC: NCT03424005; MORPHEUS-CRC: NCT03555149.

Ethics Approval The trial was conducted according to the principles of the Declaration of Helsinki. All patients provided written informed consent. Protocol approval was obtained from independent review boards or ethics committees at each site.

T CELL INFILTRATING REPERTOIRE DIVERSITY IS ASSOCIATED WITH ENHANCED SURVIVAL FOLLOWING NEOADJUVANT THERAPY IN PATIENTS WITH RESECTABLE PANCREATIC CANCER

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Abstract 260 Figure 1 Following neoadjuvant therapy, patients with resectable pancreatic cancer with a higher than median intratumoral TCR Vβ Diversity 50 (n=9, 4.624 HR: 95 CI [0.971, 21.83]) have greater overall survival compared to patients with lower than median intratumoral TCR Vβ Diversity 50 (n=10, 0.2163 HR: 95 CI [0.458, 1.021]). Representative tree maps of high and low TRC Vβ D50, where each rounded rectangle represents a unique CDR3, with the size of the rectangle corresponding to the relative frequency of the CDR3 clones across the entire repertoire.