breast cancer (BC), yet about 30% remain unresponsive. Since the potency of ICIs depends on the efficient presentation of tumor-specific antigens by cancer cells, compounds which increase such presentation could increase efficacy of ICIs. METHODS/STUDY POPULATION: A library of the ester and urethane derivatives of polyether ionophore antibiotic, monensin (MON) has been synthesized. MTT cell viability assays were performed on the panel of human and mouse BC cell lines, and non-cancerous breast epithelial cells to determine IC50 values of MON and its derivatives. Selectivity Indexes were calculated to identify the most selective compounds towards cancer versus non-cancer cells. Major Histocompatibility Complex (MHC) class I and II presentation and Programmed death-ligand 1 (PD-L1) expression have been determined using flow cytometry. Proteins involved in apoptosis, autophagy and immunogenic cell death were identified through immunoblotting. At least three biological replicates have been performed for each experiment. RESULTS/ANTICIPATED RESULTS: MON and several of its derivatives shown activity in nanomolar range against MDA-MB-231 human BC cell line. MON and its most potent derivatives significantly increased MHC class I and II presentation and downregulated the expression of PD-L1 in BC cell lines. DISCUSSION/SIGNIFICANCE: Present findings will lead to the development of new therapeutic approaches that can serve as single agents or be used in combination with existing ICIs for the treatment of metastatic BC. By pushing the boundaries of our understanding and developing new therapies, this research can make an impact in improving outcomes for patients with metastatic BC.

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The Analysis of N-glycans and Collagen to Predict Prostate Adenocarcinoma Outcome*

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OBJECTIVES/GOALS: Distinguishing indolent from aggressive prostate cancer and early identification of men at risk of developing aggressive, metastatic disease is of great importance. We aim to explore the relationship between N-glycan and collagen composition in prostate tumor tissue and the long-term outcome of the disease. METHODS/STUDY POPULATION: Matrix assisted laser desorption/ionization mass spectrometry can be utilized to characterize N-glycan profiles in formalin fixed paraffin embedded tissues. Collagen may also be characterized using ECM-targeted collagenase MALDI imaging. These approaches were used to analyze prostatectomy samples with different clinical outcomes. Tissue microarrays containing tissues from 75 non-progressors (no evidence of disease; NED) and 50 metastatic cases (MET) were examined. From a combined list of 90 N-glycans and 500 collagenase peptides, the average AUC intensity value for each glycan and collagen peptide was extracted and assessed as a predictor of metastatic progression. Ancestral informative markers were analyzed and polygenic hazard risk scores were generated for samples as well. RESULTS/ANTICIPATED RESULTS: Three N-glycans and three collagen peptides were found to discriminate between NED and MET cases with statistical significance. The best performing N-glycan was Hex6HexNAc6Fuc1 with an AUC of 0.77 ($p<0.001$). While the best performing collagen peptide was COL1A2 with an AUC of C 0.77 ($p<0.001$). DISCUSSION/SIGNIFICANCE: Both a collagen peptide and N-glycan were discovered as promising biomarkers to predict metastasis. Future validation studies are needed to confirm biomarker potential and to determine if the addition of these biomarkers can strengthen current genomic classifier's ability to predict metastatic prostate cancer.

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Pathogenicity of a CCDC6-RET Fusion in Malignant Peripheral Nerve Sheath Tumor (MPNST)

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OBJECTIVES/GOALS: RETgene fusions in sarcoma are rare and their impact on pathogenicity is unknown. Malignant peripheral nerve sheath tumors (MPNST) are a deadly, genomically heterogenous soft tissue sarcoma rarely harboring targetable aberrations. We present a case of a CCDC6-RET fusion MPNST sensitive to RET-inhibitor therapy in a xenograft model. METHODS/STUDY POPULATION: Lung tumor tissue was obtained per an approved collection protocol from a 21yo male patient with a spontaneous MPNST harboring an inactivating mutation in NF-1 and a CCDC6-RET gene fusion detected by a commercially available sequencing panel (Signatera). To confirm pathogenicity of the RET fusion, fresh tumor tissue was engrafted into immunocompromised NSG mice in the anterior and posterior flanks, harvested at ~10 weeks, and re-transplanted into bilateral flanks. When tumor diameters reached 0.5-1cm (~4 weeks), mice were randomized into 3 groups (n=6/group) and treated with either vehicle (V) (PBS), the RET-specific inhibitor selpercatinib (S) (20mg/kg twice daily), or the multi-kinase inhibitor cabozantinib (C) (30mg/kg daily) by oral gavage. Mice were monitored weekly for weight and tumor size. RESULTS/ANTICIPATED RESULTS: 92% (33/36) of implanted tumors were evaluable for treatment response. Pre-treatment tumor volumes (mm3) across all three groups were similar (mean/Std Dev – V: 230/111, S: 271/132, C: 230/123). At day 7, tumor growth was significantly inhibited by S and C versus V (ANOVA $p < 0.001$, post-hoc Tukey's V vs S $p= 0.0178$, V vs C $p< 0.0001$, S vs C $p= 0.0005$). V-treated tumors increased in volume by 60% while S reduced tumor volume by ~80% and C reduced tumor volume by ~20%. S and C treatments were tolerated well. and S improved survival with 100% of mice alive at day 63 vs 0% in V and C groups. 6 of the 12 implanted tumors treated with S, 50% increased in size after ~6-weeks following a >90% initial tumor reduction in tumor volume. Follow-on molecular studies in S-resistant tumors are ongoing. DISCUSSION/SIGNIFICANCE: Targetable genomic changes in MPNST, especially in RET, are infrequent and often considered stochastic. Our findings suggest that precision medicine approaches pairing genomic sequencing and in vivotesting of target gene pathogenicity may guide treatment planning and novel discovery for rare, difficult to treat sarcomas.

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Prototyping a mobile phone application for Chimeric Antigen Receptor (CAR) T-cell therapy patient monitoring and data collection post-discharge

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OBJECTIVES/GOALS: Research objectives include prototyping a mobile phone application that allows physicians to monitor CD19-directed CAR T-cell therapy patients remotely after discharge. This app will also enable standardized data collection across different

https://doi.org/10.1017/cts.2024.339

centers that provide CAR-T cell therapy and allow for the harmonization of follow-up protocols. METHODS/STUDY POPULATION: Literature review and semi-structured interviews with patients, clinical coordinators, and other experts in the field will be used to determine what parameters must be included in the mobile application prototype to effectively monitor the side effects of CD19-directed CAR T-cell therapy. The mobile phone application will be designed using process mapping to integrate data from self-reporting and wearable technologies, including the Garmin smart watch. Figma will then be used to develop new screens based on an existing patient monitoring app for Allogeneic Stem Cell Transplant follow-up. Finally, a preliminary feasibility study will be conducted to collect feedback on the app prototype from CAR T-cell therapy patients, providers, and stakeholders. RESULTS/ANTICIPATED RESULTS: The anticipated results of this study include an app prototype that will include the functionalities required to monitor patients for adverse effects of CD19-directed CAR T-cell therapy. This will include the parameters that will be recorded or measured using a combination of self-reporting, a reliable body temperature sensor, and the Garmin watch which monitors basic vitals, activity, and sleep. Additional parameters may be added during the stakeholder co-design process. The app prototype will include a physician interface where doctors can monitor their patients and will be alerted if they require further physician assessment. It is expected that the app will provide standardized monitoring of patients when they are discharged from the hospital after receiving CAR T-cell therapy. DISCUSSION/SIGNIFICANCE: This app will allow physicians to monitor patients for general follow-up and adverse effects, including cytokine release syndrome and neurotoxicity. Future studies may utilize this app to develop best practices for harmonizing CAR-T follow-up protocols across Canada.

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Impaired Coronary Endothelial Response to Exercise among Postpartum Women with Preeclampsia

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OBJECTIVES/GOALS: Preeclampsia increases cardiovascular (CV) risk, likely via persistent endothelial dysfunction and angiotensin II type 1 receptor autoantibodies (AT1R-Ab). We aim to assess coronary endothelial function (CEF) and AT1R-Ab levels in postpartum preeclampsia with a hypothesis this mediates CV risk. METHODS/STUDY POPULATION: We prospectively enrolled age and CV risk factor matched postpartum women. Coronary MRI was performed at rest and with isometric handgrip stress, an endothelial dependent stressor. CEF was quantified as % stress-induced change in coronary cross-sectional area (%CSA) and in coronary blood flow (%CBF). AT1R-Ab was measured using a novel antigen capture enzyme-linked immunosorbent assay. RESULTS/ANTICIPATED RESULTS: Women with and without preeclampsia were similar in age (mean 32.7+5.0 years), BMI (mean 28.0+6.3 kg/m2) and race/ethnicity (58% White, 35% Black and 4% Hispanic). %CSA was lower with (-2.1+13.6) vs without preeclampsia (8.8+17.1), p=0.023. %CBF was also lower with (11.3 [-11.8, 25.2]) vs without preeclampsia (25.7 [-0.7, 62.9]), p=0.039. AT1R-Ab was higher among women with preeclampsia (p=0.029) and was inversely associated with %CBF (beta coefficient -4.6 [-8.9, -0.3], p=0.037) but not with %CSA. DISCUSSION/SIGNIFICANCE: Women with preeclampsia have elevated AT1R-Ab and impaired CEF demonstrated by insufficient coronary reserve with exercise. Coronary endothelial dysfunction and dysregulation of the renin-angiotensin pathway likely contribute to long-term CV risk and should be considered for targeted risk reduction.

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Value estimation of the Diabetes Prevention Program: How well does clinical trial-based cost-effectiveness apply to the real world?

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OBJECTIVES/GOALS: Many economic evaluations rely on clinical trial data that may not represent real world populations and intervention effectiveness. We compare risk and cost-effectiveness for the Diabetes Prevention Program (DPP) clinical trial cohort and a real world population eligible for the national DPP to assess the impact of using real world data. METHODS/STUDY POPULATION: To produce real world (US population) representative results, we identified National Health and Nutrition Examination Survey (NHANES) subjects eligible for the national DPP and adjusted projections using survey weights. We used clinical predictive models to estimate individual diabetes risk, and microsimulation to estimate lifetime costs, benefits, and net monetary benefits (NMB) for lifestyle intervention and metformin. We compared results across the DPP clinical trial and NHANES populations. RESULTS/ANTICIPATED RESULTS: Three-year risk of diabetes onset for the DPP trial population (mean of 19.7%, median of 10.3%) exceeded corresponding risk for the NHANES population (mean of 14.6%, median of 4.8%). The proportion of individuals with a three-year diabetes risk < 10% for the DPP trial population (49%) was less than the corresponding proportion for NHANES (67%). Mean NMB for metformin for the DPP trial population ($9,749) exceeded the corresponding value for NHANES ($5,391). The proportion of subjects with negative NMB was 49% for the DPP trial population and 67% for NHANES. Lifestyle intervention had a mean NMB of $34,889 for the DPP trial population and $28,652 for NHANES. Only 20% of the NHANES population eligible for national DPP met inclusion/exclusion criteria for the DPP trial. DISCUSSION/SIGNIFICANCE: Real world populations eligible for the national DPP include a greater proportion of low-risk individuals, and for these people, prevention programs may confer smaller benefits. Technology assessments based on clinical trial data should be revised using real world population and treatment effect data.

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Targeting One-Carbon Metabolism in Brain Cancer†

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OBJECTIVES/GOALS: Glioblastoma (GBM) is the most malignant brain tumor in adults and remains incurable with an average survival of 15 months after diagnosis. There is great need for treatment options without side effects that are devastating to the quality of life for patients. GBM tumors can circumvent cellular damage by

https://doi.org/10.1017/cts.2024.339