Research Base	Protocol #	Official Study Title	Indication/Disease	Planned Intervention	Abbreviated Eligibility Criteria Please refer to CTSU for the most recent version of the protocol.	Primary Objective	ClinicalTrials.gov NCT #	CTSU Activation Date	Approx. Target Accrual
NRG	NRG-CC017	A Randomized Phase III Study Comparing Temporally-Modulated Pulsed Radiation Therapy (TMPRT) Versus Standard Radiation Therapy with Temozolomide for Adults with Newly Diagnosed MGMT-Unmethylated Glioblastoma	CNS Cancer (Primary tumor)	Arm 1 Radiation Therapy (RT) with Concomitant and Adjuvant Temozolomide Arm 2 Temporally Modulated Pulsed Radiation Therapy (TMPRT) with Concomitant and Adjuvant Temozolomide	**PVD: 03/16/2026** Patients must have adequate health that permits completion of the study requirements and the required follow-up. • For patients with known HIV, HBC, and/or HCV: o HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. o For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. o Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load. • Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. • Participants of childbearing potential (participants who may become pregnant or who may impregnate a partner) must be willing to use highly effective contraceptives during therapy and for up to 6 months after completing study therapy because the treatment in this study may be significantly teratogenic (See protocol section 9 for definition of highly effective contraception).	To determine whether TMPRT concurrently with TMZ can significantly improve time to NCF failure compared to standard RT with temozolomide for patients with MGMTunmethylated GBM.	n/a	4/1/26	398
	NRG-GY035	A Randomized Phase III Trial of Carboplatin, Paclitaxel, Pembrolizumab Versus Carboplatin, Paclitaxel, Bevacizumab Versus Carboplatin, Paclitaxel, Pembrolizumab, Bevacizumab in the Treatment of pMMR, TP53 Mutated Advanced or Recurrent Endometrial Cancer	Female Reproductive System Cancer	Arm 1 Paclitaxel + Carboplatin + Pembrolizumab every 3 weeks for 6-10 cycles Pembrolizumab maintenance every 6 weeks for 14 additional cycles See Section 5.1 Arm 2 Paclitaxel + Carboplatin + Bevacizumab (or anti-VEGF antibody biosimilar) every 3 weeks for 6-10 cycles Bevacizumab maintenance every 3 weeks for 28 additional doses See Section 5.1 Arm 3 Paclitaxel + Carboplatin + Pembrolizumab + Bevacizumab (or anti-VEGF antibody biosimilar) every 3 weeks for 6-10 cycles Pembrolizumab maintenance every 6 weeks for 14 additional cycles and Bevacizumab maintenance every 3 weeks for 28 additional doses See Section 5.1	**PVD: 10/09/2025** Stage III and Stage IVA endometrial cancer (with measurable disease), • Stage IVB endometrial cancer (with or without measurable disease), or • Recurrent endometrial cancer (with or without measurable disease) See Appendix I for FIGO 2009 Staging In patients with measurable disease, lesions will be defined and monitored by RECIST 1.1. Measurable disease (RECIST 1.1) is defined as at least one lesion that can be accurately measured in at least one dimension (longest diameter to be recorded). Each lesion must be ≥ 10 mm when measured by CT or MRI. Lymph nodes must be ≥ 15 mm in short axis when measured by CT or MRI. Histologic confirmation of the original primary tumor is required (submission of pathology report(s) is required). Patients with the following histologic types are eligible: endometrioid, serous, dedifferentiated/undifferentiated, clear cell, mixed epithelial, carcinosarcoma, adenocarcinoma not otherwise specified (N.O.S.) Patients must have: • Tumoral mismatch repair proficient (pMMR) disease as assessed by immunohistochemistry (IHC) AND • P53 IHC with aberrant staining pattern (aberrant p53 expression is consistent with mutant TP53). TP53 mutation by next-generation sequencing will also be accepted. A pathology report demonstrating results of institutional MMR IHC and p53 IHC and/or TP53 by next-generation sequencing	To demonstrate that bevacizumab, an anti-VEGF antibody therapy, (or an anti-VEGF antibody biosimilar) in combination with carboplatin, paclitaxel, and pembrolizumab is superior to carboplatin, paclitaxel, and pembrolizumab (the control arm) or carboplatin, paclitaxel, and bevacizumab in prolonging PFS in patients with pMMR, TP53 mutated advanced stage (III or IV) or recurrent endometrial cancer.	NCT07198074	**1/12/26**	**255**
	NRG-HN015	A Phase II Randomized Trial of Neoadjuvant Chemotherapy or Chemo-Immunotherapy in Patients with Recurrent/Persistent PD-L1 Enriched Squamous Cell Carcinoma of the Head and Neck Undergoing Salvage Surgery (NEOPOLIS)	Head and Neck Cancer	STRATIFY • Primary tumor site (Oropharynx or oral cavity vs. Larynx or hypopharynx) • Stage (rT4a or rN3a vs. other) • Prior use of (PD1/PDL1 inhibitors in the definitive setting (yes vs. no) Arm 1 Salvage Surgery (SS) Arm 2 Carboplatin + Paclitaxel + SS Arm 3 Carboplatin + Paclitaxel + Cemiplimab (REGN2810) + SS	**PVD: 10/10/2025** Patients must have adequate health that permits completion of the study requirements and required follow-up. • Patients with HIV, HBV, and/or HCV infection: o HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. o For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. o Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load. • Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. Persistent Grade 3-4 (CTCAE version 5.0) electrolyte abnormalities must be reversible with replacement.	Primary Objective To assess and compare investigator-assessed event-free survival (EFS) of patients treated with chemotherapy (carboplatin + paclitaxel) or chemo-immunotherapy (carboplatin + paclitaxel + cemiplimab [REGN2810]) prior to salvage surgery (SS) versus patients undergoing standard of care SS.	NCT07195733	**1/12/26**	180
	NRG-HN016	Radiotherapy with Concurrent Cetuximab vs. Carboplatin and Paclitaxel in Patients with Locoregionally Advanced Head and Neck Cancer with a Contraindication to Cisplatin: A Pragmatic Phase III Randomized Trial (CONCISE)	Head and Neck Cancer	STRATIFY: • P16 status: p16+ oropharynx vs. p16- oropharynx or non-oropharynx • Stage (AJCC 9 th edition) p16+ oropharynx: T1-2 and N2 or T3 and N0-2 (stage II) vs. T4 or N3 (stage III) p16- oropharynx or non-oropharynx: (T1-3 and N0-2b) vs. (T4a-b or N2c-3) • ECOG/Comorbidities: PS=0 and (modified) Charlson Comorbidity Index (CCI)=0 vs. PS=1-2 or (modified)	**PVD: 6/26/2025** Documentation of Disease • Patients must have pathologically confirmed, previously untreated, unresected squamous cell carcinoma of the larynx, hypopharynx, oropharynx, or oral cavity. • Local evaluation of p16 status is required for all oropharynx patients prior to registration. • Local evaluation of p16 status is recommended for non-oropharynx patients prior to registration. Definition of Disease Locoregionally advanced HNSCC defined as: • Non-oropharynx and p16-negative oropharynx cancer: AJCC 9th edition stage	To determine whether radiation therapy (RT) and concurrent carboplatin and paclitaxel (RT+CP) improves progression-free survival (PFS) compared to RT with concurrent cetuximab (RT+Cetux) in patients with locoregionally advanced head and neck cancer (HNC) who have a contraindication to cisplatin.	NCT07442681	6/10/26	454
	NRG-GI012	Phase III Randomized Trial of IO-Based Systemic Treatment +/- Liver SBRT in Hepatocellular Cancer with Macrovascular Invasion (HELIO-RT)	Gastrointestinal Cancer	Patients will recieve MD's choice of Neoadjuvant Therapy (NAT). After Central Radiation plan approval, bladder radiotherapy will commence, followed by x12 months of Pembro (MK-3475).	**PVD 9/10/2025** **Must have:** Patients must have adequate health that permits completion of the study requirements and required follow-up. • For patients with known HIV, HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. • Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial. **Must not have:** • No prior systemic therapy or transarterial radioembolization (TARE) for HCC. • No history of liver transplantation. • No prior radiotherapy to the region of the study cancer that would result in significant overlap of radiation therapy fields that would lead to excessive cumulative toxicity at the discretion of the investigator. • No medical contraindication to the standard of care immunotherapy. • For patients to be treated with atezolizumab/bevacizumab: · No history of a GI bleed or other clinically significant bleeding event within 6 months prior to study registration.	To determine if liver SBRT in combination with IO-based systemic therapy improves survival compared to IO-based systemic therapy alone, in patients with hepatocellular cancer with macrovascular invasion.	NCT07166406	10/7/25	476
SWOG	S2506	MOZART MZL: A Randomized Phase II Study Evaluating Mosunetuzumab Alone and in Combination with Either Zanubrutinib or Polatuzumab Vedotin for the Treatment of Participants with Relapsed/Refractory Marginal Zone Lymphoma	Lymphoma	Participants will be randomized between Arm 1, Arm 2, and Arm 3 using a dynamic balancing algorithm with stratification factors based on: a. Prior lines of systemic therapy: 1 vs ≥ 2 b. Marginal zone lymphoma subtype: nodal vs splenic vs extranodal	**PVD: 6/12/26** Disease Related Criteria a. Participants must have histologically diagnosed CD20+ marginal zone lymphoma (MZL) as per WHO criteria (see Section 4.0) including splenic, nodal, and extranodal subtypes, but excluding gastrointestinal-only MZL with disease assessments that can only be evaluated through endoscopic methods and cutaneous-only MZL. NOTE: A repeat biopsy to confirm MZL diagnosis is NOT required at time of relapse unless: • The participant has received prior CD3/CD20 bispecific antibody, then a repeat biopsy to document continued CD20+ MZL disease is required after the completion of the prior CD3/CD20 bispecific antibody therapy and prior to study registration. • The participant has splenic MZL in which a bone marrow biopsy preregistration is required within 42 days prior to registration. b. Participants must have measurable disease by PET-CT (preferred), or CT as defined by extranodal lesion >1cm or nodal lesion >1.5cm. • Participants with splenic MZL are included in the study if spleen SUV (or any splenic masses) is >liver SUV background and/or spleen size is >13cm. • Participants must have staging imaging performed within 42 days prior to registration, as follows. PET-CT baseline scans are preferred. If a baseline PET-CT scan cannot be obtained, CT scans of the neck, chest, abdomen, and pelvis, are acceptable. All disease must be assessed and documented on the Baseline Tumor Assessment Form. c. Participants must have one or more of the following criteria for further systemic therapy as per the discretion of the treating physician: • Symptoms due to progressive or bulky nodal disease.	a. To compare complete response (CR) rates in participants with relapsed/refractory marginal zone lymphoma randomized to mosunetuzumab SQ with or without zanubrutinib (Arm 2 versus Arm 1). b. To compare CR rates in participants with relapsed/refractory marginal zone lymphoma randomized to mosunetuzumab SQ with or without polatuzumab vedotin (Arm 3 versus Arm 1).	NCT07618722	8/18/26	138
	S2511	Randomized Phase III Trial of Multimodality Therapy Versus Standard of Care Systemic Therapy in HER2 Positive (HER2+) De Novo (AJCC Stage IV) Oligometastatic Breast Cancer with Response to Initial Chemotherapy	Breast Cancer	At Step 2 Registration, participants with clinical response after Step 1 therapy will be assigned to Cohort A and participants with disease progression or no clinical response after Step 1 therapy will be assigned to Cohort B. Participants assigned to Cohort A will be randomized between the two treatment arms according to a dynamic balancing scheme, with the randomization stratified by the following factors: 1. Initial systemic therapy: T-DXd containing vs. other 2. Number of metastatic lesions at Step 1 registration: 1 vs. 2-5 3. ER status: ER+ vs. ER- Response to systemic therapy: clinical PR in the breast vs. clinical CR in the breast or no breast lesion at diagnosis	**PVD: 6/25/26** Disease Related Criteria 1. Participants must have histologically confirmed de novo metastatic (i.e. AJCC stage IV, no prior history of breast cancer) HER2+ breast cancer with 1 to 5 distant metastatic lesions (oligometastatic). Metastatic breast cancer must be histologically confirmed through biopsy of a distant metastatic lesion unless it is not feasible or safe to biopsy a metastatic lesion, then there must be unequivocal evidence of metastasis on imaging and laboratory studies. HER2+ status must be confirmed in the breast tumor and distant metastatic site as defined per NCCN guidelines version 4.2025. NOTE: If HER2 positivity at metastatic site is equivocal due to limitations in HER2 analysis in bone, or it is not feasible or safe to biopsy the metastatic lesion, then HER2 positivity based on breast tumor only is acceptable. If there is no breast lesion, HER2+ must be confirmed in at least one metastatic site. 2. Participants with brain metastases are eligible if they meet all of the following criteria at baseline: a) There are 5 or fewer intracranial lesions. b) Each intracranial lesion is no larger than 2cm in longest dimension. NOTE: The brain is counted as 1 distant site towards the oligometastatic definition. Brain imaging is not required for participants who have no neurological signs or symptoms suggestive of CNS involvement; however, assessment of neurological symptoms and brain MRI is strongly encouraged to rule out CNS disease. 3. Participants must have no known leptomeningeal disease. b. Prior/Concurrent Therapy Criteria 1. Participants must meet one of the following criteria prior to Step 1	Randomized Cohort A: To compare overall survival (OS) between participants with de novo stage IV oligometastatic HER2+ breast cancer who experience at least a partial response (PR) after initial systemic therapy similar to those used in stage III disease with curative intent, and are randomized to a multimodality approach including definitive locoregional therapy with surgery and radiotherapy and ablative distant metastatic radiotherapy to detectable metastatic lesions followed by additional HER2-directed systemic therapy, similar to those used for residual disease after neoadjuvant therapy, (Cohort A, Arm 1) versus those who are randomized to physician's choice standard of care HER2-directed systemic therapies without local and metastatic directed ablative therapies(Cohort A, Arm 2). b. Observational Cohort B: To evaluate the distribution of progression-free survival (PFS) and overall survival (OS) among participants with de novo stage IV oligometastatic HER2+ breast cancer who do not experience a response after systemic therapy	NCT07578116	8/18/26	562
	S1900N	A Randomized Phase II Study of Sacituzumab Govitecan Alone, Ivonescimab Alone, or Sacituzumab Govitecan and Ivonescimab in Participants with Previously-Treated Actionable Genomic Alteration Positive Stage IV or Recurrent Non-Small Cell Lung Cancer (Lung-MAP Sub-Study)	Lung, Mediastinal, and Pleural Cancer	STRATIFICATION AND DESCRIPTIVE FACTORS Participants will be randomized to their treatment assignment using a dynamic balancing algorithm. Randomization will be stratified by AGA-based on EGFR driver mutation status (yes versus no) and presence of brain metastasis (yes versus no)	**PVD: 2/12/26** Disease Related Criteria a. Participants must have been assigned to S1900N by the SWOG Statistics and Data Management Center (SDMC). Assignment to S1900N is determined by submission of documentation of NSCLC harboring an actionable genomic alteration (AGA) in the LUNGMAP protocol (Section 7). AGA is defined in this protocol as an activating driver alteration with an approved targeted therapy for lung cancer in one of the following genes: ALK, EGFR, HER2 (ERBB2), MET, NTRK, RET, and ROS1. b. Participants must have measurable disease documented by CT or MRI. The CT from a combined PET/CT may be used to document only non-measurable disease unless it is of diagnostic quality as defined in Section 10.1c. Measurable disease must be assessed within 28 days prior to randomization. Pleural effusions, ascites and laboratory parameters are not acceptable as the only evidence of disease. Non-measurable disease must be assessed within 42 days prior to randomization. All disease must be assessed and documented on the Baseline Tumor Assessment Form. Participants whose only measurable disease is within a previous radiation therapy port must demonstrate clearly progressive disease (in the opinion of the treating investigator) prior to randomization. c. Participants must have a CT or MRI scan of the brain to evaluate for CNS disease within 42 days prior to randomization. d. Participants with spinal cord compression or brain metastases must not have residual neurological dysfunction, unless no further recovery is expected, and the participant has been stable on weaning doses of corticosteroids (≤ 10 mg daily prednisone or equivalent) prior to randomization. Participants with spinal cord compression or brain metastases that require local treatment must have received local treatment to these metastases and remained clinically controlled and asymptomatic for at least 7 days following stereotactic radiation and/or 14 days	The primary objectives are: Within participants with actionable genomic alteration positive NSCLC, previously treated with standard of care lines of targeted therapy and platinum-based chemotherapy randomized to sacituzumab govitecan plus ivonescimab, or sacituzumab govitecan alone, or ivonescimab alone: a. Comparison between arms 1. To compare progression-free survival (PFS) between participants randomized to the combination of sacituzumab govitecan plus ivonescimab (SG-I) and sacituzumab govitecan (SG) alone. 2. To compare progression-free survival (PFS) between participants randomized to SG-I and ivonescimab (I) alone. b. Single Arm evaluation 1. To evaluate the response (confirmed and unconfirmed, complete and partial) rate of SG against historical response rates. 2. To evaluate the response (confirmed and unconfirmed, complete and partial) rate of I against historical response rates. 3. To evaluate the response (confirmed and	NCT07393555	8/5/26	117
	MM1OA-S04	A Randomized Phase II Trial of ASTX727 with Standard Duration Versus Shorter Duration of Venetoclax in Genomically Heterogenous AML Among Adults Aged 60 or Older and Less Fit for Intensive Therapy: A MyeloMATCH Substudy	Leukemia	For purposes of this study, Acute Myeloid Leukemia (AML) is defined as having ≥ 20% blasts in the bone marrow and/or peripheral blood or having recurrent AML-specific genetic abnormalities with ≥ 10% blasts in the bone marrow and/or peripheral blood.	**PVD: 5/7/26** Disease Related Criteria a. Participants must have been registered to the MYELOMATCH Master Screening and Reassessment Protocol prior to consenting to this study. Participants must have been assigned to this clinical trial via MATCHBox prior to registration to this study. Note: Pre-enrollment/diagnosis labs must have already been performed under MYELOMATCH. See Section 15 of the MYELOMATCH protocol for details. b. Participants must have newly diagnosed, untreated acute myeloid leukemia (AML) defined by - having ≥ 20% blasts in the bone marrow and/or peripheral blood or - having recurrent AML-specific genetic abnormalities with ≥ 10% blasts in the bone marrow aspirate and/or peripheral blood c. Participants with acute promyelocytic leukemia (APL) with PML-RARA are not eligible. d. Participants must not have FLT3 mutations (ITD or TKD). e. Participants must not have TP53 mutations.	With hierarchical testing: a. To compare whether the proportion of participants with a measurable residual disease (MRD) negative complete remission (CR) at 180 days (6 months) is not more than 12% worse between participants randomized to venetoclax for 14 days versus 28 days per cycle (non-inferiority assessment). b. If 14 days of venetoclax is found to be non-inferior to 28 days, to test whether the proportion of participants with an MRD-negative CR at 180 days (6 months) after randomization is significantly higher in the 14 days per cycle compared to the 28- days per cycle (superiority assessment).	NCT07437950	7/22/26	126
	S2504	A Randomized Phase III Study of Pirtobrutinib Plus R-CHOP vs. R-CHOP for Participants with Previously Untreated Richter Transformation (PIRAMID)	Lymphoma	SCHEMA Previously Untreated Richter Transformation Safety Run-In (Arm 1) 1 During the Safety Run-in, 6 participants under 75 and 6 participants age ≥ 75 will be non-randomly assigned to Arm 1. Participants will be monitored for toxicity through Cycle 2. 1:1 Randomization **Arm 1:** Pirto + R-CHOP 2 Cycles 1-6 --> Pirtobrutinib (Until PD or discontinuation for other reasons) Off Protocol Treatment **Arm 2:** R-CHOP 2 Cycles 1-6 --> Off Protocol Treatment PD: Progressive Disease R-CHOP: rituximab/rituximab hyaluronidase, cyclophosphamide, doxorubicin, vincristine, and prednisone 1 Refer to Sections 7.4 and 15.6 for Safety Run-In	**PVD: 2/20/2026** 5.1 Disease Related Criteria a. Participants must have been diagnosed with Richter Transformation (RT) (CLL/SLL to LBCL). 1. Participants must have histologically or cytologically confirmed LBCL. b. Participants must have measurable disease as described in Section 10 determined by PET/CT or hematopathology (by morphology or FLOW cytometry) assessment within 42 days prior to registration. c. Participants must have staging PET/CT imaging performed within 42 days prior to registration. 5.2 Prior/Concurrent Therapy Criteria a. Participants are allowed prior treatments for CLL/SLL or its complications (AIHA, ITP), with the exception of pirtobrutinib b. Participants must not have prior treatment for Richter transformation except for corticosteroids up to equivalent dose of prednisone 700 mg total for less than 7 days for disease control. Treatment for CLL/SLL with CLL/SLL directed drugs (including BTK inhibitors with the exception of pirtobrutinib) after the Richter transformation diagnosis is allowed for the purpose of disease control. CLL targeted therapies must be stopped within 3 days before initiation of therapy on protocol. Chemotherapy or anti-CD20 monoclonal antibody therapy must be stopped within 2 weeks before initiation of therapy on protocol. c. Participants must not have contraindication for receiving anthracycline. Participants must not have received more than a cumulative dose of 100mg/m2 in those participants who will receive R-CHOP or not more than 250 mg/m2 in those participants who will receive R-mini-CHOP of prior doxorubicin (or equivalent dose of another anthracycline, such as epirubicin) therapy (at any time prior to registration). d. Patients requiring strong CYP3A inducers are not eligible and can only be enrolled	a. Safety run-in: 1. In participants aged 74 and younger, to evaluate the safety of the addition of pirtobrutinib to R-CHOP before initiating randomization in participants with untreated Richter Transformation to large B-cell lymphoma (LBCL). 2. In participants aged 75 and older, to evaluate the safety of the addition of pirtobrutinib to R-mini-CHOP before initiating randomization in this patient population. b. Randomized comparison: 1. Primary objective: To evaluate whether the addition of pirtobrutinib to RCHOP improves investigator-assessed progression-free survival (PFS) compared to R-CHOP alone in this patient population. 2. Second primary objective (hierarchical testing): If investigator-assessed PFS is improved with the addition of pirtobrutinib, then to evaluate whether the addition of pirtobrutinib improves overall survival (OS) in this patient population.	NCT07220087	6/1/26	102
	S2419	Phase III Double Blinded Trial of Immune-Based Therapy with a Live Biotherapeutic MO-03 or Placebo for Frontline Therapy of Advanced Clear Cell Renal Cell Carcinoma [BioFront Trial]	Kidney Cancer	Participants will be randomized in a 1:1 allocation using a dynamic balancing algorithm15 with stratification based on: 1. IMDC risk group: favorable* vs. intermediate vs. poor 2. Tumor with sarcomatoid/rhabdoid features: Yes vs. No 3. Intended SOC treatment type: IO-IO vs. IO-TKI	**PVD: 2/23/2026** **Must have:** Participants must have histologically confirmed renal cell carcinoma (RCC) with clear cell component that is advanced (not amenable to curative surgery or radiation therapy) or metastatic RCC at the time of registration on study. b. The intended standard of care (SOC) treatment regimen must be decided prior to registration.	To compare investigator assessed progression-free survival of participants with advanced clear cell renal cell carcinoma (ccRCC) randomized to standard of care immunotherapy (IO)-based combination regimen plus placebo versus IO-based combination regimen plus MO-03 in an intent-to-treat analysis.	NCT07383441	4/22/26	718
	S2505	Phase III Randomized Study Testing Non-Inferiority of Short-Course Ultra-Hypofractionated Radiation (UHRT-5) Versus Standard Fractionation (RT-25) for Stage II-IIIB, Extremity, Resectable Soft Tissue Sarcoma	Soft Tissue Cancer/Sarcoma	Pathologically confirmed, stage II-IIIB, resectable extremity soft tissue sarcoma 1:1 Randomization Arm 1: RT - 25 50Gy in 25 fractions Arm 2: UHRT-5 30Gy in 5 fractions	**PVD: 5/20/26** a. Participants must have histological evidence of a soft tissue sarcoma from core or incisional biopsy. Participants must have a primary or locally recurrent tumor. Stage II-IIIB (by AJCC 8th edition) soft tissue sarcoma is required (Appendix 18.3) • Participants must not have prior partial excision or partial excisional biopsy of the tumor, even if there is evidence of gross residual disease.	To evaluate whether the incidence of local tumor recurrence at 2-years after randomization with short-course radiation is non-inferior to standard-course radiation among participants with high-risk, resectable soft tissue sarcoma	NCT07615949	7/6/26	296
	S2433	Randomized Phase III Study of Second-Line Chemotherapy with or Without Panitumumab for KRAS Wild Type, Locally Advanced or Metastatic Pancreatic Adenocarcinoma	Gastrointestinal Cancer	Arm A Panitumumab + Chemotherapy Arm B Chemotherapy	**PVD: 10/10/2025** a. Participants must have a histologically or cytologically confirmed diagnosis of ductal adenocarcinoma of the pancreas. b. Participants must have previously documented KRAS wild type (i.e., absence of any KRAS mutation) and BRAF V600E wild type (i.e., absence of a BRAF V600E mutation) status determined by tumor tissue-based NGS assay. The testing must be done within a laboratory with CLIA, ISO/IEC, CAP, or similar certification status. Sites must confirm eligibility criterion 5.1. b. with at least one of the study chairs via email to S2433SC@swog.org prior to registration. See Section 18.7 for the study chair approval process. NOTE: Blood-based NGS assays, such as circulating tumor DNA (ctDNA) or liquid biopsies, will not be accepted for meeting eligibility criteria. c. Participants must have documented unresectable and/or metastatic disease on CT or MRI imaging completed prior to randomization. Imaging must have been completed within 28 days prior to randomization for participants with measurable disease. CT scans or MRIs used to assess non-measurable disease must have been completed within 42 days prior to randomization. All disease must be assessed and documented on the Baseline Tumor Assessment Form. d. Participants must not have known mutations in PTEN, NRAS, EGFR extracellular domain exons 1-16, no amplifications of HER2 and MET, and no gene fusions of RET, NTRK1, and ALK by tumor tissue-based NGS analysis. e. Participants must not have known brain metastases or cranial epidural disease unless adequately treated with radiotherapy and/or surgery and stable for at least 28 days before randomization.	To compare overall survival (OS) between participants with locally advanced or metastatic KRAS wild type (WT) pancreatic ductal adenocarcinoma (PDA) randomized to panitumumab plus second-line cytotoxic chemotherapy (5FU- or gemcitabine-based) versus chemotherapy alone.	NCT06998940		94
	EA1242	A Phase III Trial of Rx Therapy Guided by Genomic Risk Assessment For High Anatomic Stage ER-pos/HER2-neg Breast Cancer with RS	Breast Cancer	Arm A: SOC Chemotherapy followed by SOC Endocrine Therapy + Ribociclib Arm B: SOC Endocrine Therapy + Ribociclib	**PVD 3/3/26** Key Eligibility: • Post-menopausal women or men with ER-pos (>10%)/HER2-neg breast cancer without evidence of distant metastases • Completed primary surgery with pathologic stage (AJCC 8th Edition):	To determine whether optimal adjuvant endocrine therapy with CDK4/6 inhibitor is non-inferior to adjuvant chemotherapy followed by optimal endocrine therapy with CDK4/6 inhibitor	NCT07391774	5/20/26	1978
	EA1241	Extended Clinical Follow up and Biospecimen Collection for Patients Enrolled in TAILORx and RxPONDER: A Companion Protocol	Breast Cancer	After registration, primary tumor and relapse tumor specimens must be submitted and shipped to the ECOG-ACRIN Central Biorepository and Pathology Facility (CBPF) within 30 days of the date of registration as outlined in Sections 7 and 9. Patients enrolled on this study will receive standard of care therapy as determined by their treating physician. Patients will be followed for recurrence and survival data for 5 years according to the schedule outlined in Section 7.	**PVD: 10/1/2025** Cohort 1: Previously enrolled on TAILORx (PACCT-1) with recurrence score (RS) 0-100 AND had a biopsyconfirmed locoregional, distant, or both locoregional and distant recurrence prior to registration on this protocol. Cohort 2: Previously enrolled on Step 2 of RxPONDER (S1007) with a recurrence score (RS) of 0-25 AND had a biopsy-confirmed locoregional, distant, or both locoregional and distant recurrence prior to registration on this protocol. Cohort 3: Previously enrolled on Step 1 of RxPONDER and found to have a high Oncotype DX RS 26-100. NOTE: Only for patients enrolled at US sites. NOTE: To facilitate accrual, a list of potentially eligible participants who enrolled on TAILORx or RxPONDER, who meet Cohort 1-3 requirements, are last reported to be alive in follow-up will be provided to all currently active sites that open EA1241 and who enrolled patients on TAILORx or RxPONDER.	To assess patterns of clonal evolution and the landscape of somatic alterations in paired primary tumor samples and recurrence samples (Cohorts 1, 2, and 3). To determine prevalence of the integrative cluster (IntClust) and intrinsic (PAM50) subtypes and of subtype switching in paired primary tumor samples and recurrence samples (Cohorts 1, 2, and 3). To identify molecular signatures, including the SET 2/3 RNA expression assay, of primary tumor specimens associated with recurrence in patients with high genomic risk and high clinical risk (Cohort 3) who received adjuvant chemotherapy plus endocrine therapy. This may ultimately identify those identify individuals at highest recurrence risk and thus most likely to benefit from a 2-3 year course of currently approved adjuvant CDK 4/6 inhibitors.	NCT06786585	12/4/25	600
	EA6232	A Phase II Double-Blind Trial of Sulforaphane for Therapeutic Prevention of Melanoma in Patients with Multiple Atypical Nevi and a Prior History of Melanoma	Skin Cancer	Experimental: A Three tablets of Avmacol® Extra Strength [Nutramax] by mouth, once daily, for 12 months Placebo Comparator: B Placebo - Three tablets by mouth, once daily, for 12 months	**PVD: 1/13/26** **Inclusion Criteria:** Patient must have ≥ 3 clinically atypical nevi, assessed within 30 days prior to randomization, that are consistent with the International Agency for Research on Cancer (IARC) definition as follows.27 Must have a diameter of ≥ 5mm in one dimension Must include a macular component in at least one area Must have at least two of the following features: ill-defined borders, color variegation, uneven contour, and erythema Patient must have a prior diagnosis of early-stage melanoma, defined as either melanoma in situ, localized resected stage I-II node negative melanoma, or resected node positive stage III melanoma who in the assessment of their physician have a low risk of relapse of their prior melanoma within one year of randomization. Patient must not be currently on targeted or checkpoint immunotherapy or treated within 365 days prior to randomization. Patient must be ≥ 18 years of age. Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible. Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of randomization are eligible for this trial. For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated. Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are currently on treatment, they are eligible if they have an undetectable HCV viral load. Patients with a prior or concurrent malignancy (other than the melanoma for which they are on this study) whose natural history or treatment does not have the potential to interfere with the	To evaluate the effects of oral sulforaphane vs placebo on change in the total area of atypical and common pigmented nevocellular nevi on the posterior trunk at 12 months after randomization as assessed by digital photographic imaging and analysis using Derma-AI image analysis software, specifically assessed in patients treated for the entire 12-month treatment period (per-protocol analysis).	NCT07040280	2/20/26	120