NCI Updates

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Cancer Therapy Evaluation Program (CTEP)

Division of Cancer Treatment & Diagnosis

NCI National Clinical Trials Network

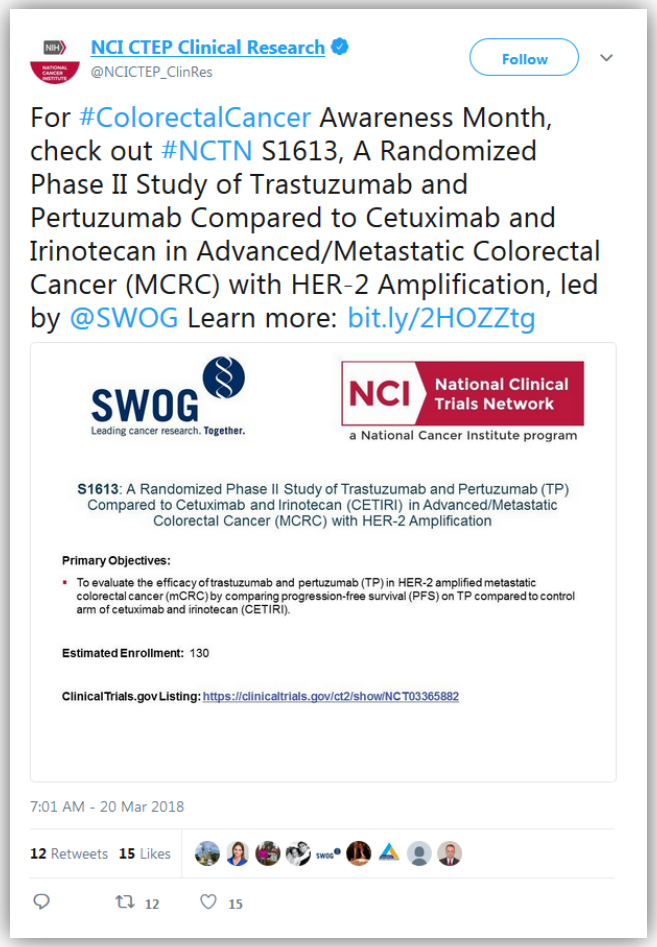
a National Cancer Institute program

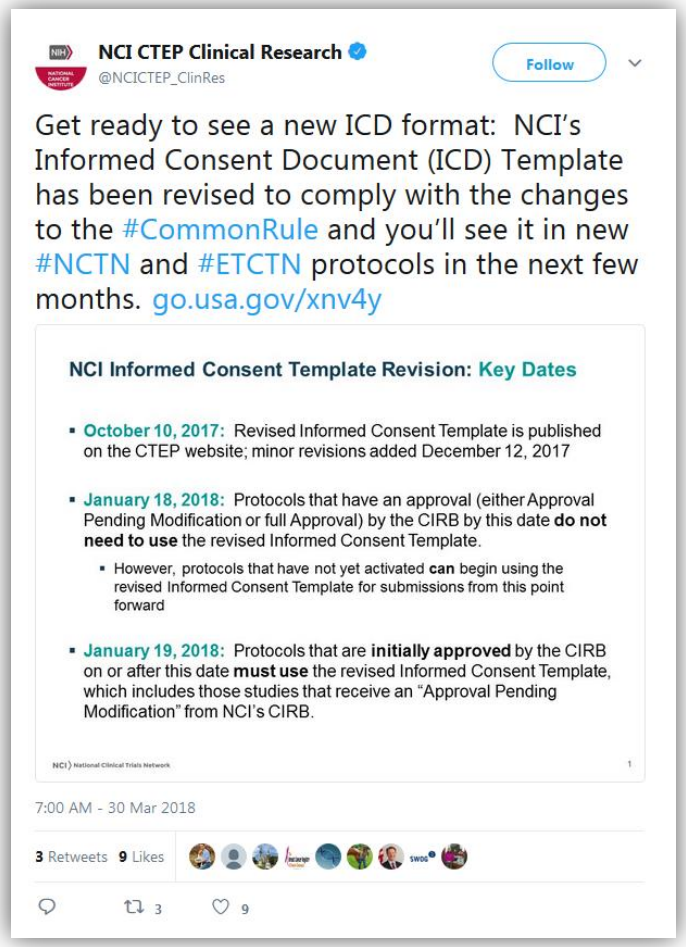
April 11, 2018

Agenda

- Brief Updates
  - CTEP Twitter Account: @NCICTEP_ClinRes
  - NCTN Navigator: https://navigator.ctsu.org/
- NCTN Trial Portfolios by Disease: https://go.usa.gov/xQT4q
- Informed Consent Implementation Update

New CTEP Twitter Account: @NCICTEP_ClinRes

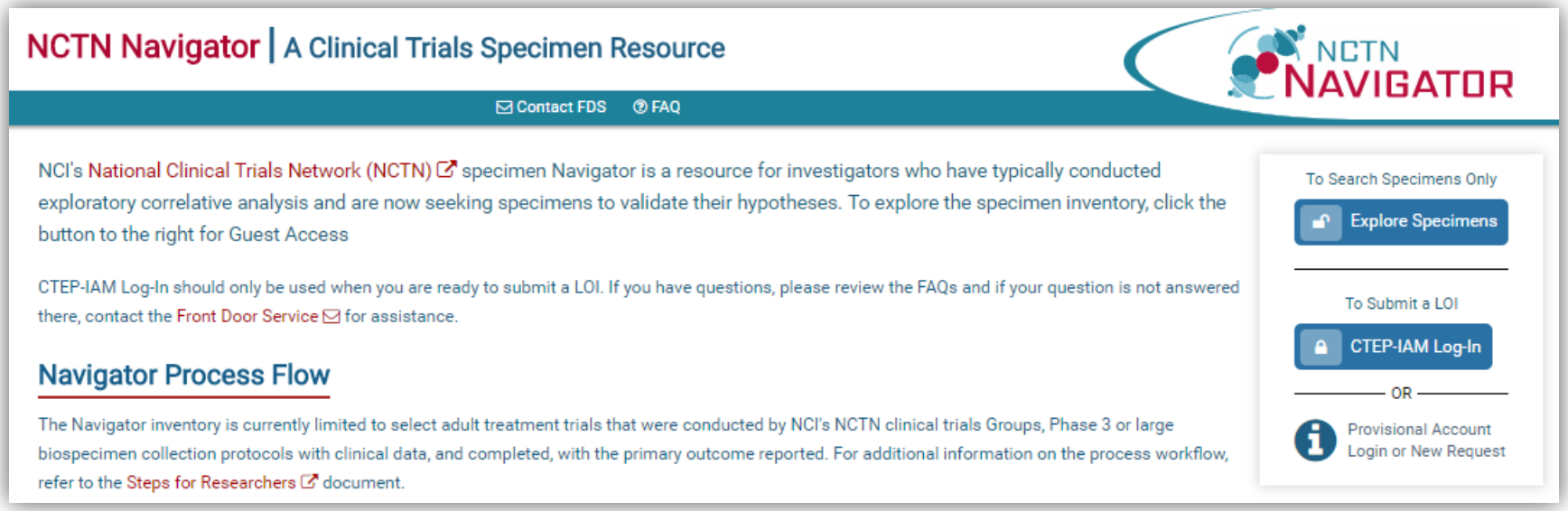




https://twitter.com/NCICTEP_ClinRes

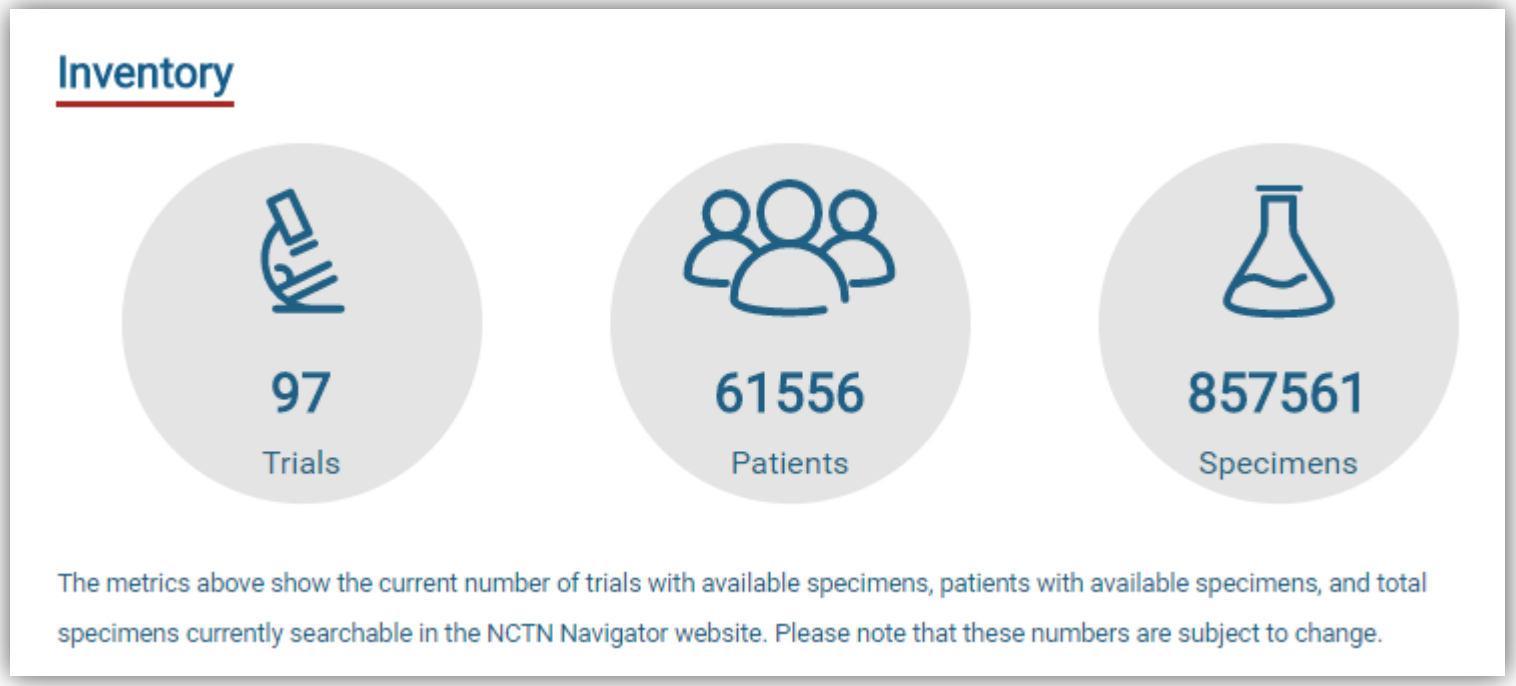
NCTN Navigator

- **NCTN Navigator website:** Inventory resource for external investigators to identify specimens of interest
- **NCTN Navigator associated processes:** Processes through which investigators can submit queries, LOIs, and proposals and carry out approved proposals for specimens and data of interest



https://navigator.ctsu.org/

NCTN Navigator



https://navigator.ctsu.org/

NCI Cancer Currents Blog Post:
https://www.cancer.gov/news-events/cancer-currents-blog/2018/nctn-navigator-cancer-clinical-trial-specimens

NCTN Trial Portfolios by Disease

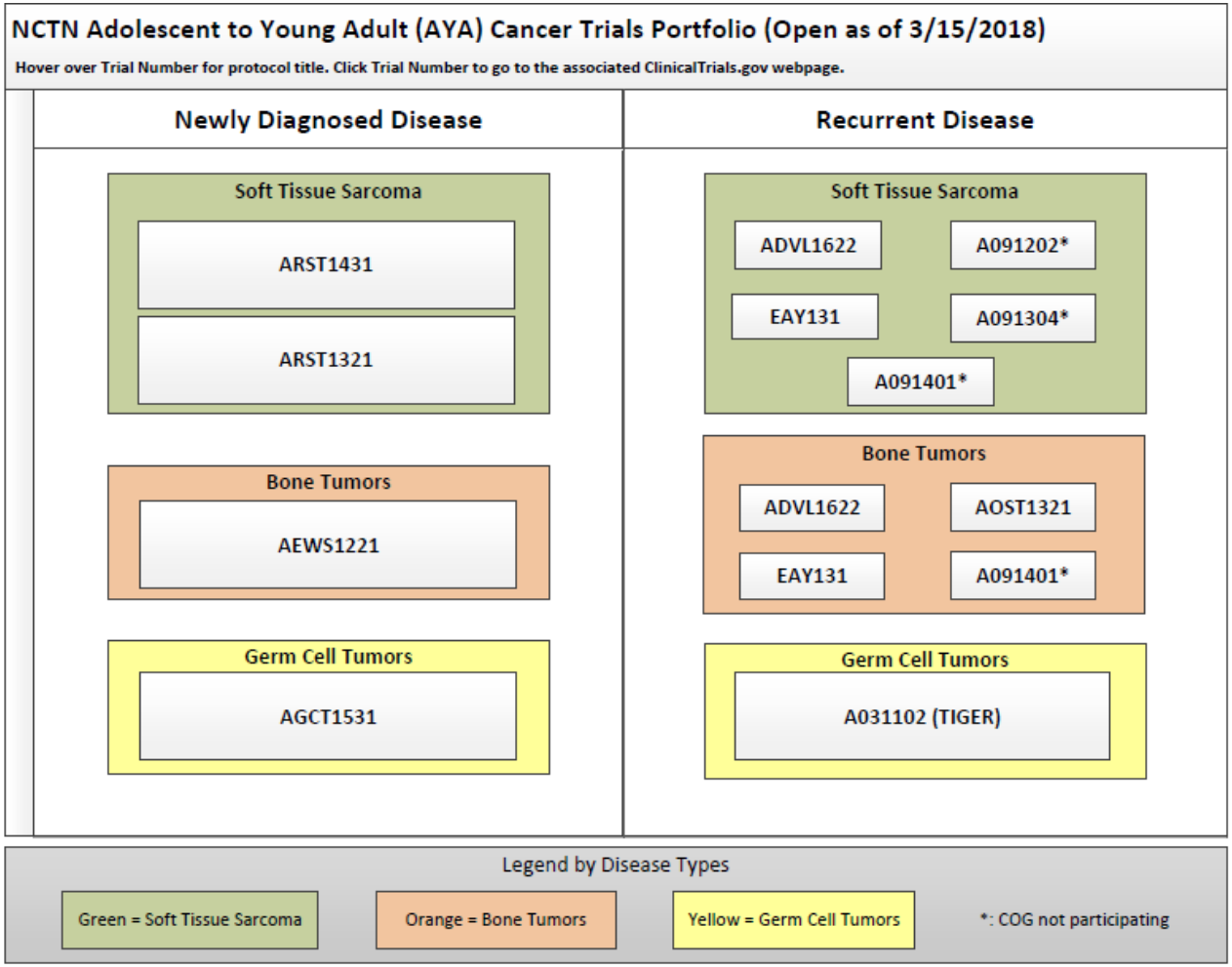
New NCTN Trial Portfolios by Disease

- Posted as separate PDFs by disease area: https://go.usa.gov/xQT4q (https://ctep.cancer.gov/initiativesPrograms/nctn_trials_by_disease.htm)
- Each document heading includes the date the diagrams were last updated
- Can be viewed on the computer
  - Hover over the trial number to see the protocol title
  - Click the trial number to go to the protocol's ClinicalTrials.gov webpage
- Can be printed out and used in hardcopy format
  - First page(s) include disease diagram
  - Last page includes a table with the protocol number and title for reference

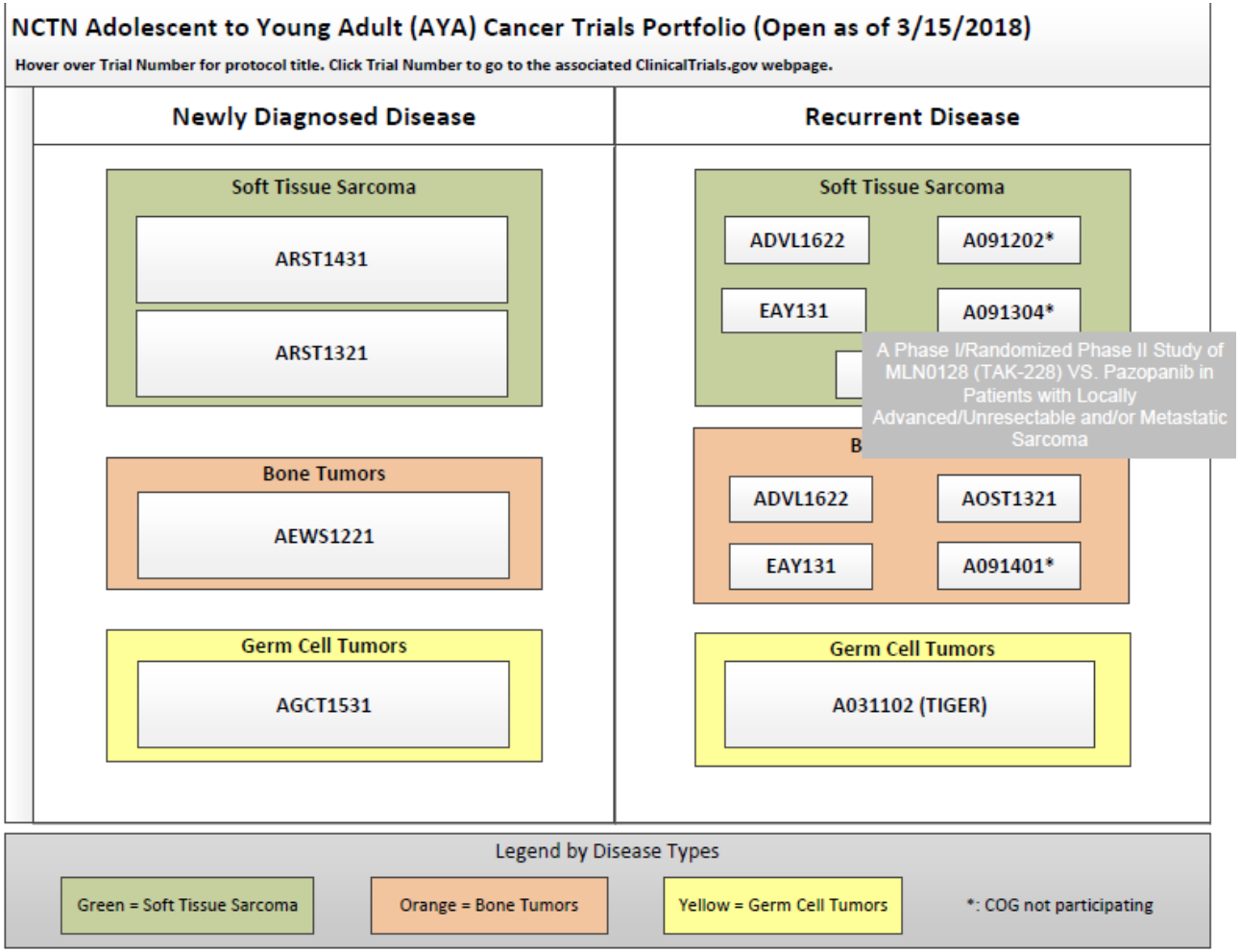
New NCTN Trial Portfolios by Disease

https://ctep.cancer.gov/initiativesPrograms/nctn_trials_by_disease.htm

New NCTN Trial Portfolios by Disease: AYA Trials



New NCTN Trial Portfolios by Disease: AYA Trials



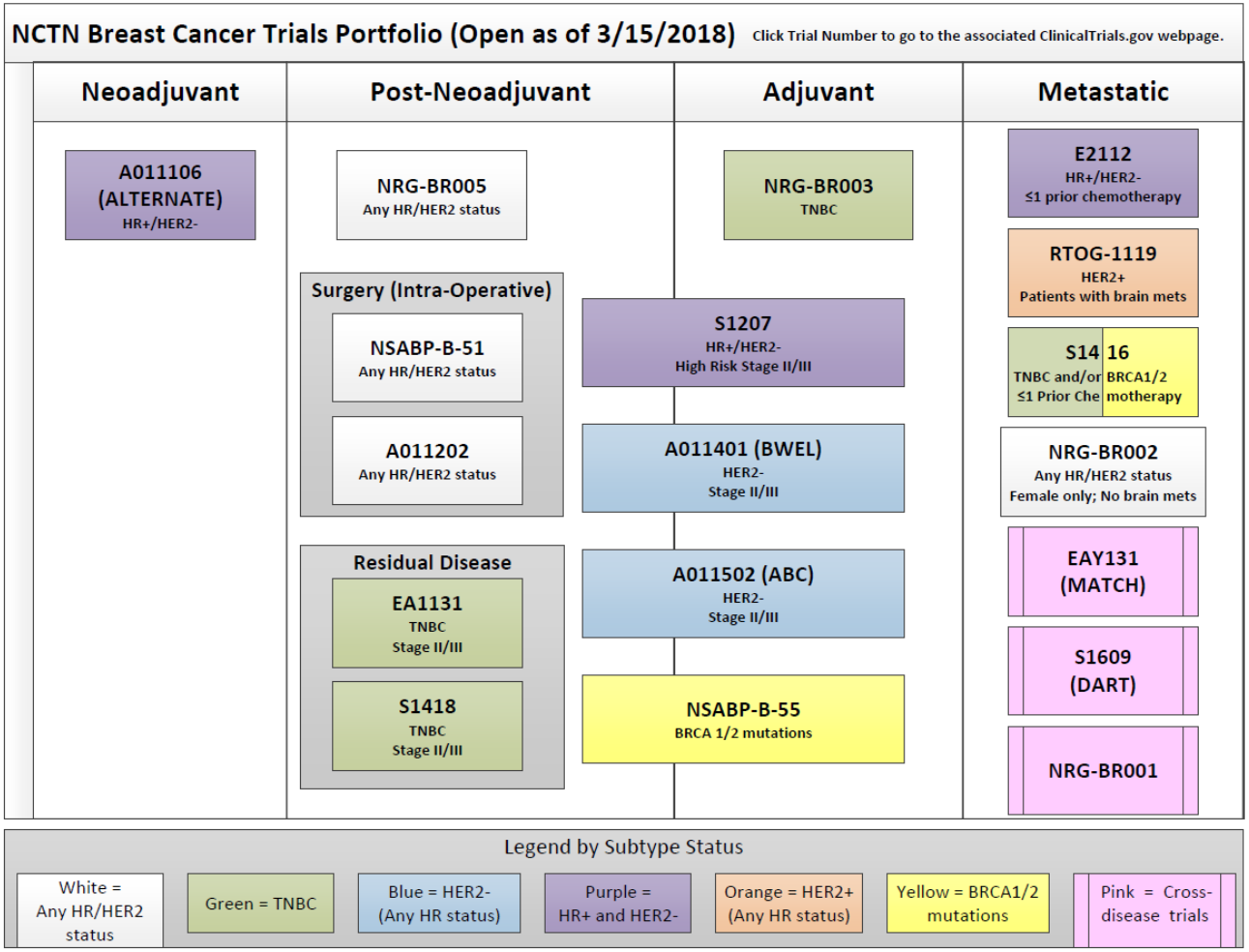
New NCTN Trial Portfolios by Disease: AYA Trials

NCTN Adolescent to Young Adult (AYA) Cancer Trials (Open as of 3/15/2018)

Protocol Number	Phase	Protocol Title
A031102	III	A Randomized Phase III Trial Comparing Conventional-Dose Chemotherapy Using Paclitaxel, Ifosfamide, and Cisplatin (TIP) with High-Dose Chemotherapy Using Mobilizing Paclitaxel Plus Ifosfamide Followed by High-Dose Carboplatin and Etoposide (TI-CE) as First Salvage Treatment in Relapsed or Refractory Germ Cell Tumors
A091202*	II	A Phase II Study of the Peroxisome Proliferator-Activated Receptor Gamma Agonist, Efatutazone in Patients with Previously Treated, Unrespecatble Myxoid Liposarcoma
A091304*	I/II	A Phase I/Randomized Phase II Study of MLN0128 (TAK-228) VS. Pazopanib in Patients with Locally Advanced/Unresectable and/or Metastatic Sarcoma
A091401*	II	Randomized Phase II Study of Nivolumab with or Without Ipilimumab in Patients with Metastatic or Unresectable Sarcoma
ADVL1622	II	Phase 2 Trial of XL184 (Cabozantinib) an Oral Small-Molecule Inhibitor of Multiple Kinases, in Children and Young Adults with Refractory Sarcomas, Wilms Tumor, and Other Rare Tumors
AEWS1221	III	Randomized Phase 3 Trial Evaluating the Addition of the IGF-1R Monoclonal Antibody Ganitumab (AMG 479, NSC# 750008, IND# 120449) to Multiagent Chemotherapy for Patients with Newly Diagnosed Metastatic Ewing Sarcoma
AGCT1531	III	A Phase 3 Study of Active Surveillance for Low Risk and a Randomized Trial of Carboplatin vs. Cisplatin for Standard Risk Pediatric and Adult Patients with Germ Cell Tumors
AOST1321	II	Phase 2 Study of Denosumab (IND# 127430, NSC# 744010), a RANK Ligand Antibody, for Recurrent or Refractory Osteosarcoma
ARST1321	II/III	Pazopanib Neoadjuvant Trial in Non-Rhabdomyosarcoma Soft Tissue Sarcomas (PAZNTIS): A Phase II/III Randomized Trial of Preoperative Chemoradiation or Preoperative Radiation Plus or Minus Pazopanib (NSC# 737754, IND# 118613)
ARST1431	III	A Randomized Phase 3 Study of Vincristine, Dactinomycin, Cyclophosphamide (VAC) Alternating with Vincristine and Irinotecan (VI) Versus VAC/VI Plus Temsirolimus (TORI, Torisel, NSC# 683864) in Patients with Intermediate Risk (IR) Rhabdomyosarcoma (RMS)
EAY131	II	Molecular Analysis for Therapy Choice (MATCH)

*: COG not participating

New NCTN Trial Portfolios by Disease: Breast Cancer



New NCTN Trial Portfolios by Disease: Breast Cancer

NCTN Breast Cancer Trials (Open as of 3/15/2018)

Protocol Number	Phase	Protocol Title
A011106	III	ALTernate Approaches for Clinical Stage II and III Estrogen Receptor Positive Breast Cancer NeoAdjuvant TrEatment (ALTERNATE) in Postmenopausal Women: A Phase III Study
A011202	III	A Randomized Phase III Trial Comparing Axillary Lymph Node Dissection to Axillary Radiation in Breast Cancer Patients (cT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy
A011401	III	Randomized Phase III Trial Evaluating the Role of Weight Loss in Adjuvant Treatment of Overweight and Obese Women with Early Breast Cancer
A011502	III	A Randomized Phase III Double Blinded Placebo Controlled Trial of Aspirin as Adjuvant Therapy for HER2 Negative Breast Cancer: The ABC Trial
E2112	III	A Randomized Phase III Trial of Endocrine Therapy Plus Entinostat/Placebo in Patients with Hormone Receptor-Positive Advanced Breast Cancer
EA1131	III	A Randomized Phase III Post-Operative Trial of Platinum Based Chemotherapy Vs. Capecitabine in Patients with Residual Triple-Negative Basal-Like Breast Cancer following Neoadjuvant Chemotherapy
NRG-BR002	II/III	A Phase IIR/III Trial of Standard of Care Therapy with or Without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer
NRG-BR003	III	A Randomized Phase III Trial of Adjuvant Therapy Comparing Doxorubicin Plus Cyclophosphamide Followed by Weekly Paclitaxel with or Without Carboplatin for Node-Positive or High-Risk Node-Negative Triple-Negative Invasive Breast Cancer
NRG-BR005	II	A Phase II Trial Assessing the Accuracy of Tumor Bed Biopsies in Predicting Pathologic Response in Patients with Clinical/Radiologic Complete Response After Neoadjuvant Chemotherapy in Order to Explore the Feasibility of Breast Conserving Treatment Without Surgery
NSABP-B-51	III	A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy
NSABP-B-55	III	A Randomised, Double-Blind, Parallel Group, Placebo-Controlled Multi-Centre Phase III Study to Assess the Efficacy and Safety of Olaparib Versus Placebo as Adjuvant Treatment in Patients with Germline BRCA1/2 Mutations and High Risk HER2 Negative Primary Breast Cancer Who Have Completed Definitive Local Treatment and Neoadjuvant or Adjuvant Chemotherapy
RTOG-1119	II	Phase II Randomized Study of Whole Brain Radiotherapy/Stereotactic Radiosurgery in Combination with Concurrent Lapatinib in Patients with Brain Metastasis From HER2-Positive Breast Cancer: A Collaborative Study of NRG Oncology and KROG
S1207	III	Phase III Randomized, Placebo-Controlled Clinical Trial Evaluating the Use of Adjuvant Endocrine Therapy +/- One Year of Everolimus in Patients with High-Risk, Hormone Receptor-Positive and HER2/Neu Negative Breast Cancer. e^3 Breast Cancer Study-Evaluating Everolimus with Endocrine Therapy.
S1416	II	Phase II Randomized Placebo-Controlled Trial of Cisplatin with or Without ABT-888 (Veliparib) in Metastatic Triple-Negative Breast Cancer and/or BRCA Mutation-Associated Breast Cancer
S1418	III	A Randomized, Phase III Trial to Evaluate the Efficacy and Safety of MK-3475 (Pembrolizumab) as Adjuvant Therapy for Triple Receptor-Negative Breast Cancer with >/= 1 CM Residual Invasive Cancer or Positive Lymph Nodes (ypN+) after Neoadjuvant Chemotherapy
EAY131	II	Molecular Analysis for Therapy Choice (MATCH)
NRG-BR001	I	A Phase 1 Study of Stereotactic Body Radiotherapy (SBRT) for the Treatment of Multiple Metastases
S1609	II	DART: Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors

Implementation of the NCI Informed Consent Template Revision

NCI ICD Template Revision:
Process

- **Internal revision process in 2016**
  - Revised key sections identified through prior evaluations, including costs, extra tests, and general integration of biomarker research
  - Met internally to review and finalize **Revision #1**
- **Stakeholder review in 2016**
  - Distributed **Revision #1** to prior working group members, Groups, and other NCI entities
  - Received 29 responses (450+ comments or changes); reviewed and reconciled comments and edits
- **Final Revisions to the Common Rule, January 2017**
  - Released by OHRP on January 19, 2017 and effective January 19, 2018
  - NCI implemented changes to the consent template to comply with the Final Rule requirements[1]
  - Conducted iterative review with plain language specialist and finalized **Revision #2**
- **Stakeholder review in 2017**
  - Circulated **Revision #2** & received 20 responses (200+ comments or changes); reviewed and reconciled comments and edits
- **Final revised template published, October 2017**
- **Two minor updates published December 12, 2017**

NCI ICD Template Revision:
Key Dates

- **October 10, 2017:** Revised Informed Consent Template is published on the CTEP website
- **December 12, 2017:** Template updated with CoC and new risk

- **January 19, 2018:** Protocols **initially** submitted to CTEP on or after this date **must use** the revised Informed Consent Template.
  - Protocols that were submitted to CTEP before this date but not yet CIRB approved are encouraged to transition to the revised Informed Consent Template.
- **July 19, 2018:** Protocols that do not have an IRB approval (either Approval Pending Modification or full Approval by the CIRB) are **required** to use the revised template.
  - Review your protocol timelines and revise consent forms in your protocols that do not have an IRB approval as needed to meet this deadline.

NCI ICD Template Revision:
Certificate of Confidentiality (CoC) Updated 12/12/2017

- NIH Certificate of Confidentiality Policy – updated 10/01/2017
  - https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html
  - NIH CoC "kiosk": https://humansubjects.nih.gov/coc/index
  - "(A)ll ongoing or new research funded by NIH … that is collecting or using identifiable, sensitive information is automatically issued a CoC."

- NIH CoC website has suggested consent language. The NCI template edited the NIH's version to align with our health literacy and plain language goals. This update was added to the NCI consent in the section, "Who will see my medical information?" on page 43.
  - Please note that currently NCI CIRB approved consent forms do not need to have this addition, but this paragraph should be used in all consent forms being updated with amendments.

ICD Requirements: ICH GCP, 21 CFR 50 (FDA-regulated trials), 45 CFR 46.116 (Common Rule and Final Rule)

Category	Element	ICH GCP	FDA CFR 21	Common Rule	Final Rule
General element	Key Information				X
General element	Trial involves research	X	X	X	X
General element	Purpose	X	X	X	X
General element	Probability for random assignment	X			
General element	Procedures	X	X	X	X
General element	Subject responsibilities	X			
General element	What is experimental	X	X	X	X
General element	Risks to subject	X	X	X	X
General element	Risks to fetus/infant	X	X	X	X
General element	Benefits	X	X	X	X
General element	Alternative / usual course	X	X	X	X
General element	Trial-related injury	X	X	X	X
General element	Compensation	X			
General element	Cost	X	X	X	X
General element	Voluntariness and right of withdrawal	X	X	X	X
General element	Medical records access	X	X		
General element	Confidentiality of records and if published	X	X	X	X
General element	New findings & informing	X	X	X	X

ICD Requirements: ICH GCP, 21 CFR 50 (FDA-regulated trials), 45 CFR 46.116 (Common Rule and Final Rule)

Category	Element	ICH GCP	FDA CFR 21	Common Rule	Final Rule
General element	Contacts	X	X	X	X
General element	Potential for stopping participation	X	X	X	X
General element	Duration	X	X	X	X
General element	Number of participants	X	X	X	X
General element	Unforeseeable risks		X	X	X
General element	Withdrawal consequences and procedures		X	X	X
General element	CT.gov language		X		
General element	Identifiable information / specimens				X
General element	Commercial profit				X
General element	Return of research results				X
General element	Whole genome sequencing				X
Biospecimens	Types of research				X
Biospecimens	Identifiable information / specimens				X
Biospecimens	Period of time				X
Biospecimens	Unknown future research				X
Biospecimens	Return of results				X
Biospecimens	Contacts				X

NCI ICD Template Revision:
Page Counts for Select Submitted NCTN ICDs

Key Information Pages	Total Pages (including key information and optional studies)	Optional Pages
3.1	12.75	3.5
2.75	14.5	2.5
3.5	15	3
2.5	15	3
3	15.25	3
3	16.5	3
3.1	16.5	2.5
2.8	18.3	3.5
3.25	18.5	2.5
3.25	18.5	2.5
3.3	19.5	4
3	22.5	4
Average	**3.0**	**16.9**	**3.1**

Draft Initial Numbers

Questions & Discussion