NCTN Colorectal Cancer Trials

NCI National Clinical Trials Network

a National Cancer Institute program

December 14, 2017

Agenda

- NCTN Colorectal Cancer Trial Portfolio, Dr. Carmen Allegra (CTEP)
- A021502, Dr. Frank Sinicrope
  - Q&A Session for A021502
- NRG-GI004, Dr. James Lee
  - Q&A Session for NRG-GI004
- S1613, Dr. Kanwal Raghav
  - Q&A Session for S1613

Questions/Feedback during the webinar?

Directions:

- Please use the “CHAT BOX” to submit a question.
- The chat box is located below the list of panelists on the right.
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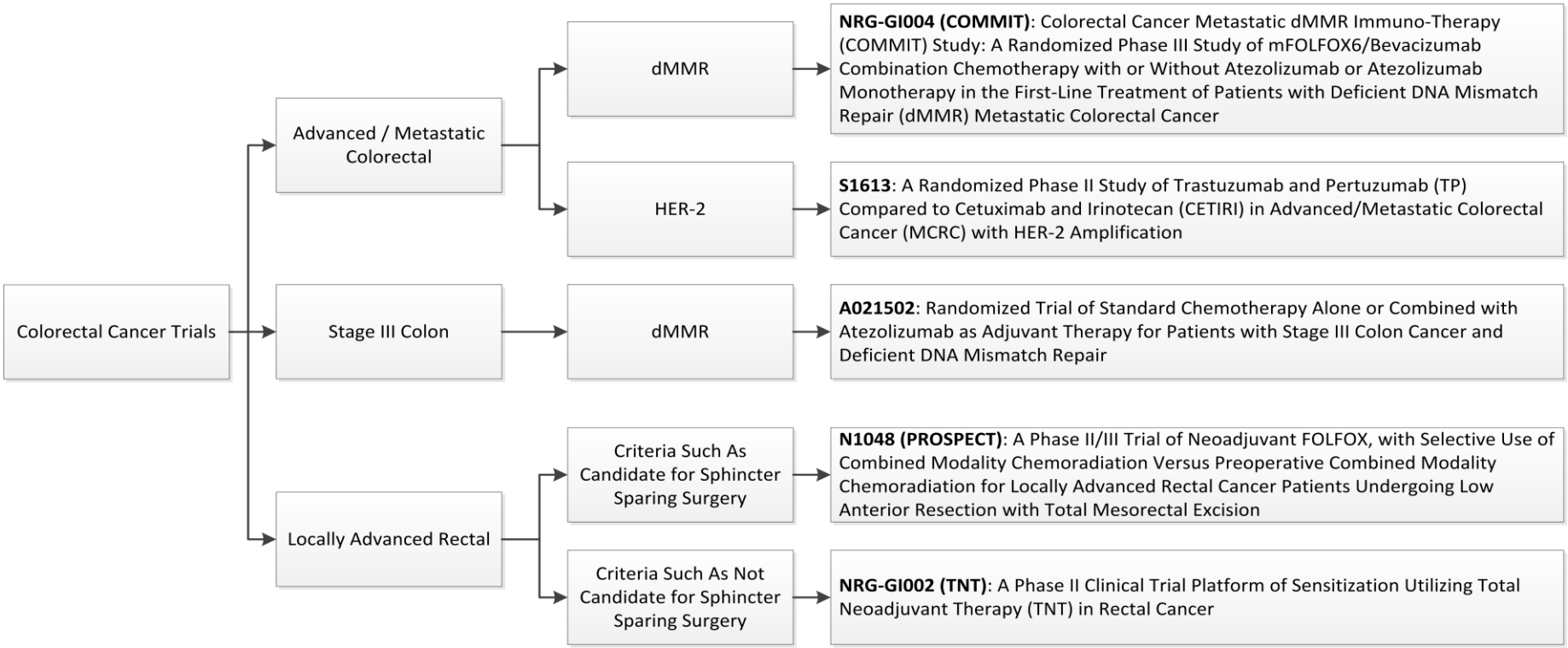
NCTN Colorectal Cancer Trials Portfolio



Two Complementary Locally Advanced Rectal Cancer Trials Open in the NCTN

Current Treatment Paradigm:		Chemoradiation therapy	Surgery	Post-op Rx (MD Discretion)
PROSPECT Trial: Candidate for LAR	Chemotherapy	Chemoradiation therapy (only if needed)	Sphincter sparing surgery	Post-op Rx (MD Discretion)
TNT Trial: Not LAR Candidate	Chemotherapy	Chemoradiation therapy +/- novel	Surgery	Post-op Rx (MD Discretion)

Two Complementary Locally Advanced Rectal Cancer Trials Open in the NCTN

- For more information about the locally advanced rectal cancer trials, see the overview presentation slides available within the protocol pages on the CTSU (instructions next slide)

- And contact the study chairs with questions:
  - N1048 (PROSPECT) Study Chair: Deb Schrag, MD, MPH

    deb_schrag@dfci.harvard.edu
  - NRG-GI002 (TNT) Study Chair: Thomas George, MD, FACP

    thom.george@medicine.ufl.edu

N1048 and NRG-GI002 Overview Information

Home | Funding Information | Documents | Drug Safety Notification | Study Agent | Protocol Requirements

NCI National Clinical Trials Network — N1048

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A Phase II/III Trial of Neoadjuvant FOLFOX, with Selective Use of Combined Modality Chemoradiation Versus Preoperative Combined Modality Chemoradiation for Locally Advanced Rectal Cancer Patients Undergoing Low Anterior Resection with Total Mesorectal Excision

CIRB Details

#	Documents used for CIRB approval	Post Date	Document Change Date
1	Protocol Version Date 09/06/17	17-Oct-2017	17-Oct-2017
2	Consent Form (Protocol Version Date 09/06/17)	17-Oct-2017	17-Oct-2017
3	Consent Form (Protocol Version Date 09/06/17): Spanish	07-Dec-2017	07-Dec-2017

CIRB Documents | Supplemental Documents | Education and Promotion | Case Report Forms | Site Registration

Patient Enrollment | Adverse Event Reporting | Pharmacy | Remote Data Capture | Miscellaneous

Documents

#	Document Title	Document Date	Format	Post Date
	Education and Promotion Materials			
1	Study Calendar	06-Sep-2017	PDF	17-Oct-2017
2	Schema	06-Sep-2017	PDF	17-Oct-2017
3	Frequently Asked Questions (FAQs) for N1048	15-Jun-2017	PDF	19-Jun-2017
4	Protocol Card	03-Feb-2016	PDF	25-Mar-2016
5	Physician Fact Sheet **NOTE:** The Physician Fact Sheets are intended for promotional use among health care professionals and are NOT intended for use as patient educational materials. **NOTE:** If you are having problems accessing the Physician Fact Sheet, the Protocol Card contains comparable content. If you need assistance obtaining any information, please refer to the CTSU Accessibility Policy to request a reasonable accommodation.	06-Sep-2017	PDF	05-Dec-2017
6	PROSPECT Summary Slides for Clinicians (including sample TME photos for surgical QA)		PDF	15-Sep-2015
7	PROSPECT Patient FAQs **NOTE:** Taken from the protocol document (Appendix II) so has been CIRB-approved.	09-Jul-2012	PDF	31-Oct-2014
8	PROSPECT Patient Reference Cards for the PRO-CTCAE Companion Study	15-Oct-2014	PDF	19-Jan-2015
9	N1048 Data Entry Instructions and Tips	01-Mar-2017	PDF	03-Mar-2017
10	CRA [illegible]		PDF	06-Mar-2017
11	PROSPECT (N1048) and TNT (NRG-GI002) Clinical Trials – November 2017		PDF	03-Nov-2017

Alliance A021502 (ATOMIC) - Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair

Frank Sinicrope, MD – Study Chair

Kabir Mody, MD – Study Co-Chair

Walter Peters, MD – Study Co-Chair

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A021502 Study Overview: Background

A021502 Background – General

- The PD-1/PD-L1 pathway acts to protect tumor cells from immune attack by T cells which can be circumvented by checkpoint inhibitors.

- Targeting PD-1 with pembrolizumab or nivolumab for treatment of refractory metastatic colorectal cancers with deficient DNA mismatch repair (d-MMR) produced frequent and durable responses. These data led to FDA approval of both drugs for d-MMR tumors.

References: Le, D et al, NEJM 2015;372:2509-20.

Overman, M, et al, Lancet Oncol. 2017; 18:1182-91.

A021502 Background – Atezolizumab

- Atezolizumab is a monoclonal antibody that binds to PD-L1 and blocks its interaction with PD-1, thereby enhancing T-cell activity against tumor cells.

- Atezolizumab is well tolerated with no dose-limiting toxicities; data include a phase I trial of atezolizumab plus bevacizumab +/- FOLFOX.

- Atezolizumab is FDA-approved for treatment of platinum-resistant metastatic non-small cell lung cancer (NSCLC) and locally advanced or metastatic urothelial cancer.

A021502 Background – Checkpoint Inhibitor + Chemotherapy

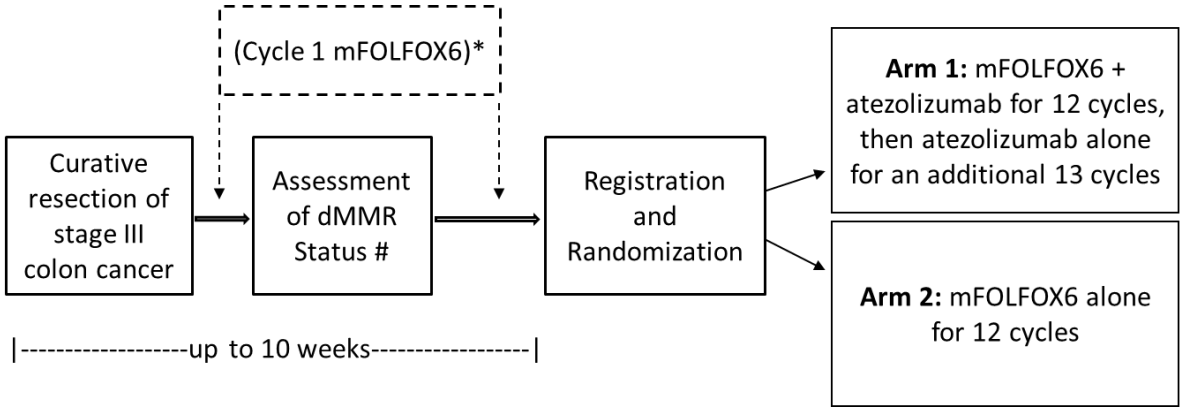
- Atezolizumab was shown to enhance the efficacy of platinum-containing chemotherapy in NSCLC (IMpower150, ESMO ImmunoOnc 2017).
- Oxaliplatin has been shown to induce immunogenic tumor cell death.
- *We hypothesize that atezolizumab can enhance the efficacy of standard adjuvant FOLFOX chemotherapy for stage III colon cancer with d-MMR.*

A021502 Background – d-MMR Colon Cancer

- d-MMR results in microsatellite instability (MSI).
- d-MMR tumors are hypermutated with abundant neoantigens that trigger tumor infiltrating lymphocytes (TILs); factors associated with response to checkpoint inhibitors.
- d-MMR cancers include both sporadic and hereditary (e.g. Lynch Syndrome) types.
- About 12% of stage III colon cancers show d-MMR or MSI.
- NCCN Guidelines recommend d-MMR/MSI testing of all newly diagnosed CRC cases.

A021502 Study Overview: Trial Design

A021502 Trial Design – Schema



* One cycle of mFOLFOX6 is allowed prior to registration

dMMR status assessed via local or reference lab testing of MMR proteins by IHC

- Stratification Factors: T, N stage, tumor location.
- Dosing Schedule (one cycle = 2 weeks):
  - Atezolizumab 840 mg IV q2 weeks.
  - Oxaliplatin 85 mg/m^2 IV q2 weeks.
  - Leucovorin 400 mg/m^2 IV q2 weeks.
  - Fluorouracil 400 mg/m^2 IV bolus + 2400 mg/m^2 IV q2 weeks.

A021502 Trial Design – Objectives

- **Primary:** to determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve *disease-free survival (DFS)* compared to FOLFOX alone in patients with stage III colon cancers and d-MMR.
- **Secondary:** to determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve *overall survival* compared to FOLFOX alone in patients with stage III colon cancers and d-MMR.
- **Secondary:** to assess the adverse event profile and safety of each treatment arm using CTCAE and PRO-CTCAE.

A021502 Trial Design – Statistical Analyses

- Primary endpoint is DFS.
  - Target Hazard Ratio = 0.60 (equivalent to achieving DFS of 84% at 3-year mark for atezolizumab arm [2-sided alpha = 0.05, 90% power]); N = 700 patients.
  - Interim analyses at 50% and 75% of events.
  - Total number of DFS events required = 165.
- Secondary endpoints are OS, immune-related and other adverse events, and QOL.
- Toxicity monitoring via CTCAE v4.0, PRO-CTCAE (Patient Reported Outcomes Measurement System), and HRQOL (Health-related Quality of Life) Instruments.

A021502 Trial Design – Patient Impact

- The addition of atezolizumab to FOLFOX has the potential to significantly reduce colon cancer recurrence and prolong disease-free survival compared to FOLFOX alone (i.e. current standard of care).
- Using patient-reported adverse event data provides additional and valuable information on treatment safety (i.e. using PRO-CTCAE to consider emotional aspects and unreported side effects).

A021502 Trial Design – Eligibility Summary

- Curative resection of stage III colon adenocarcinoma with d-MMR.
- Tumor evaluation for d-MMR:
  - MMR protein expression (MLH1, MSH2, MSH6, or PMS2) by IHC.
    - Even if MSI-H by PCR is known, d-MMR by IHC is still required.
  - Local testing is acceptable. If not available, then tissue can be sent to a site-selected reference lab for MMR testing by IHC.
- Mandatory submission of FFPE tumor tissue to enable retrospective central confirmation of d-MMR by IHC.
  - Retrospective central confirmation is <u>not</u> for eligibility.

A021502 Trial Design – Eligibility Summary (2)

- ECOG Performance Status: 0-2.
- One cycle of mFOLFOX6 may be given prior to registration.
  - Allows additional time for a patient to decide whether or not to participate and for sufficient time to obtain a local MMR IHC result while the patient starts treatment.
- For patients who are randomized to Arm 1 (mFOLFOX6 + atezolizumab) and had received Cycle 1 of mFOLFOX6 prior to registration, atezolizumab will begin with Cycle 2 of mFOLFOX6.

A021502 Trial Design – Adjuvant Treatment Duration

- Regardless of IDEA trial results, the duration of adjuvant mFOLFOX6 treatment on A021502 is 6 months. Justification for this is based upon:
  - No data exists for adjuvant treatment duration (3 months vs. 6 months) in d-MMR colon cancers.
  - Risk stratification based upon T and N stage is unknown among d-MMR cancers.
  - A021502 is an FDA registration trial and uniformity is optimal.

A021502 Trial Design – Additional Key Issues

- FFPE tumor tissue submission to the central lab required for all patients.
  - Tissue submission must be accompanied by electronically-completed, printed A021502 Requisition Form.
    - Fillable PDF can be found on the study-specific Alliance and CTSU websites.
- A021502 is an FDA Registration trial and thus includes the following:
  - Central and on-site monitoring.
  - Collection of major and critical protocol deviations via Medidata Rave®.
  - Utilization of the centralized Delegation Task Log (DTL) via the CTSU.

A021502 Trial Design – Biospecimen Collection

	Prior to treatment	3 weeks after treatment initiation	2 months after Cycle 5, Day 1	6 months after end of adjuvant Rx	Time of recurrence
Mandatory Submissions for <u>All Patients</u> Registered to the A021502 Main Study:					
Tissue	X				
Optional Submissions for Patients Registered to the PP1 and/or ST1 Substudies:					
Tissue	X				X
Blood	X	X	X	X	X
Stool	X		X	X	

- Each specimen type has a separate consent question for optional future correlative science studies.

A021502 Accrual Update

- Accrual goal is 700 patients.
- As of December 11th, 11 patients have been registered/randomized, and 511 sites have been approved by the CTSU.

THANK YOU!

A021502 Contact Information

- Study Chair, Dr. Frank Sinicrope
  - sinicrope.frank@mayo.edu or (507) 266-5365
- Study Co-Chairs, Dr. Walter Peters and Dr. Kabir Mody
  - walter.peters@baylorhealth.edu or (469) 800-7600
  - mody.kabir@mayo.edu or (904) 953-2795
- Protocol Coordinator, Alexandra LeVasseur
  - alevasseur@uchicago.edu or (773) 834-4518

Q&A – A021502

Directions:

- Please use the “CHAT BOX” to submit a question.
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- Please select “All Participants” from the drop-down menu when sending your question or comment.

NRG-GI004/SWOG-S1610 Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) Study: A Randomized Phase III Study of mFOLFOX6/Bevacizumab Combination Chemotherapy with or without Atezolizumab or Atezolizumab Monotherapy in the First-Line Treatment of Patients with Deficient DNA Mismatch Repair (dMMR) Metastatic Colorectal Cancer

PI (NRG Oncology): James J. Lee, MD PhD
Co-PI (SWOG): Michael Overman, MD

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NRG-GI004/SWOG-S1610 Deficient DNA Mismatch Repair (dMMR) CRC

- The DNA mismatch repair (MMR) system is involved in recognition and repair of erroneous bases or insertion-deletion loops of newly replicated DNA strands.
- About 5% of metastatic CRCs are hypermutated due to DNA mismatch repair defect (dMMR) by promoter hypermethylation of MLH1 promoter or germline MMR mutations (Lynch syndrome).
- Functional loss of the MMR system (dMMR) leads to length variations in tracts of mono- or polynucleotides in short, tandem repeated sequences, termed microsatellite instability (MSI).
- Recently the NCCN recommended that “all patients with a personal history of colon or rectal cancer” undergo MSI testing (NCCN guidelines version 2.2017).

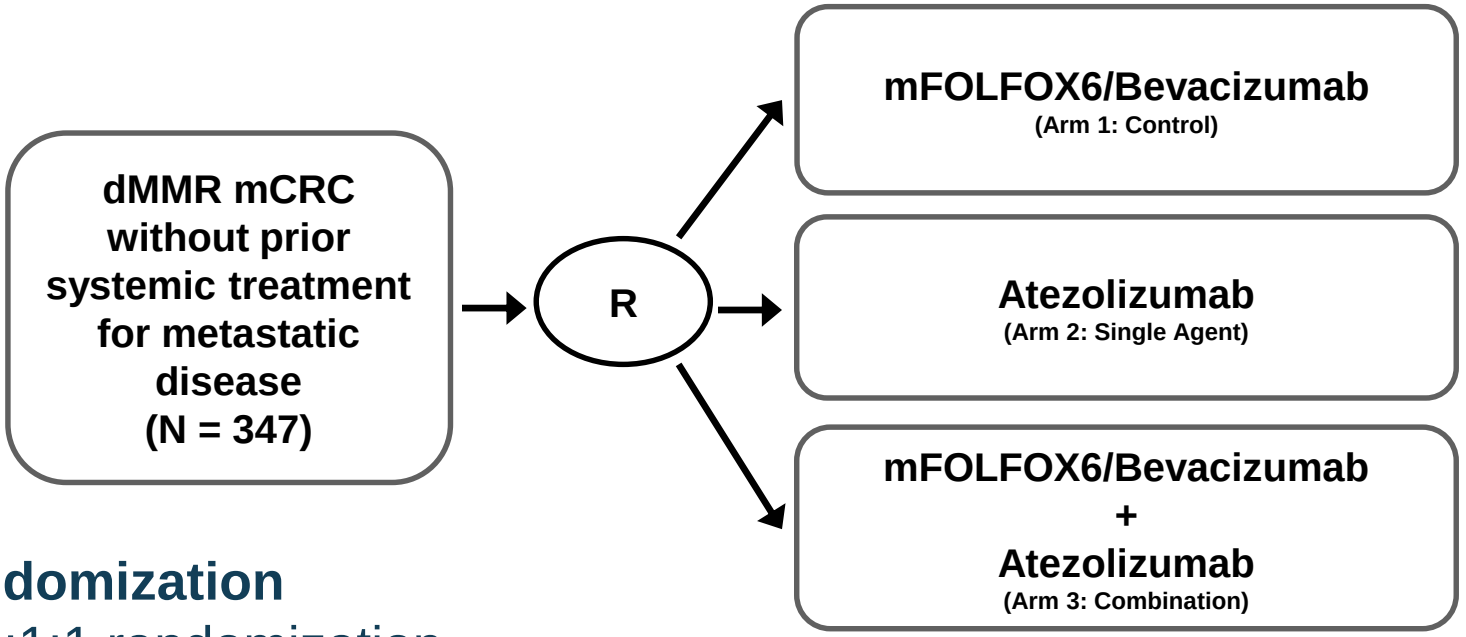
NRG-GI004/SWOG-S1610 Rationale for the Combination of mFOLFOX6/Bevacizumab and Atezolizumab in dMMR mCRC

- Oxaliplatin-containing chemotherapy induces immunogenic cell death.
- Synergistic anti-tumor activity by oxaliplatin/anti-VEGF chemotherapy and PD-1 blockade in murine CRC tumor models.
- dMMR CRC derived statistically significant survival benefit from the addition of bevacizumab in the adjuvant therapy trial of NSABP C-08.
- Pembrolizumab and nivolumab have been approved in the U.S. for the treatment of patients with MSI-H/dMMR mCRC that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

NRG-GI004/SWOG-S1610 Study Hypothesis

- We hypothesize that the PD-1/PD-L1 pathway may play a critical role in impeding T cell response to dMMR CRC cells and that mFOLFOX6 in combination with anti-VEGF blockade will potentiate the effect of PD-1 blockade. Therefore, we expect that the dMMR subset of mCRC may be effectively targeted with the combination of PD-L1 blockade and mFOLFOX6 plus anti-VEGF-A inhibition to promote tumor regression.
- The main hypothesis of this study is that the addition of atezolizumab to standard mFOLFOX6/bevacizumab as first line therapy will improve progression-free survival in patients with dMMR mCRC as compared to standard mFOLFOX6/bevacizumab combination chemotherapy.

NRG-GI004/SWOG-S1610 Study Schema



Randomization

- 1:1:1 randomization.
- Stratified according to BRAF mutation (V600E; non-V600E, WT, or Unknown), metastatic disease: (liver-only; extra-hepatic), and prior adjuvant therapy for CRC (yes; no).

NRG-GI004/SWOG-S1610 Study Objectives

- **Primary objective**:
  - To determine the efficacy of mFOLFOX6 + bevacizumab + atezolizumab (combination) and atezolizumab (single agent) as compared to mFOLFOX6 + bevacizumab (control).
  - Primary endpoint: PFS.
- **Secondary objectives**:
  - To compare OS, ORR, safety profile, surgical conversion rate, DCR, duration of response and stable disease.
- **Exploratory objectives**:
  - Health-related QoL.
- **Translational objectives:** To bank tissue and blood samples for other future correlative studies from patients enrolled on the study.

NRG-GI004/SWOG-S1610 Key Eligibility Criteria

- Metastatic CRC without prior chemotherapy for mCRC.
- Tumor determined to be mismatch-repair deficient (dMMR) by **CLIA-certified immunohistochemical (IHC) assay** *with a panel of all four IHC markers, including MLH1, MSH2, PMS2, and MSH6.*
  - *Note: MSI-H diagnosed by other MSI testing (e.g., either Bethesda markers or Pentaplex panel or by next-generation sequencing (NGS)) is not eligible unless dMMR is confirmed by CLIA-certified IHC assay.*
- An adequate amount of archived tumor tissue, either from primary colorectal cancer site or metastatic lesions, for central confirmation of dMMR status: Either FFPE block *or* at least 8 unstained slides.
- Measurable disease per RECIST 1.1

NRG-GI004/SWOG-S1610 Treatment

- **Arm 1: mFOLFOX6/Bevacizumab**
  - Oxaliplatin 85 mg/m^2 IV (up to 10 cycles).
  - Bevacizumab 5 mg/kg IV.
  - 5-FU 400 mg/m^2 IV bolus on day 1 followed by 5-FU 2400 mg/m^2 IV over 46 hours.
- **Arm 2: Atezolizumab monotherapy**
  - Atezolizumab 800 mg IV on day 1 of every cycle.
    - Not to exceed 48 cycles (= about 2 years).
- **Arm 3: mFOLFOX6/Bevacizumab + Atezolizumab**
  - mFOLFOX6/Bevacizumab as in arm 1 (oxaliplatin up to 10 cycles).
  - Atezolizumab 800 mg IV on day 1 of every cycle.
    - Not to exceed 48 cycles (= about 2 years).

NRG-GI004/SWOG-S1610 Statistical Plan

- Median PFS for the control arm (FOLFOX/Bev arm) is assumed to be 7 months based on historical data.
- 223 PFS events are required to provide 90% power to detect a true hazard ratio (H_A) of 0.59 (mPFS, 7 months vs 11.86 months) with the log-rank test at $\alpha = 0.025$ one-sided for both pairwise comparisons.
- Centrally Confirmed Intention To Treat (CCITT): The CCITT population will include all randomized patients who have central confirmation of dMMR status (assuming <10% discordance between local lab and central confirmation).
- 347 patients accrued over 35 months and followed an additional 8 months (47 months total) will provide the needed events.

NRG-GI004/SWOG-S1610 Study Leadership Team (Contact Information)

- PI (NRG Oncology): James J. Lee, MD PhD (leejj@upmc.edu)
- Co-PI (SWOG): Michael Overman, MD (moverman@mdanderson.org)
- Protocol Officer: Sam Jacobs, MD (samuel.jacobs@nsabp.org)
- Translational Chair: Scott Kopetz, MD PhD (skopetz@mdanderson.org)
- Pathology Chair: Peter Lucas, MD PhD (nrgbiobankpgh@nrgoncology.org)
- Stats Chair: Greg Yothers, PhD (yothersg@nrgoncology.org) and Katherine Guthrie, PhD (kguthrie@fredhutch.org)
- QoL Chair: Norah Henry, MD PhD (lynn.henry@hci.utah.edu) and Patricia Ganz, MD (pganz@mednet.ucla.edu)
- NRG Co-Investigator: Thomas George, MD (thom.george@medicine.ufl.edu)
- SWOG Co-Investigator: Howard Hochster, MD (howard.hochster@yale.edu)
- ALLLIANCE Co-Chair: Hanna Sanoff, MD (hanna_sanoff@med.unc.edu)
- ECOG-ACRIN Co-Chair: Deirdre Cohen, MD (deirdre.cohen@nyumc.org)
- Coordinating Center: NRG Oncology (info@nrgoncology.org)

Q&A – NRG-GI004/SWOG-S1610

Directions:

- Please use the “CHAT BOX” to submit a question.
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NCI - S1613: A Randomized Phase II Study of Trastuzumab & Pertuzumab (TP) vs. Cetuximab & Irinotecan (CETIRI) in Metastatic Colorectal Cancer (mCRC) with HER2 Amplification

NCT03365882

Kanwal Raghav, MD
SWOG & MD Anderson Cancer Center, Houston TX (Study Chair)

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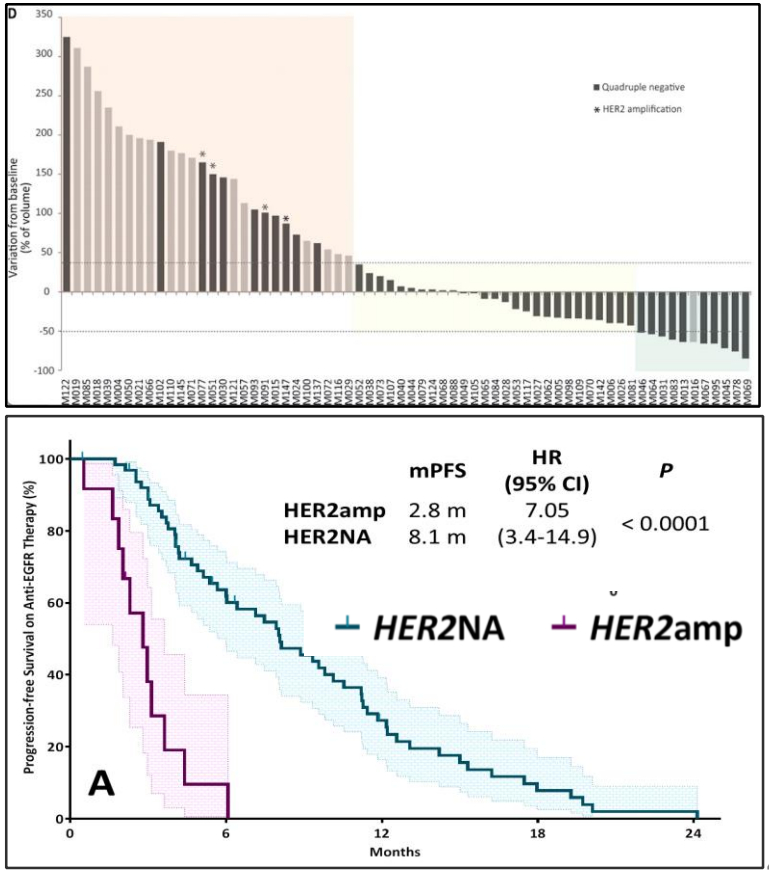
December 14, 2017

S1613 Study Rationale

Background and Hypothesis

S1613 Prevalence & Impact of HER2 Amplification in mCRC

- HER2 amplification is found predominantly in KRAS-WT (5-6%) mCRC.
- HER2 amplification in PDXs blunts response to anti-EGFR therapy **(Fig)** (*Bertotti et. al. 2011*).
- HER2 amplified mCRC patients have shorter median PFS on anti-EGFR therapy (2.9 v. 8.1 months; P < 0.001) compared to non-amplified cases **(Fig)** (*Raghav et al. 2016*).



S1613 Targeting HER2 Amplification in mCRC

- HER2 amplified mCRC PDXs resistant to anti-EGFR respond to dual-anti-HER2 inhibition **(Fig)** (*Bertotti et. al. 2011*).

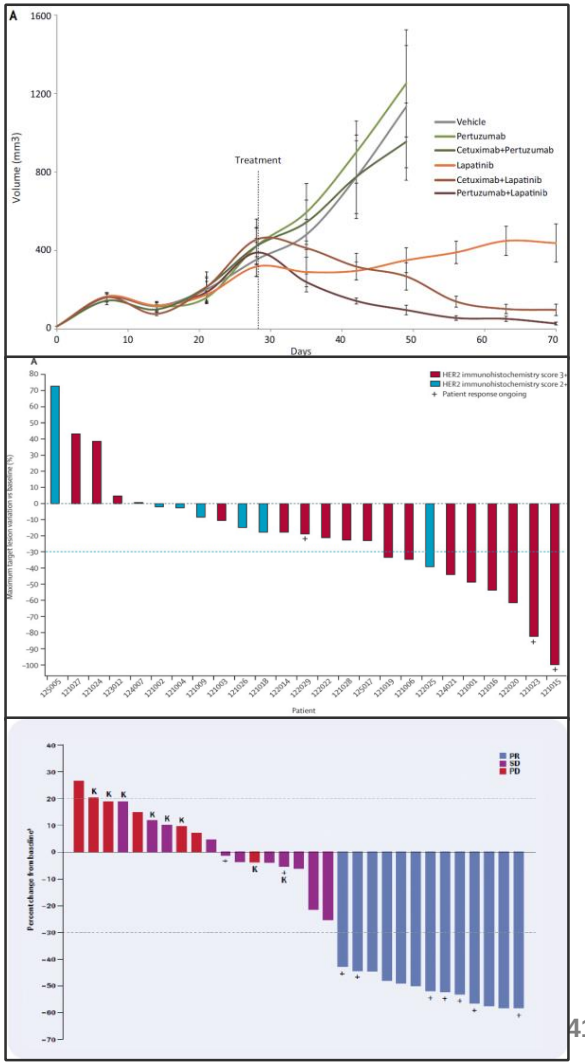
- Dual anti-HER2 inhibition has activity in in refractory HER2 amplified mCRC (early phase II studies):

  - **HERACLES Study (Fig)** (*Siena et. al. 2016*).

    - Trastuzumab + Lapatinib: ORR: 30%; mPFS: 5.2 m

  - **My Pathway Study (Fig)** (*Hurwitz et. al. 2017*).

    - Trastuzumab + Pertuzumab: ORR: 38%; mPFS: 4.6 m



S1613 Working Hypothesis

- Recognizing that HER-2 amplification:
  - Adversely influences the clinical response to therapy with anti-EGFR-antibody, cetuximab (negative predictor of response to EGFR inhibition) and
  - Is predictive of response to dual anti-HER-2 therapy (positive predictor of response to HER-2-targeting agents), we hypothesize that
  - Dual anti-HER-2 inhibition using trastuzumab and pertuzumab, will result in enhanced efficacy thereby resulting in improved PFS compared to standard of care therapy with cetuximab and irinotecan.

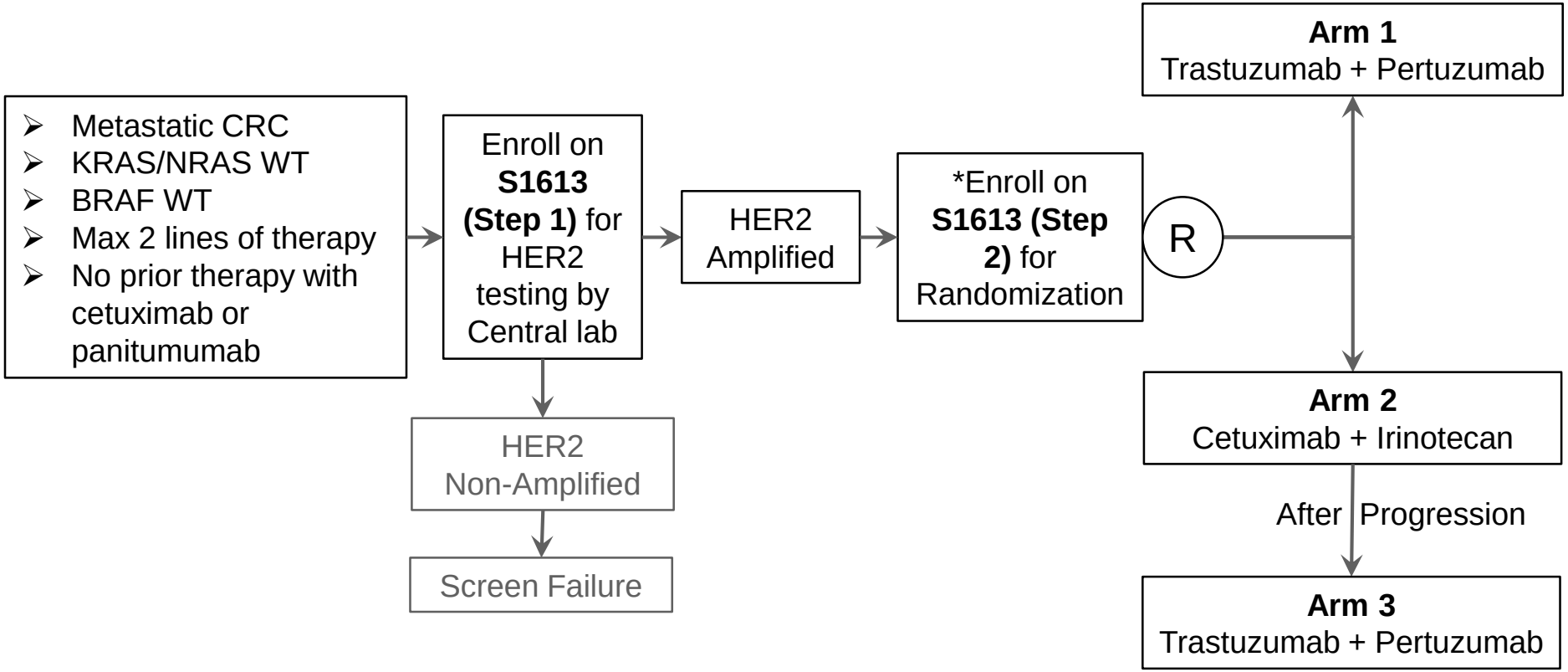
S1613 Study Design

Study Methodology, Eligibility criterion and Statistical Methods

S1613 Study Methodology

- **Step 1: Registration (Screening):**
  - All RAS/BRAF-WT mCRC can be screened, at any time during their treatment course, as long as they have not received anti-EGFR therapy.
  - HER2 Screening at central lab with IHC & Dual ISH.
  - If local HER2 IHC shows 2+/3+ expression or sequencing shows HER2 amplification, central confirmation is needed.
- **Step 2: Randomization (Treatment):**
  - HER2 amplified patients will be randomized after progression on at least one prior line of therapy.
- **Crossover (Optional):** To Arm 3 (anti-HER2 therapy) allowed for control group.

S1613 Study Schema



*Enrollment on Step 2 requires progression on at least one line of therapy.

S1613 Study Eligibility

- **Step 1: Registration (Screening):**
- Metastatic/Locally advanced and unresectable adenocarcinoma of colon/rectum.
- No mutation in exon 2 [codons 12 and 13], exon 3 [codons 59 and 61] and exon 4 [codons 117 and 146]) of KRAS/NRAS genes and exon 15 (BRAFV600E mutation) of BRAF gene.
- No prior treatment with cetuximab or panitumumab or HER2 therapy for CRC.
- No history of severe toxicity/intolerance/hypersensitivity to irinotecan.
- Must have tumor slides for HER2 testing.
- **Step 2: Randomization (Treatment):**
- HER2 amplification by central testing [3+/2+ IHC & ISH (HER2/CEP17 ≥ 2.0)].
- Measurable disease per RECIST 1.1
- Must have had progression on at least one prior regimen for mCRC. Prior treatment with irinotecan is allowed. Patients with ≥3 lines of therapy ineligible.
- ECOG PS 0/1.

S1613 Study Treatments

- **Arm 1: Experimental (TP)**
  - Pertuzumab @ 840 mg IV over 60 mins (cycle 1) followed by 420 mg IV over 30 mins (cycle 2+) every 21 days.
  - Trastuzumab @ 8 mg/kg IV over 90 mins (cycle 1) followed by 6 mg/kg IV over 30 mins (cycle 2+) every 21 days.
- **Arm 2: Control (CETIRI)**
  - Cetuximab @ 500 mg IV over 120 mins (cycle 1) followed by 500 mg IV over 60 mins (cycle 2+) every 14 days.
  - Irinotecan @ 180 mg/m^2 IV over 90 mins every 14 days.
- **Arm 3: Cross-Over (TP)**
  - Same as Arm 1.

S1613 Statistical Methods

- **Primary Objective**
  - Efficacy by PFS
- **Secondary Objectives**
  - ORR per RECIST 1.1
  - OS
  - Safety and toxicity
- **Translational Objective**
  - Predictive: HER-2/CEP17 ratio and HER-2 GCN
  - Bank tissue and blood

- **Primary Endpoint:** PFS
- **Primary Analysis:** ITT
- **Sample Size:** 130 randomized patients
  - 122 eligible patients
  - **Type 1 error (one-sided):** 5%
  - **Power:** 90%
  - PFS (control arm) (null hypothesis): 3 m
  - PFS (experimental arm) (alternate hypothesis): 5.1 m
- 33 months accrual

S1613 Key Issues For Study Execution

- **HER2 is not tested routinely in clinical practice**
  - Study allows for testing on protocol.
- **Study requires anti-EGFR naïve population**
  - Since HER2 amplified CRC unlikely to get significant benefit from anti-EGFR therapy, we endorse HER2 testing prior to exposure to anti-EGFR therapy.
  - Step 1 registration can be done early on in treatment course.
- **HER2 amplified patients are a rare subset**
  - More and more centers getting NGS panels for CRC which can identify HER2 amplifications without specific testing (i.e. local screening).
  - Promising results of phase II studies.
  - Study endorsed by patient advocacy as a less toxic and more efficacious precision treatment option for this subset of CRC.

S1613 Contact Information

- Benjamin Tan, Jr. MD (Washington University, WA) [btan@wustl.edu] **(ALLIANCE)**
- Crystal Denlinger [Crystal.Denlinger@fccc.edu] (**ECOG-ACRIN)**
- Marwan Fakih, MD (City of Hope Medical Center, CA) [mfakih@coh.org] **(NRG)**
- Kanwal Raghav, MD (MD Anderson Cancer Center, TX) [kpraghav@mdanderson.org] (**SWOG)(Study Chair)**
- Scott Kopetz, MD (MD Anderson Cancer Center, TX) [skopetz@mdanderson.org] **(Translational Medicine)**
- Anthony Magliocco, MD (H Lee Moffitt Cancer Center, FL) [anthony.magliocco@moffitt.org] **(Central Lab :HER2 Screening)**

Q&A –S1613

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www.allianceforclinicaltrialsinoncology.org
www.ctsu.org