NRG-GI004/SWOG-S1610: Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) Study—A randomized phase III study of atezolizumab (atezo) monotherapy versus mFOLFOX6/bevacizumab/atezo in the first-line treatment of patients (pts) with deficient DNA mismatch repair (dMMR) or microsatellite instability high (MSI-H) metastatic colorectal cancer (mCRC).

Background: Despite activity of programmed cell death-1 (PD-1) pathway inhibition in dMMR/MSI-H mCRC, approximately one-third of patients demonstrate progressive disease as best response to anti-PD1 monotherapy. Preclinical models have demonstrated synergistic interactions between FOLFOX, anti-VEGF, and anti-PD-1. We hypothesize that the dMMR/MSI-H mCRC subset may be more effectively targeted by the combination of PD-1 pathway blockade and mFOLFOX6/bevacizumab (bev) rather than with anti-PD-1 therapy (atezo) alone. Methods: Initially a three-arm study, the mFOLFOX6/bev arm was closed to new enrollment on 6-4-20 due to emerging data; the redesigned COMMIT is a prospective phase III open-label trial that will randomize (1:1) mCRC dMMR/MSI-H pts (N=211) to either atezo monotherapy or mFOLFOX6/bev+atezo combination. Stratification factors include BRAFV600E status, metastatic site, and prior adjuvant CRC therapy. Primary endpoint is progression-free survival (PFS) as assessed by site investigator. Secondary endpoints include OS, objective response rate, safety profile, disease control rate, duration of response, and centrally-reviewed PFS. Health-related quality of life is an exploratory objective. Archived tumor tissue and blood samples will be collected for correlative studies. Key inclusion criteria are: mCRC without prior chemotherapy for advanced disease; dMMR tumor determined by local CLIA-certified IHC assay (MLH1/MSH2/MSH6/PMS2) or MSI-H by local CLIA-certified PCR or NGS panel; and measurable disease per RECIST. Support: U10CA180868, -180822, -180888, -180819, U10CA189867, U24CA196067; Genentech, Inc. Clinical trial information: NCT02997228. Research Sponsor: U.S. National Institutes of Health, Pharmaceutical/Biotech Company.