Alliance Study A021502 – 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

Data as of 08/28/2023

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1.0 OBJECTIVES

Primary

- To determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve DFS compared to FOLFOX alone in patients with stage III colon cancers and dMMR.

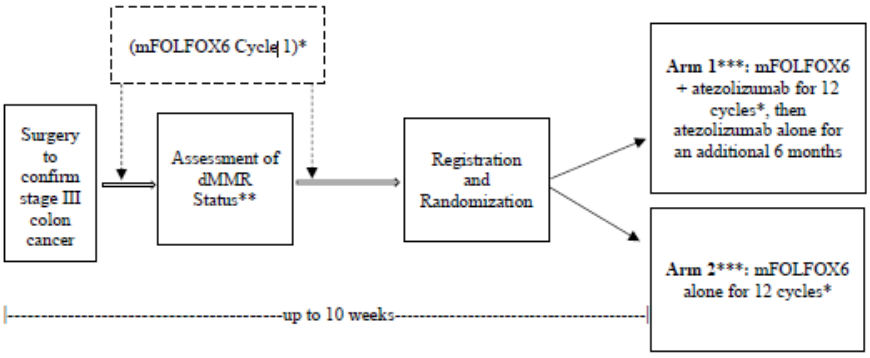
Secondary

- 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 dMMR.

- To assess the adverse events (AE) profile and safety of each treatment arm, using the CTCAE and PRO-CTCAE (among patients aged ≥ 18).

2.0 CURRENT SCHEMA

Schema



* 1 cycle = 14 days. One cycle of mFOLFOX6 is allowed prior to registration. If Cycle 1 of mFOLFOX6 is started prior to registration, then the first post-registration cycle will be mFOLFOX6 Cycle 2. For patients who received Cycle 1 of mFOLFOX6 prior to registration and who are randomized to Arm 1, atezolizumab will start with Cycle 2 of mFOLFOX6.

** Assessment of dMMR status for eligibility may be performed locally or at a site-selected reference laboratory. Retrospective central confirmation of dMMR testing is required for all patients to gauge the false-positive rate in local testing (not for eligibility). See Section 6.2 for specimen submission requirements.

*** The standard of care for the time window between the end of mFOLFOX6 Cycle 1 and the start of mFOLFOX6 Cycle 2 is 14 days; however, up to 28 days are allowed between the end of Cycle 1 and the start of Cycle 2 if delays are made due to toxicity.

Patients will be followed for recurrence and survival every 6 months for the first two years after registration, then survival every 6 months and recurrence once annually for years 3-5 after registration, and then survival every 6 months for years 5-8 after registration.

3.0 ELIGIBILITY CRITERIA

- Histologically proven stage III colon adenocarcinoma
- Presence of deficient MMR (dMMR) via IHC
- Completely resected tumors
- Entire tumor in colon

- No evidence of residual involved lymph node disease or metastatic disease
- Patients known to have Lynch Syndrome are eligible
- No other planned concurrent investigational agents or other tumor directed therapy
- No active autoimmune disease, including colitis, panhypopituitarism, adrenal insufficiency
- No known active hepatitis B or C infection
- No active pulmonary disease with hypoxia
- No grade ≥ 2 peripheral motor or sensory neuropathy
- Non-pregnant, non-nursing
- Age ≥ 12 years
- Performance Status: Lansky ≥ 50% (patients <16 years), Karnofsky ≥ 50% (patients 16 to <18 years), or ECOG PS≤ 2 (patients ≥ 18 years)

Required Initial Laboratory Values

- Absolute Neutrophil Count (ANC) ≥ 1500/mm3
- Platelet Count ≥ 100,000/mm3*
- AST/ALT ≤ 2.5 x ULN
- Bilirubin ≤ 1.5 x ULN***
- TSH WNL****
- Creatinine ≤ 1.5 x ULN**
  OR
- Calculated Creatinine Clearance ≥ 45 mL/min

* Platelets ≥ 75,000 for patients who received Cycle 1 of mFOLFOX6 prior to registration
** By Cockcroft-Gault equation. Alternatively, for patients <18 years of age, maximum serum creatinine ≤the age-gender-specific norms listed in the protocol Section 3.2.7
*** Except in the case of Gilbert disease
**** Supplementation is acceptable to achieve a TSH WNL

4.0 TREATMENT SCHEDULE

Arm 1: mFOLFOX6 Plus Atezolizumab

The agents in the table below are listed in the order of intended administration.

Agent	Dose	Route	Duration	Days	Cycle
Atezolizumab	840mg*	IV	Over 60 min (+/- 15 min) for 1st dose, then Over 30min (+/- 10 min) for all subsequent doses	Day 1	Every 14 days
Oxaliplatin	85mg/m^2	IV	Over 2 hours (+/- 30 min)	Day 1	Every 14 days
Leucovorin**	400mg/m^2	IV	Over 2 hours (+/- 30 min)	Day 1	Every 14 days
Fluorouracil	400mg/m^2 + 2400mg/m^2	IV	Bolus + Over 46 hours (+/- 4 hours)	Day 1 + Days 1-3	Every 14 days

* Patients 12 to < 18 years of age will receive a dose of 10 mg/kg up to a maximum flat dose of 840 mg. The patient's age on the day of treatment should be used to determine whether to use weight-based dosing.
** Alternatively, leucovorin may be administered (via separate infusion containers) concurrently with oxaliplatin. Infusion duration may be adjusted according to institutional practice.

Note: if the minimum durations are followed and/or concurrent administration of leucovorin and oxaliplatin occurs, then fluorouracil administration could be completed on Days 1-2.

Atezolizumab should be the first drug administered for Cycle 1 as no premedication is allowed prior to the first dose of atezolizumab; see Section 7.0 and Section 8.1.4 in the protocol for additional details.

Patients should receive 6 months (12 cycles total) of mFOLFOX6, including the cycle that may have been received prior to registration.

For patients who started mFOLFOX6 after registration, atezolizumab should start on Day 1 Cycle 1 of mFOLFOX6 (12 cycles in combination with mFOLFOX6 followed by 13 cycles as monotherapy); for a total of 25 cycles of atezolizumab).

For patients who receive one cycle of mFOLFOX6 prior to registration, atezolizumab should start on Day 1 Cycle 2 of mFOLFOX6 (11 cycles in combination with mFOLFOX6 followed by 13 cycles as monotherapy for a total of 24 cycles of atezolizumab).

Arm 2: mFOLFOX6

The agents in the table below are listed in the order of intended administration.

Agent	Dose	Route	Duration	Days	Cycle
Oxaliplatin	85mg/m^2	IV	Over 2 hours (+/- 30min)	Day 1	Every 14 days
Leucovorin*	400mg/m^2	IV	Over 2 hours (+/- 30 min)	Day 1	Every 14 days
Fluorouracil	400mg/m^2 + 2400mg/m^2	IV	Bolus + Over 46 hours (+/- 4 hours)	Day 1 + Days 1-3	Every 14 days

* Alternatively, leucovorin may be administered (via separate infusion containers) concurrently with oxaliplatin. Infusion duration may be adjusted according to institutional practice.

Note: if the minimum durations are followed and/or concurrent administration of leucovorin and oxaliplatin occurs, then fluorouracil administration could be completed on Days 1-2.

Patients should receive 6 months (12 cycles total) of mFOLFOX6, including the cycle that may have been received prior to registration.

5.0 STUDY DESIGN

5.1 Study Phase/Type of Design/Stratification Factors

This study is a two-arm randomized phase III trial comparing the outcomes of patients with stage III colon cancer whose tumors have dMMR status treated with 1) mFOLFOX6 with atezolizumab and its continuation as monotherapy and 2) mFOLFOX6 alone. Patients will be assigned to one of two treatment arms (Arm 1 vs Arm 2) in a 1:1 fashion using a permuted block design.

The stratification factors are as follows:

1) Number of Positive Lymph Nodes: N1 (1-3 positive nodes)/N1C vs N2 (≥4 positive nodes) (per AJCC 7),
2) T Stage: Tx/T1-T3 vs T4,
3) Primary Tumor Location: proximal (cecum, ascending colon, hepatic flexure, and transverse colon) vs. distal (splenic flexure, descending colon, sigmoid colon, and rectosigmoid junction).

5.2 Primary Endpoint

Endpoint Definition: The primary endpoint of this study is the disease-free survival (DFS), defined as the time from randomization to first documentation of disease recurrent or death. Patients who do not have a DFS event will be censored for DFS at their last disease assessment date. Confirmed second primary colon cancer and second primaries of other types will not be included as an event for the DFS endpoint.
Efficacy analyses will be based on the intention to treat principle and all randomized patients (including adult and patients aged < 18 years) will be included for the analysis i.e. patients will be assigned to the treatment group they were randomized to regardless of the actual treatment received.

DFS will be compared between treatment arms using the stratified log-rank test at one-sided level 0.025.

Power/Sample Size:
We anticipate randomizing a maximum of 700 adult patients (350 per arm) per statistical design. Patients aged 12 to < 18 years old will be accrued and randomized, but they will not be counted toward the sample size of 700. If the study reaches full accrual of 700 adult patients, enrollment will be closed to both adult and patients aged 12 to < 18 years at the same time.

When both NSABP C-08 and NCCTG N0147 adjuvant trials were simultaneously accruing patients, the NSABP C-08 trial accrued 110-130 patients/month and NCCTG N0147 concurrently accrued 20-30 patients/month. Of these 150 patients/month accrual capacity, we estimate that 12% of colon cancers will show dMMR which calculates to 18 patients/month or 216 patients/year. One and a half years after trial opening, if the accrual rate exceeds the projection (e.g. >25 patients /month), we will consider amending the protocol to raise the accrual target and to allow the detection of a hazard ratio (HR) of > 0.6.

The best historical data available on the outcome of patients with stage III colon cancer comes from Intergroup Study N0147, where the 3-year DFS in MSI-H stage III patients treated with mFOLFOX6 was 75%. We assume an accrual period of 3.24 years, minimum follow-up on all patients of 2.05 years, exponential survival, and that a one-sided log-rank test for superiority will be conducted at level 0.025. Additionally, we assume a dropout rate of 1.25% per year. Based on these assumptions, a sample size of 350 adult patients per arm (700 adult patients in total) will result in 165 events which are required to provide 90% power to detect a hazard ratio (HR) of 0.6 between the two treatment arms. The 3-year DFS estimate for the atezolizumab arm corresponding to this HR is 84.147%.

Two interim analyses will be performed to assess treatment futility and superiority. The first interim analysis, for both efficacy and futility, will be performed at the time at which 50% of the projected number of events has occurred. The second interim analysis is for efficacy only and will be performed at the time at which 75% of the projected number of events has occurred. The number of DFS events will be the total number of DFS events observed from both adult and patients aged <18 years. The statistical analysis will be conducted by pooling the adult and patients aged <18 years.

5.3 Target Accrual

The target accrual for this study is 700 patients using a 1:1 randomization (permuted block randomization). The target accrual rate is 18 patients per month.

6.0 CURRENT ACCRUAL

Study Activation Date	09/12/2017
Closure Date	01/17/2023
Target Accrual	700
Final Accrual	712 (including 1 patient < 18 years old)

7.0 CURRENT STUDY STATUS

- This study was activated on 9/12/2017. It was closed on 1/17/2023 after reaching full enrollment.
- Update #1 (posting date: 12/15/2017): Clarifications and administrative changes.
- Update #2 (posting date: 07/16/2018): Adverse event stopping rule is amended.
- Update #3 (posting date: 08/02/2018): Upgrade CTCAE to version 5.0
- Update #4 (posting date: 10/05/2018): Updated CAEPR for Atezolizumab

- Update #5 (posting date: 03/01/2019): Updated the plan for retrospective central review of dMMR status
- Update #6 (posting date: 08/01/2020): Eligibility changes, therapy/dose modification/study calendar changes, inform consent changes, editorial/administrative changes.
- Update #7 (posting date: 12/15/2020): Addition of Arbeitsgemeinschaft Internistische Onkologie (AIO) as a non-member collaborator. Therapy/dose modifications, study calendar changes, informed consent changes, editorial/administrative changes. Added group-specific appendixes for AIO.
- Update #8 (posting date: 05/01/2021): Incorporated the addition pediatric patients ages 12 and over. Eligibility changes, therapy/dose modifications, study calendar changes, informed consent changes, scientific/statistical considerations changes, and editorial/administrative changes.
- Update #9 (posting date: 06/23/2021): Informed consent changes and updated CAEPR for Atezolizumab.
- Update #10 (posting date: 12/15/2021): Minor changes to study calendar footnotes, primary and secondary analysis endpoints, and adverse events and reporting. Updated Atezolizumab preparation instructions, dose modifications, and hypersensitivity/infusion reactions. Modified sections throughout the AIO Group-specific Appendix.
- Update #11 (posting date: 09/01/2022): Editorial/administrative changes.
- Update #12 (posting date: 09/30/2022): Updated trial personnel, CTSU language, and AE reporting language. Minor update to Statistical section to address FDA comments.
- Update #13 (posting date: 12/01/2022): Atezolizumab section updated to align with the most recent drug language for atezolizumab. Editorial/administrative changes.
- Update #14 (posting date: 07/14/2023): Added and/or modified language in the Study Calendar, Supporting Documentation to be Submitted to Alliance, and Protocol-specific Monitoring Plan sections to support the data mitigation effort for anticipated FDA filing. Updated the Patient Registration and Data and Specimen Submission sections to use the current CTSU template language. Modified the Inclusion of Women and Minorities section to align the current Alliance model protocol template. Editorial/administrative changes.

8.0 PATIENT CHARACTERISTICS

The primary endpoint analysis population for this study follows intent-to-treat principle; therefore, all patients who were randomized are included in the table below in the arm which they were assigned to regardless their actual treatment assignment.

Table 8a. Demographics

	Arm 1: mFOLFOX6 + atezo (N=355)	Arm 2: mFOLFOX6 alone (N=357)	Total (N=712)
Age (in years)			
Median (Q1, Q3)	64.0 (50.0, 72.0)	63.0 (47.0, 72.0)	64.0 (49.0, 72.0)
Range	13.0, 91.0	20.0, 89.0	13.0, 91.0
Race			
American Indian or Alaska Native	2 (0.6%)	2 (0.6%)	4 (0.6%)
Asian	10 (2.8%)	12 (3.4%)	22 (3.1%)
Black or African American	28 (7.9%)	22 (6.2%)	50 (7.0%)
White	302 (85.1%)	305 (85.4%)	607 (85.3%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)	1 (0.3%)	1 (0.1%)
Not Reported	4 (1.1%)	9 (2.5%)	13 (1.8%)
Unknown	8 (2.3%)	6 (1.7%)	14 (2.0%)

	Arm 1: mFOLFOX6 + atezo (N=355)	Arm 2: mFOLFOX6 alone (N=357)	Total (N=712)
Other	1 (0.3%)	0 (0.0%)	1 (0.1%)
Gender			
Female	186 (52.4%)	206 (57.7%)	392 (55.1%)
Male	169 (47.6%)	151 (42.3%)	320 (44.9%)
Lymph nodes examined category			
Missing	0	1	1
Nodes examined < 12	3 (0.8%)	5 (1.4%)	8 (1.1%)
Nodes examined 12+	352 (99.2%)	351 (98.6%)	703 (98.9%)
Perforation			
Yes	36 (10.1%)	30 (8.4%)	66 (9.3%)
No	319 (89.9%)	327 (91.6%)	646 (90.7%)
Obstruction			
Yes	63 (17.7%)	62 (17.4%)	125 (17.6%)
No	292 (82.3%)	295 (82.6%)	587 (82.4%)
Adherence			
Yes	65 (18.3%)	74 (20.7%)	139 (19.5%)
No	290 (81.7%)	283 (79.3%)	573 (80.5%)

Table 8b. Stratification Factors (if applicable)

	Arm 1: mFOLFOX6 + atezo (N=355)	Arm 2: mFOLFOX6 alone (N=357)	Total (N=712)
Number of Positive Lymph Nodes			
N1/N1C	227 (63.9%)	227 (63.6%)	454 (63.8%)
N2	128 (36.1%)	130 (36.4%)	258 (36.2%)
T Stage			
Tx/T1-T3	247 (69.6%)	248 (69.5%)	495 (69.5%)
T4	108 (30.4%)	109 (30.5%)	217 (30.5%)
Primary Tumor Location			
Proximal	299 (84.2%)	298 (83.5%)	597 (83.8%)
Distal	56 (15.8%)	59 (16.5%)	115 (16.2%)

9.0 ADVERSE EVENTS

Adverse events are reported using CTCAE version 5.0, regardless of attribution.

Among the 712 patients randomized, 679 patients are evaluable for adverse event (AE) analyses (Arm 1: 350, Arm 2: 329) and 33 patients (Arm 1: 5, Arm 2: 28) have submitted only baseline AE data.

Commonly occurring grade 3+ AEs (occurring in 10% or more overall or by arm) include Neutrophil count decreased (Arm 1: 43%, Arm 2: 35%), Peripheral sensory neuropathy (Arm 1: 19%, Arm 2: 15%), Diarrhea (Arm 1: 12%, Arm 2: 9%), and Hypertension (Arm 1: 7%, Arm 2: 12%).

The only commonly occurring grade 4 AE (occurring in 10% or more overall or by arm) is Neutrophil count decreased (Arm 1: 14%, Arm 2: 7%).

Of the 679 evaluable patients, 8 patients reported a grade 5 AE in a treatment cycle (Arm 1: 6 (0.9%), Arm 2: 2 (0.3%)). **There are no additional deaths on study since the last Study Summary report.**

Grade 5 AE, previously reported, contributes to the AE stopping rule:

- Arm 1 patient, CTCAE term: Sudden death NOS (possibly related to study drug). Death date: 06/20/2018, 51 days since initiation of mFOLFOX6+Atezo.
- Arm 1 patient, CTCAE term: Sepsis (possibly related to study drug). Death date: 9/18/2021, 39 days since initiation of mFOLFOX6+Atezo.

Grade 5 AE, previously reported, does not contribute to the AE stopping rule:

- Arm 1 patient, CTCAE term: Death NOS (unrelated to study drug). Death date: 09/19/2019, 202 days since initiation of mFOLFOX6+Atezo.
- Arm 1 patient, CTCAE term: Infections and infestations - Oth spec (COVID-19 unrelated to study drug). Death date: 04/21/2020, 132 days since initiation of mFOLFOX6+Atezo.
- Arm 1 patient, CTCAE term: Death NOS (unlikely related to study drug). Death date: 1/11/2022, 106 days since initiation of mFOLFOX6+Atezo.
- Arm 1 patient, CTCAE term: Sudden Death NOS (unlikely related to study drug). Death date: 3/17/22, 365 days since initiation of mFOLFOX6+Atezo.
- Arm 2 patient, CTCAE term: Cardiac arrest (unrelated to study drug). Death date: 5/31/2018, 58 days since initiation of mFOLFOX6.
- Arm 2 patient, CTCAE term: Cardiac arrest (unrelated to study drug). Death date: 1/31/2021, 216 days since initiation of mFOLFOX6.

Number of Evaluable Patients Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329		
Patients with a maximum*:	**Arm**	**N (%)**
Total		
Grade 3 Event	Arm 1: mFOLFOX6 + atezo	220 (62.9%)
	Arm 2: mFOLFOX6 alone	203 (61.7%)
Grade 4 Event	Arm 1: mFOLFOX6 + atezo	61 (17.4%)
	Arm 2: mFOLFOX6 alone	32 (9.7%)
Grade 5 Event	Arm 1: mFOLFOX6 + atezo	6 (1.7%)
	Arm 2: mFOLFOX6 alone	2 (0.6%)
Hematologic Adverse Events		
Grade 3 Event	Arm 1: mFOLFOX6 + atezo	111 (31.7%)
	Arm 2: mFOLFOX6 alone	103 (31.3%)
Grade 4 Event	Arm 1: mFOLFOX6 + atezo	48 (13.7%)
	Arm 2: mFOLFOX6 alone	25 (7.6%)
Grade 5 Event	Arm 1: mFOLFOX6 + atezo	0 (0.0%)
	Arm 2: mFOLFOX6 alone	0 (0.0%)
Non-Hematologic Adverse Events		
Grade 3 Event	Arm 1: mFOLFOX6 + atezo	212 (60.6%)

Number of Evaluable Patients Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329		
Patients with a maximum*:	**Arm**	**N (%)**
	Arm 2: mFOLFOX6 alone	165 (50.2%)
Grade 4 Event	Arm 1: mFOLFOX6 + atezo	18 (5.1%)
	Arm 2: mFOLFOX6 alone	8 (2.4%)
Grade 5 Event	Arm 1: mFOLFOX6 + atezo	6 (1.7%)
	Arm 2: mFOLFOX6 alone	2 (0.6%)
Note: Summaries are based on available patient data		

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	**4-LifeThr**	**5-Lethal**
		N (%)	**N (%)**	**N (%)**
Hematologic Adverse Events				
Blood/Bone Marrow				
Anemia	Arm 1: mFOLFOX6 + atezo	12 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	11 (3%)	0 (0%)	0 (0%)
Blood and lymphatic system disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Leukocytosis	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Lymphocyte count decreased	Arm 1: mFOLFOX6 + atezo	9 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	4 (1%)	0 (0%)	0 (0%)
Neutrophil count decreased	Arm 1: mFOLFOX6 + atezo	101 (29%)	48 (14%)	0 (0%)
	Arm 2: mFOLFOX6 alone	93 (28%)	23 (7%)	0 (0%)
Platelet count decreased	Arm 1: mFOLFOX6 + atezo	7 (2%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	10 (3%)	3 (1%)	0 (0%)
White blood cell decreased	Arm 1: mFOLFOX6 + atezo	20 (6%)	4 (1%)	0 (0%)
	Arm 2: mFOLFOX6 alone	6 (2%)	1 (0%)	0 (0%)
Non-Hematologic Adverse Events				
Blood and lymphatic system disorders				
Febrile neutropenia	Arm 1: mFOLFOX6 + atezo	3 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	5 (2%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Cardiac disorders				
Atrial fibrillation	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Cardiac arrest	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	2 (1%)
Cardiac disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Chest pain - cardiac	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Heart failure	Arm 1: mFOLFOX6 + atezo	2 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Myocardial infarction	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Restrictive cardiomyopathy	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Sick sinus syndrome	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Supraventricular tachycardia	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ventricular fibrillation	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ear and labyrinth disorders				
Hearing impaired	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Middle ear inflammation	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Endocrine disorders				
Adrenal insufficiency	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Eye disorders				

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Eye disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Retinal detachment	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Gastrointestinal disorders				
Abdominal pain	Arm 1: mFOLFOX6 + atezo	16 (5%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	7 (2%)	0 (0%)	0 (0%)
Colitis	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Colonic obstruction	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Colonic ulcer	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Dental caries	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Diarrhea	Arm 1: mFOLFOX6 + atezo	42 (12%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	29 (9%)	0 (0%)	0 (0%)
Duodenal obstruction	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Duodenal ulcer	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Enterocolitis	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Esophagitis	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Gastric hemorrhage	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Gastrointestinal disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Gastrointestinal pain	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ileal obstruction	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ileus	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Jejunal ulcer	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Lower gastrointestinal hemorrhage	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Mucositis oral	Arm 1: mFOLFOX6 + atezo	10 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	4 (1%)	0 (0%)	0 (0%)
Nausea	Arm 1: mFOLFOX6 + atezo	16 (5%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	4 (1%)	0 (0%)	0 (0%)
Pancreatitis	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Rectal hemorrhage	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Small intestinal obstruction	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Typhlitis	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Upper gastrointestinal hemorrhage	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Vomiting	Arm 1: mFOLFOX6 + atezo	8 (2%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	4 (1%)	0 (0%)	0 (0%)
General disorders and administration site conditions				
Death NOS	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	2 (1%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Fatigue	Arm 1: mFOLFOX6 + atezo	31 (9%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
	Arm 2: mFOLFOX6 alone	10 (3%)	0 (0%)	0 (0%)
Fever	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Flu like symptoms	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Multi-organ failure	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Non-cardiac chest pain	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Pain	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Sudden death NOS	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	2 (1%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hepatobiliary disorders				
Cholecystitis	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hepatobiliary disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Portal vein thrombosis	Arm 1: mFOLFOX6 + atezo	2 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Immune system disorders				
Allergic reaction	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Anaphylaxis	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Infections and infestations				
Abdominal infection	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Device related infection	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
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Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Encephalitis infection	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Enterocolitis infectious	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Infections and infestations - Other, specify	Arm 1: mFOLFOX6 + atezo	5 (1%)	0 (0%)	1 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	1 (0%)	0 (0%)
Lung infection	Arm 1: mFOLFOX6 + atezo	6 (2%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Otitis media	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Penile infection	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Pharyngitis	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Sepsis	Arm 1: mFOLFOX6 + atezo	5 (1%)	1 (0%)	1 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Sinusitis	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Skin infection	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Upper respiratory infection	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Urinary tract infection	Arm 1: mFOLFOX6 + atezo	4 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Wound infection	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Injury, poisoning and procedural complications				
Fall	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
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Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Fracture	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hip fracture	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Infusion related reaction	Arm 1: mFOLFOX6 + atezo	5 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Injury, poisoning and procedural complications - Other, specify	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Vascular access complication	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Investigations				
Alanine aminotransferase increased	Arm 1: mFOLFOX6 + atezo	5 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Alkaline phosphatase increased	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Aspartate aminotransferase increased	Arm 1: mFOLFOX6 + atezo	11 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Blood bilirubin increased	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Cardiac troponin I increased	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Cholesterol high	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Creatinine increased	Arm 1: mFOLFOX6 + atezo	2 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ejection fraction decreased	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
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Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Electrocardiogram QT corrected interval prolonged	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Investigations - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Lipase increased	Arm 1: mFOLFOX6 + atezo	1 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Serum amylase increased	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Weight gain	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Weight loss	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Metabolism and nutrition disorders				
Anorexia	Arm 1: mFOLFOX6 + atezo	9 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Dehydration	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Hyperglycemia	Arm 1: mFOLFOX6 + atezo	6 (2%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	4 (1%)	0 (0%)	0 (0%)
Hyperkalemia	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hypertriglyceridemia	Arm 1: mFOLFOX6 + atezo	2 (1%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Hypoalbuminemia	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Hypocalcemia	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Hypoglycemia	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
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Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Hypokalemia	Arm 1: mFOLFOX6 + atezo	28 (8%)	3 (1%)	0 (0%)
	Arm 2: mFOLFOX6 alone	15 (5%)	0 (0%)	0 (0%)
Hypomagnesemia	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Hyponatremia	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hypophosphatemia	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Metabolism and nutrition disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Obesity	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Musculoskeletal and connective tissue disorders				
Arthralgia	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Back pain	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Chest wall pain	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Flank pain	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Generalized muscle weakness	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Muscle cramp	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Myalgia	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Pain in extremity	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
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Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Neoplasms benign, malignant and unspecified (incl cysts and polyps) - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Nervous system disorders				
Dizziness	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Dysesthesia	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	3 (1%)	0 (0%)	0 (0%)
Encephalopathy	Arm 1: mFOLFOX6 + atezo	1 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Headache	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Intracranial hemorrhage	Arm 1: mFOLFOX6 + atezo	1 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Muscle weakness left-sided	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Nervous system disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Paresthesia	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	9 (3%)	0 (0%)	0 (0%)
Peripheral motor neuropathy	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	5 (2%)	0 (0%)	0 (0%)
Peripheral sensory neuropathy	Arm 1: mFOLFOX6 + atezo	66 (19%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	50 (15%)	0 (0%)	0 (0%)
Seizure	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Stroke	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)

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Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Syncope	Arm 1: mFOLFOX6 + atezo	10 (3%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	7 (2%)	0 (0%)	0 (0%)
Vasovagal reaction	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Pregnancy, puerperium and perinatal conditions				
Pregnancy loss	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Psychiatric disorders				
Confusion	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	0 (0%)	0 (0%)
Delirium	Arm 1: mFOLFOX6 + atezo	1 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Insomnia	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Psychiatric disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Psychosis	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Renal and urinary disorders				
Acute kidney injury	Arm 1: mFOLFOX6 + atezo	9 (3%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Chronic kidney disease	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Hematuria	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Renal and urinary disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	0 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Renal calculi	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
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Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
Reproductive system and breast disorders				
Dyspareunia	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Ovarian rupture	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Respiratory, thoracic and mediastinal disorders				
Aspiration	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Cough	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Dyspnea	Arm 1: mFOLFOX6 + atezo	5 (1%)	2 (1%)	0 (0%)
	Arm 2: mFOLFOX6 alone	2 (1%)	1 (0%)	0 (0%)
Hypoxia	Arm 1: mFOLFOX6 + atezo	4 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Laryngopharyngeal dysesthesia	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Respiratory failure	Arm 1: mFOLFOX6 + atezo	0 (0%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	1 (0%)	0 (0%)
Respiratory, thoracic and mediastinal disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Wheezing	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Skin and subcutaneous tissue disorders				
Palmar-plantar erythrodysesthesia syndrome	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	6 (2%)	0 (0%)	0 (0%)
Pruritus	Arm 1: mFOLFOX6 + atezo	2 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Rash maculo-papular	Arm 1: mFOLFOX6 + atezo	3 (1%)	0 (0%)	0 (0%)

Listing of Grade 3+ Adverse Events
Max Grade per Patient Per Event
Regardless of Attribution
Number of Evaluable Patients
Arm 1: mFOLFOX6 + atezo=350 Arm 2: mFOLFOX6 alone=329

		Grade of Adverse Event		
		3-Severe	4-LifeThr	5-Lethal
		N (%)	N (%)	N (%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Skin and subcutaneous tissue disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Urticaria	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Surgical and medical procedures				
Surgical and medical procedures - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)
Vascular disorders				
Hypertension	Arm 1: mFOLFOX6 + atezo	24 (7%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	38 (12%)	0 (0%)	0 (0%)
Hypotension	Arm 1: mFOLFOX6 + atezo	5 (1%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	0 (0%)	0 (0%)	0 (0%)
Thromboembolic event	Arm 1: mFOLFOX6 + atezo	11 (3%)	1 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	10 (3%)	2 (1%)	0 (0%)
Vascular disorders - Other, specify	Arm 1: mFOLFOX6 + atezo	1 (0%)	0 (0%)	0 (0%)
	Arm 2: mFOLFOX6 alone	1 (0%)	0 (0%)	0 (0%)

10.0 IMBEDDED CORRELATIVES

Mandatory Sample Collection Biomarker Studies – dMMR Concordance Analysis

- Number of Consented Patients at Enrollment: 712(100%)
- Current Status: Samples are being collected on all patients and sent to a central laboratory for dMMR confirmation testing. Patient data is being sent to Alliance SDC monthly.

Optional Quality of Life Study in Alliance A021502: A021502-HO1

- Number of Consented Patients at Enrollment: 580 (81%)
- Current Status: Since enrollment 19 patients have withdrawn consent. QOL booklets are being collected on consented 561 (79%) patients at various time points.

Optional (A021502-PP1 and A021502-ST1) Sample Collection Biomarker Studies

- Number of Consented Patients at Enrollment:
  - PP1 (Blood): 554 (78%)
  - ST1 (Blood): 554 (78%)

- ST1 (Tissue): 552 (78%)
- ST1 (Stool): 372 (52%)

- Current Status: Samples are being collected on all consented patients. Alliance SDC is working with BIOMS to track samples, and make sure specimen submission is up to date. Number of patients with consent intact for specimens:
  - PP1 (Blood): 528 (74%)
  - ST1 (Blood): 528 (74%)
  - ST1 (Tissue): 536 (75%)
  - ST1 (Stool): 338 (47%)