



Targeting RAS-mutated Metastatic Colorectal Cancer with a Selective PLK1 Inhibitor

SEPTEMBER 2026

Forward-looking statements

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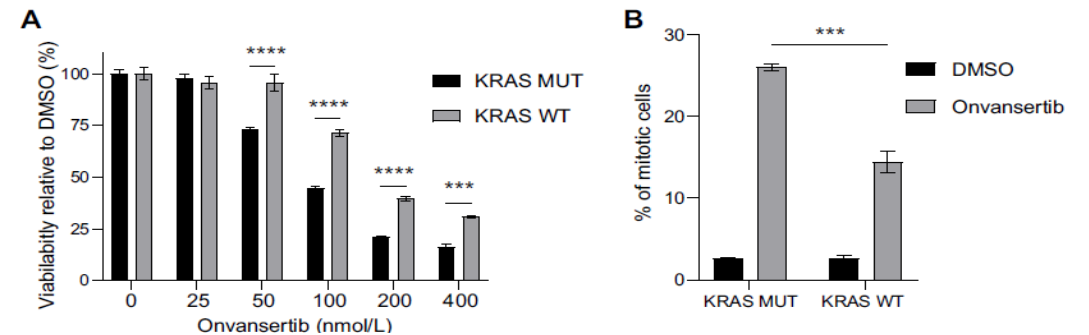
harm our financial condition and increase our costs and expenses; uncertainties of government or third party payer reimbursement; dependence on key personnel; limited experience in marketing and sales; substantial competition; uncertainties of patent protection and litigation; dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. There are no guarantees that our product candidate will be utilized or prove to be commercially successful. Additionally, there are no guarantees that future clinical trials will be completed or successful or that our product candidate will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in our Form 10-K for the year ended December 31, 2025, and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and we do not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Targeting PLK1-dependent mitotic vulnerability of RAS mutant colorectal cancer

Mechanistic rationale

- 1 Genome-wide RNAi screen identified multiple mitotic proteins, including PLK1 (a key regulator of mitosis), as synthetic lethal dependencies in RAS-mutant cells.¹
- 2 PLK1 depletion or inhibition preferentially impaired KRAS-mutant CRC cells and increased mitotic arrest.^{1,2}
- 3 Hypothesis: oncogenic RAS increases mitotic stress, creating greater dependence on PLK1-controlled mitotic progression.

Onvansertib confirms KRAS-mutant dependency in isogenic CRC cells²



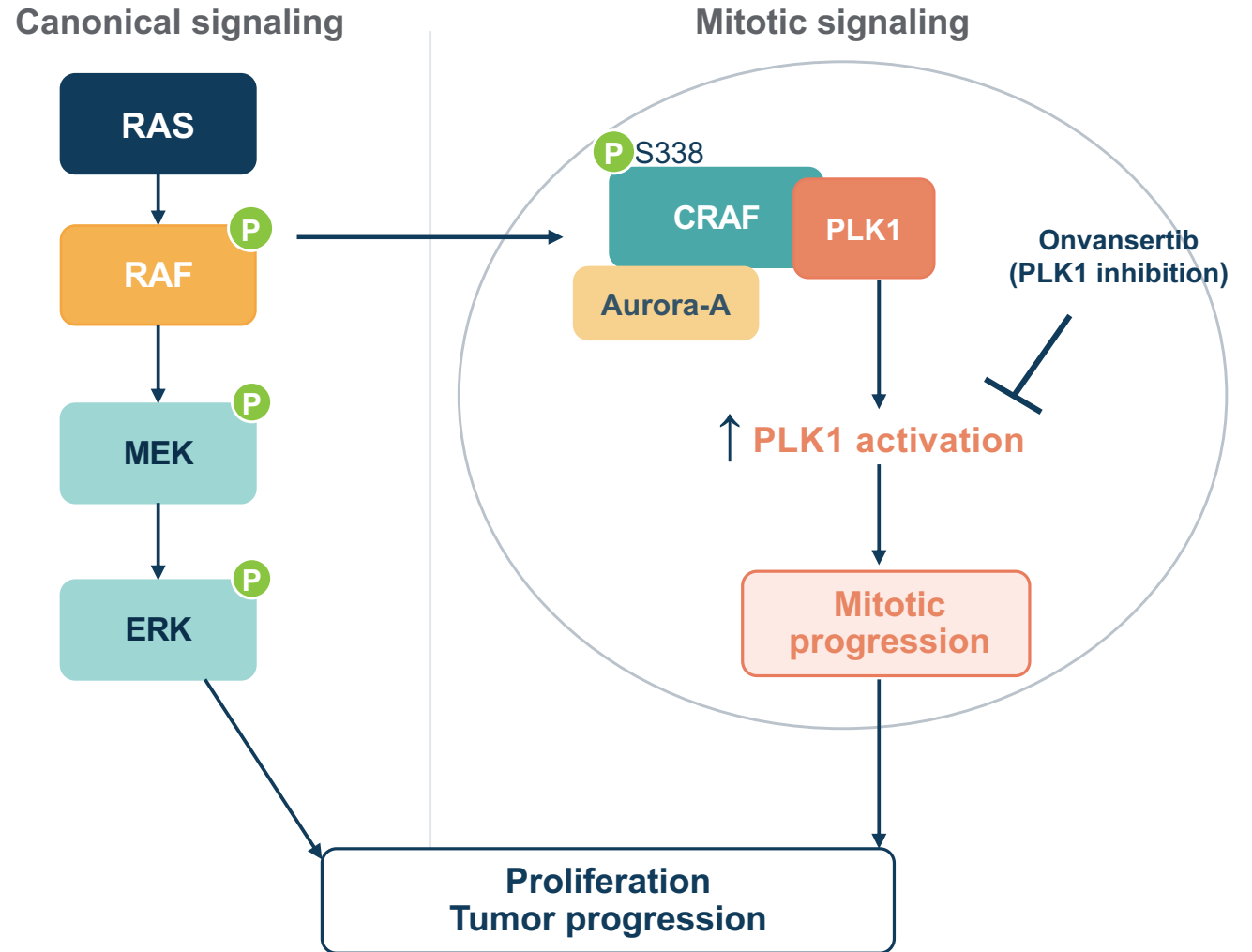
Greater loss of viability and mitotic accumulation in KRAS-mutant versus KRAS-WT DLD1 cells



CRAF provides a MEK/ERK-independent link from RAS signaling to PLK1

Mielgo et al. mechanism¹

- 1 pSer338 CRAF localizes to centrosomes and spindle poles during G2/M.
- 2 CRAF associates with kinases such as Aurora-A and PLK1, promoting PLK1 activation and kinetochore accumulation.
- 3 This mitotic signaling pathway operates beyond canonical RAF–MEK–ERK signaling and further supports mitotic/tumor progression.



Onvansertib: highly selective, clinical stage PLK1 inhibitor for first-line RAS-mutant metastatic colorectal cancer (mCRC)

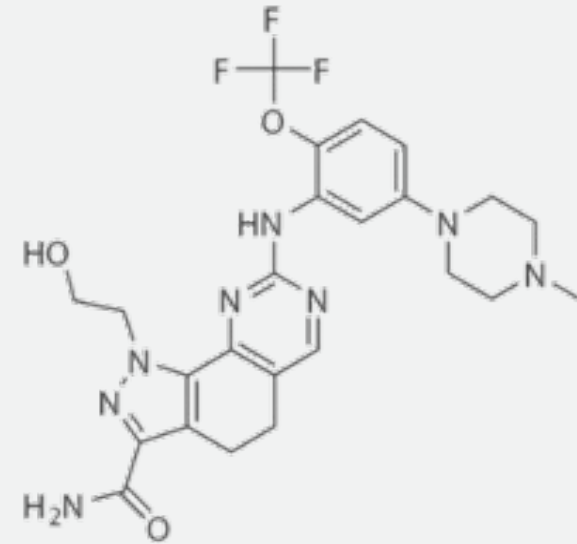
SPECIFICITY

Exquisitely specific for PLK1

ENZYME	IC ₅₀ (μM)
PLK1	0.002
PLK2	>10
PLK3	>10
CK2	0.4
FLT3	0.4
CDK1/CycB	>10
42 other kinases and >140 in the Millipore panel	>10

PROPERTIES

- Small molecule
- Oral dosing
- 24-hour half-life



Onvansertib: highly selective PLK1 inhibitor with practice-changing potential in first-line RAS-mut mCRC

Strong Efficacy in RAS-mutated mCRC

- 72% ORR in randomized first-line Ph 2 trial, 30% absolute ORR improvement over SoC; median PFS not reached vs 12.2 months in SoC*
- Synergy with FOLFIRI/bev in RAS-mut mCRC with a favorable safety profile
- Confirms earlier efficacy shown in Ph 1b/2 trial in second-line KRAS-mut mCRC in bev-naïve patients

Large Commercial Opportunity

- First-line RAS-mutated mCRC, is an area of high unmet need and limited innovation
- Practice-changing potential in large, underserved populations
- Opportunity for market expansion, including in rare RAS-driven cancers such as CMML

Clear Registrational Path

- Successful End-of-Phase 2 FDA meeting: aligned on the registrational trial in first-line RAS-mutated mCRC
- Dose and chemo regimen selected: 30 mg onvansertib + FOLFIRI/bev
- Ph 3 designed to allow for Accelerated Approval (ORR) and full approval (PFS)

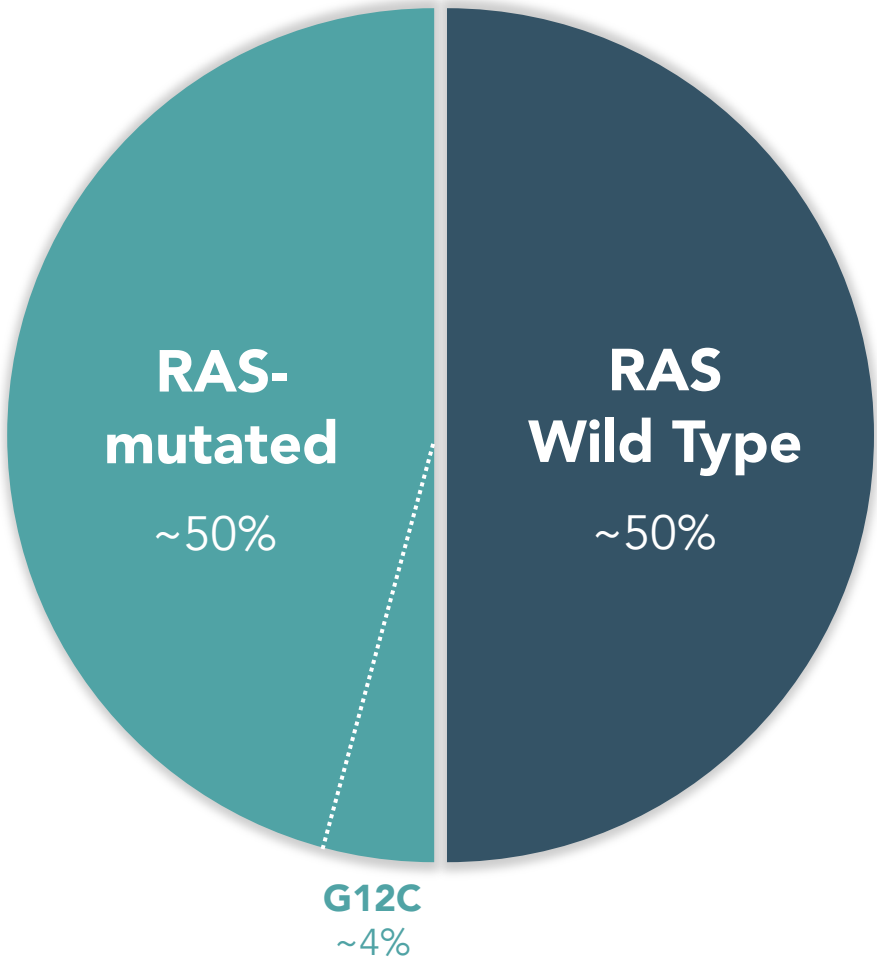
ORR reflects BICR. PFS reflects Investigator Assessment

ORR: Objective Response Rate; PFS: Progression Free Survival; BICR: Blinded Independent Central Review

Positioned to address the first-line RAS-mutated mCRC market

~150,000 newly diagnosed CRC patients in U.S.; 20% present metastatic disease*

Blockbuster potential:
Onvansertib targets **All RAS-mut mCRC**



1st Line Standard-of-Care Remains Unchanged for Two Decades

Chemotherapy + Bevacizumab
(FOLFOX/FOLFIRI/FOLFOXIRI) (Avastin®)

No approvals specific to panRAS-mut mCRC

For patients with mCRC

15%
5-year relative OS

Less than 12 months
median PFS

*American Cancer Society; NCI SEER database
CRC, colorectal cancer; mCRC, metastatic colorectal cancer



ONVANSERTIB

FIRST-LINE RAS-MUTATED mCRC

Mechanistic Rationale for FOLFIRI/bev Combination

Positive Data from the Phase 2 CRDF-004 Trial

Broader Opportunity

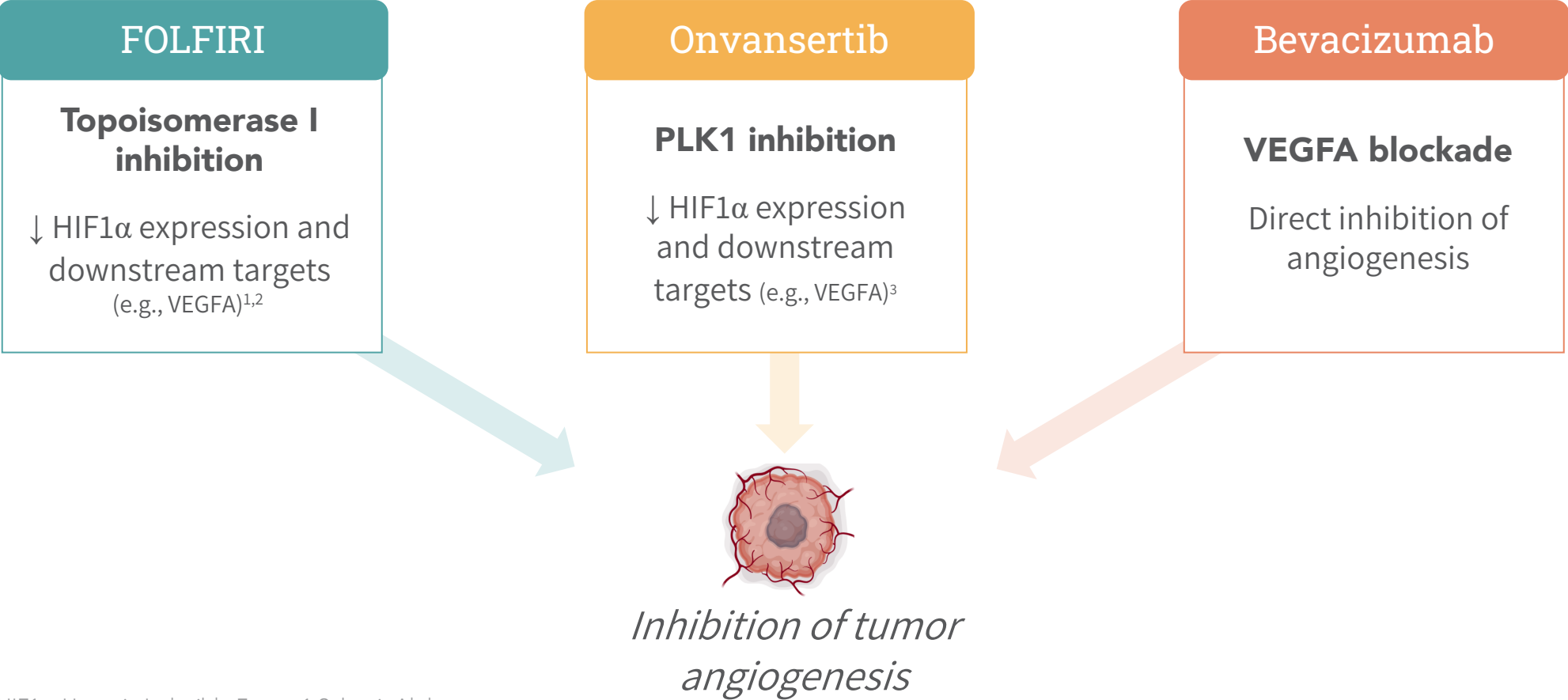
Multiple onvansertib MOAs underlie our focus on RAS-mutated mCRC

Two clinical studies demonstrated improved outcomes with FOLFIRI/bev in bev-naïve patients, validating the combination approach

Onvansertib targets RAS-mutated mCRC in three potential ways

- | | | |
|---|---|--|
| 1 | Synthetic lethality in RAS-mut background | RAS-mut mCRC tumor cells are hypersensitive to onvansertib |
| 2 | Synergy with FOLFIRI chemo | Onvansertib inhibits repair of chemo-induced DNA damage |
| 3 | Synergy with bevacizumab | Onvansertib inhibits creation of new blood vessels |

Combination rationale further supported by synergistic anti-angiogenic effects of FOLFIRI, onvansertib, and bev



Bev, bevacizumab; HIF1α, Hypoxia Inducible Factor 1 Subunit Alpha

1. Rapisarda et al., Cancer Res 2004 Oct 1;64(19); 2. Rapisarda et al., Cancer Res. 2002 Aug 1;62(15); 3. Ahn et al., J Clin Oncol. 2025 Mar;43(7)

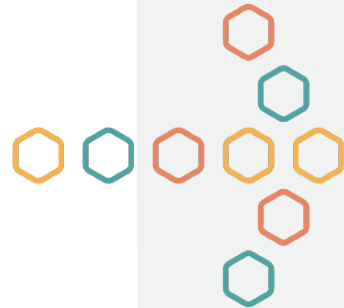
ONVANSERTIB

FIRST-LINE RAS-MUTATED mCRC

Mechanistic Rationale for FOLFIRI/bev Combination

Positive Data from the Phase 2 CRDF-004 Trial

Broader Opportunity



Ph 1b/2 trial in second-line KRAS-mutated mCRC combined onvansertib with FOLFIRI+bev

ENROLLMENT CRITERIA

Second-line mCRC

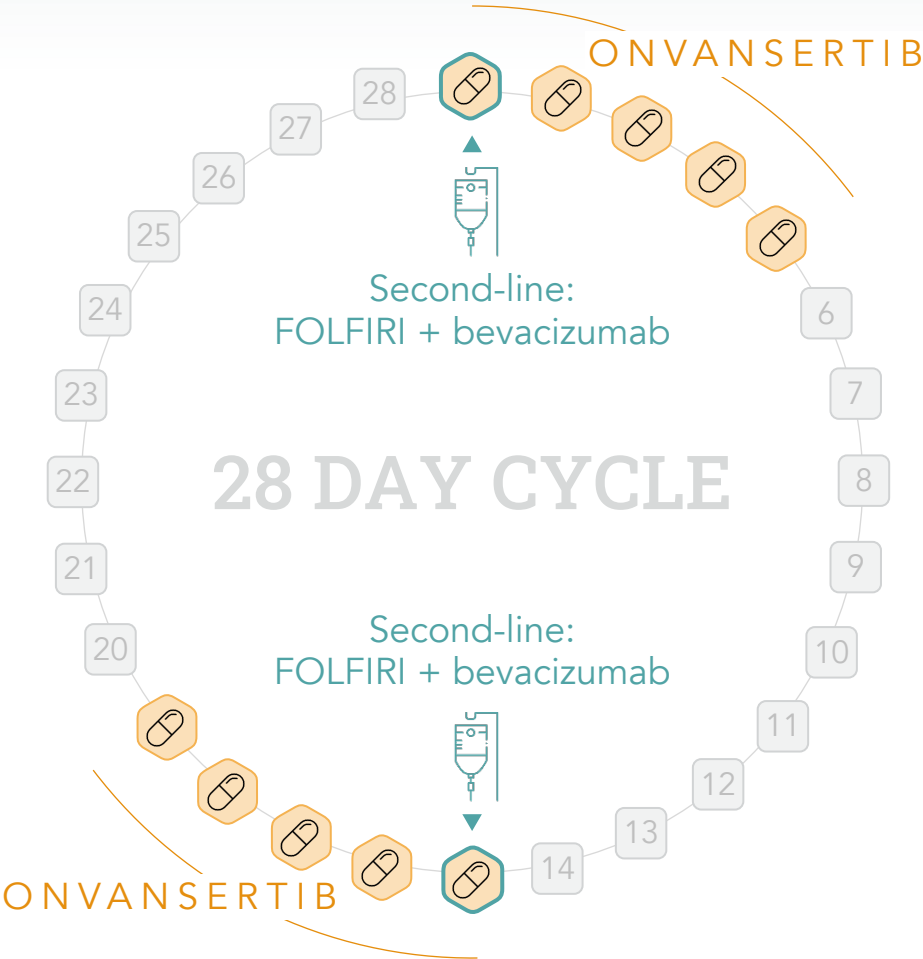
KRAS+

Unresectable

N=68

ENDPOINTS

Primary: ORR
Secondary: DoR and PFS



Patient's tumors are scanned every 8 weeks

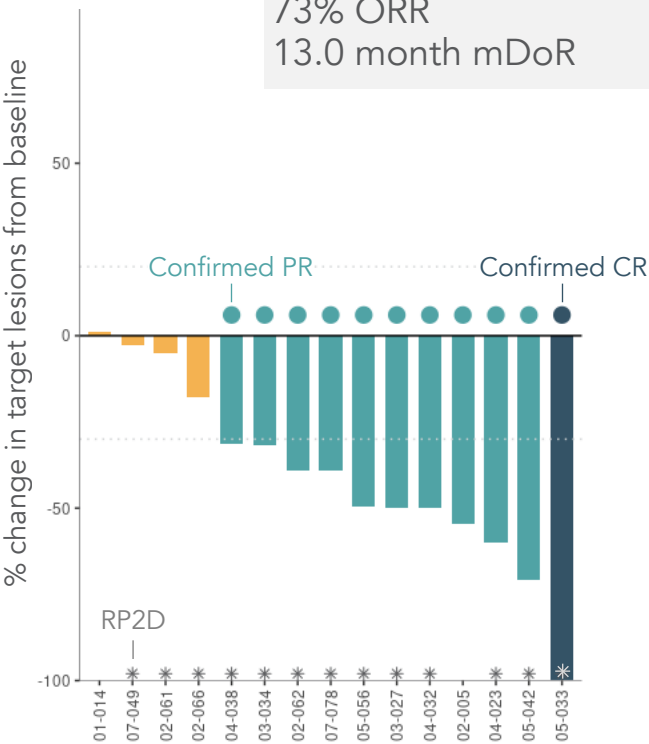
Ph 1b/2 trial: Bev-naïve patients treated with onvansertib + FOLFIRI/bev achieved higher response rates

Best Radiographic Response and Duration of Response*

66 evaluable patients (as of June 16, 2023)

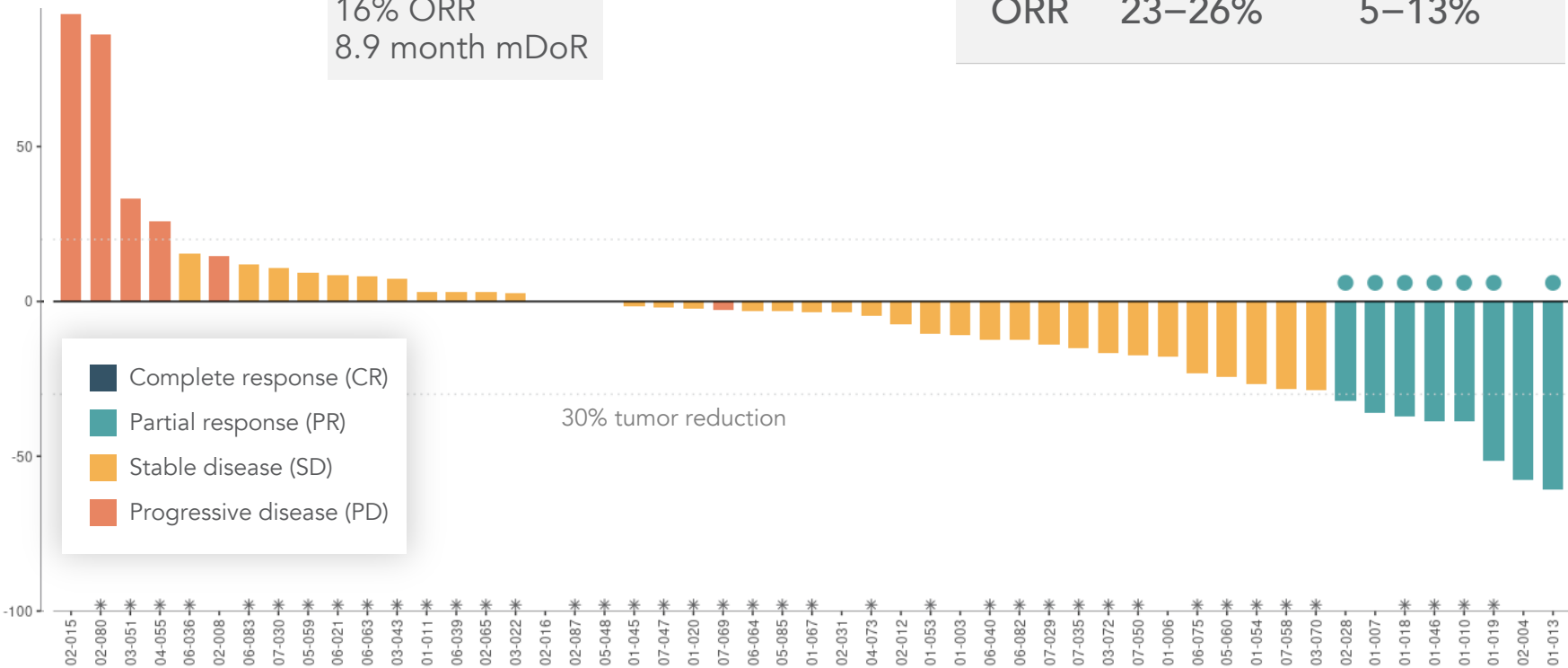
Bev-naïve: 15 of 66 patients (23%)

73% ORR
13.0 month mDoR



Bev-exposed: 51 of 66 (77%)

16% ORR
8.9 month mDoR



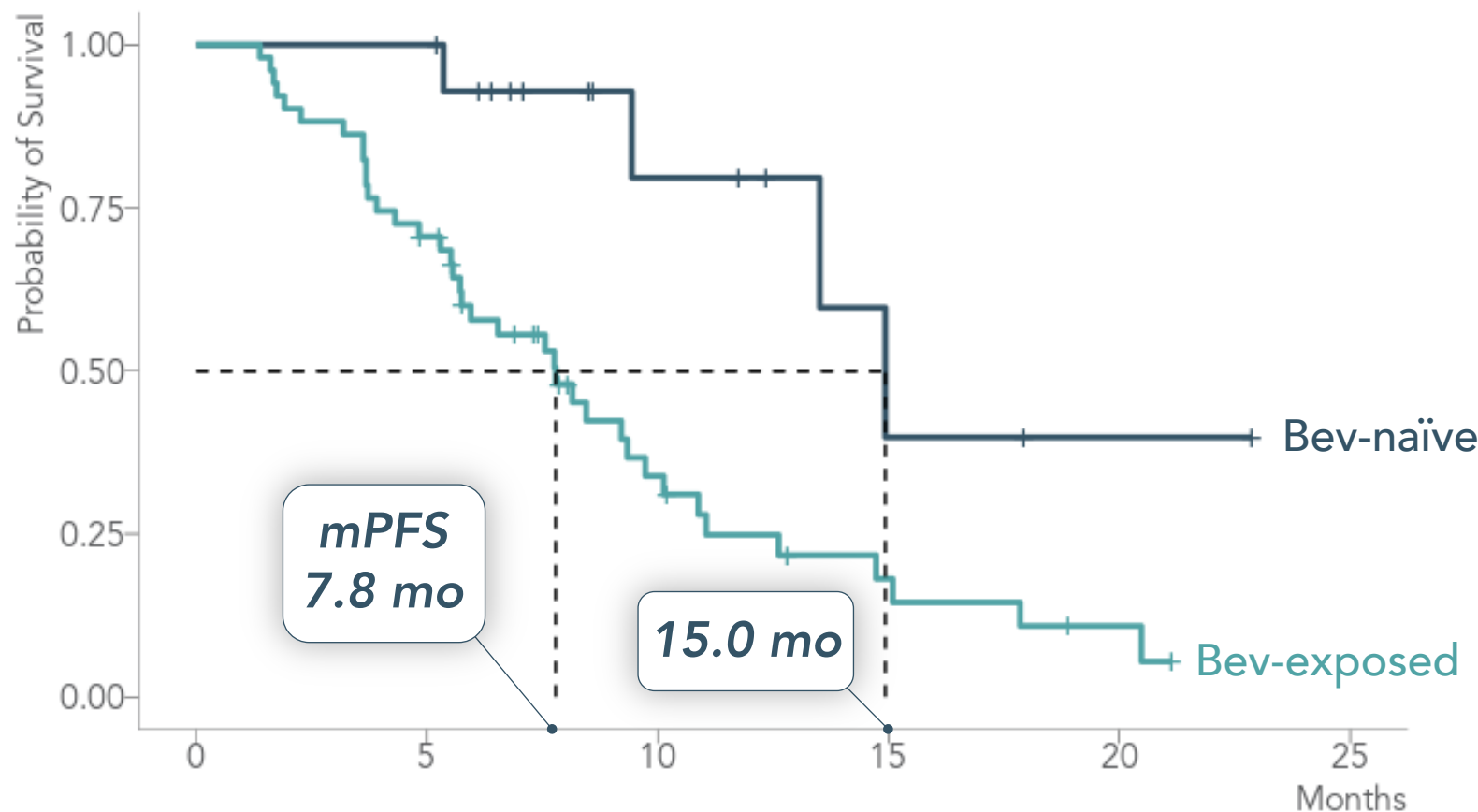
	Historical controls**	
	Bev-naïve	Bev-exposed
ORR	23–26%	5–13%

Bev, bevacizumab; ORR, objective response rate; DoR, duration of response; RP2D, recommended phase 2 dose
*Radiographic response determined per RECIST 1.1. Waterfall plot and table reflect interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database.
*Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187–193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539–1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al., Med Oncol 2013, 30:486.

Ph 1b/2 trial: Bev-naïve patients treated with onvansertib + FOLFIRI/bev achieved higher mPFS

Progression-free survival*

66 evaluable patients (as of June 16, 2023)



	Historical controls**	
	Bev naïve	Bev exposed
mPFS (mo)	6.9–8.5	4.5–6.7

*Onvansertib mPFS are interim data as of June 16, 2023 from an ongoing trial and unlocked EDC database. PFS, progression free survival; bev, bevacizumab; mo, months

** Bennouna et al., Lancet Oncol 2013; 14: 29–37; Giessen et al., Acta Oncologica, 2015, 54: 187–193; Cremolini et al., Lancet Oncol 2020, 21: 497–507; Antoniotti et al., Correspondence Lancet Oncol June 2020. Giantonio et al., 2007, J Clin Oncol 25:1539–1544; Moriwaki et al., Med Oncol, 2012, 29:2842–2848; Beretta et al., Med Oncol 2013, 30:486.

CRDF-004: dose-finding, randomized, controlled Phase 2 trial in first-line patients with RAS-mutated mCRC

ENROLLMENT CRITERIA

- First-line mCRC
- KRAS+/NRAS+
- No BRAF-V600 or MSI-H/dMMR
- Unresectable
- No prior bev

R

ITT=110

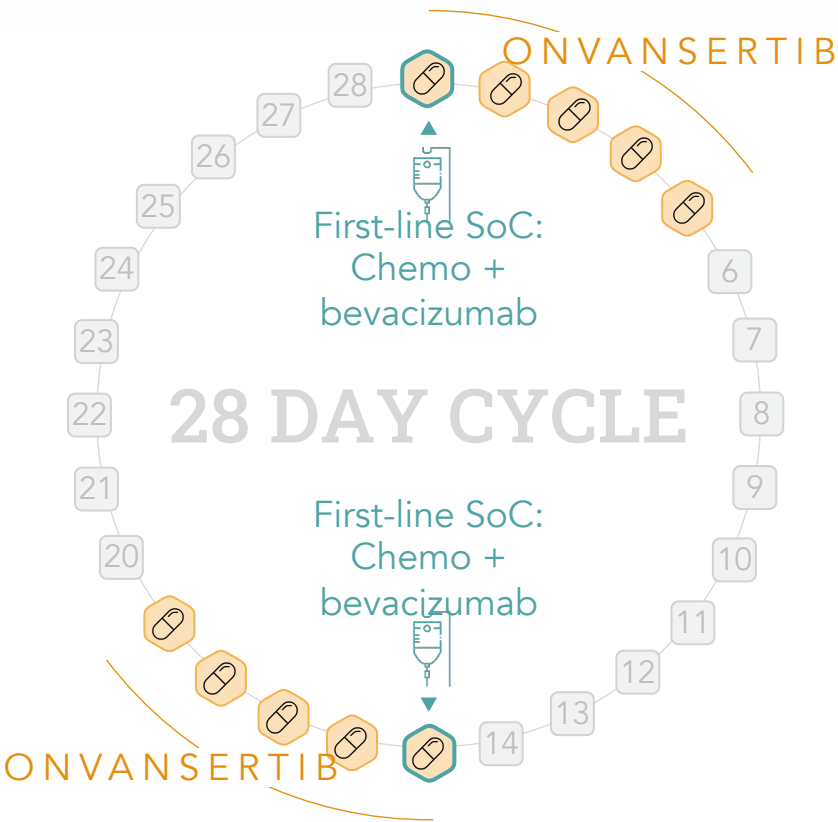
6 RANDOMIZATION ARMS

SoC alone	1. FOLFIRI/bev 2. FOLFOX/bev
Onv 20mg +	3. FOLFIRI/bev 4. FOLFOX/bev
Onv 30mg +	5. FOLFIRI/bev 6. FOLFOX/bev

ENDPOINTS*

Primary: ORR
Secondary: DoR and PFS

* Assessed by blinded independent central review (BICR)



Trial conducted in partnership with Pfizer Ignite, an end-to-end service for biotech companies

mCRC: metastatic colorectal cancer; ORR: objective response rate; DoR: duration of response; PFS: progression free survival; SoC: standard of care; onv: onvansertib; bev: bevacizumab

Demographics and baseline characteristics

	FOLFIRI/bev (N=19)	Onv 20 mg + FOLFIRI/bev (N=18)	Onv 30 mg + FOLFIRI/bev (N=18)	FOLFOX/bev (N=18)	Onv 20 mg + FOLFOX/bev (N=18)	Onv 30 mg + FOLFOX/bev (N=19)
Age (years)						
Mean (SD)	55.41 (14.34)	52.41 (13.13)	59.67 (12)	56.24 (12.04)	59.41 (14.5)	60.11 (14.1)
Median (Min, Max)	53 (32, 81)	52 (30, 78)	60 (34, 81)	57 (34, 82)	66 (34, 79)	59.5 (39, 86)
ECOG						
0	6 (31.6%)	13 (72.2%)	11 (61.1%)	7 (38.9%)	10 (55.6%)	11 (57.9%)
1	11 (57.9%)	4 (22.2%)	7 (38.9%)	10 (55.6%)	7 (38.9%)	7 (36.8%)
Stage at initial diagnosis*						
STAGE IV	9 (47.4%)	10 (55.6%)	14 (77.8%)	9 (50.0%)	11 (61.1%)	13 (68.4%)
STAGE III	4 (21.1%)	4 (22.2%)	2 (11.1%)	6 (33.3%)	2 (11.1%)	3 (15.8%)
STAGE II	3 (15.8%)	2 (11.1%)	2 (11.1%)	2 (11.1%)	3 (16.7%)	1 (5.3%)
STAGE I	0	1 (5.6%)	0	0	1 (5.6%)	1 (5.3%)
Side of tumor						
RIGHT	5 (26.3%)	8 (44.4%)	6 (33.3%)	8 (44.4%)	7 (38.9%)	7 (36.8%)
LEFT	6 (31.6%)	7 (38.9%)	6 (33.3%)	5 (27.8%)	8 (44.4%)	4 (21.1%)
BILATERAL	6 (31.6%)	2 (11.1%)	6 (33.3%)	4 (22.2%)	2 (11.1%)	7 (36.8%)
Liver metastasis at study entry						
Yes	10 (52.6%)	10 (55.6%)	14 (77.8%)	10 (55.6%)	12 (66.7%)	14 (73.7%)
No	7 (36.8%)	7 (38.9%)	4 (22.2%)	7 (38.9%)	5 (27.8%)	4 (21.1%)
Liver only disease						
No	15 (78.9%)	15 (83.3%)	11 (61.1%)	14 (77.8%)	16 (88.9%)	15 (78.9%)
Yes	2 (10.5%)	2 (11.1%)	7 (38.9%)	3 (16.7%)	1 (5.6%)	3 (15.8%)
Number of metastatic organs						
Multiple	11 (57.9%)	9 (50.0%)	9 (50%)	9 (50.0%)	13 (72.2%)	15 (78.9%)
Single	6 (31.6%)	8 (44.4%)	9 (50%)	8 (44.4%)	4 (22.2%)	3 (15.8%)
Prior adjuvant or neo-adjuvant chemo						
No	13 (68.4%)	12 (66.7%)	14 (77.8%)	12 (66.7%)	12 (66.7%)	16 (84.2%)
Yes	4 (21.1%)	5 (27.8%)	4 (22.2%)	5 (27.8%)	5 (27.8%)	2 (10.5%)

*Missing in one patient

As of the March 18, 2026 data cut-off, 13 of 14 remaining patients continue on onvansertib + SoC chemo/bev

Population, n	FOLFIRI/bev	Onv 20mg + FOLFIRI/bev	Onv 30mg + FOLFIRI/bev	FOLFOX/bev	Onv 20mg + FOLFOX/bev	Onv 30mg + FOLFOX/bev	Total
Intent-to-treat (ITT)	19	18	18	18	18	19	110
Safety population (dosed)	17	17	18	17	17	18	104
Patients still on study treatment	1	5	4	0	3	1	14

Onv 30 mg + FOLFIRI/bev delivers superior ORR & depth of response: 30% improvement in ORR over FOLFIRI/bev

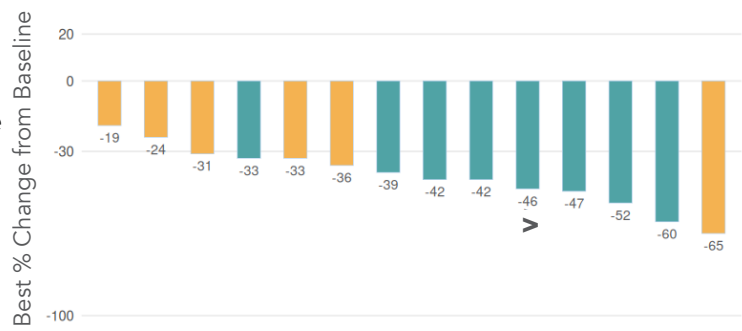
Objective Response Rate (per BICR) - ITT Analysis

FOLFIRI/bev
(n=19)

Confirmed ORR (n)
42.1% (8/19)

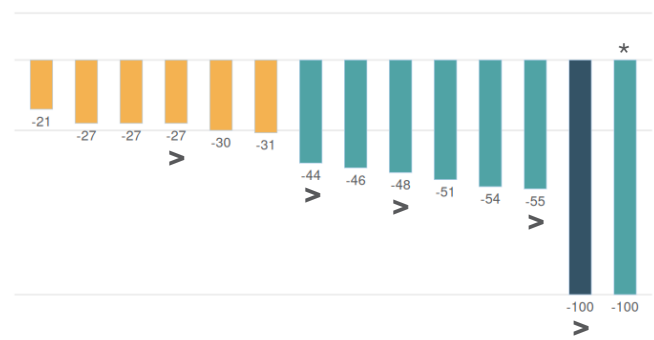
■ CR
■ PR
■ Stable
■ Progressive Disease

> On Treatment



Onv 20 mg + FOLFIRI/bev
(n=18)

Confirmed ORR (n)
44.4% (8/18)

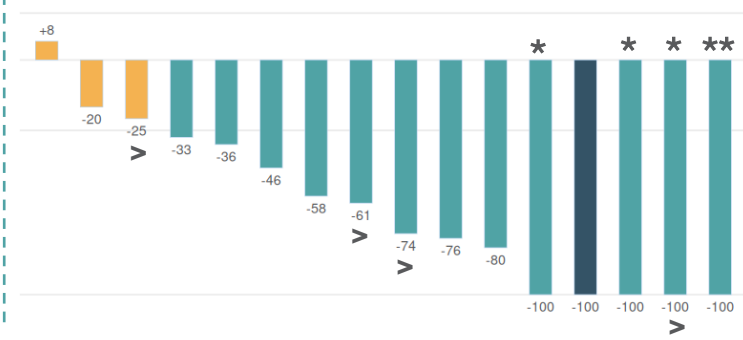


Onv 20 mg/Onv 30 mg + FOLFIRI/bev
(n=36)

Combined ORR: 58.3% (21)

Onv 30 mg + FOLFIRI/bev
(n=18)

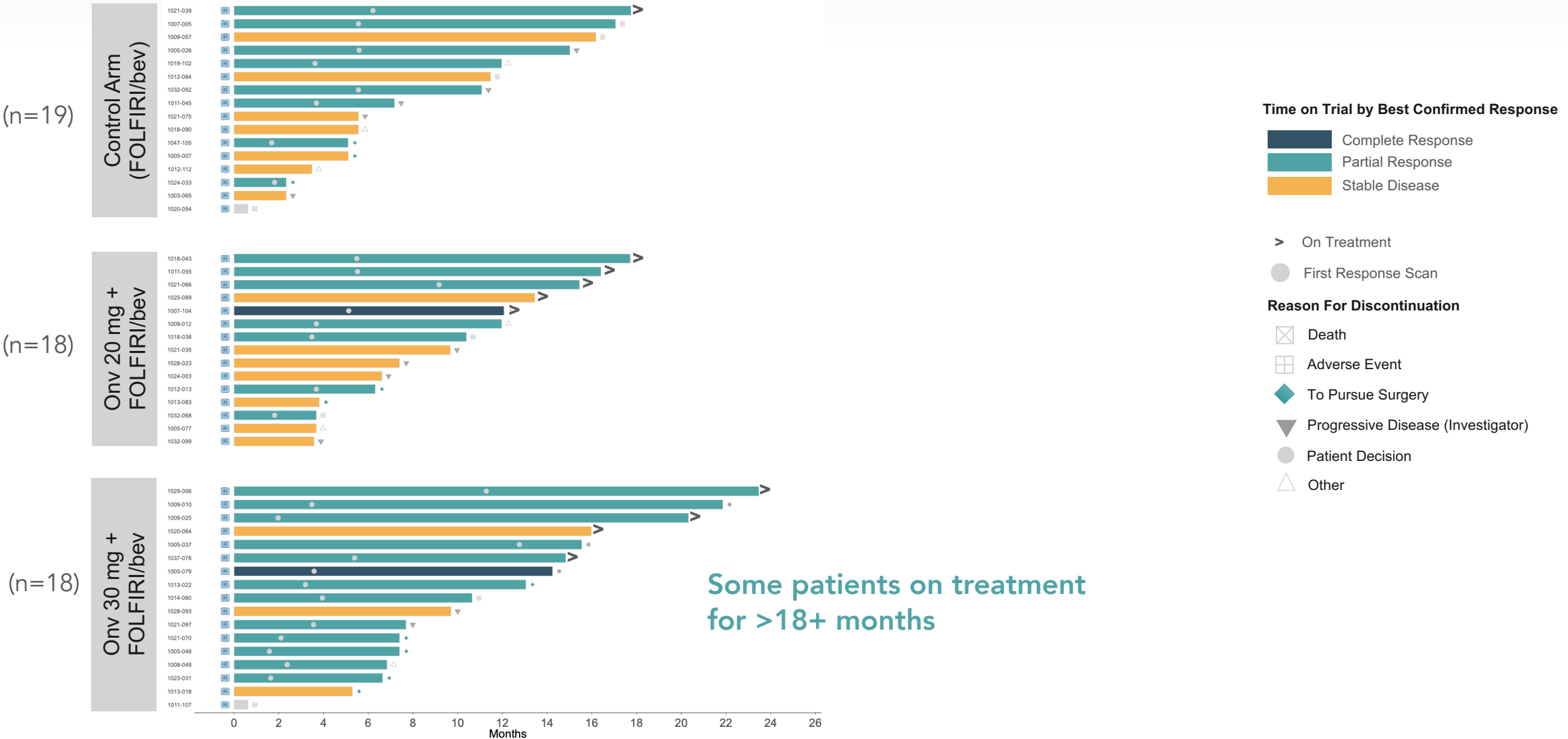
Confirmed ORR (n)
72.2% (13/18)



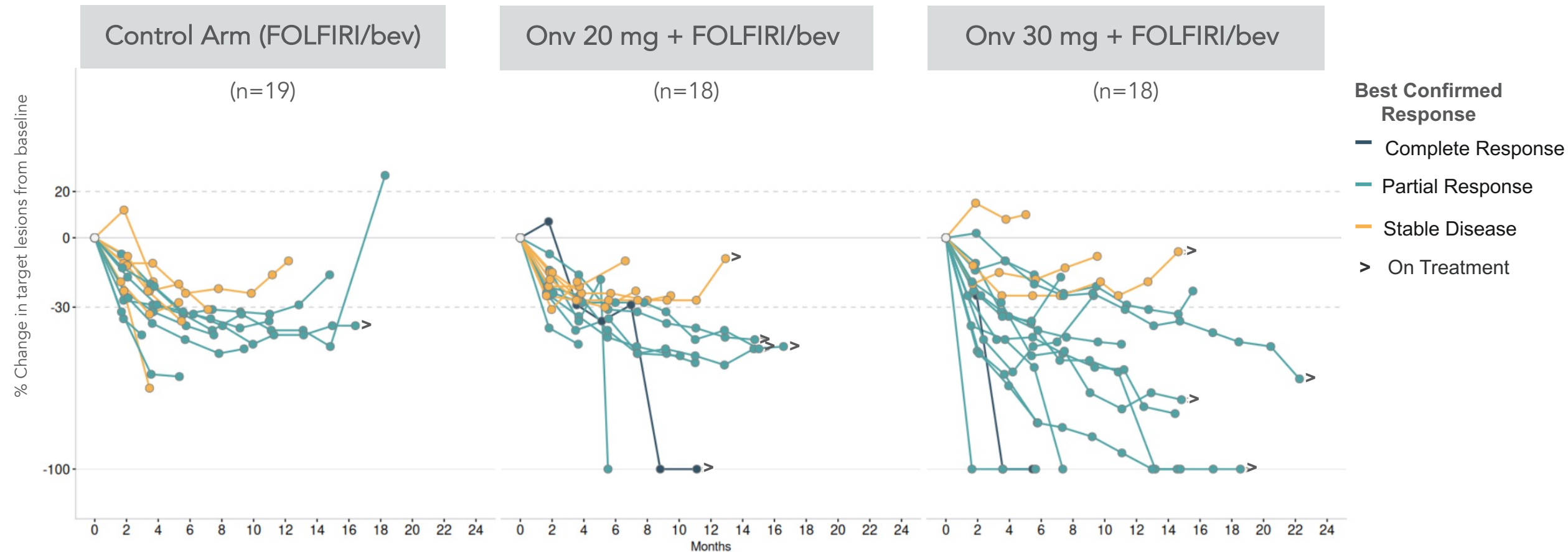
Data cutoff: March 18, 2026
** CR at last assessment; unconfirmed due to discontinuation for curative surgery
* Residual non-target disease (Non-CR/Non-PD)
Patients that are not-evaluative or do not have target lesions are not shown in the plots

Onv 30 mg + FOLFIRI/bev demonstrates longer duration of treatment

9 of 10 remaining patients on onv + FOLFIRI/bev

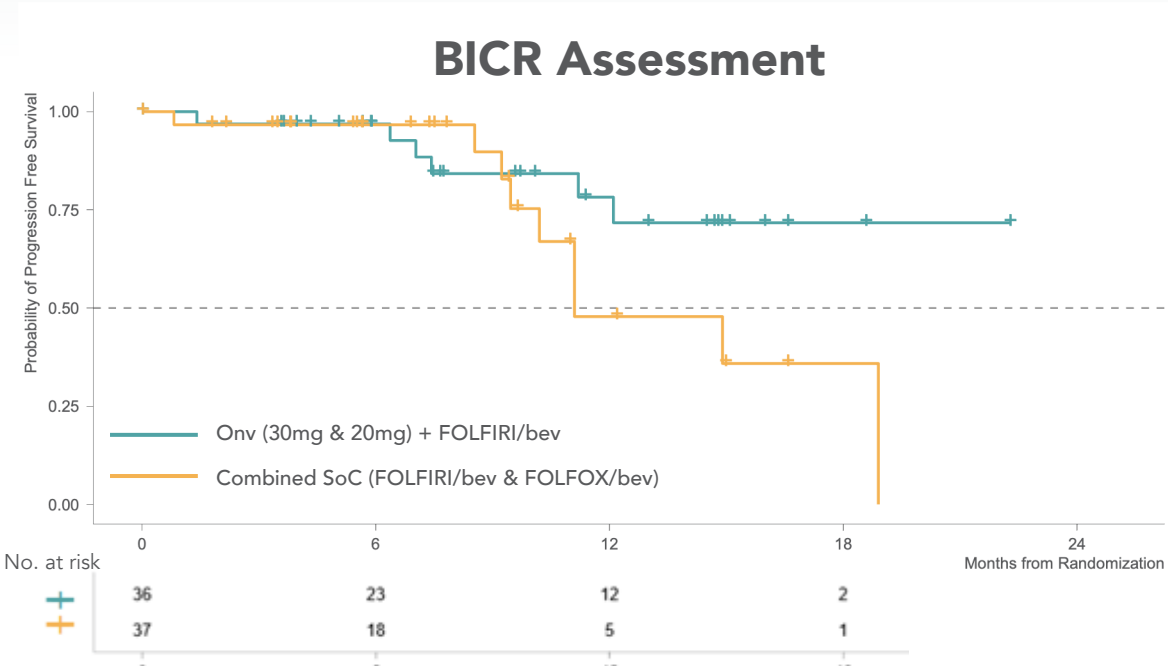


Onv 30 mg + FOLFIRI/bev demonstrates deep and durable tumor shrinkage over time

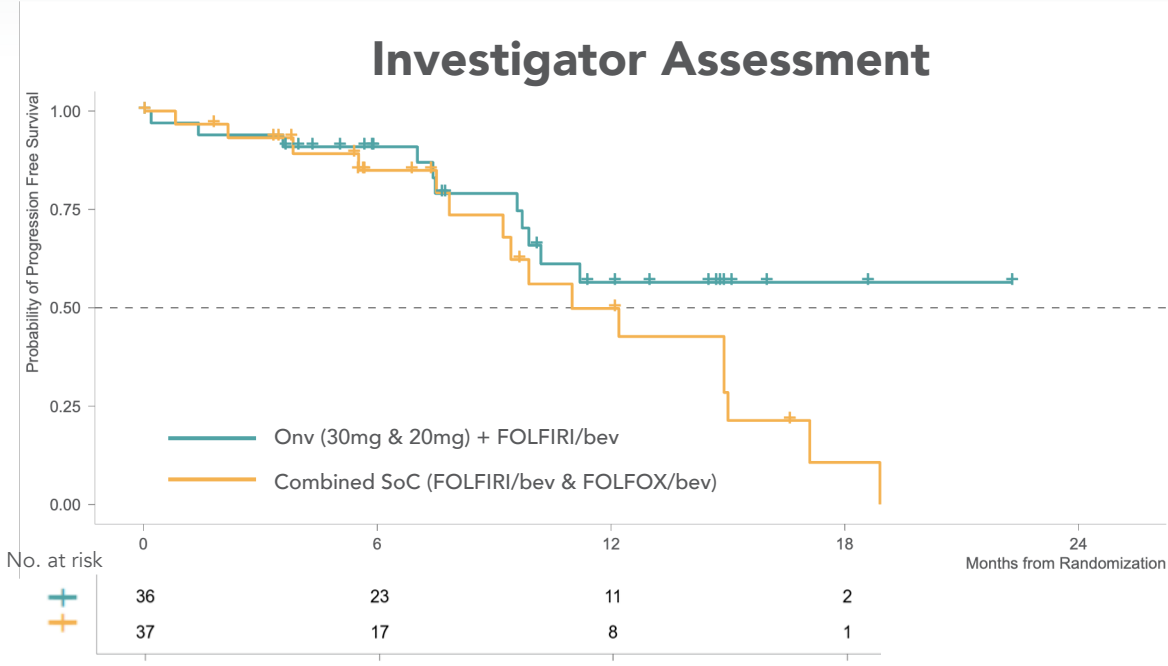


Data cutoff: March 18, 2026
Patients that are not-evaluable or do not have target lesions are not shown in the plots.

Onv (20 & 30 mg) + FOLFIRI/bev shows improved PFS vs SoC (FOLFIRI/bev & FOLFOX/bev)

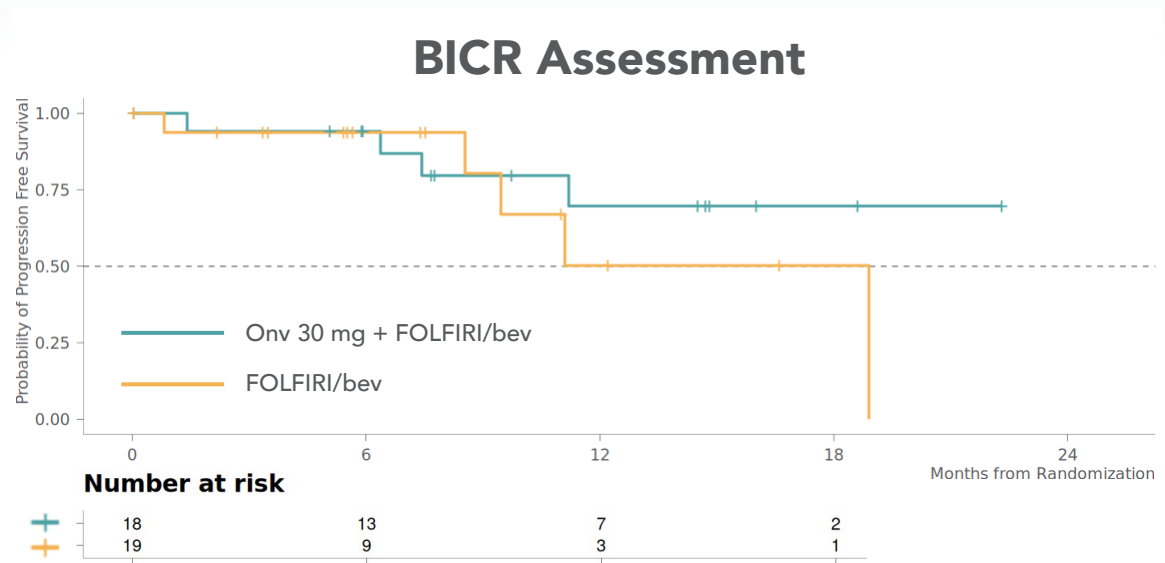


	FOLFIRI/bev + FOLFOX/bev	Onv (20 & 30mg) + FOLFIRI/bev
N	37	36
Median PFS	11.07	NR*
HR (95% CI)	0.44 (0.15, 1.25)	

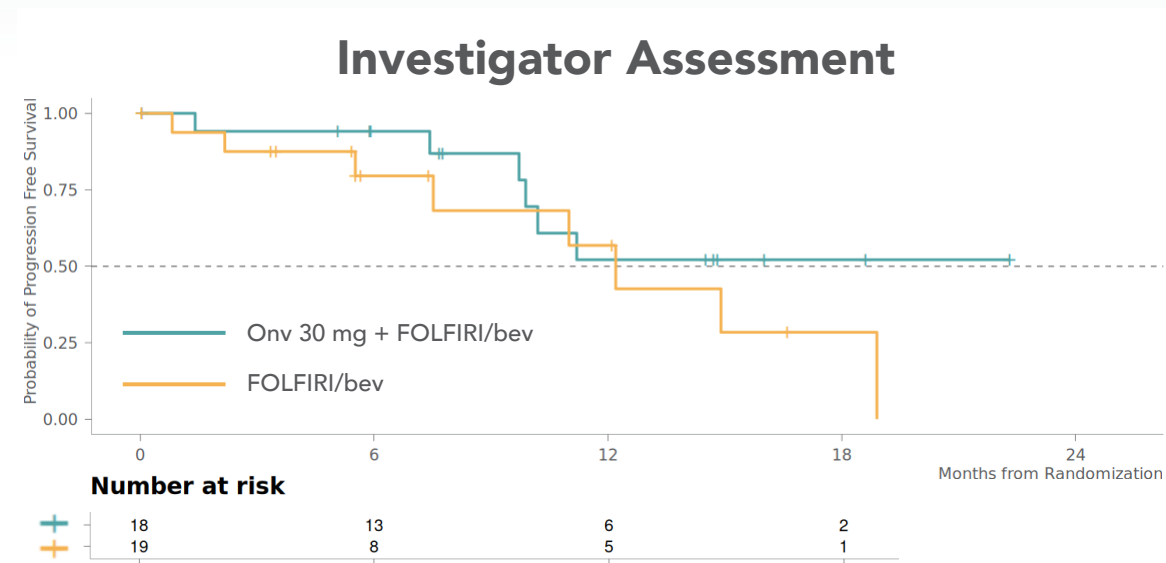


	FOLFIRI/bev + FOLFOX/bev	Onv (20 & 30mg) + FOLFIRI/bev
N	37	36
Median PFS	10.97	NR*
HR (95% CI)	0.53 (0.25, 1.15)	

Onv 30 mg + FOLFIRI/bev shows improved PFS vs FOLFIRI/bev



	FOLFIRI/bev	Onv 30 mg + FOLFIRI/bev
N	19	18
Median PFS	18.89*	NR**
HR (95% CI)	0.55 (0.15, 2.09)	



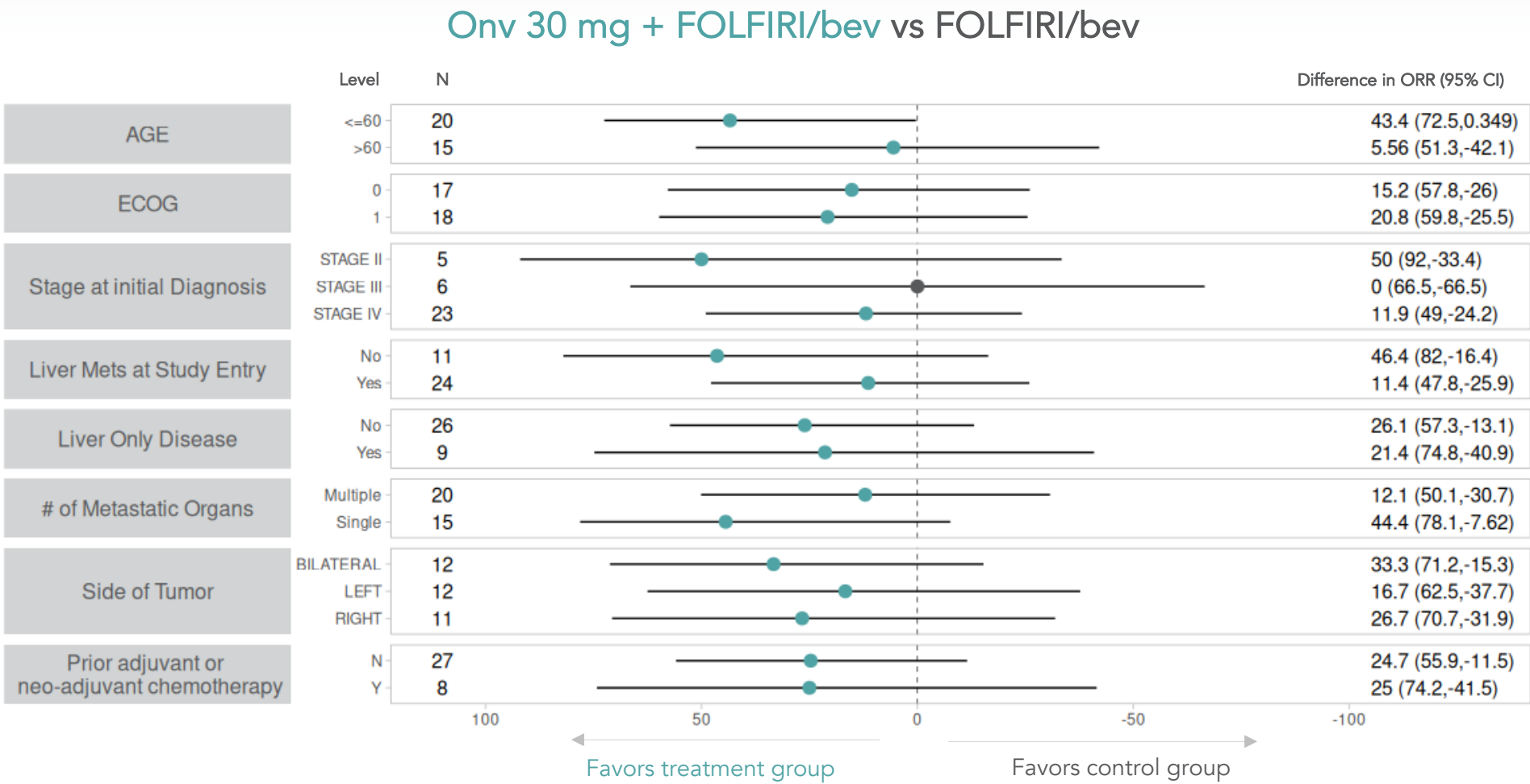
	FOLFIRI/bev	Onv 30 mg + FOLFIRI/bev
N	19	18
Median PFS	12.22*	NR**
HR (95% CI)	0.57 (0.2, 1.65)	

Data cutoff: March 18, 2026

*Discordance in median PFS in FOLFIRI/ bev arm due to investigator-assessed progressive disease (PD) and discontinuation prior to BICR confirmation of progression

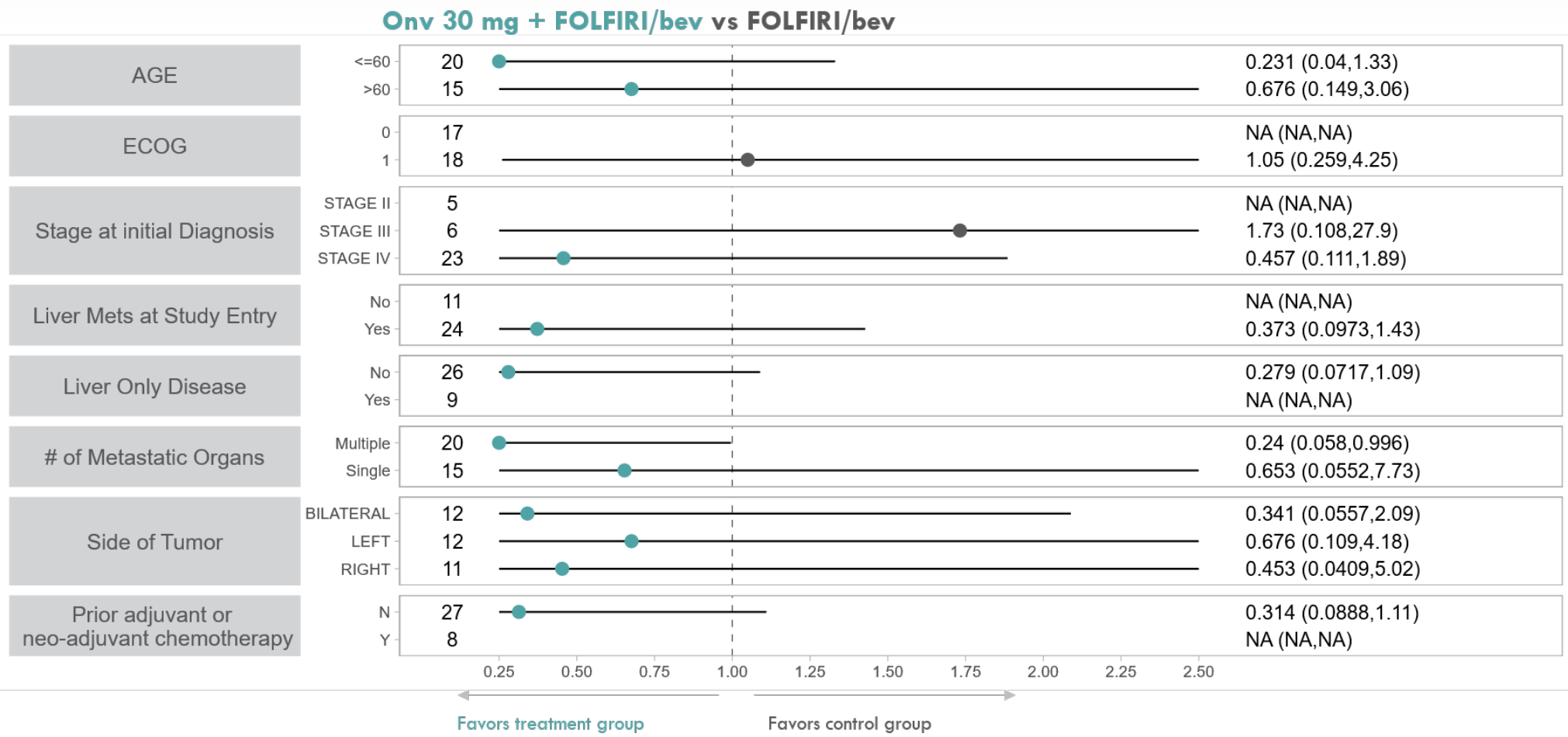
**Four patients still on study

Forest plot of ORR (BICR) by baseline characteristics demonstrates consistent benefit across subgroups with Onv 30 mg + FOLFIRI/bev



STAGE I at initial diagnosis excluded due to too few patients to meaningfully analyze.

Forest plot of PFS* by baseline characteristics demonstrates trends in benefit across subgroups with Onv 30 mg + FOLFIRI/bev

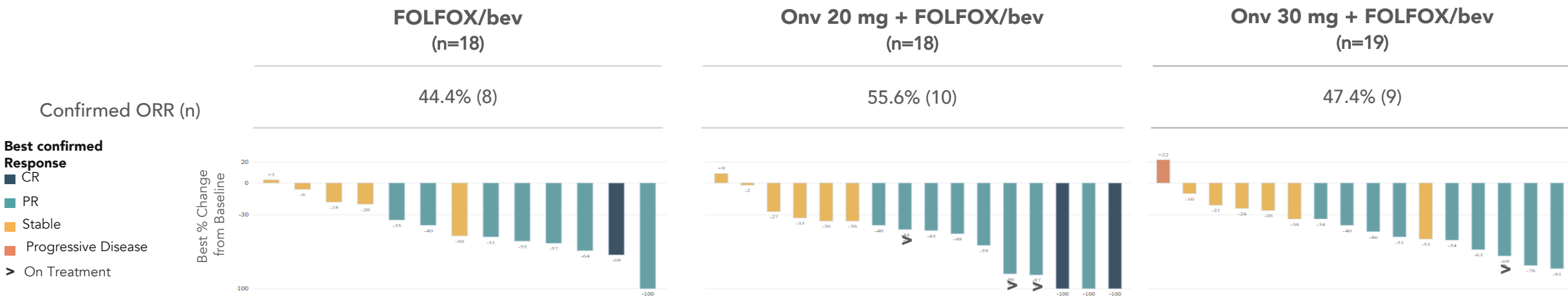


* Progressive disease events were based on events of BICR and Investigator assessments. The earliest reported date was used for a conservative estimate
STAGE I at initial diagnosis excluded due to too few patients to meaningfully analyze.

24

Onvansertib adds no consistent meaningful benefit to FOLFOX/bev

Objective Response Rate (per BICR)^a - ITT Analysis



Progression Free Survival		FOLFOX/bev (n=18)		Onv 20 mg + FOLFOX/bev (n=18)		Onv 30 mg + FOLFOX/bev (n=19)	
		Median (95% CI)		Median (95% CI)	Hazard Ratio (95% CI)	Median (95% CI)	Hazard Ratio (95% CI)
BICR only		11.07 (10.18-NR)		14.13 (10.94-NR)	1.14 (0.32, 4.04)	11.37 (9.4-NR)	2.2 (0.67, 7.28)
Investigator only		9.89 (9.23-NR)		12.78 (7.39-NR)	1.02 (0.39, 2.64)	11.37 (8.15-NR)	1.81 (0.64, 5.08)

Data cutoff: March 18, 2026

Patients that are not evaluable are not shown in the plots

Onvansertib shows no unexpected, overlapping, or new toxicities when added to FOLFIRI/bev or FOLFOX/bev

	FOLFIRI/bev (N=17)		Onv 20 mg + FOLFIRI/bev (N=17)		Onv 30 mg + FOLFIRI/bev (N=18)		FOLFOX/bev (N=17)		Onv 20 mg + FOLFOX/bev (N=17)		Onv 30 mg + FOLFOX/bev (N=18)	
Number (%) of Participants: by Preferred Term	Any Grade n (%)	Gr ≥ 3 n (%)	Any Grade n (%)	Gr ≥ 3 n (%)	Any Grade n (%)	Gr ≥ 3 n (%)	Any Grade n (%)	Gr ≥ 3 n (%)	Any Grade n (%)	Gr ≥ 3 n (%)	Any Grade n (%)	Gr ≥ 3 n (%)
Participants with events	17 (100.0)	15 (88.2)	17 (100.0)	13 (76.5)	18 (100.0)	15 (83.3)	16 (94.1)	11 (64.7)	17 (100.0)	12 (70.6)	18 (100.0)	16 (88.9)
Nausea	9 (52.9)	1 (5.9)	13 (76.5)	1 (5.9)	12 (66.7)	0	11 (64.7)	1 (5.9)	12 (70.6)	0	11 (61.1)	0
Fatigue	9 (52.9)	0	12 (70.6)	0	11 (61.1)	0	10 (58.8)	2 (11.8)	12 (70.6)	1 (5.9)	10 (55.6)	0
Diarrhea	11 (64.7)	1 (5.9)	13 (76.5)	2 (11.8)	9 (50.0)	0	8 (47.1)	1 (5.9)	7 (41.2)	1 (5.9)	7 (38.9)	0
Neutrophil count decreased	9 (52.9)	5 (29.4)	5 (29.4)	2 (11.8)	7 (38.9)	3 (16.7)	5 (29.4)	5 (29.4)	7 (41.2)	4 (23.5)	7 (38.9)	4 (22.2)
Peripheral sensory neuropathy	5 (29.4)	0	2 (11.8)	0	3 (16.7)	0	6 (35.3)	0	10 (58.8)	2 (11.8)	11 (61.1)	1 (5.6)
Vomiting	6 (35.3)	1 (5.9)	8 (47.1)	0	7 (38.9)	0	5 (29.4)	1 (5.9)	7 (41.2)	1 (5.9)	4 (22.2)	0
Hypertension	6 (35.3)	2 (11.8)	8 (47.1)	3 (17.6)	7 (38.9)	3 (16.7)	3 (17.6)	0	5 (29.4)	1 (5.9)	7 (38.9)	5 (27.8)
Constipation	3 (17.6)	1 (5.9)	6 (35.3)	0	5 (27.8)	0	2 (11.8)	0	10 (58.8)	0	8 (44.4)	0
Abdominal pain	5 (29.4)	2 (11.8)	4 (23.5)	1 (5.9)	7 (38.9)	1 (5.6)	4 (23.5)	0	6 (35.3)	1 (5.9)	7 (38.9)	1 (5.6)
Decreased appetite	7 (41.2)	1 (5.9)	5 (29.4)	0	7 (38.9)	1 (5.6)	4 (23.5)	0	7 (41.2)	0	3 (16.7)	0
Epistaxis	4 (23.5)	0	9 (52.9)	0	7 (38.9)	0	4 (23.5)	0	5 (29.4)	0	4 (22.2)	0
Anemia	4 (23.5)	1 (5.9)	7 (41.2)	1 (5.9)	5 (27.8)	1 (5.6)	3 (17.6)	0	4 (23.5)	1 (5.9)	8 (44.4)	4 (22.2)
Platelet count decreased	2 (11.8)	1 (5.9)	4 (23.5)	0	3 (16.7)	1 (5.6)	7 (41.2)	1 (5.9)	7 (41.2)	0	8 (44.4)	2 (11.1)
Weight decreased	7 (41.2)	2 (11.8)	2 (11.8)	1 (5.9)	6 (33.3)	0	2 (11.8)	0	3 (17.6)	0	5 (27.8)	1 (5.6)
Alopecia	5 (29.4)	0	4 (23.5)	0	6 (33.3)	0	2 (11.8)	0	5 (29.4)	0	2 (11.1)	0
Dizziness	3 (17.6)	0	4 (23.5)	0	2 (11.1)	0	3 (17.6)	0	5 (29.4)	0	7 (38.9)	0
Headache	4 (23.5)	0	7 (41.2)	0	2 (11.1)	0	4 (23.5)	0	6 (35.3)	0	1 (5.6)	0
Hypokalemia	4 (23.5)	1 (5.9)	3 (17.6)	2 (11.8)	5 (27.8)	2 (11.1)	5 (29.4)	1 (5.9)	3 (17.6)	0	4 (22.2)	1 (5.6)
Insomnia	0	0	5 (29.4)	0	4 (22.2)	0	3 (17.6)	0	6 (35.3)	0	6 (33.3)	0
Stomatitis	3 (17.6)	1 (5.9)	7 (41.2)	0	3 (16.7)	0	6 (35.3)	0	3 (17.6)	0	1 (5.6)	0
White blood cell count decreased	5 (29.4)	1 (5.9)	5 (29.4)	0	5 (27.8)	0	6 (35.3)	2 (11.8)	0	0	2 (11.1)	1 (5.6)
Dysgeusia	2 (11.8)	0	1 (5.9)	0	4 (22.2)	0	5 (29.4)	0	5 (29.4)	0	5 (27.8)	0

*Data cut-off March 18, 2026, from an ongoing trial and unlocked EDC database. events shown occurred in ≥20% of total patients; Subjects reporting more than one adverse event (AE) within a preferred term are counted only once in that preferred term. For subjects reporting more than one AE within a preferred term, the AE with maximum grade is included in the table.

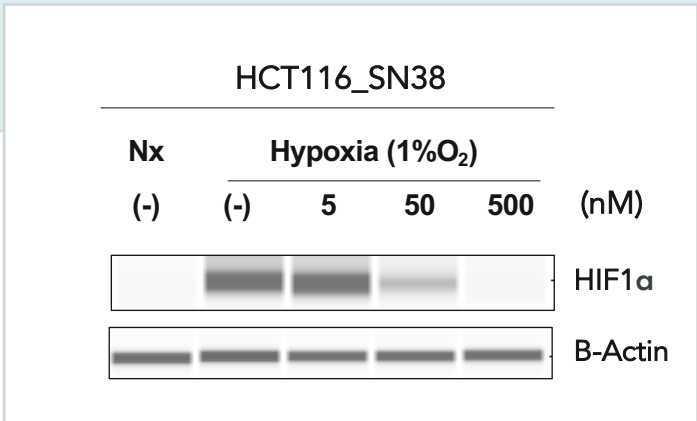
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Mechanistic rationale for onvansertib's synergy with FOLFIRI but not FOLFOX

Onvansertib may complement irinotecan via HIF1 α suppression and inhibition of DNA repair pathways

Topoisomerase I inhibitors (Irinotecan/SN38) + Onvansertib

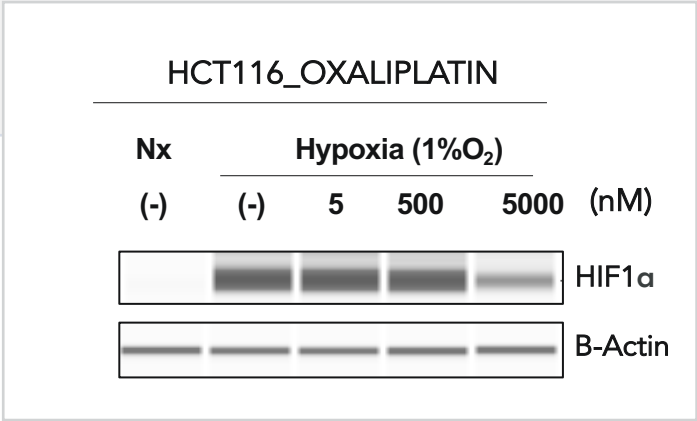
- ✓ Both suppress HIF1 α → dual anti-angiogenic effect
- ✓ Irinotecan-induced double stranded breaks (DSBs) rely on PLK1-dependent Homologous Recombination repair



SN38 decreases HIF1 α in a dose-dependent manner; HIF1 α less sensitive to oxaliplatin

Oxaliplatin + Onvansertib

- ✗ Oxaliplatin has low impact on HIF1 α suppression — no shared antiangiogenic effect
- ✗ Oxaliplatin induced DNA damage uses Nucleotide Excision Repair mechanism — limited/no role of PLK1



CRDF-004 Phase 2 trial: key goals/endpoints achieved

Primary Goal: DOSE + CHEMO SELECTION

**30 mg onvansertib
+ FOLFIRI/bev**

Selected the efficacious
and safe dose of
onvansertib + SoC for the
registrational program

Primary Endpoint: ORR

**30% absolute
improvement
in ORR**

30 mg onvansertib +
FOLFIRI/bev demonstrated
improvement in ORR
compared to SoC

Secondary Endpoint: PFS

**Median PFS not yet
reached vs SoC**

9 of 14 patients remain on
onvansertib + FOLFIRI/bev
treatment; median PFS not
reached but reached in SoC

CRDF-005: Proposed pivotal trial in first-line RAS-mutated mCRC

FDA End-of-Phase 2 meeting completed in 2Q 2026

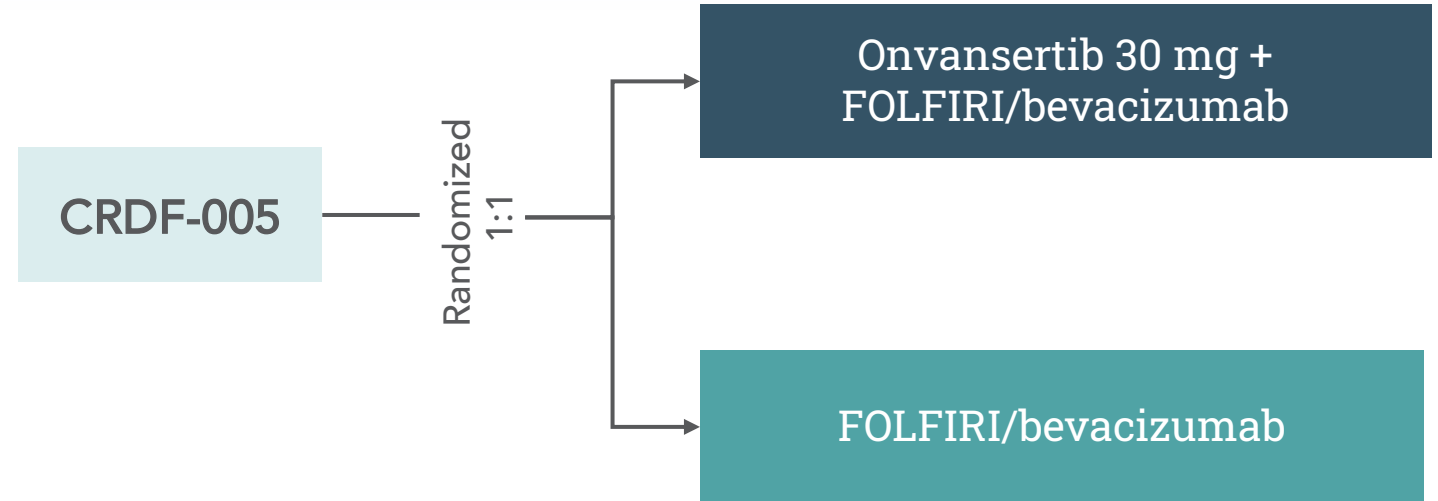
ENROLLMENT CRITERIA

- First-line mCRC
- KRAS+/NRAS+
- No BRAF-V600 or MSI-H/dMMR
- Unresectable
- No prior bev

ENDPOINTS

Dual Primary Endpoints: ORR and PFS

Secondary: DoR and OS



Design details:

- Proposed sample size ~ 640 patients
- >90% power to detect PFS and ORR difference in the two arms
- Potential for accelerated approval based on ORR and durability of responses
- FDA feedback received, EMA feedback pending

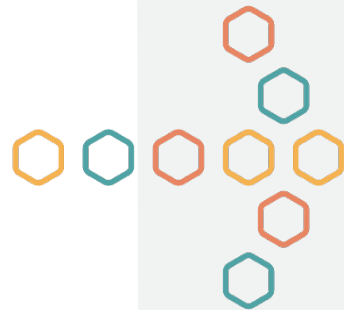
ONVANSERTIB

FIRST-LINE RAS-MUTATED mCRC

Mechanistic Rationale for FOLFIRI/bev Combination

Positive Data from the Phase 2 CRDF-004 Trial

Broader Opportunity



Our pipeline opens many attractive opportunities for onvansertib

	Line of Therapy	Trial	IIT*	Ph1	Ph2	Ph3	Combination with:
mCRC (RAS-mut)	1 st line	CRDF-004 (w/Pfizer)			<i>randomized</i>		FOLFIRI/bev and FOLFOX/bev
	2 nd line	Ph 1b/2			<i>completed</i>		FOLFIRI/bev
CMML	2 nd line	Ph 1	 MAYO CLINIC Rochester, Minnesota		<i>expansion ongoing</i>		None (monotherapy)
mPDAC	1 st line	Ph 2	 KU MEDICAL CENTER The University of Kansas				NALIRIFOX
	2 nd line	Ph 2			<i>completed</i>		Nal-IRI/leucovorin/5-FU
SCLC	2 nd line	Ph 2	 UNIVERSITY of MARYLAND MARLENE AND STEWART GREENEBAUM COMPREHENSIVE CANCER CENTER				None (monotherapy)
TNBC	2 nd line	Ph 2	 Dana-Farber Cancer Institute				Paclitaxel

* For investigator-initiated trials (IITs) only, the investigator's institution is provided., CMML, chronic myelomonocytic leukemia; mPDAC, metastatic pancreatic ductal adenocarcinoma; SCLC, small-cell lung cancer; TNBC, triple-negative breast cancer.

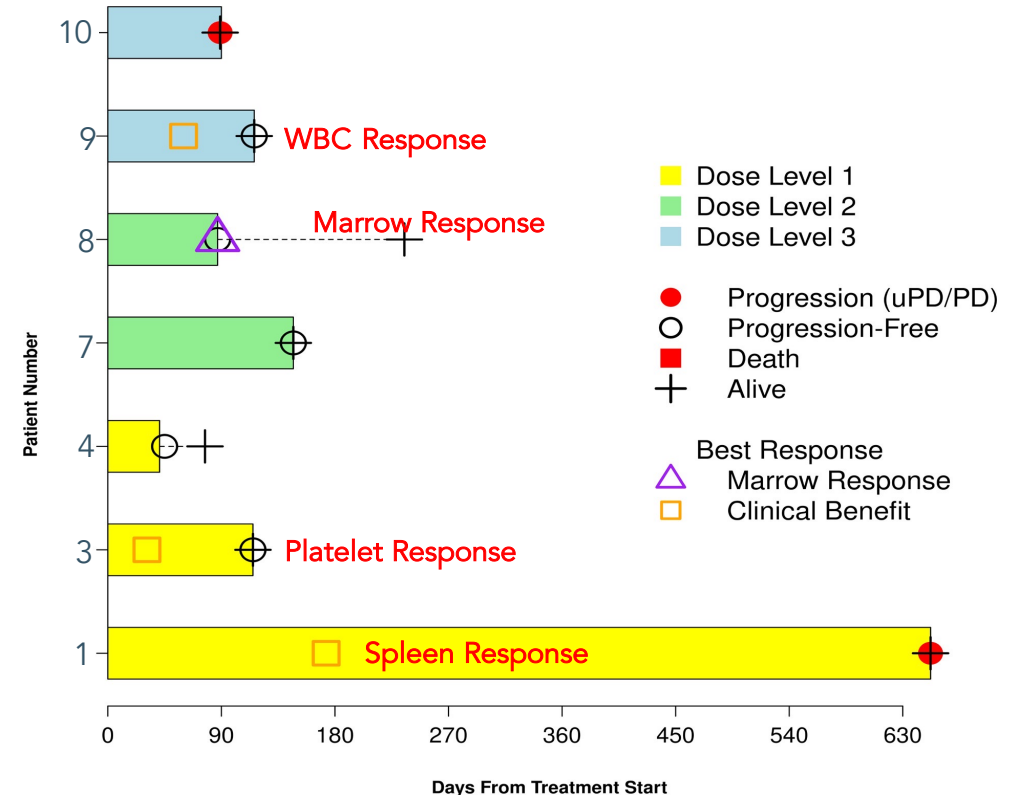
Investigator-initiated Phase 1 trial in CMML: onvansertib shows encouraging early activity as monotherapy in orphan disease

Chronic Myelomonocytic Leukemia (CMML)

- Aggressive hematologic malignancy (median age ~76; median survival <3 years)
- Overlapping features of MDS and MPN; marked by monocytosis, cytopenias, and bone marrow dysplasia
- Poor clinical outcomes; high risk of bone marrow failure and progression to AML
- Hypomethylating agents (HMAs): only approved therapy but no sig effect on natural history of disease

Phase 1 trial assessing safety & efficacy of onvansertib in relapsed/refractory CMML (n=10)

- Onvansertib was generally well tolerated and showed preliminary efficacy in ~40% of patients, including:
 - 100% platelet response
 - Normalization of white blood cell (WBC) count
 - Spleen response
 - Optimal bone marrow response: blast reduction from 8% to 2%, enabling allogeneic stem cell transplant
 - 3 patients with stable disease
- Dose expansion is currently open and recruiting



Swimmers' plot showing for those who received at least 1 cycle (n=8) with 3 (38%) patients meeting criteria for either hematological or optimal marrow response. One patient (not pictured here) was also progression free but did not complete the assessable DLT period.