2026 ASCO ANNUAL MEETING

Onvansertib Plus Standard-of-Care Chemotherapy plus Bevacizumab in First-Line RAS-Mutated Metastatic Colorectal Cancer: Interim Results from the Phase 2 Randomized CRDF-004 Trial

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Key Takeaway Points

Onvansertib is a highly selective, oral, small molecule inhibitor of PLK1. Treatment with onvansertib blocks mitotic progression, DNA repair and tumor cell adaptation to hypoxia

1

Data from the Phase 2 CRDF-004 trial show Onv 30 mg + FOLFIRI/bevacizumab (bev) improved efficacy (ORR and PFS) vs. standard of care

Data cut-off: Mar 18, 2026

2

The safety profile of Onv in combination with FOLFIRI/bev is consistent with the known profiles of the individual agents, with no new safety signals identified

3

CRDF-004 data confirm prior Ph 2 results observed in second-line mCRC patients and support the planned Ph3 evaluation of Onv 30 mg + FOLFIRI/bev in first-line RAS-mutated mCRC

Study Design
CRDF-004: Dose-finding Phase 2 trial in first-line RAS-mutated mCRC

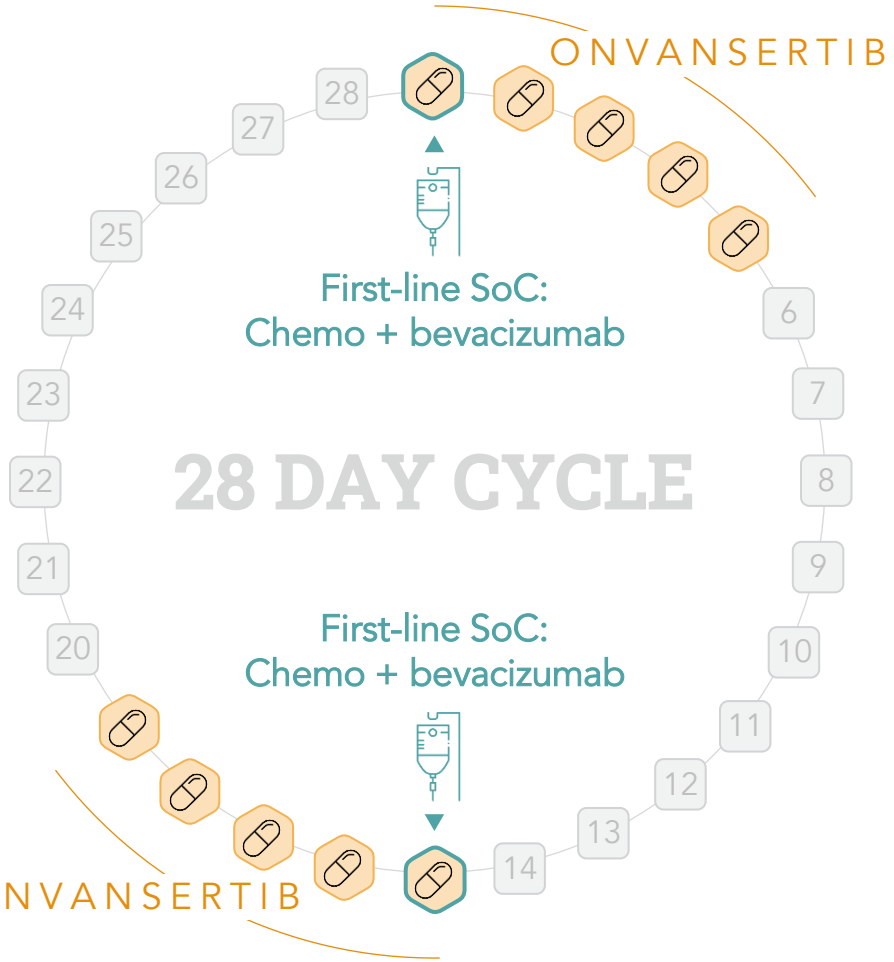
ENROLLMENT CRITERIA

- 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



Patient's tumors are scanned every 8 weeks

ENDPOINTS*

Primary:	ORR
Secondary:	DoR and PFS

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

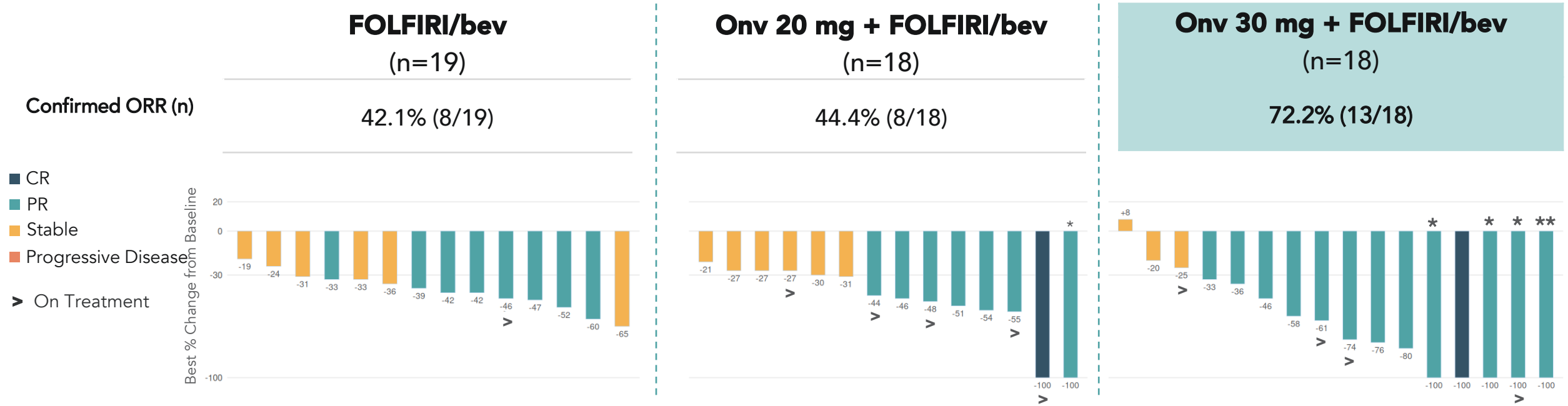
* Assessed by blinded independent central review (BICR)

Patient Demographics and Baseline Characteristics (ITT)

	FOLFIRI/bev (N=19)	Onv 20 mg + FOLFIR/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%)

Onvansertib + FOLFIRI/bev improves both ORR and depth of response in first-line RAS-mutated mCRC

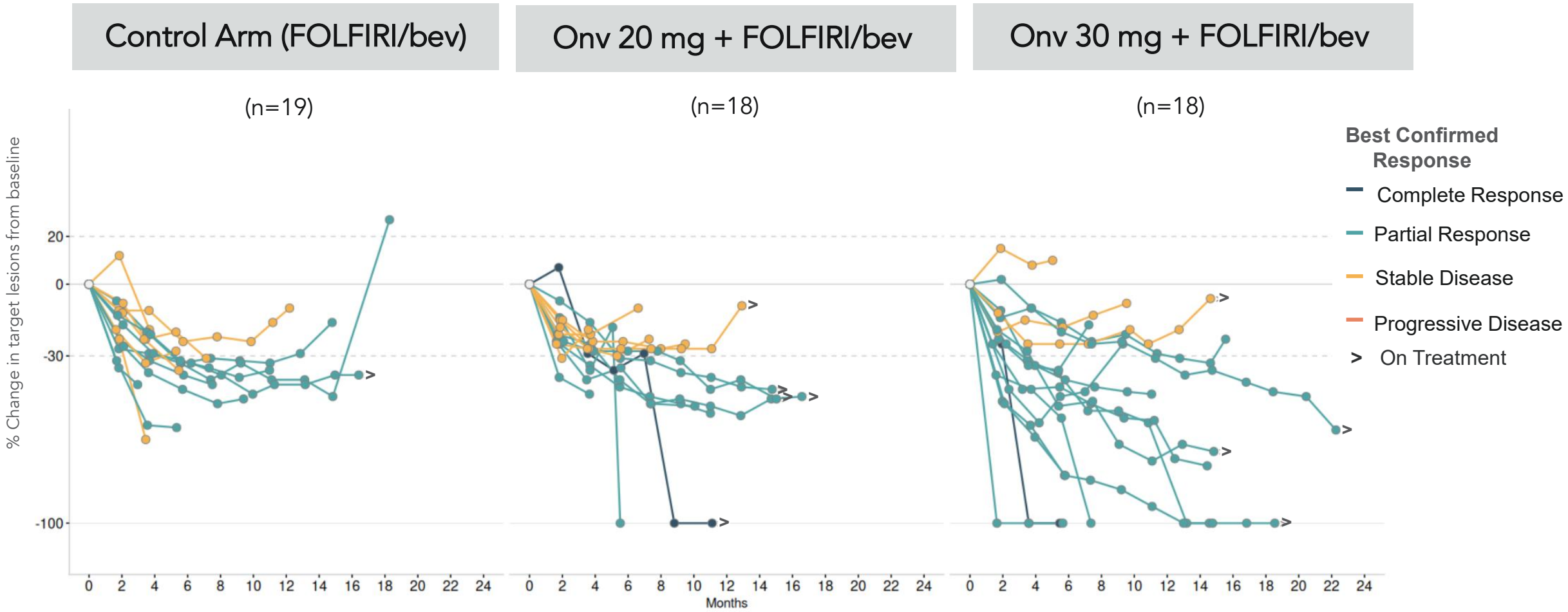
Objective Response Rate (per BICR)[a] - ITT Analysis



** CR at last assessment; unconfirmed due to discontinuation for curative surgery
* Residual non-target disease (Non-CR/Non-PD)

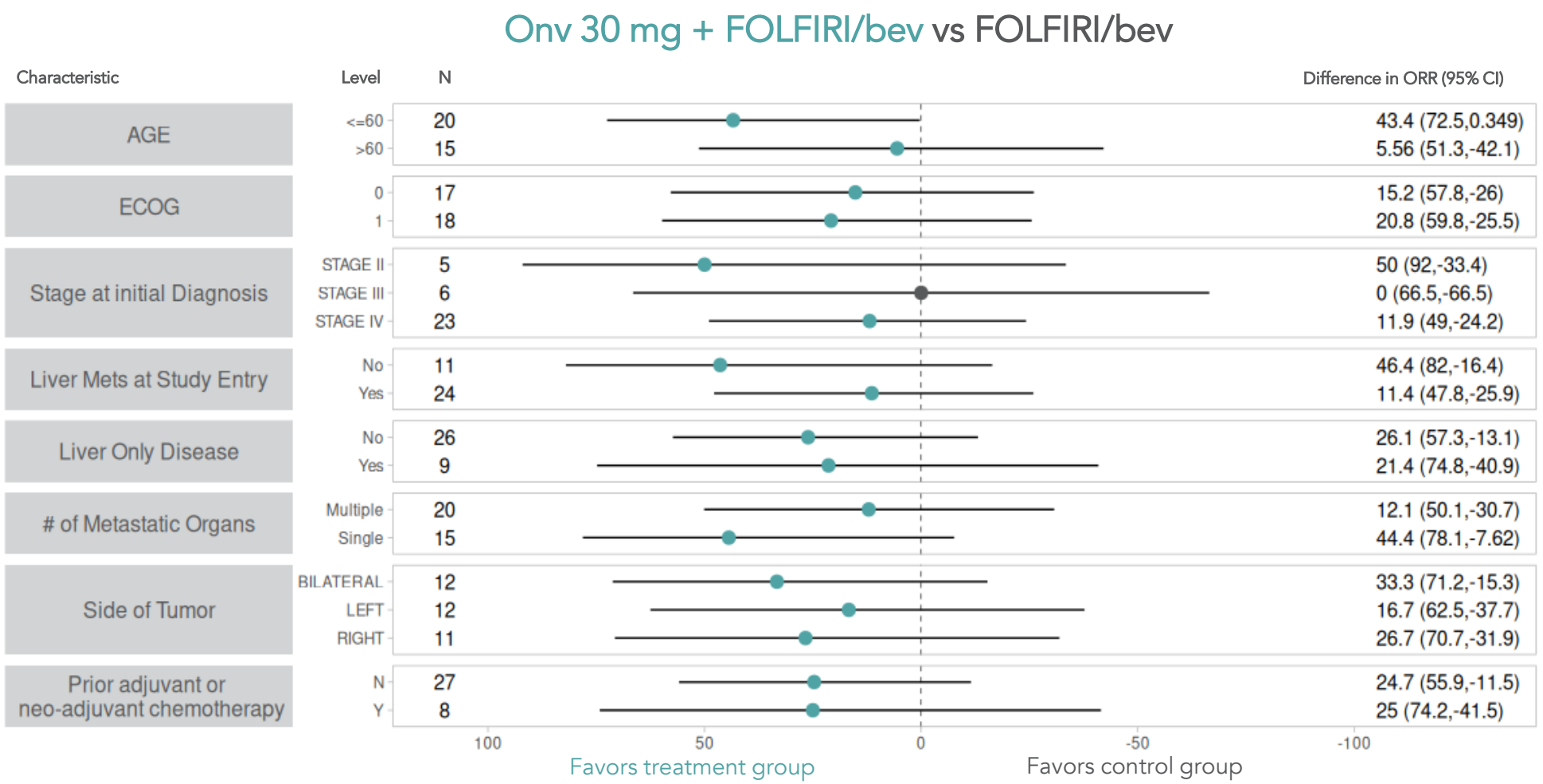
Bev, bevacizumab; BICR, Blinded Independent Central Review; CR, confirmed response; Onv, onvansertib; ORR, objective response rate; PR, partial response; SoC, standard of care.
[a]ORR is based on confirmed responses
Patients that are not-evaluable or do not have target lesions are not shown in the plots

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



Patients that are not-evaluable or do not have target lesions are not shown in the plots

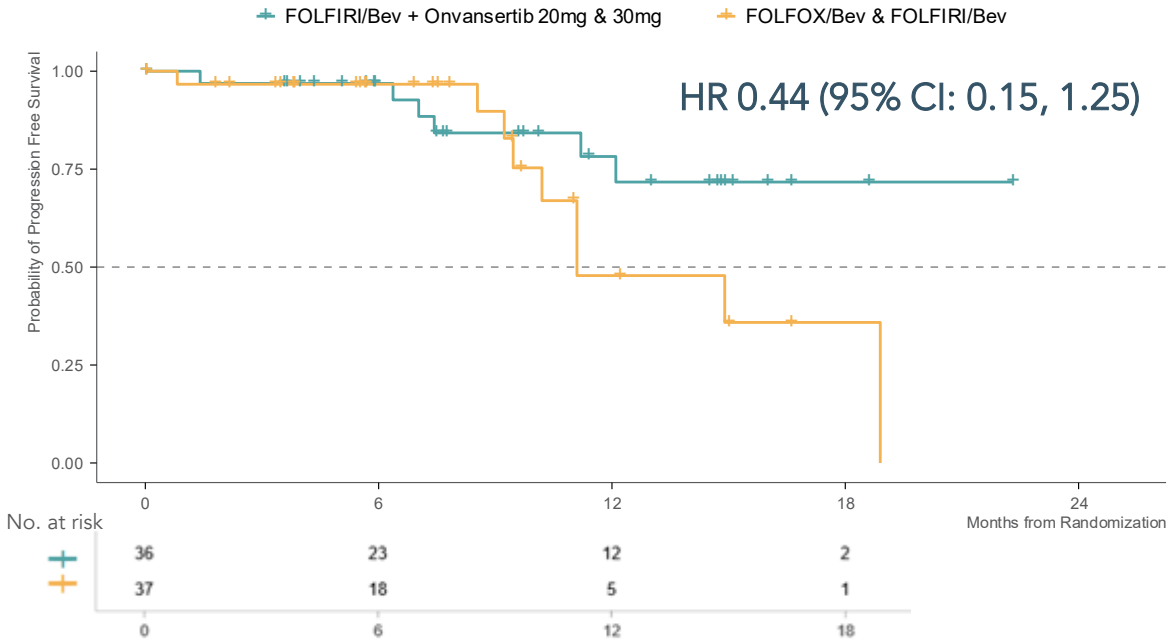
Forest plot of ORR (BICR) based on baseline characteristics: Consistent benefit across subgroups



[a] Based on BICR
STAGE I at initial diagnosis excluded due to too few patients to meaningfully analyze

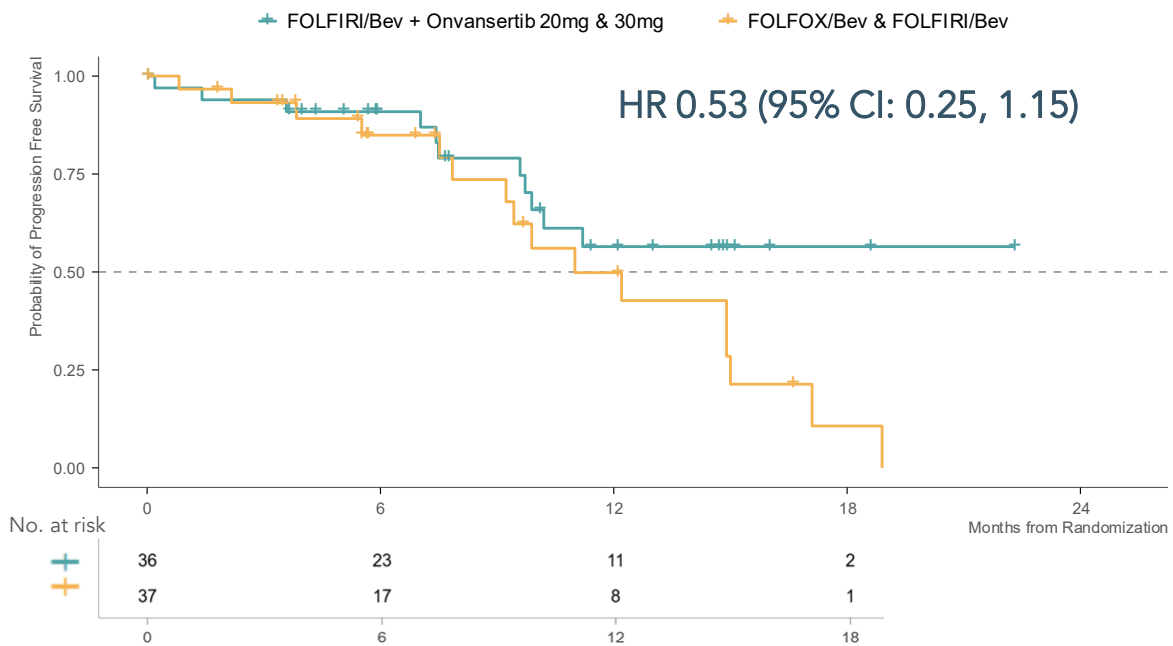
Onvansertib (20mg & 30mg) + FOLFIRI/bev shows improved PFS vs SOC (FOLFIRI/bev & FOLFOX/bev): ITT population

BICR Assessment



Arm	PFS Events	PFS (mo)
FOLFIRI/bev + FOLFOX/bev	9	11.07 (10.18-NA)
Onv (20 mg + 30mg) + FOLFIRI/bev	6	NR (NR-NR)

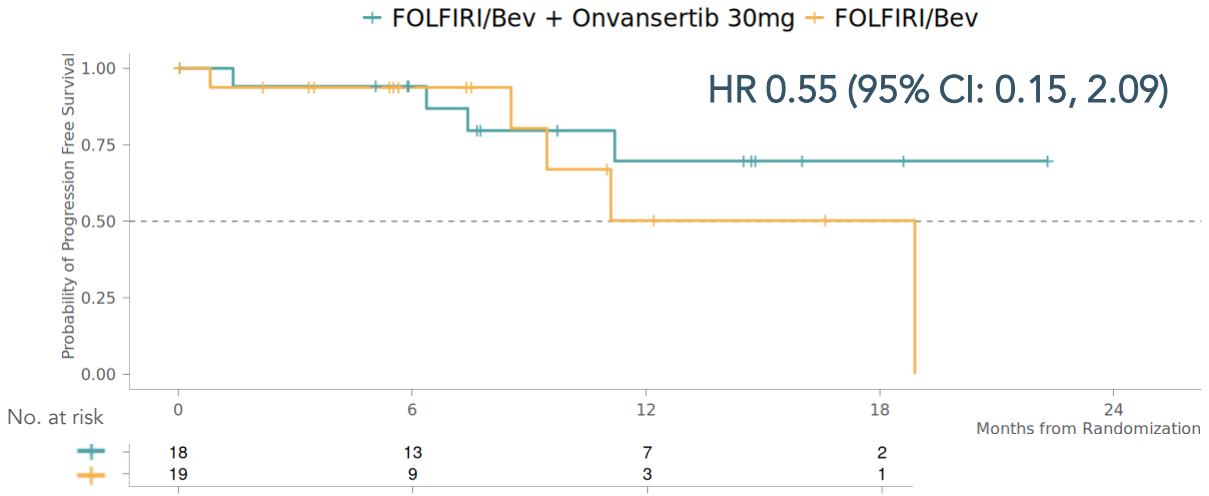
Investigator Assessment (IA)



Arm	PFS Events	PFS (mo)
FOLFIRI/bev+ FOLFOX/bev	16	10.97 (9.43-NR)
Onv (20 mg + 30mg) + FOLFIRI/bev	11	NR (9.89-NR)

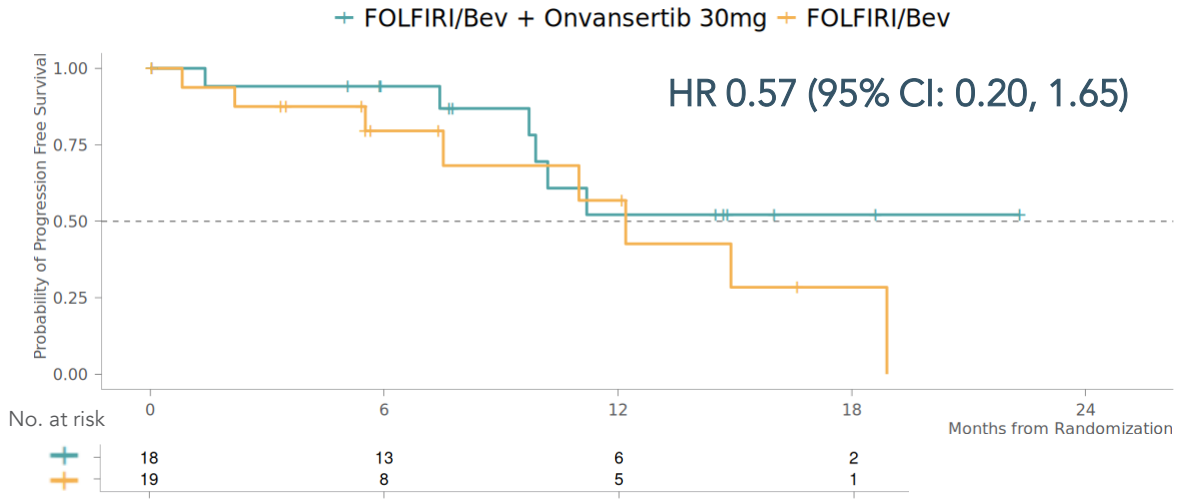
Onvansertib 30mg + FOLFIRI/bev shows improved PFS vs FOLFIRI/bev: ITT population

BICR Assessment



Arm	PFS Events	PFS (mo)
FOLFIRI/bev	5	18.89* (9.46-NR)
Onv 30mg + FOLFIRI/bev	4	NR (11.2-NR)

Investigator Assessment (IA)



Arm	PFS Events	PFS (mo)
FOLFIRI/bev	8	12.22* (7.52-NA)
Onv 30mg + FOLFIRI/bev	5	NR (9.89-NR)

* Discordance in PFS observed where investigator-assessed PD led to treatment discontinuation prior to BICR confirmation of progression.

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. bev, bevacizumab; onv, onvansertib

Conclusions

- Onvansertib plus FOLFIRI/bevacizumab regimen demonstrated improved efficacy in first-line RAS-mutated mCRC; well tolerated with no new or unexpected toxicities observed
    - The data confirm prior Phase 2 results in second-line KRAS-mutated bev-naïve mCRC patients
- Onvansertib 30 mg + FOLFIRI/bevacizumab arm showed a dose-dependent improvement in ORR (72.2% vs 42.1%) and PFS, with median PFS not yet reached in the treatment arm
- Onvansertib plus FOLFOX/bevacizumab did not demonstrate benefit in first-line RAS-mutated mCRC (data not shown)
- These results support the planned confirmatory Phase 3 evaluation of onvansertib 30 mg plus FOLFIRI/bevacizumab vs FOLFIRI/bevacizumab in first-line RAS-mutated mCRC

Thank You

Acknowledgments

- All patients and their families for participating in the clinical trial
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