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MEETING SUMMARY
ASCO GI 2018, San Francisco, USA

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CANCERS OF THE LOWER GI TRACT

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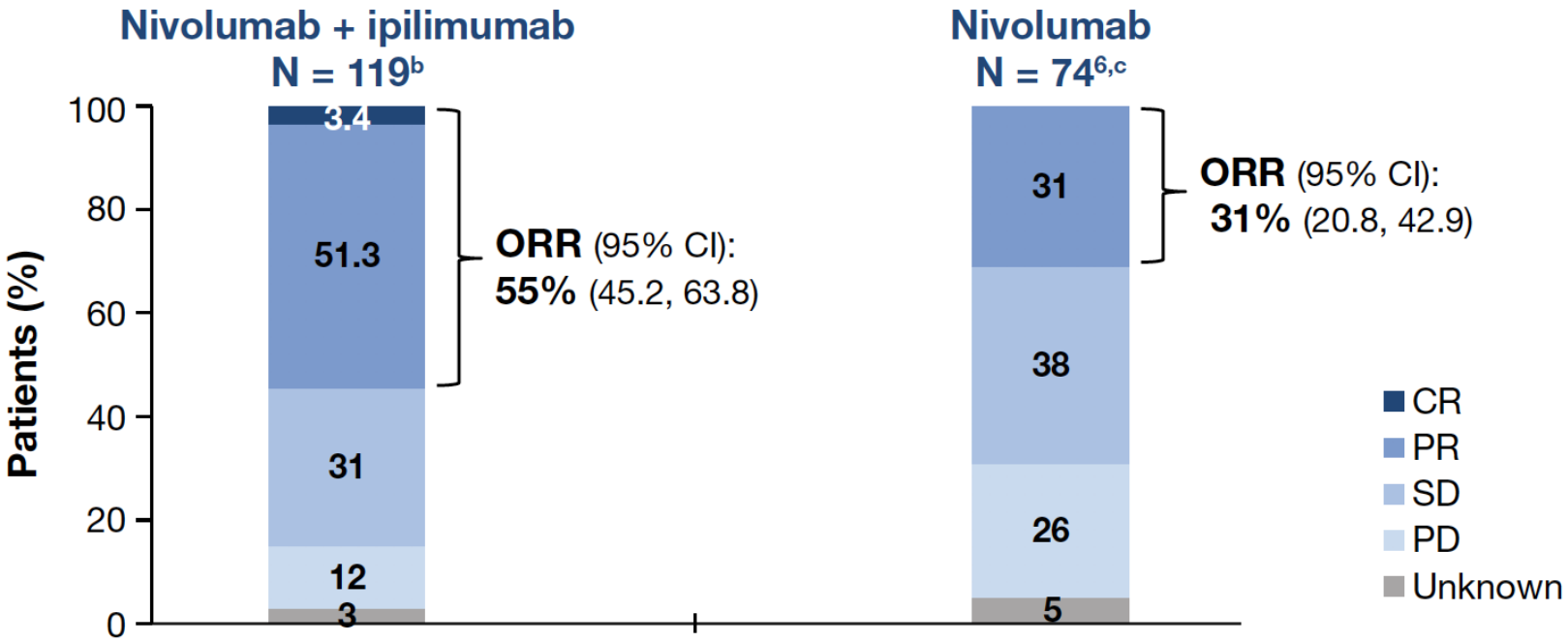
NIVOLUMAB + IPILIMUMAB COMBINATION IN PATIENTS WITH DNA MISMATCH REPAIR-DEFICIENT/MICROSATELLITE INSTABILITY-HIGH (DMMR/MSI-H) METASTATIC COLORECTAL CANCER (mCRC): FIRST REPORT OF THE FULL COHORT FROM CHECKMATE-142

Andre et al. Abstract #553

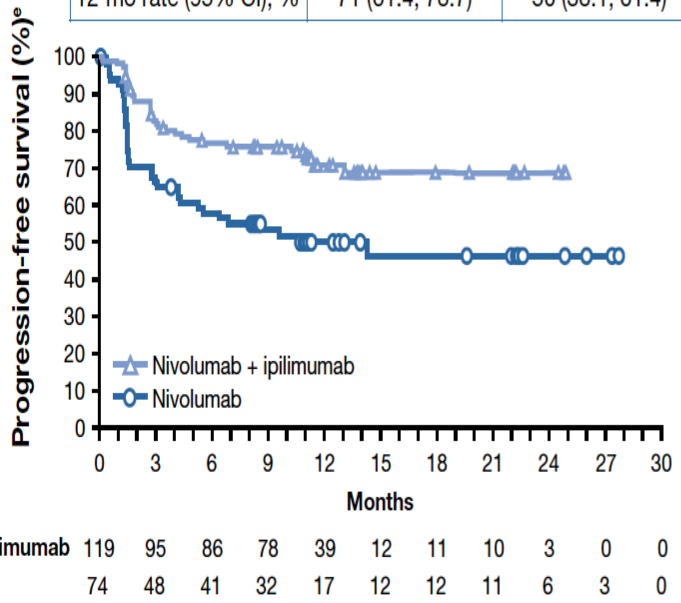
CHECKMATE-142: RESPONSE



Presented at ASCO GI 2018, Andre et al. Abstract #553

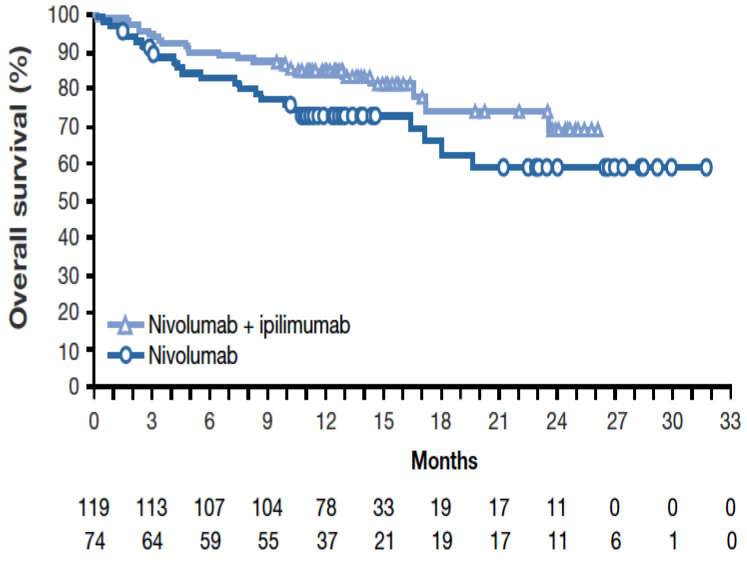
CHECKMATE-142: PFS AND OS

	Nivolumab + ipilimumab[b,c]	Nivolumab[6,d]
9-mo rate (95% CI), %	76 (67.0, 82.7)	54 (41.5, 64.5)
12-mo rate (95% CI), %	71 (61.4, 78.7)	50 (38.1, 61.4)



No. at Risk											
Nivolumab + ipilimumab	119	95	86	78	39	12	11	10	3	0	0
Nivolumab	74	48	41	32	17	12	12	11	6	3	0

	Nivolumab + ipilimumab[b,f]	Nivolumab[6,d]
9-mo rate (95% CI), %	87 (80.0, 92.2)	78 (66.2, 85.7)
12-mo rate (95% CI), %	85 (77.0, 90.2)	73 (61.5, 82.1)



Nivolumab + ipilimumab	119	113	107	104	78	33	19	17	11	0	0	0
Nivolumab	74	64	59	55	37	21	19	17	11	6	1	0

Presented at ASCO GI 2018, Andre et al. Abstract #553

PFS, Progression Free Survival; OS, Overall Survival

A PHASE IB STUDY OF SAFETY AND CLINICAL ACTIVITY OF ATEZOLIZUMAB AND COBIMETINIB IN PATIENTS WITH METASTATIC COLORECTAL CANCER (mCRC)

Bendell et al. Abstract #560

MSS mCRC COMBINATION ATEZOLIZUMAB AND COBIMETINIB: RESPONSE TO THERAPY

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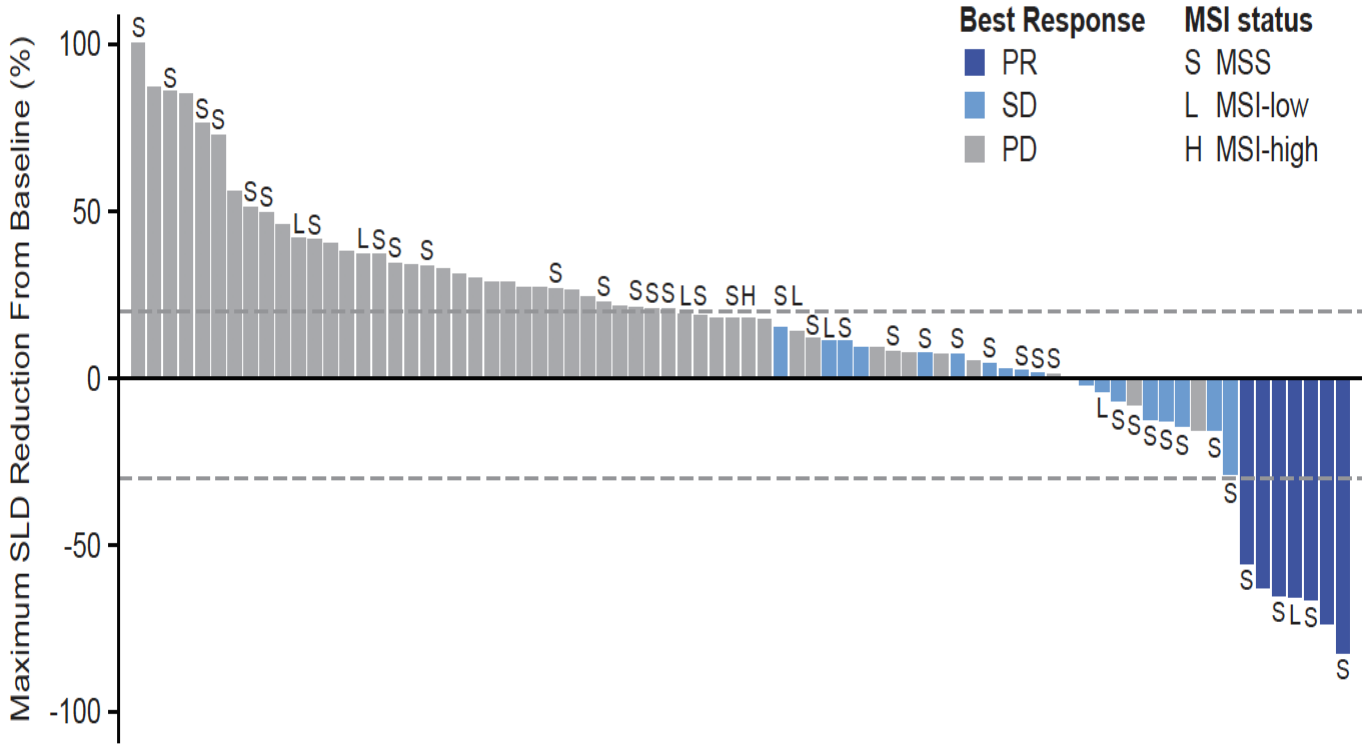

Presented at ASCO GI 2018, Bendell et al. Abstract #560

OS AND PFS INVESTIGATOR ASSESSED AND BY MAPK PATHWAY ACTIVATION

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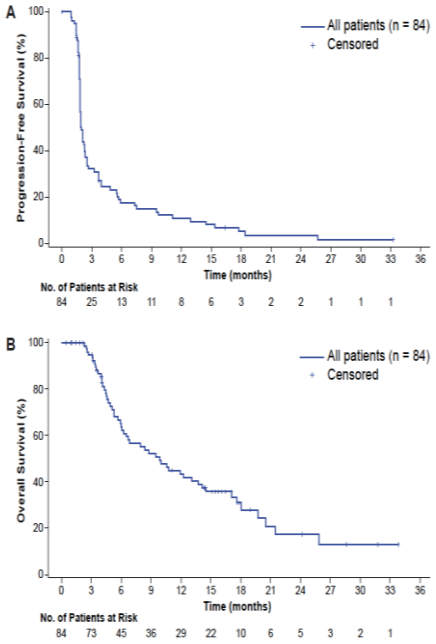
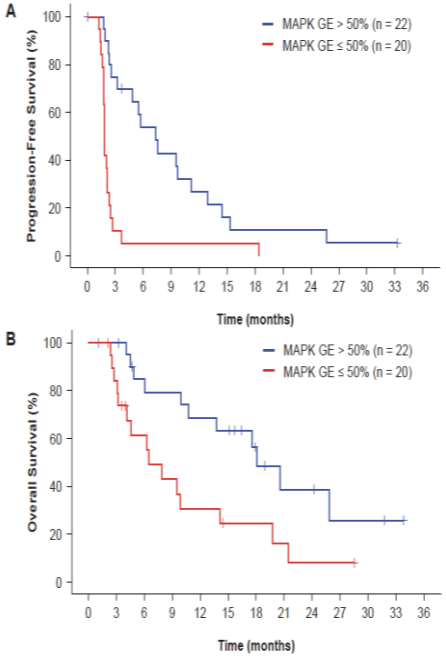
Investigator-Assessed (A) PFS and (B) OS for the mCRC Patient Cohort



Patients	PFS		OS		
	Median (95% CI), mo	6-mo, %	Median (95% CI), mo	6-mo, %	12-mo, %
All (n=84)	1.9 (1.8, 2.3)	18%	9.8 (6.2, 14.1)	65%	43%
MSS (n=42)	2.5 (1.8, 3.7)	27%	13.0 (6.0, 25.8)	71%	51%

Of the remaining 42 non-MSS patients, 32 patients had unknown MSI status, 9 patients were MSI-low and 1 patient was MSI-high.

(A) PFS and (B) OS by MAPK Pathway Transcriptional Activity



Patients	PFS		OS		
	Median (95% CI), mo	6-mo, %	Median (95% CI), mo	6-mo, %	12-mo, %
MAPK GE >50%[a]	7.3 (2.6, 11.1)	54%	18.0 (10.0, NR)	85%	69%
MAPK GE ⩽50%[a]	1.8 (1.7, 2.1)	5%	6.5 (3.2, 14.1)	61%	31%

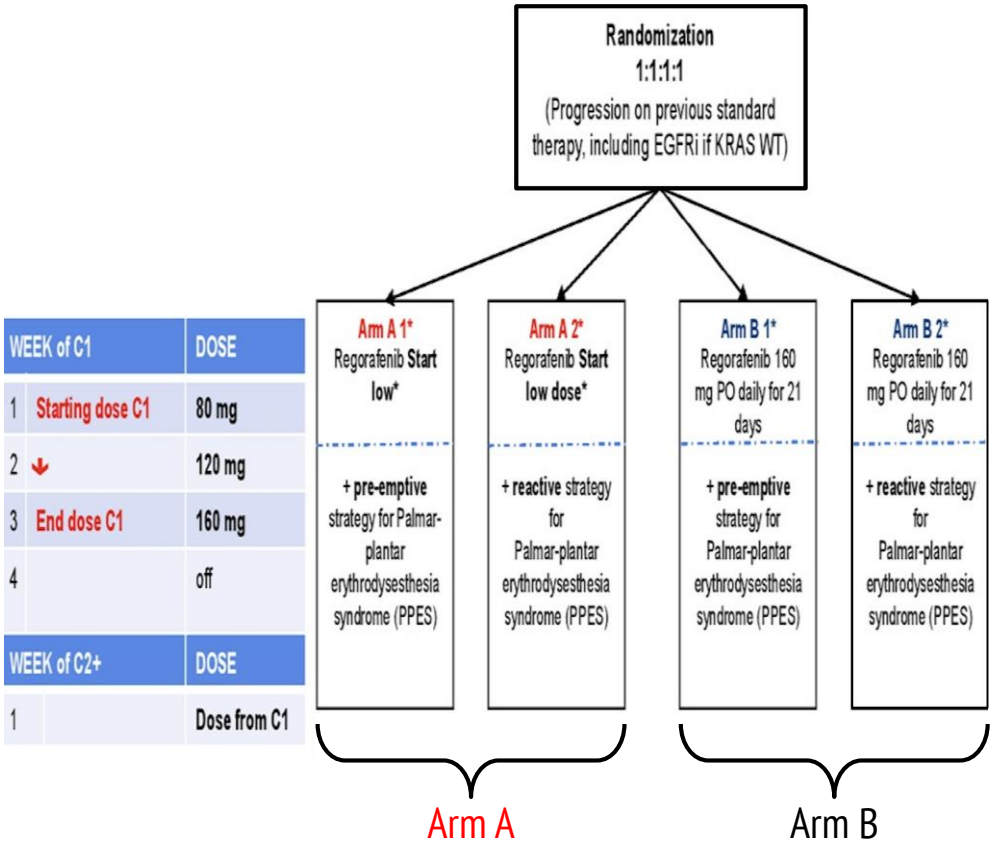
GE, gene expression, NR, not reached. [a]Defined by mRNA expression of CCND1, DUSP4, DUSP6, ETV4, ETV5, NT5E (CD73), SPRY2 and SPRY4.

Presented at ASCO GI 2018, Bendell et al. Abstract #560
PFS, Progression Free Survival; OS, Overall Survival

REGORAFENIB DOSE OPTIMIZATION STUDY (ReDOS): RANDOMIZED PHASE II TRIAL TO EVALUATE DOSING STRATEGIES FOR REGORAFENIB IN REFRACTORY METASTATIC COLORECTAL CANCER (mCRC)—AN ACCRU NETWORK STUDY

Bekaii-Saab et al. Abstract #511

ReDOS STUDY: TRIAL DESIGN

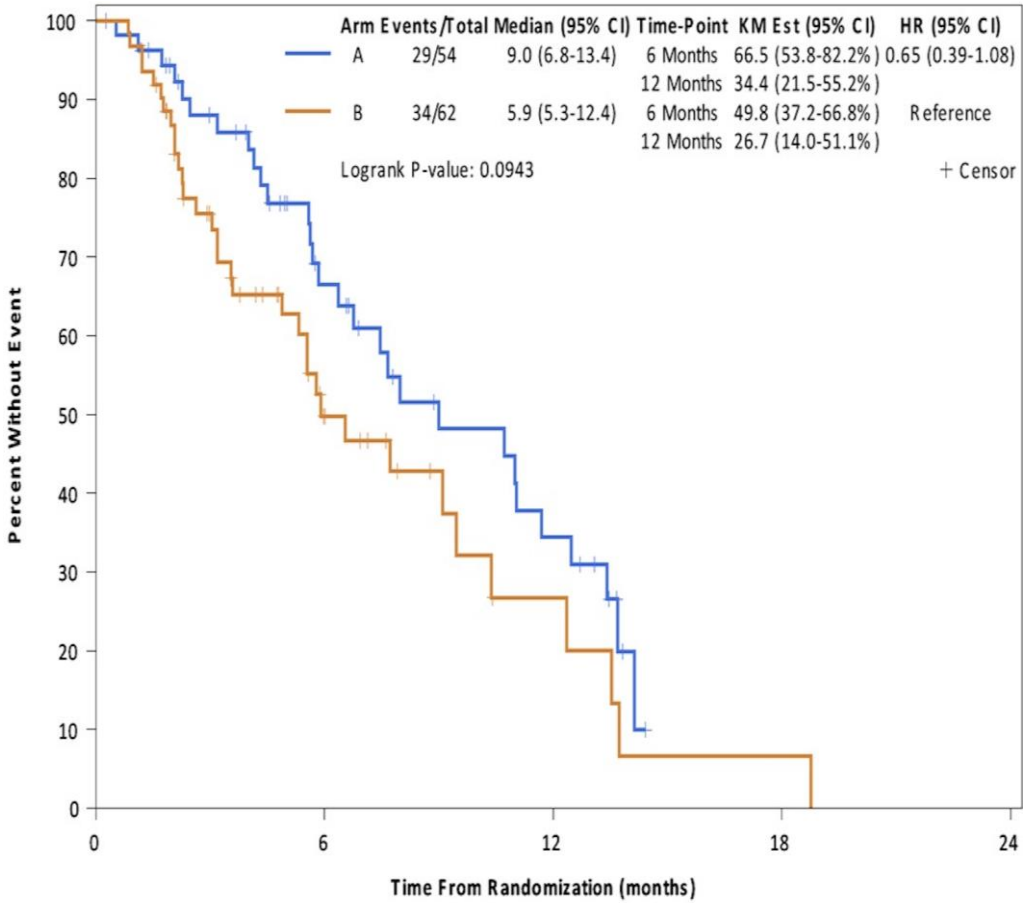


WEEK of C1		DOSE
1	Starting dose C1	80 mg
2	↓	120 mg
3	End dose C1	160 mg
4		off
WEEK of C2+		**DOSE**
1		Dose from C1

1ary endpoint: proportion of patients who complete 2 cycles of protocol treatment and initiate cycle 3 in arm A and arm B
2ary endpoints: OS, PFS, TTP

Presented at ASCO GI 2018, Bekaii-Saab et al. Abstract #511

ReDOS OS: REGORAFENIB LOW DOSE (A) VERSUS HIGH DOSE (B)



Presented at ASCO GI 2018, Bekaii-Saab et al. Abstract #511

SUMMARY

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- Impressive data on Checkpoint inhibition in MSI-high mCRC with nivolumab and ipilimumab
  - Challenge to identify patients who need combination treatment or who can be salvaged by combination treatment
- MSS mCRC benefit from combination of atezolizumab and cobimetinib
  - Especially if MAPK pathway is activated
- ReDOS study shows improved OS and beneficial toxicity profile by using dose escalation strategy

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