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MEETING SUMMARY

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CANCERS OF THE LOWER GI TRACT

NIVOLUMAB IN PATIENTS WITH DNA MISMATCH REPAIR DEFICIENT/MICROSATELLITE INSTABILITY HIGH METASTATIC COLORECTAL CANCER: UPDATE FROM CHECKMATE 142

OVERMAN ET AL

SUMMARY

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- 74 patients with dMMR/MSI-H mCRC who progressed on or were intolerant to ⩾ 1 prior line of therapy
  - 84% received ⩾ 2 prior lines of therapy
- Nivolumab 3 mg/kg every 2 weeks
- Overall response rate: 27%
- Disease control rate: 62%
- Median PFS: 9.6 months
- 12 month overall survival 73.8% (median OS not reached)

****Clinical benefit regardless of KRAS, BRAF status, h/o Lynch syndrome****

CONCLUSION

- Nivolumab has clear activity in MSI-H mCRC

- These are more data to support the use of checkpoint inhibitors in this population

RANDOMIZED TRIAL OF IRINOTECAN AND CETUXIMAB WITH OR WITHOUT VEMURAFENIB IN BRAF-MUTANT METASTATIC COLORECTAL CANCER (SWOG 1406)

KOPETZ ET AL

SUMMARY

- 106 patients with *BRAF*^{V600} mutated and *RAS* wild-type mCRC
  - 39% prior irinotecan, no prior EGFR inhibitor use

	ironotecan + cetuximab vemurafenib	ironotecan + cetuximab	
PFS	4.4 months	2.0 months	(HR: 0.42, P < 0.001)
RR	16%	4%	(*P*=0.09)
SD	48%	17%	
DCR	67%	22%	(*P* < 0.001)

- Grade 3/4 adverse events were higher, and included neutropenia (28% vs 7%), anemia (13% vs 0%), and nausea (15% vs 0%)
- Overall survival results not yet mature

CONCLUSION

- This regimen shows promise in this difficult to treat population

PERTUZUMAB + TRASTUZUMAB FOR HER2-AMPLIFIED/OVEREXPRESSED METASTATIC COLORECTAL CANCER (MCRC): INTERIM DATA FROM MYPATHWAY

HURWITZ ET AL

SUMMARY

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- 34 patients with heavily pre-treated mCRC
  - (median # prior regimens = 4)
- Overall RR 13 (38.2%), stable disease 4
- Clinical benefit rate 17 (50%)
- Median PFS 4.6 months
  - 5.7 months for KRAS wild type patients
  - 1.4 months for KRAS mutant patients
- Median OS 10.3 months
  - 14 months for KRAS wild type patients
  - 5 months for KRAS mutant patients

CONCLUSION

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- Active regimen in patients with heavily pretreated HER2+ mCRC

MOLECULAR VARIANCES BETWEEN RECTAL AND LEFT-SIDED COLON CANCERS

SALEM ET AL

SUMMARY

- 1,457 primary tumors
  - 125 splenic flexure to descending colon (SFT)
  - 460 sigmoid colon (SgT)
  - 872 rectum (RT)

- Tumors evaluated with protein expression, gene amplification and NextGen sequencing, PCR for microsatellite instability (MSI)

- Somatic nonsynonymous missense mutations used to calculate tumor mutational load (TML)

RESULTS

	RT	SFT	
TP53	71%	57%	P=0.03
APC	66%	49%	P=0.01
PIK3CA	11%	22%	P=0.02
BRAF	3%	15%	P=0.0001
GNAS	0.9%	4%	P=0.04
HNF1A	0.7%	5%	P=0.01
CTNNB1	0.3%	4%	P=0.003
TOPO1	52%	31%	P=0.0001
ERCC1	29%	15%	P=0.03
MGMT	64%	53%	P=0.048

	SgT	RT	
TLE3	33%	23%	P=0.007
TOPO1	52%	35%	P<0.001
TUBB3	41%	28%	P=0.003
MGMT	64%	54%	P=0.003

No differences in

- PD-L1 expression frequency on tumor cells or tumor-infiltrating lymphocytes
- HER-2 expression and amplification

MSI was seen in 7% of SFT, 4% of SgT, and 0.7% of RT (total LT vs RT, the frequency of =0.01)

In all three cohorts, aTML > 17 mut/MB was highly concordant with MSI

SFT = splenic flexure to descending colon, SgT = sigmoid colon, RT = rectum

Presented by Salem et al at ASCO GI 2017

CONCLUSION

- The rectum has biologic differences from the “left colon”; clinical trials should stratify on molecular features as well as left vs. right

THE INTERNATIONAL WATCH AND WAIT DATABASE (WWD) FOR RECTAL CANCER: AN UPDATE

Maxime van der Valk et al

SUMMARY

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- Included 679 patients who exhibited a clinical complete response to neoadjuvant chemoradiation therapy for rectal cancer
- Median follow-up time 2.6 years (range 0-24 years)
- A total of 167 patients (25%) experienced local regrowth, 84% of which occurred in the first 2 years of follow-up in 84%
  - 96% had endoluminal local regrowth (n=161)
  - 4% in the loco-regional lymph nodes (n=7)
  - 7% had distant metastasis occurred (n=49)
- The overall 3-year-survival of all patients was 91%, and 87% in those with a local regrowth

RESULTS

		N=679
Sex	Male	449 (66%)
	Female	230 (34%)
Age	Mean	63.6 years
BMI	Mean	26.7 kg/m^2
Imaging	Endo/rectoscopy	598 (87%)
	MRI	434 (64%)
	ERUS	42 (6%)
	CT-pelvis	172 (25%)
T stage baseline	cT1	13 (2%)
	cT2	146 (28%)
	cT3	335 (64%)
	cT4	27 (5%)
N stage baseline	cN0	208 (40%)
	cN1	185 (35%)
	cN2	132 (25%)
M stage baseline	M0	635 (99%)
	M+	8 (1%)

CONCLUSION

- This approach may be safe with strict follow up, but it is unknown if it should be routinely offered to patients with CCR to neoadjuvant therapy for rectal cancer

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