maintenance therapy group (161 patients), 95 (59.0%) patients had KRAS WT and 66 (41.0%) had KRAS MT tumours. In the Bev maintenance therapy group(170 patients), 85 (50.0%) patients had KRAS WT and 85 (50.0%) had KRAS MT tumours. ORR, PFS and OS by mutation status are shown in the table.

Parameter	All patients (n = 331)	XELOX-Bev (n = 161)	Bev (n = 170)	Odds ratio/Hazard ratio (95% CI)
ORR, %				
KRAS WT	59	62	56	1.26 (0.70–2.30)
KRAS MT	43	39	46	0.77 (0.40–1.47)
Odds ratio (95% CI)	1.94 (1.25–3.02) p = 0.0031			
Median PFS, mo				
KRAS WT	10.9	13.1	9.9	1.19 (0.84–1.67) p = 0.33
KRAS MT	8.7	9.4.	8.3	0.92 (0.63–1.32) p = 0.63
Hazard ratio (95% CI)	0.67 (0.54–0.89) p = 0.0044			
Median OS, mo				
KRAS WT	25.8	27.2	24.3	1.15 (0.81–1.64); p = 0.43
KRAS MT	17.2	17.2	17.2	0.94 (0.65–1.35) p = 0.73
Hazard ratio (95% CI)	0.61 (0.47–0.79) p = 0.0001			

Conclusions: Patients with KRAS WT tumours had significantly improved outcomes compared with patients with KRAS MT tumours. Outcomes in patients with WT or MT tumours were not influenced by the type of maintenance therapy received (i.e. chemotherapy plus Bev or single-agent Bev).

6004 ORAL

Role of Baseline Circulating Tumour Cells and KRas Status in Patients With Metastatic Colorectal Cancer Treated With First-line Chemotherapy Plus Bevacizumab: a TTD Spanish Group Cooperative Study

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Background: Recent data suggest that baseline circulating tumour cell (CTC) count is a marker for clinical outcomes in patients with metastatic colorectal cancer (mCRC) treated with chemotherapy plus bevacizumab [Tol et al. Ann Oncol 2010; 21: 1006−12; Sastre et al. ESMO 2010, abstract 3476]. An exploratory, retrospective analysis of the MACRO randomized phase III study [Tabernero et al. ASCO 2010, abstract 3501] was performed to investigate the relationship between baseline CTC count and tumour Kirsten-ras (KRAS) mutational status and clinical outcome in patients with mCRC who received first-line treatment with chemotherapy plus bevacizumab followed by maintenance therapy with bevacizumab ± chemotherapy.
Methods: Patients with mCRC received capecitabine/oxaliplatin (XELOX) plus bevacizumab for 6 cycles followed by maintenance therapy with bevacizumab ± XELOX. Of the 480 randomized patients, baseline blood samples for determining CTC count by Veridex Cell Search method were collected in 180 patients; a cut-off value of 3 CTCs was selected based on the literature. Baseline tumour samples for determining KRAS status were collected in 331 patients. The relationship between CTC count (<3 or ⩾3 CTC) plus KRAS status (wild-type [WT] or mutant [MT]) and progression-free survival (PFS) and overall survival (OS) was analyzed.
Results: Data on both CTC count and KRAS status were available in 130 patients. Efficacy outcomes for each patient subgroup according to CTC count and KRAS status are shown in the Table.
Conclusions: Baseline CTC count and tumour KRAS status combined are strong markers for PFS and OS in patients with mCRC treated with chemotherapy and bevacizumab.

Parameter	KRAS WT		KRAS MT	
	CTC < 3 (n = 35)	CTC ⩾ 3 (n = 37)	CTC < 3 (n = 33)	CTC ⩾ 3 (n = 25)
Median PFS, mo	12.2	8.4	11.5	6.2
Log-rank	p = 0.0021			
Median OS, mo	30.7	15.4	19.8	12.9
Log-rank	0.0034			

6005 ORAL

A Multicenter, Randomized, Double-blind, Phase II Study of TAS-102 (A) Plus Best Supportive Care (BSC) Versus Placebo (P) Plus BSC in Patients (pts) With Chemotherapy-refractory Metastatic Colorectal Cancer (mCRC)

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Background: TAS-102 is a novel oral nucleoside antitumour agent, consisting of trifluorothymidine and thymidine phosphorylase inhibitor. This agent showed promising results with a disease control rate of 50.0% in 18 mCRC pts in the previous phase I study. This phase II study evaluated the efficacy and safety of TAS-102 compared with placebo after failure of standard therapy for mCRC.
Material and Methods: Patients with mCRC who had received standard therapy including fluoropyrimidine, irinotecan and oxaliplatin, adequate organ functions, and ECOG PS 0 to 2 were randomly assigned 2:1 to receive TAS-102 versus placebo. They were administered orally twice daily for day 1 to 5 and day 8 to 12 per every 4 weeks at 70 mg/m^2/day. Primary endpoint was overall survival (OS). *KRAS* test (codons 12 and 13) was evaluated by Scorpion-ARMS. In addition, the association among OS and *KRAS* status was analyzed.
Results: From August 2009 to April 2010, 172 pts were enrolled, 170 pts were received and 169 pts were assessable (A, 112; P, 57). There was no significant imbalance in baseline pts background between the two arms: males (A, 57.1%; P, 49.1%); median age (A, 63 yrs; P, 62 yrs); ECOG PS 0 (A, 64.3%; P, 61.4%); 2/>=3 prior regimen (A, 15.2/84.8%; P, 22.8/77.2%); prior treatment with bevacizumab (A, 76.8%; P, 82.5%); with cetuximab (A, 63.4%; P, 63.2%). TAS-102 significantly improved OS compared with placebo (median OS, 9.0 vs.6.6 months, HR, 0.56; p = 0.001). Among 170 pts, the observed toxicities of grade 3/4 more than 5% were neutropenia (17.6%) and leucopenia (9.4%), without treatment-related deaths. *KRAS* status was ascertained in 149 of 169 pts (A, 99, P, 50). *KRAS* status was wild-type (wt)/mutant-type (mt) (A, 54/45; P, 24/26). In the *KRAS* wt subset, HR was 0.70, with no significant trend for favoring TAS-102. In the mt subset, HR was 0.44, with a statistically significance for favoring TAS-102. No interaction was observed between wt and mt.

Patients	Group	N	Median OS (months)	HR	95% CI	P value
All	A	112	9.0	0.56	[0.39, 0.81]	0.001
	P	57	6.6			
wt	A	54	7.2	0.70	[0.41, 1.20]	0.191
	P	24	7.0			
mt	A	45	13.0	0.44	[0.25, 0.80]	0.006
	P	26	6.9			

Conclusions: TAS-102 significantly improved OS with a good safety profile in pts with mCRC who failed to conventional cytotoxic agents and targeting agent. TAS-102 is the first cytotoxic agent that showed significant survival prolongation for mCRC in this setting, though this should be confirmed in a phase III study including *KRAS* status analysis.