IMPACT OF SECOND-LINE CETUXIMAB-CONTAINING THERAPY IN PATIENTS WITH KRAS WILD TYPE METASTATIC COLORECTAL CANCER: RESULTS FROM ITACA TRIAL.

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Background

The ITACA trial was an academic study on the management strategy for patients with metastatic colorectal cancer, designed to define the role of cetuximab (Cet) and bevacizumab (Bev) in combination with standard chemotherapy (CT, FOLFIRI or FOLFOX4) in first- and second-line treatment (Fig 1).

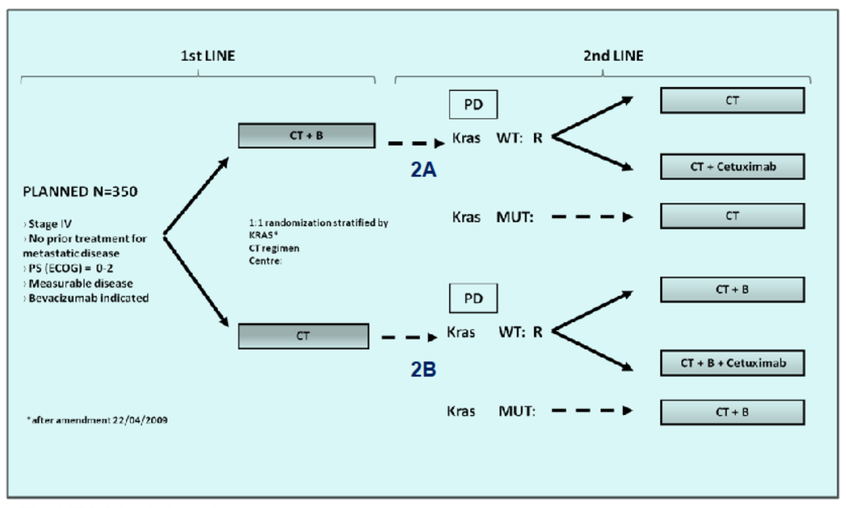

Fig.1 ITACA trial design

Results from the first-line trial (Arm A: CT+Bev vs Arm B: CT alone) were recently published (Passardi et al, Ann Oncol 2015); the second-line trial results are presented here.

Methods

All patients randomized in the first-line trial who fulfilled inclusion criteria were randomized onto two independent second-line trials (Fig.1):

•Study 153 01/2A: Arm A patients with wild type (WT) KRAS were randomized to the other CT regimen or the other CT plus Cet. Arm A patients with mutated KRAS were not randomized and treated with the other CT regimen alone.

•Study 153 01/2B: Arm B patients with WT KRAS were randomized to the other CT plus Bev or the other CT plus Bev plus Cet. Arm B patients with mutated KRAS were not randomized and treated with the other CT plus Bev.

The primary objective was to determine, separately for each study, whether the addition of Cet to CT or to CT plus Bev, would improve efficacy in terms of PFS.
Secondary objectives were to determine the ORR, OS and the safety profile of the treatments administered.

Results

Of the 370 patients recruited in the first-line trial, 48 and 56 KRAS WT patients were randomized onto Study 153 01/2A and 153 01/2B, respectively, while 31 and 40 KRAS mutated patients were treated without randomization in the 2 study groups. Patients' characteristics of KRAS WT patients are shown in Table 1.

Patient Characteristics	CT (N=25) No. (%)	CT+cet (N=23) No. (%)	CT+bev (N=31) No. (%)	CT+bev+cet (N=25) No. (%)
Age: median years (range)	63 (44-82)	65 (35-82)	64 (45-81)	65 (33-79)
Gender				
Male	16 (64.0)	16 (69.6)	20 (64.5)	16 (64.0)
Female	9 (36.0)	7 (30.4)	11 (35.5)	9 (36.0)
Performance Status (ECOG)				
0	20 (80.0)	16 (69.6)	25 (83.3)	17 (68.0)
1-2	5 (20.0)	7 (30.4)	5 (16.7)	8 (32.0)
Tumor localization				
rectum	8 (32.0)	3 (13.0)	10 (32.3)	4 816.0)
colon	17 (68.0)	20 (87.0)	21 (67.7)	21 (84.0)
Stage at diagnosis				
I-III	6 (24.0)	3 (13.6)	7 (23.3)	6 (25.0)
IV	19 (76.0)	19 (86.4)	23 (76.7)	18 (75.0)
CT regimen				
FOLFOX	9 (36.0)	9 (39.1)	15 (48.4)	10 (40.0)
FOLFIRI	16 (64.0)	14 (60.9)	16 (51.6)	15 (60.0)

KRAS WT patients

Efficacy data (PFS, OS) of both study groups are summarized in Fig 2. ORR is reported in Table 2.

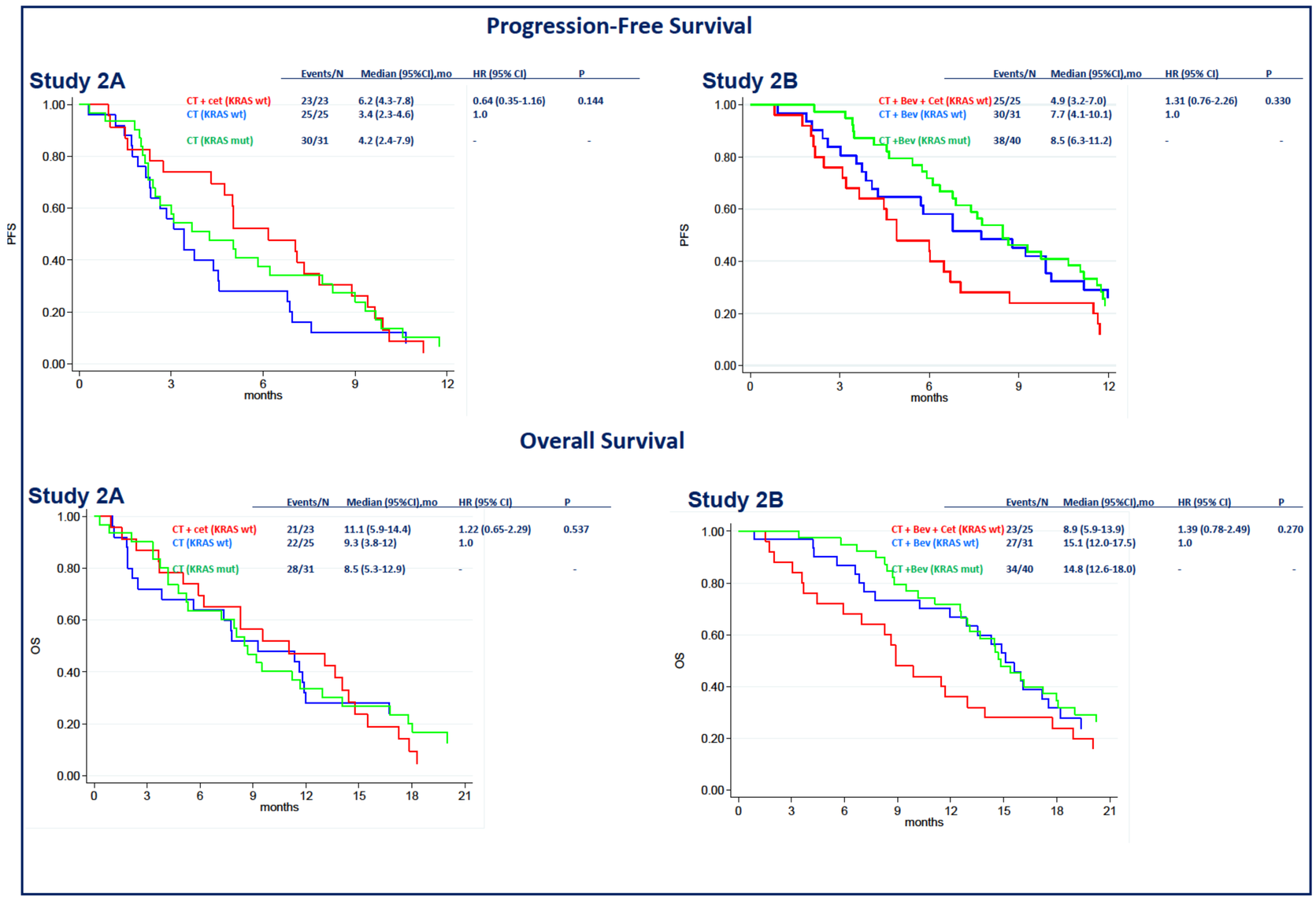

Fig.2 Kaplan-Meier curves for PFS and OS by treatment group

	ORR (CR or PR/No. patients)
Study 2A	
CT	16%
CT+Cet	30.5%
p	p=0.398 (Chi-square test)
CT (mut KRAS)	25.8%
Study 2B	
CT+Bev	32.2%
CT+Bev+Cet	16%
p	p=0.277 (Chi-square test)
CT+Bev (mut KRAS)	25%

Table 2. ORR by treatment group (Study 2A and Study 2B).

Discussion

Notwithstanding limitations due to the small sample size, our results suggest that, among patients with WT KRAS, the addition of Cet to second-line CT increased PFS, while the addition of Cet to CT + Bev was associated with decreased PFS.

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