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# Maintenance treatment with cetuximab versus observation in RAS wild-type metastatic colorectal cancer: First results of the randomized phase II TIME-PRODIGE28 UNICANCER study according to RAS/BRAF status

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## Background

Although anti-EGFR monoclonal antibodies are active as single-agent therapy in *RAS* wild-type (wt) metastatic colorectal cancer (mCRC), few studies are available on their role in maintenance therapy during chemotherapy (CT)-free intervals (CFI).

## Methods

*RAS* wt unresectable mCRC patients with controlled disease after FOLFIRI + cetuximab (8 cycles) were randomized (1:1) to receive maintenance with bi-weekly cetuximab alone (arm A) or observation (arm B) until disease progression (PD)/unacceptable toxicity/death. Randomization was stratified according to tumor response, center, baseline Köhne score, CEA and platelet count. In case of tumor progression during the CFI, FOLFIRI + cetuximab was to be reintroduced for 8 cycles, followed by a new CFI. The primary objective of this multicenter non-comparative randomized phase II trial was the 6-month progression-free rate (PFR) after initiation of maintenance therapy. A total of 134 randomized and evaluable patients (67 per arm) were required (Fleming's one-step design, one-sided  $\alpha=5\%$ ,  $\beta=20\%$ ,  $H_0: 40\%$ ;  $H_1: 55\%$ ). Among secondary endpoints, overall response rate (ORR) and progression-free survival (PFS) from randomization are available. *RAS* and *BRAF* status were centrally validated by NGS using the AmpliSeq™ Colon and Lung Panel v2.

## Results

214 patients were included according to *RAS* status locally assessed in each center, and 139 randomized (67 arm A/72 arm B). Baseline characteristics were: median age, 64/68 years; ECOG PS 0, 55%/49%; single metastatic site, 58%/47%; right-sided primary, 24%/18%. The median follow-up was 29.6 months. Table: 429P

Results according to *RAS* and *BRAF* status

	Included		Randomized		Arm B - Observation	
	All n=214	BRAF <sup>V600E</sup> +RASwt n=184 (86%)	All n=67	BRAF <sup>V600E</sup> +RASwt n=60 (90%)	All n=72	BRAF <sup>V600E</sup> +RASwt n=66 (92%)
ORR (%) before randomization	55	58	75	78	69	68
6-month PFR (%) after randomization [95% CI]	-	-	39 [27; 52]	42 [29; 55]	7 [2; 16]	8 [3; 17]
Median PFS (months) after randomization [95% CI]	-	-	5.3 [3.7; 7.4]	5.7 [3.7; 7.7]	2.0 [1.8; 2.4]	2.0 [1.8; 2.7]

## Conclusions

Although the cetuximab maintenance arm did not meet the primary objective, a clinically meaningful difference in PFS in favor of cetuximab maintenance was found in *RAS/BRAF* wt mCRC patients.

## Clinical trial identification

NCT02404935.

## Legal entity responsible for the study

UNICANCER.

## Funding

Merck Serono S.A.S.

## Disclosure

V. Boige: Financial Interests, Personal and Institutional, Other, consulting, training, clinical research, travel, accomodations, expenses: Merck; Financial Interests, Personal, Other, consulting: Eisai; Ipsen; BMS; Financial Interests, Personal, Other, consulting, training, clinical research, travel, accomodations, expenses: Bayer; Roche; Sanofi Genzyme; Financial Interests, Personal, Other, training, clinical research, travel, accomodations, expenses: Amgen; Financial Interests, Personal, Training: MSD; Novartis; Financial Interests, Personal, Other, consulting: Daiichi Sankyo; Prestizia. E. Francois: Financial Interests, Personal, Other, consulting, honoraria, travel, accomodations, expenses: Roche; Financial Interests, Personal, Other, honoraria, travel, accomodations, expenses: Servier; MSD; Novartis; Amgen. M. Ben Abdelghani: Financial Interests, Personal, Other, consulting, travel, accomodations, expenses, expert testimony: Sanofi; Servier; Bayer; Ipsen; Amgen. Financial Interests, Personal, Other, travel, accomodations, expenses, expert testimony: Roche. J.M. Phelip: Financial Interests, Personal, Other, consulting, honoraria, travel, accomodations, expenses, research funding: Merck; Roche; Bayer; Sanofi; Financial Interests, Personal, Other, consulting, honoraria, travel, accomodations, expenses: Amgen; Servier; Msd; Pierre Fabre. V. Hautefeuille: Financial Interests, Personal, Invited Speaker: Novartis; Merck; Amgen; Financial Interests, Personal, Advisory Board: Ipsen; Sanofi Aventis; AAA. C. de la Fouchardiere: Financial Interests, Personal, Other, consulting, travel, accomodations, expenses: Servier; Eisai; Roche; Financial Interests, Personal, Other, consulting: Bayer; Lilly; Pierre Fabre; MSD; Financial Interests, Personal, Other, travel, accomodations, expenses: Amgen; BMS. H. Blons: Financial Interests, Personal, Training: AstraZeneca; BMS; MSD. O. Bouche: Financial Interests, Personal, Other, honoraria as a speaker and/or in an advisory role: Merck KgaA; Bayer; AstraZeneca; Grunenthal; MSD; Amgen; Servier; Pierre Fabre; Roche; Genentech. All other authors have declared no conflicts of interest.

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