Impact of concomitant medication on recurrence, survival and tolerability of chemotherapy in early colon cancer patients – results from the PETACC 8 study

FPN 567P Colorectal cancer

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Introduction

- Few information is available about the impact of concomitant medication (CM) on the tolerability of chemotherapy as well as on the outcome of cancer patients in general.
- We aimed to evaluate the impact of CM on disease-free survival (DFS), overall survival (OS) as well as tolerability of adjuvant chemotherapy in a large cohort of early colon cancer (CC) patients.

Methods

- PETACC8: phase III randomized trial, resection with curative intent of a stage II or III colon cancer (CC), standard adjuvant fluoropyrimidine and oxaliplatin (+/- cetuximab) over 6 months.
- 2559 patients of PETACC 8 with available information on CM intake gathered by study visits at inclusion as well as during chemotherapy were included into analysis
- CM was coded according to the WHO ATC classification system
- Focus on the most frequent 5 CM categories: Gastro-esophageal reflux disease (GERD) treatment, anticoagulants, platelet aggregation inhibitors, cardiovascular and antidiabetic drugs
- Primary objective: Association between 5 CM groups / number of CM with DFS / OS
- Secondary objective: Association between 5 CM groups / number of CM with grade 3/4 adverse events (AEs), treatment discontinuation due to toxicity, dose reductions

Results

Table 1. Patients characteristics

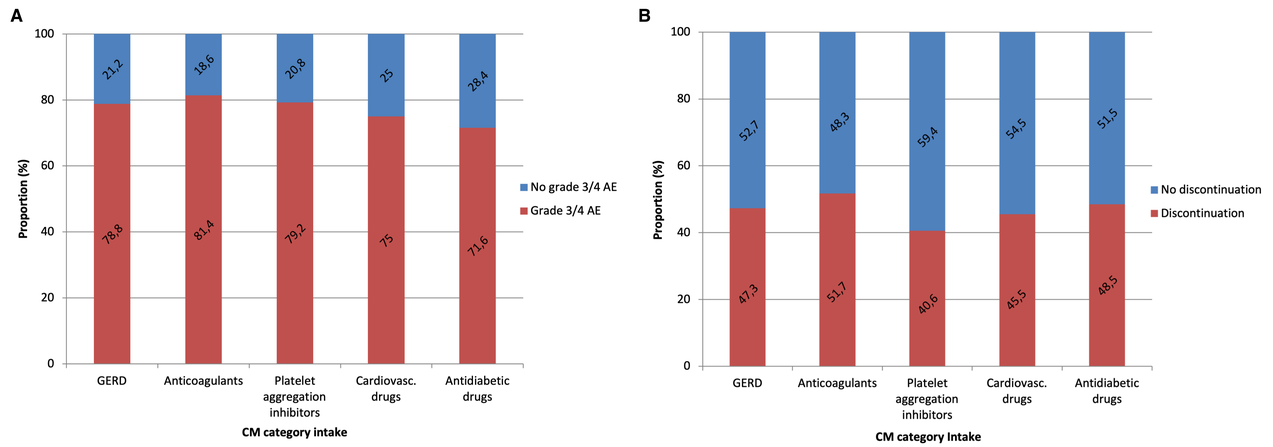
		N	%
Number of CM per patient	n	2559	
	median	8	
	range	0-25	
categorized numbers of CM per patient	n	2559	
	none	22	0.9
	< 5	395	15.4
	5-10	1307	51.1
	>10	813	31.8
CM category	n	2559	
	GERD treatments	1328	51.9
	anticoagulants	452	17.7
	platelet aggregation inhibitors	279	10.9
	Cardiovascular drugs	1028	40.2
	Antidiabetic drugs	236	9.2

Results

Table 2. Results of uni- and multivariate analyses on DFS and OS

	DFS				OS			
	uni		multi		uni		multi	
	HR [95%CI]	p	HR [95%CI]	p	HR [95%CI]	p	HR [95%CI]	p
Number of CM (*ref 0-5*)								
> 10	1.17 [0.95;1.45]	*0.139*	-	-	1.15 [0.9;1.47]	*0.274*	-	-
5-10	0.98 [0.8;1.19]	*0.809*	-	-	0.98 [0.77;1.24]	*0.867*	-	-
GERD treatments	0.95 [0.83;1.1]	*0.506*	-	-	0.94 [0.8;1.11]	*0.471*	-	-
Anticoagulants	1.34 [1.13;1.59]	***0.001***	1.29 [1.06;1.56]	***0.010***	1.33 [1.09;1.62]	***0.005***	1.28 [1.02;1.59]	***0.032***
Platelet aggregation inhibitors	1.25 [1.02;1.54]	***0.033***	1.12 [0.88;1.42]	*0.375*	1.54 [1.22;1.93]	***0.000***	1.27 [0.97;1.66]	*0.088*
Cardiovascular drugs	1.17 [1.02;1.35]	***0.025***	1.13 [0.95;1.34]	*0.163*	1.27 [1.08;1.5]	***0.004***	1.15 [0.94;1.4]	*0.177*
Antidiabetic drugs	1.37 [1.1;1.7]	***0.005***	1.25 [0.96;1.61]	*0.097*	1.48 [1.16;1.9]	***0.002***	1.30 [0.96;1.75]	*0.086*

Figure 1. Proportion of patients with and without A) grade 3/4 adverse events (AEs) and B) discontinuation of therapy due to toxicity according to CM categories



- Among 2559 patients included in the PETACC 8 trial, information regarding patient-self-reported CM was available in all patients. Therefore, all 2559 patients could be considered for this final analysis.
- Anticoagulation treatment was the only CM category being significantly and independently associated with a shorter DFS (HR 1.29, 95%CI 1.06-1.56, *p=0.010*) as well as OS (HR 1.28, 95%CI 1.02-1.59, *p=0.032*).
- No association of number of CM (<5, 5-10, >10) has been observed neither with DFS (ref.; HR 0.98; HR 1.17) nor OS (ref.; HR 0.98; HR 1.15) (*p>0.05*).
- The proportion of grade 3/4 AEs compared to no grade 3/4 AE was significantly higher in patients with GERD treatment intake (78.8% vs 21.2%, *p<0.001*), anticoagulation intake (81.4% vs 18.6%, *p<0.001*) and platelet aggregation inhibitors intake (79.2% vs 20.8%, *p=0.012*). The proportion of treatment discontinuation due to toxicity compared to no discontinuation was significantly higher in patients with anticoagulation intake (51.7% vs 48.3%, *p=0.028*).
- Grade 3/4 AEs correlated directly with number of CM with 0.0% of patients with no CM, 53.5% of patients with less than 5 CM, 73.5% with 5 to 10 CM and 84.0% with more than 10 CM experiencing a grade 3/4 AE (*p<0.001*). Treatment discontinuation due to toxicity correlated directly with number of CM with 5.9% of patients with no CM, 36.9% of patients with 1 to 5 CM, 51.2% of patients with 5 to 10 CM and 43.4% of patients with more than 10 CM (*p<0.001*).

Discussion

- Patients with a high CM intake did not experience a shorter DFS or OS under adjuvant chemotherapy for early CC.
- Patients with anticoagulants had a significantly and independently shorter DFS and OS.
- A higher rate of grade 3/4 AEs and discontinuations of therapy due to toxicity in these patients may serve as explanation.

Conflicts of interests

- J TAIEB has received travel grants and honoraria for speaker or advisory role from: Astra Zeneca, Astellas, Amgen, BMS, Merck Serono, MSD, Novartis, Ono pharmaceuticals, Pfizer, Pierre Fabre, Servier, Roche and Takeda. All other authors declare no conflicts of interest for this communication.

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