

Evolution of efficacy and safety of cetuximab with the determination of RAS status in Metastatic Colorectal Cancer (mCRC) elderly patients

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INTRODUCTION

Successive **EMA approvals** have been given for **cetuximab** : determining **wild type RAS status** (exons 2, 3 and 4 of KRAS and NRAS) is now mandatory prior to its initiation.

Influence of RAS status on the **efficacy and safety of cetuximab** in metastatic colorectal cancer elderly patients have been analyzed.

METHODS

Data from **2 studies** were compared :

- **Erbix Ouest study** with patients of **70 years and over** who s began to receive cetuximab from April 2004 to December 2006 (**115 patients – KRAS and NRAS unknown**). [Metges *et al*, 2016]

- **RAS study** with wild-type KRAS patients had began to receive cetuximab based regimen from September 2007 to November 2011 (**70 elderly patients**) for which **NRAS was defined retrospectively**.

OBSERVATORY OF CANCER BRETAGNE PAYS DE LA LOIRE

- Created in 2003 by Regional Representatives of French ministry of health
- Collects data from both private and public hospitals

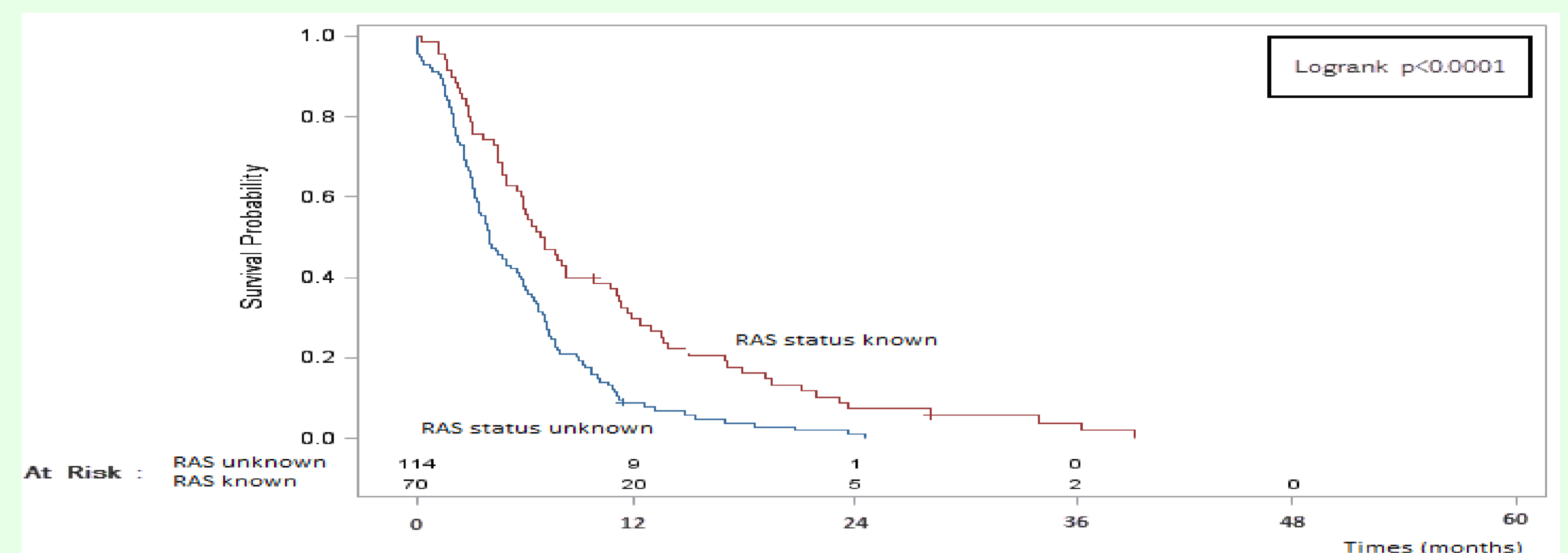
Evaluation and expertise in oncology :

- Working with practitioners to improve drug use and clinical practices
- Evaluation of drugs in current practice : benefit/risk/cost
- Healthcare coordination : care pathways and link between professionals

POPULATION DESCRIPTION

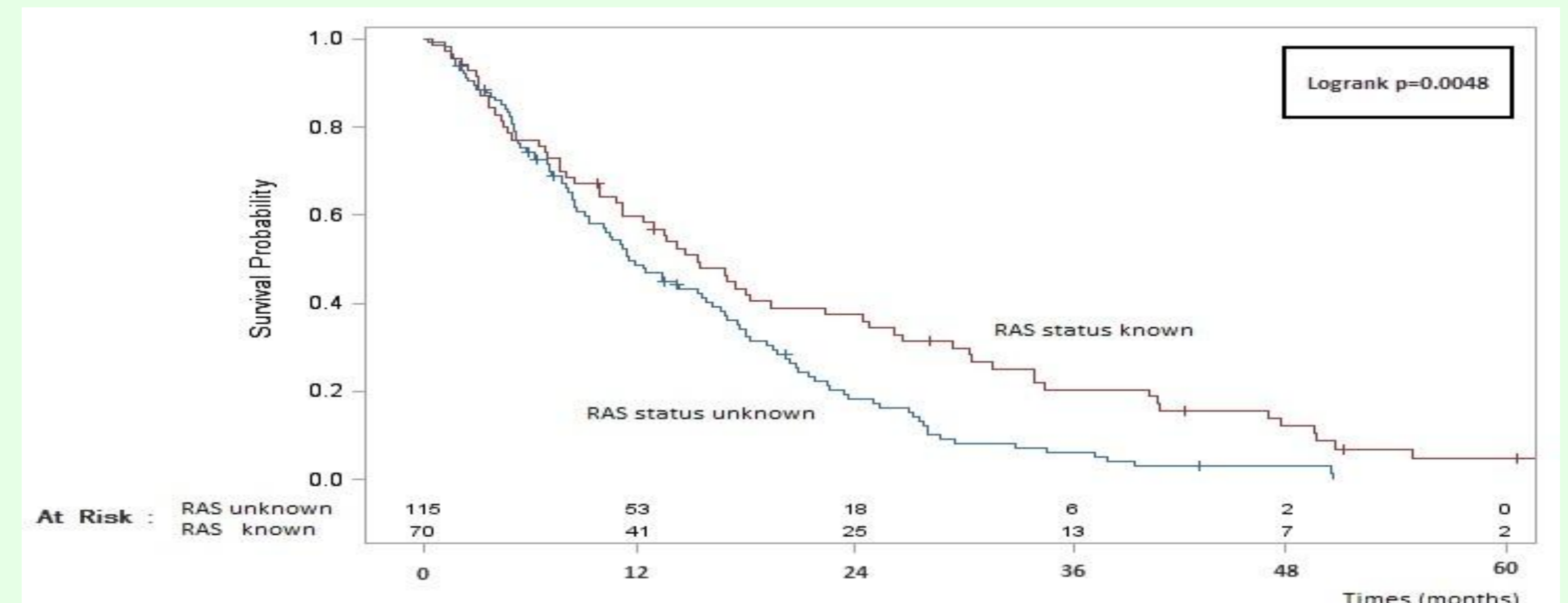
		Erbix Ouest (n=115) RAS status unknown		RAS study (n= 70) RAS status known		p
		n	%	n	%	
Sex ratio	Women	49	43%	17	24%	<0.0001
	Men	66	57%	53	76%	
Age	≥ 70-75	70	61%	29	41%	0.0807
	≥ 75-80	36	31%	30	43%	
	≥ 80	9	8%	11	16%	
	Median age [min;max]	74 years	[70;82]	75 years	[70;105]	
Primary diagnostic	Tumor surgery	97	84%	55	79%	
	Synchronous metastasis	69	60%	43	61%	
Cetuximab Treatment	Median number of line	3	[1;7]	2	[1;6]	
	Median number of cycles	6	[1;45]	6	[1;34]	
Association	Irinotecan	100	87%	15	21%	
	FOLFIRI (5-fluorouracil - 5FU, folinic acid - FA and irinotecan)	15	13%	40	57%	
	FOLFOX (5FU, FA and oxaliplatin)			10	14%	
	5 FU / capecitabine			5	7%	
Objective Response	CR	0	0%	2	3%	0.0023
	PR	22	19%	28	40%	
	SD	28	24%	12	17%	
	PD	54	47%	12	17%	
	Toxicity	4	3%	11	16%	
Reason of discontinuation	NA (Non Assessable)	7	6%	5	7%	
	End of treatment	20	17%	10	14%	
	PD	48	42%	20	29%	
	Toxicity	10	9%	11	16%	
Grade III/IV toxicities	Investigator decision	21	18%	21	30%	0.0836
	Patient wishes	4	3%	4	6%	
	Death	7	6%	2	3%	
	NA (Non Assessable)	5	4%	2	3%	
Total	Total	21	18%	23	33%	0.1101
	≥ 70-75	11	52%	8	35%	
	≥ 75-80	9	43%	10	43%	
≥ 80	1	5%	5	22%		

PROGRESSION FREE SURVIVAL (PFS)



	RAS status unknown	RAS status known	p
Median [IC95%]	3.9 [3.2 ; 5.6]	6.8 [5.5 ; 9.6]	<0.0001
One-year survival rate [IC95%]	8.7% [4.5% ; 14.8%]	29.6% [19.4% ; 40.6%]	
Two-year survival rate [IC95%]	0.9% [0.08% ; 4.7%]	7.4% [2.7% ; 15.2%]	

OVERALL SURVIVAL (OS)



	RAS status unknown	RAS status known	p
Median [IC95%]	11.3 [9.1 ; 15.6]	15.1 [11.0 ; 22.3]	0.0048
One-year survival rate [IC95%]	48.8% [39.1% ; 57.7%]	59.8% [47.4% ; 70.2%]	
Two-year survival rate [IC95%]	18.3% [11.5% ; 26.3%]	37.5% [26.1% ; 48.8%]	

DISCUSSION / CONCLUSION

- Comparison of one historical series (Erbix Ouest) and one updated series of patients (determination of RAS status).
- Good use of drug has evolved in function of scientific publications (EGFR → KRAS → RAS).
- Evolution of gold standard treatment (cetuximab alone, cetuximab irinotecan vs cetuximab FOLFIRI/FOLFOX) has lead to major risk of toxicities. But here, same profile of toxicities has been observed in the 2 arms (p=0.0836).
- Aged population seemed to have a clinical benefit to receive cetuximab based regimen (RC+PR+SD=51.5%). As expected, optimization of the drug delivery with the use of RAS status improved clinical benefit (43% vs 60%; p=0.0023).