Outcome of EGFR-mutated NSCLC patients with MET-driven resistance to EGFR tyrosine kinase inhibitors

SUPPLEMENTARY MATERIALS

Supplementary Table 1: Re-biopsy characteristics. * : range ; † : one missing data in total population ; TKI : tyrosine kinase inhibitor ; p : p value

	Overall population	*MET* amplification	MET overexpression no *MET* amplification	p	T790M+	T790M-	p
	n = 42	n = 19	n = 17		n = 11	n = 30	
Re-biopsy obtained after EGFR TKI RECIST progression	38 (90,5%)	15 (78,9%)	17 (100%)	0,11	10 (90,9%)	27 (90%)	1
Number of lines ongoing or over at the time of re-biopsy				1			1
≤2	37 (88,1%)	17 (89,5%)	15 (88,2%)		10 (90,9%)	26 (86,7%)	
≥3	5 (11,9%)	2 (10,5%)	2 (11,8%)		1 (9,1%)	4 (13,3%)	
Median time between re-biopsy and EGFR TKI initiation (months)	15,6 (2,1-61,3)*	14,1 (3,6-31,8)*	20,7 (2,1-31,3)*	0,39	22,1 (9,1-36)*	12,1 (2,1-61,3)*	**0,050**
Re-biopsy obtained while TKI EGFR is still ongoing†	28 (68,3%)	15 (79,0%)	9 (56,3%)	0,15	5 (50%)	23 (76,7%)	0,13
Re-biopsy site							
Lung	23(54,8%)	12(63,2%)	8(47,1%)		6(54,5%)	16(53,3%)	
Pleura	3(7,1%)	2(10,5%)	1(5,9%)		0(0%)	3(10%)	
Lymph node metastasis	4(9,5%)	1(5,3%)	1(5,9%)		1(9,1%)	3(10%)	
Brain	3(7,1%)	0(0%)	3(17,6%)		1(9,1%)	2(6,7%)	
Liver	4(9,5%)	2(10,5%)	1(5,9%)		2(18,2%)	2(6,7%)	
Skin	1(2,4%)	1(5,3%)	0(0%)		0(0%)	1(3,3%)	
Adrenal glands	2(4,8%)	0(0%)	2(11,8%)		0(0%)	2(6,7%)	
Bone	1(2,4%)	0(0%)	1(5,9%)		1(9,1%)	0(0%)	
Muscle	1(2,4%)	1(5,3%)	0(0%)		0(0%)	1(3,3%)	

Supplementary Table 2: First EGFR TKI therapy and MET alterations of patients with an EGFR exon 19 deletion or an EGFR exon 21 mutation on the initial biopsy. [*]: % calculated with the number of patients with a MET FISH ; [**] : % calculated with the number of patients with a MET IHC ; TKI : tyrosine kinase inhibitor ; IHC : Immunochemistry ; FISH : Fluorescence In Situ Hybridization ; p : p value

	Patients with EGFR exon 19 deletion	Patients with EGFR exon 21 L858R mutation	p
	N = 23	N =16	
First EGFR TKI			1
gefintib or erlotinib	22 (95,7%)	16 (100%)	
afatinib	1 (4,3%)	0 (0%)	
MET FISH on re-biopsy	21 (91,3%)	12 (75%)	0,21
***MET* amplified on re-biopsy**	12 (57,1%)[*]	6 (50%)[*]	0,73
MET IHC on re-biopsy	20 (87%)	13 (81,25%)	0,67
MET IHC 3+ on re-biopsy	20 (100%)[**]	13 (100%)[**]	1

Supplementary Table 3: Molecular alterations and prognosis of T790M positive patients. [*] lost of follow up immediately after EGFR TKI progression. [*] patient 45 : the T790M mutation was not detected on the re-biopsy displaying MET amplification. However, very few tumor cells were found in this sample. The T790M mutation was detected in a tumor biopsy obtained before the re-biopsy displaying MET amplification in this patient. [†] patient 46 : the research of T790M mutation was not performed on the re-biopsy displaying MET amplification. The T790M mutation was detected in circulating free DNA in this patient. OS : overall survival. PPOS : post progression overall survival. OS and PPOS are expressed in months

ID	*MET* amplification	Primary EGFR mutation	OS	PPOS
5	+	Exon 19 deletion	121,3	8,7
16	-	Exon 21 L858R mutation	26,7	16,0
18	+	Exon 21 L858R mutation	43,1	36,9
22		Exon 19 deletion	36,6	14,6
26	-	Exon 19 deletion	36,2	23,8
27		Exon 21 L858R mutation	25,0	17,0
28	+	Exon 21 L858R mutation	21,8	1,6
34[*]	-	Exon 19 deletion	37,1	0
35		Exon 19 deletion	27,7	13,7
45[**]	+	Exon 19 deletion	33,8	18,6
46[†]	+	Exon 19 deletion	44,3	12,9