Supplementary Online Content

Sacher AG, Dahlberg SE, Heng J, Mach S, Jänne PA, Oxnard GR. Association between younger age and targetable genomic alterations and prognosis in non–small-cell lung cancer. *JAMA Oncol*. Published online December 17, 2015. doi:10.1001/jamaoncol.2015.4482.

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eTable 1: patient demographic information and genotype for those included in the composite targetable genomic alteration analysis.

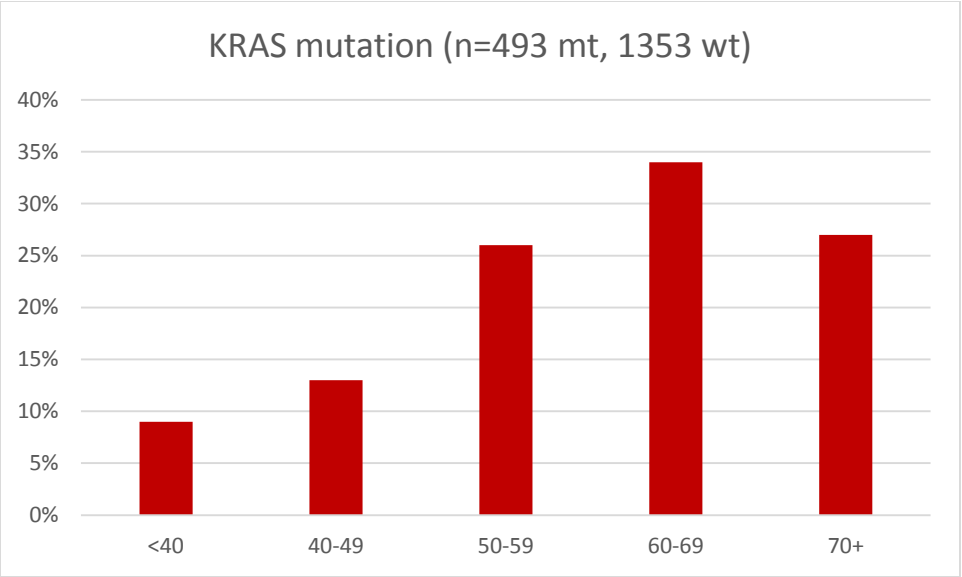
		Total		<40		40-49		50-59		60-69		70+		p-value
Patients		1325	100%	53	4%	153	12%	364	27%	432	33%	323	24%	
Sex	Male	448	34%	17	32%	42	27%	115	32%	147	34%	127	39%	0.002
	Female	877	66%	36	68%	111	73%	249	68%	285	66%	196	61%	
Race	White	1157	89%	36	71%	127	85%	311	87%	389	93%	294	92%	<0.001
	Asian	75	6%	7	14%	16	11%	24	7%	20	5%	8	3%	
	Black	40	3%	2	4%	5	3%	18	5%	6	1%	9	3%	
	Hispanic	22	2%	6	12%	2	1%	4	1%	3	1%	7	2%	
Smoker	Never	451	34%	40	75%	83	55%	126	35%	108	25%	94	29%	<0.001
	Light (≤10 py)	138	10%	5	10%	19	12%	42	12%	39	9%	33	10%	
	Heavy (>10 py)	710	54%	8	15%	49	32%	191	53%	276	64%	186	58%	
Stage	I	239	18%	5	10%	25	16%	60	16%	80	19%	69	21%	<0.001
	II	105	8%	2	4%	10	7%	21	6%	34	8%	38	12%	
	IIIA	177	13%	2	4%	16	10%	55	15%	61	14%	43	13%	
	IIIB	56	4%	7	13%	8	5%	10	3%	17	4%	14	4%	
	IV	747	56%	37	70%	94	61%	218	60%	240	57%	158	49%	
Histology	Adeno	1205	91%	44	83%	138	90%	334	92%	405	93%	284	88%	<0.001
	Squamous	5	0.04%	2	4%	0	0%	2	1%	0	0%	1	0.03%	
	NSCLC NOS	115	9%	7	13%	15	10%	28	8%	27	6%	38	12%	
Targetable Alteration	**Detected**	**707**	**53%**	**41**	**77%**	**119**	**78%**	**197**	**54%**	**194**	**45%**	**156**	**48%**	**<0.01**
	Absent†	**618**	**47%**	**12**	**23%**	**34**	**22%**	**167**	**46%**	**238**	**55%**	**167**	**52%**	
EGFR Mutation	MUT	540	41%	25	47%	80	52%	149	41%	157	36%	129	40%	0.01
	WT	785	59%	28	53%	73	48%	215	59%	275	64%	194	60%	
ALK	MUT	84	6%	13	25%	26	17%	25	7%	16	4%	4	1%	<0.001
	WT	1241	94%	40	75%	127	83%	339	93%	416	96%	319	99%	
HER2 Exon 20	MUT	44	3%	1	2%	10	7%	13	4%	10	2%	10	3%	0.15
	WT	1281	97%	52	98%	143	93%	351	96%	422	98%	313	97%	
ROS1	MUT	20	1%	3	6%	3	2%	5	1%	4	1%	5	1%	0.12
	WT	1305	99%	50	94%	150	98%	359	99%	428	99%	318	99%	
BRAF V600E	MUT	24	2%	0	0%	1	1%	6	2%	8	2%	9	3%	0.42
	WT	1301	98%	53	100%	152	99%	358	98%	424	98%	314	97%	

†Patients must have been tested for all 5 targetable genomic alterations to be considered negative for a targetable alteration (912 patients with incomplete testing were excluded from this category).

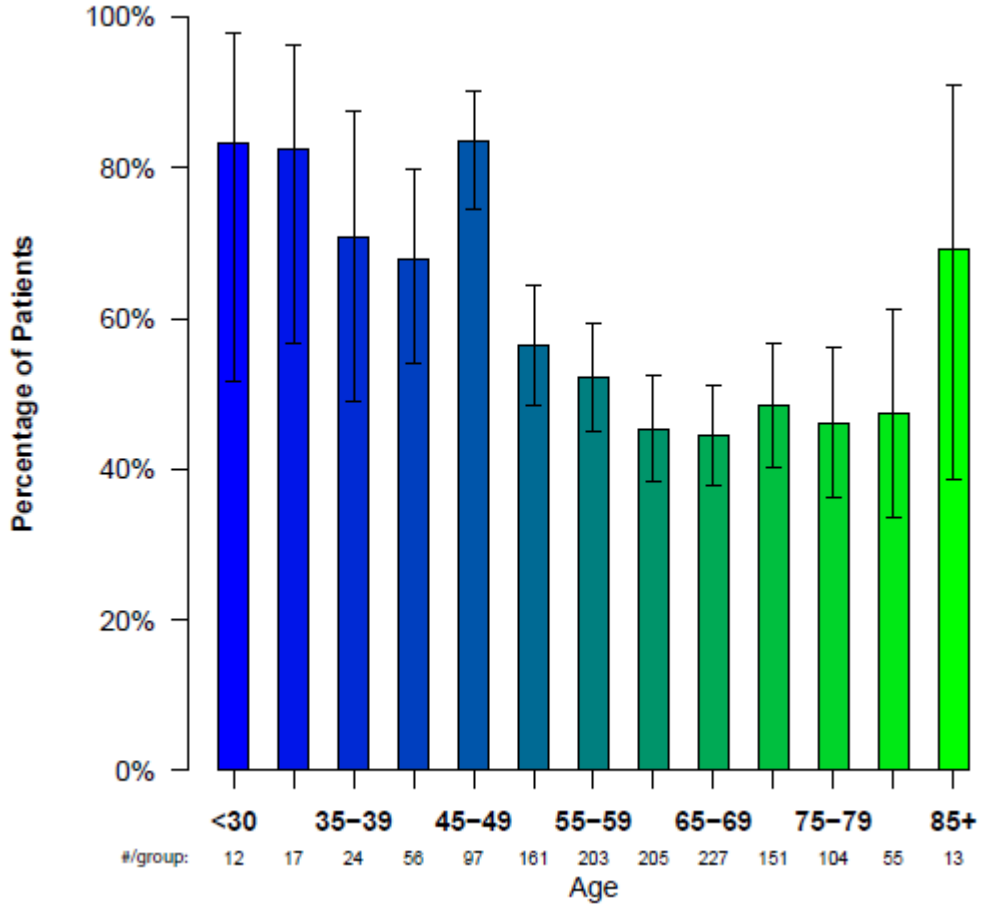
eTable 2: Cox-regression survival analysis of age category as primary predictor

	HR	95% CI	p-value
Age Category			
1: <40	0.73	0.32-1.67	0.46
2: 40-49	0.75	0.57-0.98	0.04
3: 50-59	0.66	0.54-0.82	<0.01
4: 60-69	0.73	0.60-0.89	<0.01
5: 70+	-	-	-
Presence of Targetable Genomic Alteration, Targeted Therapy Received†	0.66	0.55-0.79	<0.01
Presence of Targetable Genomic Alteration, Targeted Therapy Not Received	1.06	0.80-1.40	0.71
Metastatic at Diagnosis	1.48	1.25-1.76	<0.01
Female Sex	0.86	0.73-1.00	0.05
Adenocarcinoma Histology	0.84	0.65-1.09	0.19
Brain Mets Present	1.25	1.07-1.47	<0.01
Year of Diagnosis with Metastatic Disease	1.11	1.07-1.15	<0.01

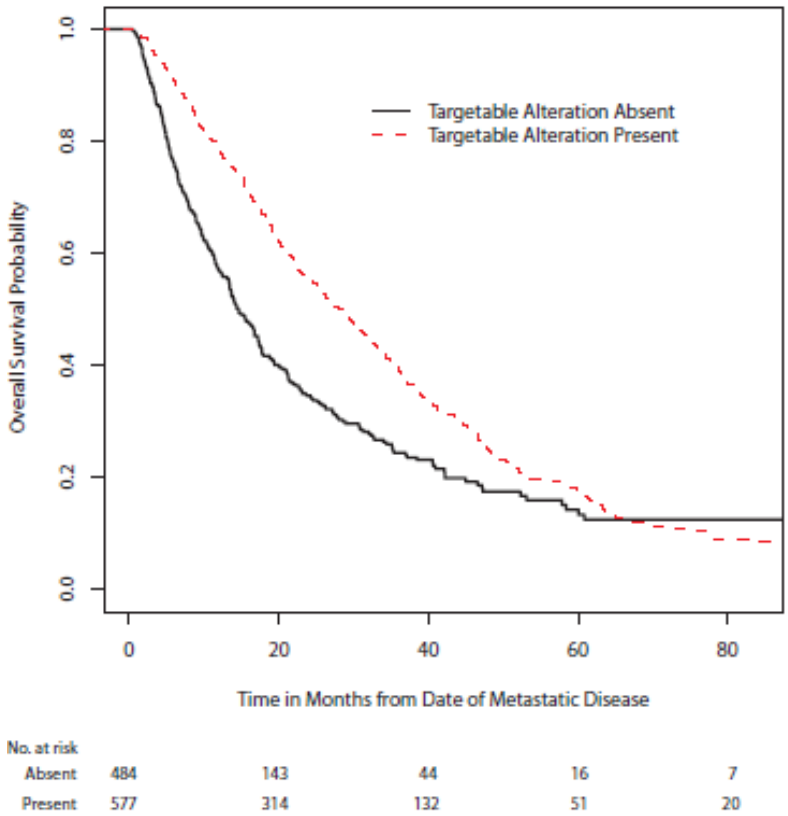
†Targeted therapy must have been directed against known targetable genomic alteration including erlotinib, gefitinib or afatinib for *EGFR* mutations, crizotinib for *ALK* or *ROS1* alterations, trastuzumab-vinorelbine or afatinib for *HER2* exon 20 insertions, dabrafenib or vemurafenib for *BRAF* V600E mutations. Of those with a targetable alteration, 468 received targetable therapy, 140 did not receive targeted therapy and 99 had incomplete treatment records.



eFigure 1: The frequency of KRAS mutations by age category.



eFigure 2: Frequency of targetable genomic alterations by age group among patients where complete testing was performed (EGFR, ALK, ROS1, HER2, BRAF). The frequency of targetable genomic alterations appears to increase below the age of 50. This age was subsequently confirmed by recursive partitioning to represent a distinct age boundary between two populations with unique rates of targetable alterations.



No. at risk					
Absent	484	143	44	16	7
Present	577	314	132	51	20

eFigure 3: The survival of patients possessing a targetable alteration compared with those not possessing a targetable alteration. OS is significantly improved in patients possessing a targetable alteration ($p<0.01$).