The GLASS trial: Retrospective Global Experience with Lorlatinib

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The most significant recent breakthroughs in ALK NSCLC

1. Diagnostic platforms are well established
2. Liquid cfDNA methods are available (upfront/PD)
3. Crizotinib, Alectinib, Brigatinib are approved for 1st line
4. 2nd line therapies (Alectinib, Ceritinib, Brigatinib)
5. ≥ 2nd line Lorlatinib is growing
6. BBB as main PD profile for crizotinib
7. Median OS ~ 8 years in sequential therapies

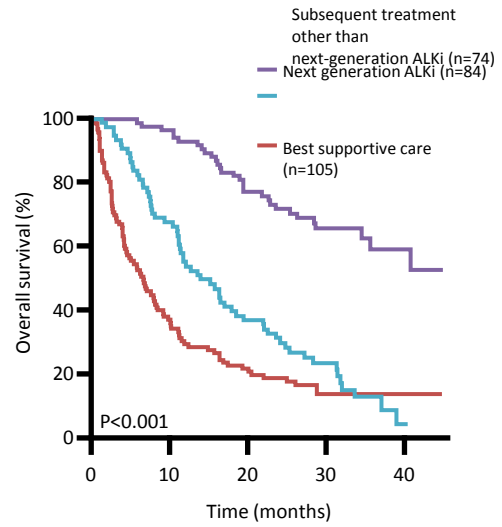
ALK+ NSCLC: sequence of crizotinib followed by next generation inhibitor: MOS of 89.6 months

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 13), pp: 21903-21917

Research Paper

Overall survival with crizotinib and next-generation ALK inhibitors in *ALK*-positive non-small-cell lung cancer (IFCT-1302 CLINALK): a French nationwide cohort retrospective study

Michaël Duruisseaux[1], Benjamin Besse[2], Jacques Cadranel[3], Maurice Pérol[4], Bertrand Mennecier[5], Laurence Bigay-Game[6], Renaud Descourt[7], Eric Dansin[8], Clarisse Audigier-Valette[9], Lionel Moreau[10], José Hureaux[11], Remi Veillon[12], Josiane Otto[13], Anne Madroszyk-Flandin[14], Alexis Cortot[15], François Guichard[16], Pascaline Boudou-Rouquette[17], Alexandra Langlais[18], Pascale Missy[19], Franck Morin[19], Denis Moro-Sibilot[1]

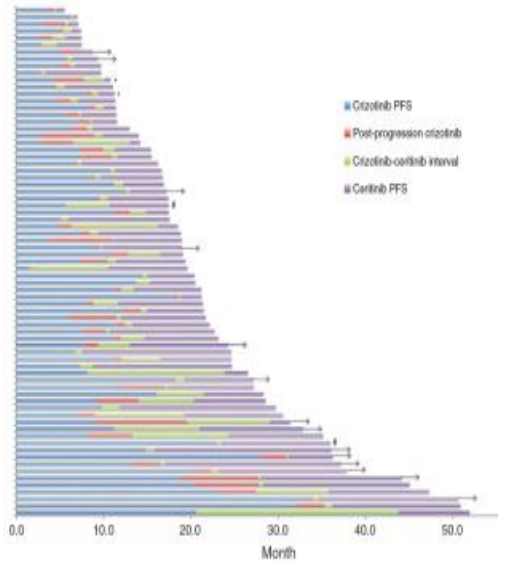


Median OS = 89.6 months

Cancer Therapy: Clinical
Clinical Cancer Research

Progression-Free and Overall Survival in ALK-Positive NSCLC Patients Treated with Sequential Crizotinib and Ceritinib

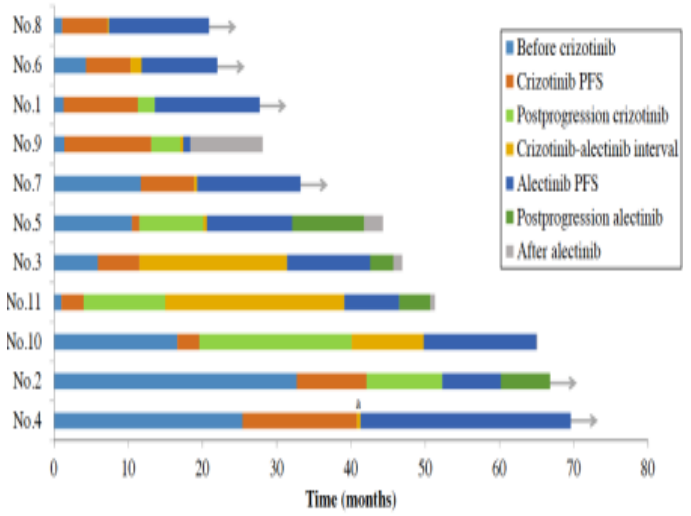
Justin F. Gainor[1], Daniel S.W. Tan[2], Tomasso De Pas[3], Benjamin J. Solomon[4], Azish Ahmad[5], Chiara Lazzari[3], Filippo de Marinis[3], Gianluca Spitaleri[3], Katherine Schultz[1], Luc Friboulet[1], Beow Y. Yeap[1], Jeffrey A. Engelman[1], and Alice T. Shaw[1]



Median combined PFS: 17.4 months
Median OS: 49.4 months

Progression-Free and Overall Survival of Patients With *ALK* Rearrangement–Positive Non–Small Cell Lung Cancer Treated Sequentially With Crizotinib and Alectinib

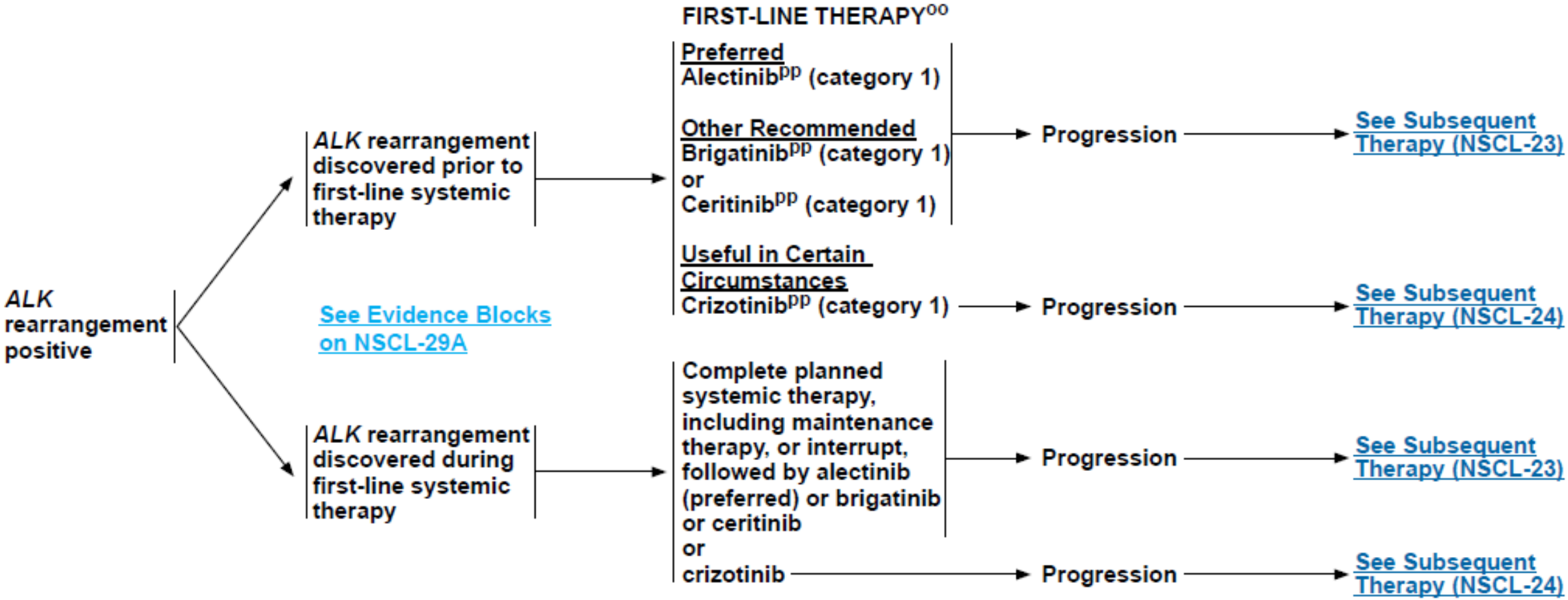
Satomi Watanabe,[1] Hidetoshi Hayashi,[1] Kunio Okamoto,[2] Kimiko Fujiwara,[3] Yoshikazu Hasegawa,[4] Hiroyasu Kaneda,[2] Kaoru Tanaka,[1] Masayuki Takeda,[1] Kazuhiko Nakagawa[1]



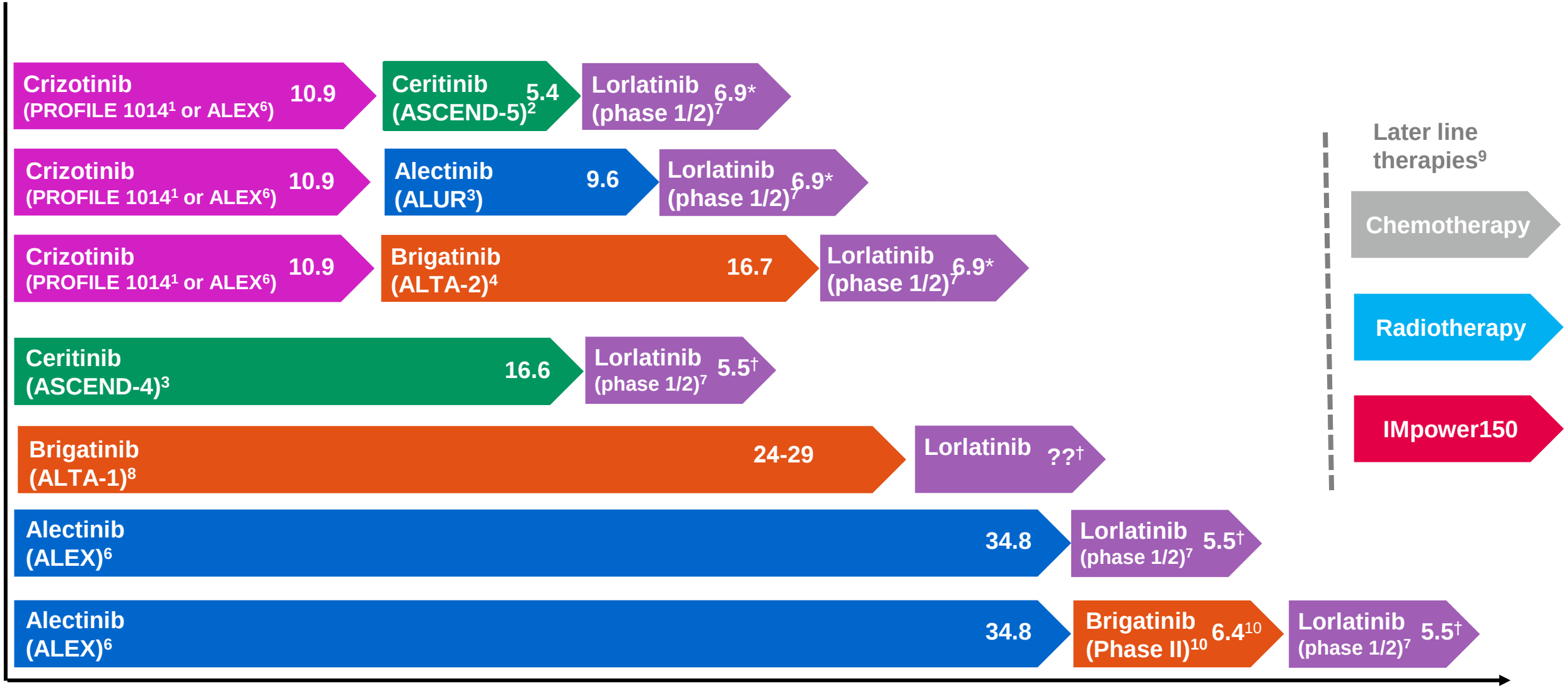
Median combined PFS: 18.2 months
Median OS: 51.1 months

Duruisseaux M, et al. Oncotarget 2017; Gainor JF, et al. Clin Cancer Res 2015; Watanabe S, et al. Clin Lung Cancer 2016

ALK REARRANGEMENT POSITIVE[jj]



Treatment sequence for ALK+ NSCLC patients – cumulative PFS



*Data are from the EXP4 and EXP5 groups (two or three prior ALK TKIs ± chemotherapy)
†Lorlatinib PFS data following ceritinib or alectinib in **any line**
‡For illustration purposes only; note that cross-trial comparisons should be interpreted with caution due to the differences in study design, size, patient population and data maturity
Not all regimens are approved

1. Solomon, et al. N Eng J Med 2014; 2. Shaw, et al. Lancet Oncol 2017
3. Novello, et al. Ann Oncol 2018; 4. Huber, et al. ASCO 2018
5. Soria, et al. Lancet Oncol 2017; 6. Camidge, et al. J Thorac Oncol 2019
7. Besse, et al. ASCO 2018; 8. Camidge, et al. ESMO ASIA 2019
9. Ferrara, et al. J Thorac Oncol 2018 10. Stinchcombe et al ASCO 2019 -The efficacy of brigatinib after NG ALK TKI)

GLASS: Global Lorlatinib for *ALK*(+) and *ROS1*(+) retrospective Study: real world data of 123 NSCLC patients

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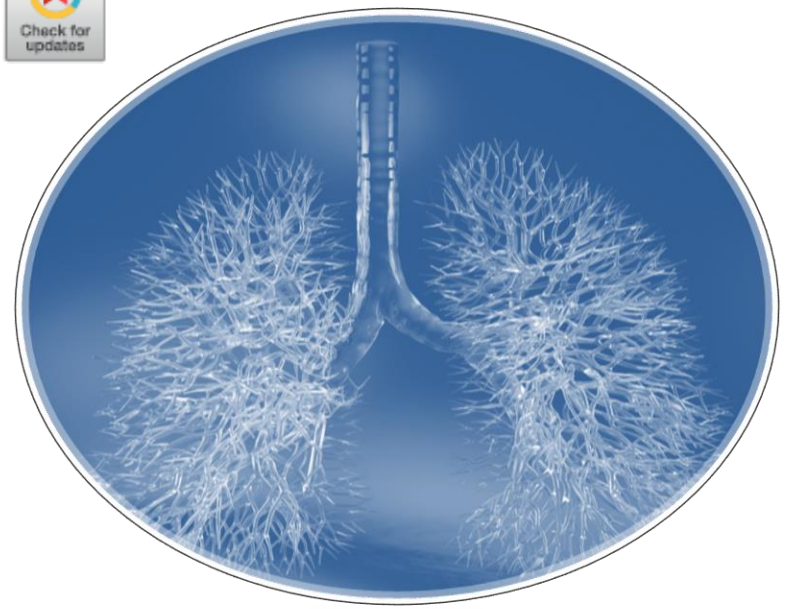
GLASS: Global Lorlatinib for *ALK*(+) and *ROS1*(+) retrospective Study: real world data of 123 NSCLC patients

Nir Peled[a,b,*], Roni Gillis[a,b], Saadettin Kilickap[c], Patrizia Froesch[d], Sergei Orlov[e], Elena Filippova[e], Umut Demirci[f], Petros Christopoulos[g], Irfan Cicin[h], Fatma Bugdayci Basal[i], Cengiz Yilmaz[j], Moiseenko Fedor[k,l], Taner Korkmaz[m], Semra Paydas[n], Oliver Gautschi[o], Alisan Zirtiloglu[p], Yesim Eralp[m], Havva Yesil Cinkir[r], Ahmet Sezer[s], Mustafa Erman[c], Deniz Tural[p], Hande Turna[t], Julien Mazieres[u], Elizabeth Dudnik[v], Noemi Reguart[w], David Ross Camidge[x], Terry L. Ng[y], Filiz Çay Şenler[z], İsmail Beypınar[A], Doğan Yazılıtaş[B], Ahmet Demirkazık[z], Aziz Karaoğlu[C], Kerem Okutur[D], Hasan Şenol Coşkun[E], Mehmet Ali Nahit Şendur[B], Abdurrahman Isikdogan[E], Devrim Cabuk[I], Perran Fulden Yumuk[F], Ibrahim Yıldız[m], M. Ali Kaplan[E], Özgür Özyılkan[s], İlhan Öztop[C], Omer Fatih Olmez[G], Kübra Aydin[J], Adnan Aydıner[q], Nezih Meydan[H], Roxana Denisa Grinberg[a,b], Laila C. Roisman[a,b]



Study Design

- An international, multicenter, retrospective study, which aimed to describe the efficacy and safety of lorlatinib in previously treated ALK/ROS1(+) NSCLC.
- All patients were treated through an early access program, when no other targeted therapy was available.
- The countries that participated in this study were Turkey, Switzerland, Russia, Israel, Germany, France and the USA.
- Between March 2015 to January 2019 (date of data cutoff).

Patients Characteristics

Characteristic	ALK (+) patients N= 106	ROS1 (+) patients N= 17
Age (Median, SD)	53.0 ± 12.7	49.0 ± 10.7
Sex (M:F)	53:53	9:18
Smoking (Current/Past/Never)	5/23/77	1/5/11
Adenocarcinoma	103 (97%)	16 (94%)
Stage III-IV at Diagnosis	102 (96%)	16 (94%)
ECOG 1-2	65 (61%)	11 (65%)
Brain Mets at Diagnosis	72 (68%)	11 (65%)

Patients Characteristics

Characteristic	ALK (+) patients N= 106	ROS1 (+) patients N= 17
Brain metastasis at diagnosis		
Brain Mets at Diagnosis	72 (68%)	11 (65%)
Absent	34 (32%)	6 (35%)
Method of diagnosis†		
FISH	81 (76%)	12 (71%)
IHC	33 (31%))	2 (12%)
NGS	8 (8%)	2 (12%)
PCR	14 (13%)	2 (12%)

Last therapy before Lorlatinib treatment – ALK+

Last Therapy before Lorlatinib	Summary of cases	Lorlatinib as 2nd Line	Lorlatinib as 3rd Line	Lorlatinib as 4th Line	Lorlatinib as 5th Line	Lorlatinib as 6th Line	Lorlatinib as 7th Line	Lorlatinib as 8th Line
ALK(+) Patients								
Crizotinib	40 (38%)	12 (75%)	22 (55%)	4 (13%)	2 (18%)			
Alectinib	15 (14%)	1 (6%)	2 (5%)	8 (24%)	1 (9%)	1 (50%)		2 (67%)
Brigatinib	13 (12%)		1 (2%)	6 (18%)	4 (36%)		1 (100%)	1 (33%)
Ceritinib	25 (24%)	3 (19%)	9 (22%)	10 (30%)	2 (18%)	1 (50%)		
Chemotherapy	13 (12%)		6 (16%)	5 (15%)	2 (18%)			
Total ALK(+) cases	106 (100%)	16 (100%)	40 (100%)	33 (100%)	11 (100%)	2 (100%)	1 (100%)	3 (100%)

N (% from summary of line of treatment)

Last therapy before Lorlatinib treatment – ROS1+

Last Therapy before Lorlatinib	Summary of cases	Lorlatinib as 2nd Line	Lorlatinib as 3rd Line	Lorlatinib as 4th Line	Lorlatinib as 5th Line	Lorlatinib as 6th Line	Lorlatinib as 7th Line	Lorlatinib as 8th Line
ROS1(+) Patients								
Crizotinib	12 (71%)	5 (83%)	5 (83%)				1 (100%)	1 (100%)
Ceritinib	2 (12%)	1 (17%)	1 (17%)					
Chemotherapy	3 (18%)			3 (100%)				
Total ROS1(+) cases	17 (100%)	6 (100%)	6 (100%)	3 (100%)			1 (100%)	1 (100%)

N (% from summary of line of treatment)

Extracranial best response to Lorlatinib treatment – ALK+

Systemic Best response to Lorlatinib treatment	Summary of cases	2nd Line	3rd Line	4th Line	5th Line	6th Line	7th Line	8th Line
ORR	52 (60%)	7 (64%)	21 (63%)	15 (54%)	7 (70%)	0 (0%)	0 (0%)	2 (67%)
DCR	79 (91%)	11 (100%)	28 (88%)	24 (86%)	10 (100%)	2 (100%)	1 (100%)	3 (100%)
CR	9 (10%)	2 (18%)	4 (13%)	1 (4%)	2 (20%)			
PR	43 (50%)	5 (46%)	17 (53%)	14 (50%)	5 (50%)			2 (67%)
SD	27 (31%)	4 (36%)	7 (22%)	9 (32%)	3 (30%)	2 (100%)	1 (100%)	1 (33%)
PD	8 (9%)	0 (0%)	4 (12%)	4 (14%)				
Available data	87 (100%)	11 (100%)	32 (100%)	28 (100%)	10 (100%)	2 (100%)	1 (100%)	3 (100%)
Indeterminate/ Missing Data	19	5	8	5	1			
Total ALK(+) cases	106	16	40	33	11	2	1	3

All percentage calculation are from the total of patients with available evaluable data
N (% from summary of line of treatment)

Extracranial best response to Lorlatinib treatment – ROS1+

Systemic Best response to Lorlatinib treatment	Summary of cases	2nd Line	3rd Line	4th Line	5th Line	6th Line	7th Line	8th Line
ORR	**8 (62%)**	**1 (25%)**	**4 (100%)**	**1 (33%)**			**1 (100%)**	**1 (100%)**
DCR	12 (92%)	4 (100%)	4 (100%)	2 (67%)			1 (100%)	1 (100%)
CR	0 (0%)							
PR	8 (61%)	1 (25%)	4 (100%)	1 (33%)			1 (100%)	1 (100%)
SD	4 (31%)	3 (75%)		1 (33%)				
PD	1 (8%)			1 (33%)				
Available data	13 (100%)	4 (100%)	4 (100%)	3 (100%)			1 (100%)	1 (100%)
Indeterminate/ Missing Data	4	2	2					
Total ROS1(+) cases	17	6	6	3			1	1

All percentage calculation are from the total of patients with available evaluable data
N (% from summary of line of treatment)

Intracranial best response to Lorlatinib treatment – ALK+

Intracranial Best response to Lorlatinib treatment	Summary of cases	2nd Line	3rd Line	4th Line	5th Line	6th Line	7th Line	8th Line
ORR	**40 (62%)**	**5 (50%)**	**12 (71%)**	**13 (52%)**	**7 (78%)**	**1 (50%)**	**1 (100%)**	**2 (67%)**
DCR	57 (88%)	10 (100%)	14 (83%)	20 (80%)	9 (100%)	2 (100%)	1 (100%)	3 (100%)
Best Overall Response								
CR	10 (16%)	2 (25%)	2 (12%)	5 (20%)	1 (11%)			
PR	30 (46%)	2 (25%)	10 (59%)	8 (32%)	6 (67%)	1 (50%)	1 (100%)	2 (67%)
SD	17 (26%)	4 (50%)	2 (12%)	7 (28%)	2 (22%)	1 (50%)		1 (33%)
PD	8 (12%)		3 (17%)	5 (20%)				
Available data	65 (100%)	8 (100%)	17 (100%)	25 (100%)	9 (100%)	2 (100%)	1 (100%)	3 (100%)
Indeterminate/ Missing Data	41	8	23	8	2			
Total ALK(+) cases	106	16	40	33	11	2	1	3

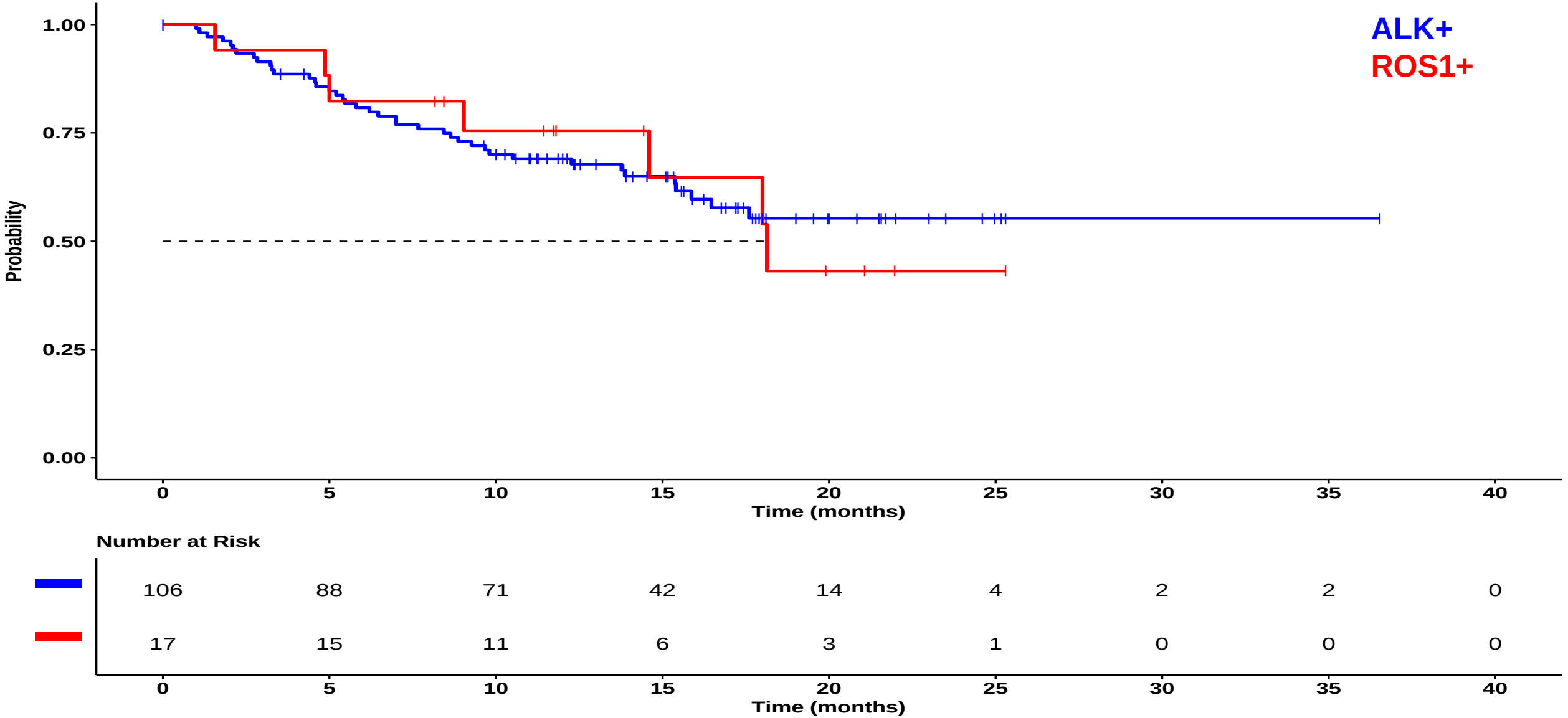
All percentage calculation are from the total of patients with available evaluable data
N (% from summary of line of treatment)

Intracranial best response to Lorlatinib treatment – ROS1+

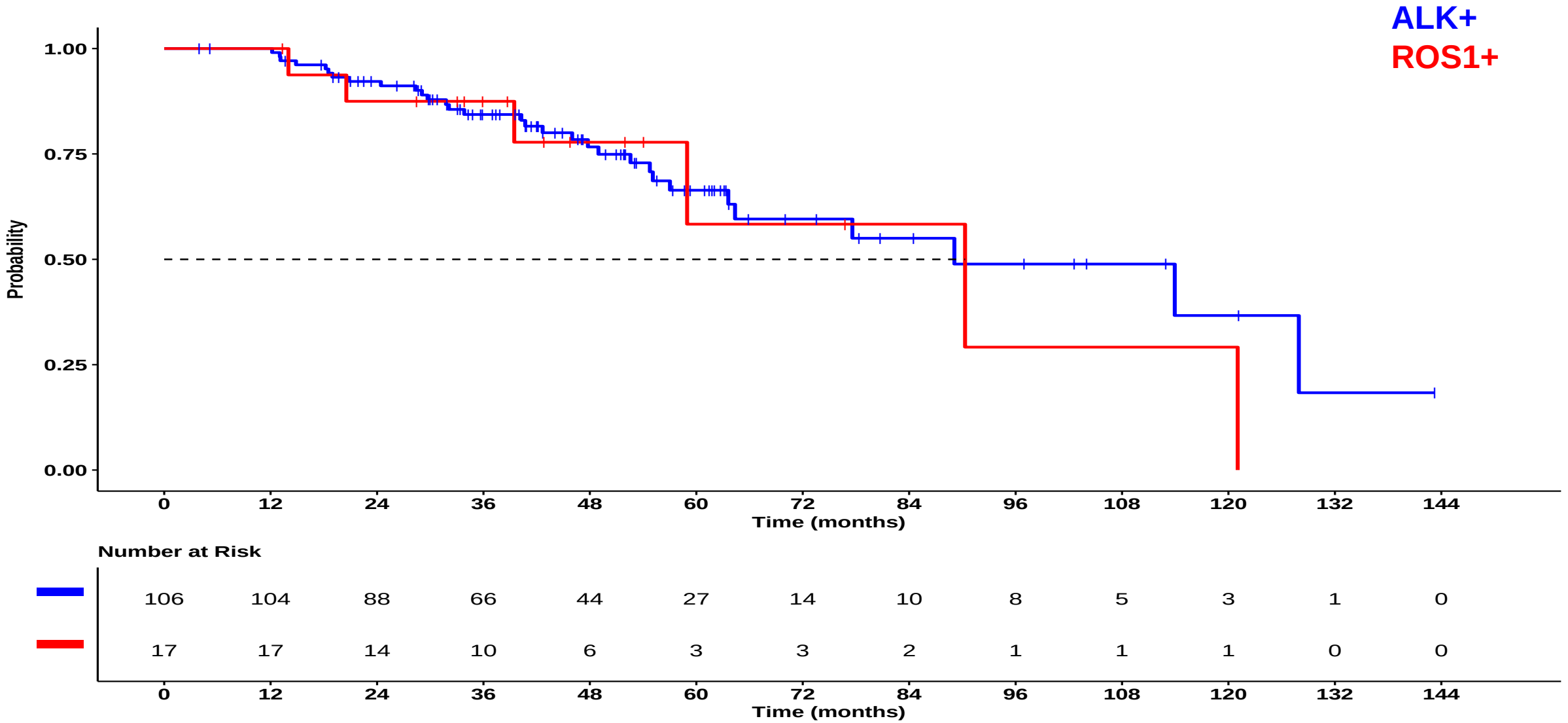
Intracranial Best response to Lorlatinib treatment	Summary of cases	2nd Line	3rd Line	4th Line	5th Line	6th Line	7th Line	8th Line
ORR	**6 (67%)**	**2 (67%)**	**2 (100%)**	**1 (33%)**			**1 (100%)**	
DCR	7 (78%)	3 (100%)	2 (100%)	1 (33%)			1 (100%)	
Best Overall Response								
CR	1 (11%)		1 (50%)					
PR	5 (56%)	2 (67%)	1 (50%)	1 (33%)			1 (100%)	
SD	1 (11%)	1 (33%)						
PD	2 (22%)			2 (67%)				
Available data	9 (100%)	3 (100%)	2 (100%)	3 (100%)			1 (100%)	
Indeterminate/ Missing Data	8	3	4				1	
Total ROS1(+) cases	17	6	6	3			2	

All percentage calculation are from the total of patients with available evaluable data
N (% from summary of line of treatment)

Duration of Therapy (DoT) of Lorlatinib



Overall survival



Safety Data

AE N=123	Grade1 N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)
Hyperlipidemia	13 (11%)	35 (28%)	8 (6%)	3 (3%)
Hypercholesterolemia	12 (10%)	34 (28%)	7 (6%)	3 (3%)
Hypertriglyceridemia	25 (20%)	24 (20%)	2 (2%)	2 (2%)
Peripheral edema	27 (22%)	29 (24%)	2 (2%)	
Weight increased	23 (19%)	5 (4%)	2 (2%)	
Fatigue	23 (19%)	6 (5%)	1 (1%)	
Peripheral neuropathy	9 (7%)	4 (3%)	2 (2%)	
Cognitive effects	16 (13%)	6 (5%)		
Mood effects	16 (13%)	3 (2%)		
Diarrhea	6 (5%)	1 (1%)		
Arthralgia	6 (5%)	3 (2%)		
Increased AST	8 (6%)	2 (2%)		

Safety Data

AE N=123	Grade1 N (%)	Grade 2 N (%)	Grade 3 N (%)	Grade 4 N (%)
Bronchial pain while breathing deeply	2 (2%)			
QTc prolongation		2 (2%)		
Creatinine elevation		1 (1%)		
Pleural and pericardial effusion		1 (1%)		
Systremma	1 (1%)			
Rash	2 (2%)			
Anemia	1 (1%)			
Dyspnea	1 (1%)			
Exanthema	1 (1%)			
Formication left arm	1 (1%)			
Ischemia	1 (1%)			
Dry skin	1 (1%)			
Double vision	1 (1%)			
Fever	1 (1%)			

Summary ALK & ROS

- Numerous alternatives for both 1st & 2nd line in ALK+ population.
- Prolong MOS (8 y) in sequential therapies (retrospective cohorts).
- Lorlatinib is highly effective post 2nd generation ALK/ROS TKIs.
- Extracranial (EC) and intracranial (IC) effective is practically similar.
- The GLASS data presents EC/IC ORR of ~60% in both ALK+ & ROS1+.
- ALK(+): Mean DoT 23.9±1.6 months; MOS 89.1±19.6 months.
- ROS1(+): median DoT of 18.1±2.5 months; MOS 90.3±24.4 months.

Thank you