Resultados clínicos de los inhibidores de NTRK de primera y segunda generación

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Disclosure

I have provided consultation, attended advisory boards and/or provided lectures for the following organizations: Merck Sharp and Dohme, Bristol-Myers Squibb, F. Hoffmann-La Roche, AstraZeneca, Boehringer-Ingelheim, Eli Lilly, Pfizer, Celgene.

I declare no conflict of interest.

TRK Receptor Signalling

Neurotrophin family of receptors

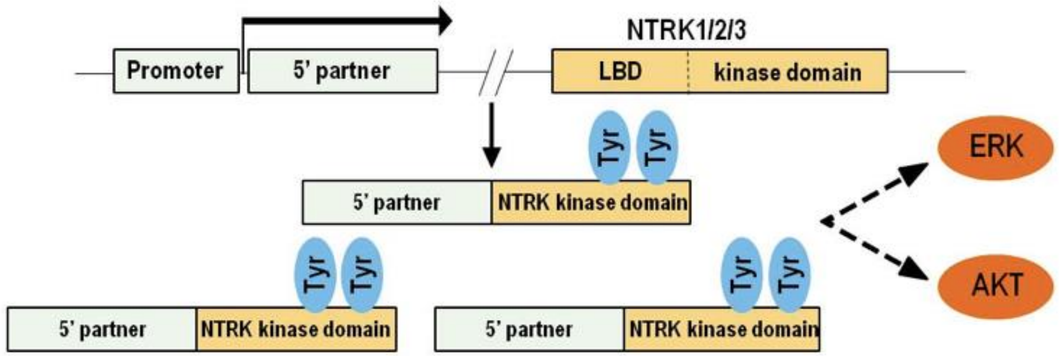
TRKA (*NTRK1*) → Pain, thermoregulation

TRKB (*NTRK2*) → Movement, memory, mood, appetite, body weight

TRKC (*NTRK3*) → Proprioception

TRK fusions

- Ligand binding domain (LBD) replaced by 5' fusion partner
- Drives overexpression and ligand-independent activation



NTRK-1, -2, -3

- Encode TrkA, TrkB and TrkC transmembrane receptors, respectively.
- Ras/Raf/MAPK pathway PI3K/Akt/mTOR pathway PLCc/PKC pathway.
- Trks are involved in physiological CNS development and maturation
- NTRK fusions in NSCLC 0.1%-~3%

TRK uncommonly expressed in normal tissues or cancer
Fusion drives abnormally high expression and activation of TRK kinase domain

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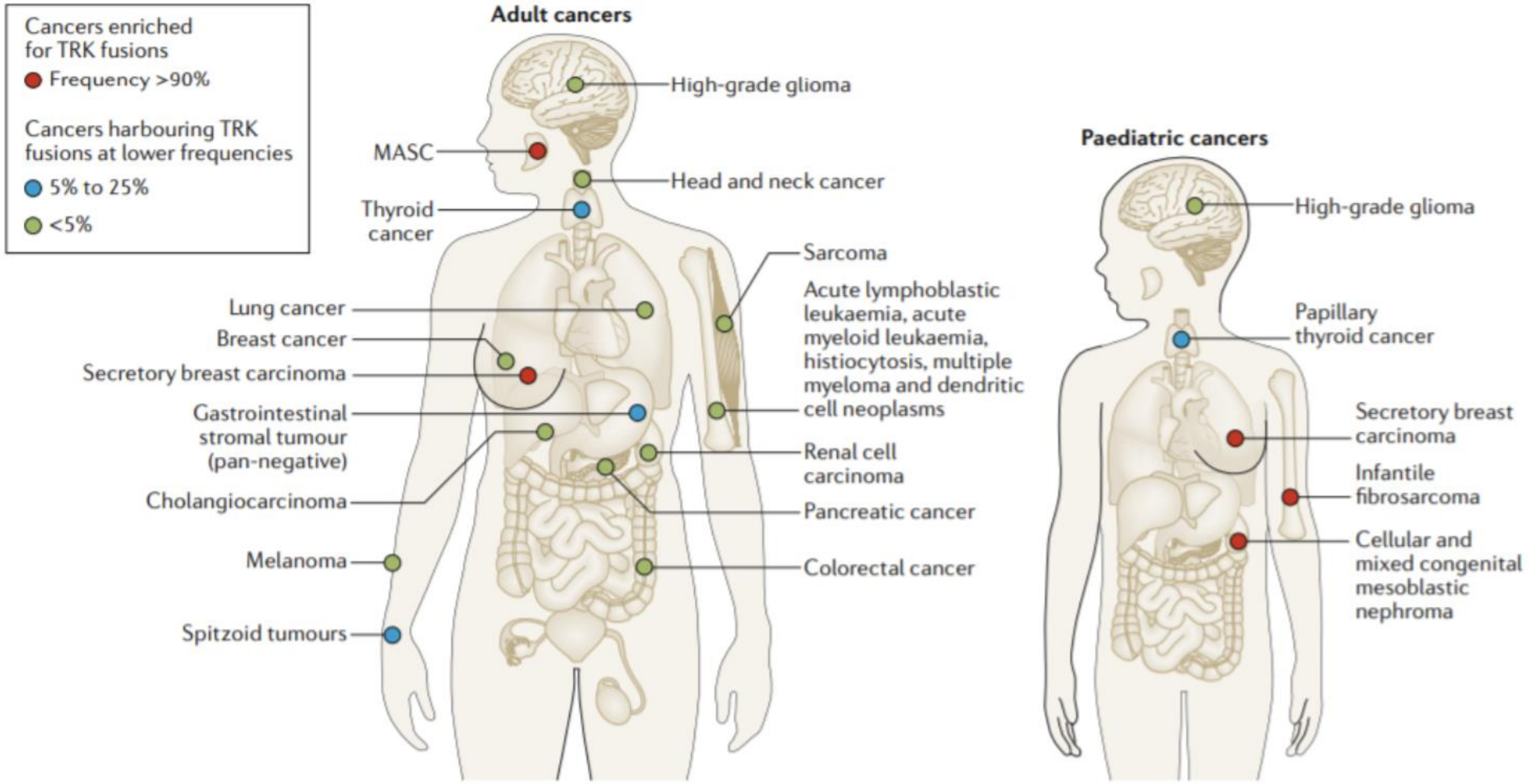
Tumor Types



Cocco E. et al, Nat Rev Clin Oncol 2018

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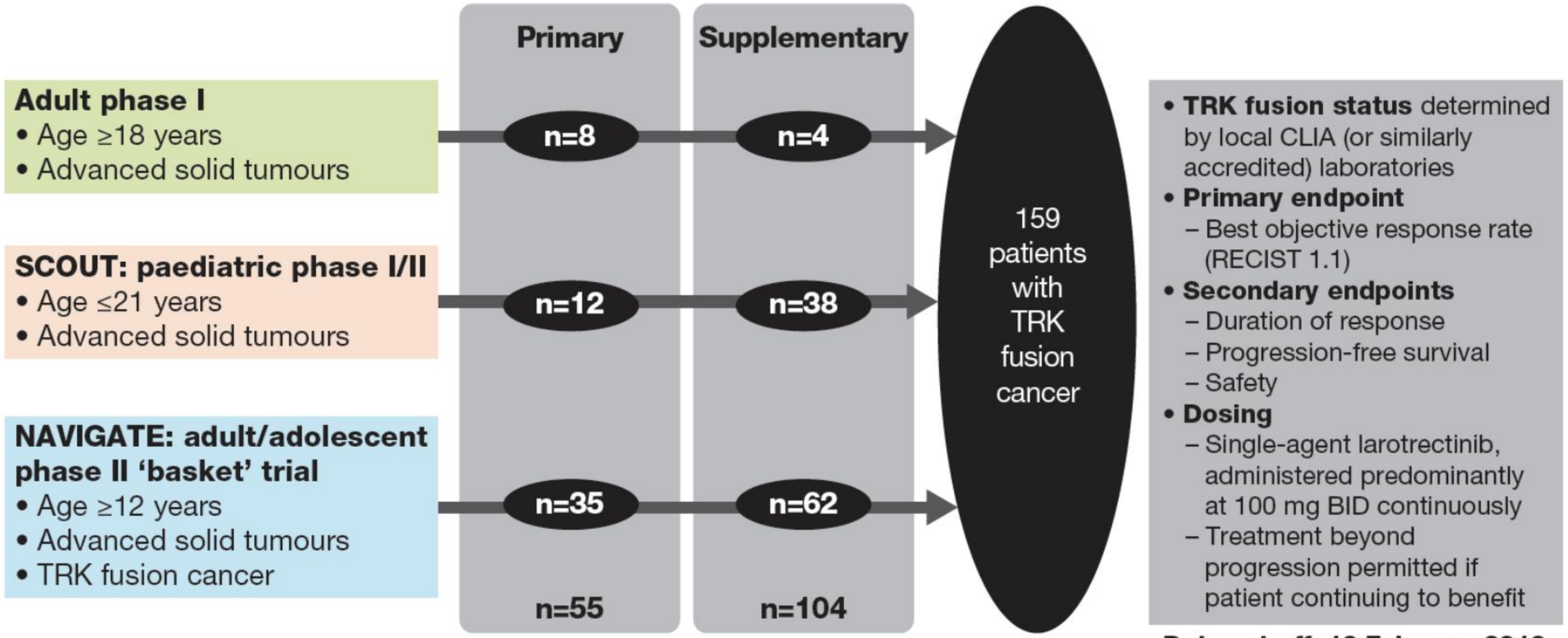

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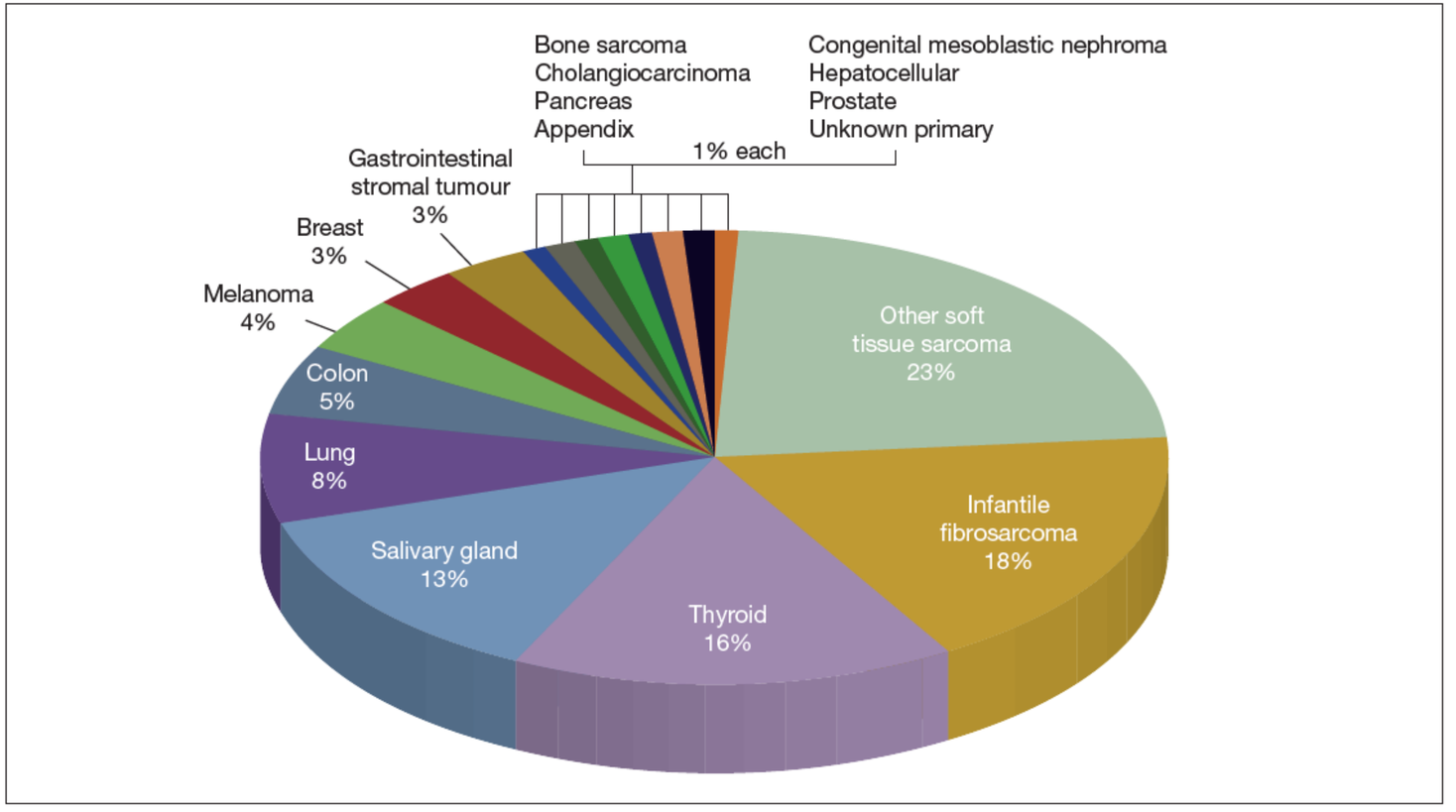
Patient Characteristics and Tumor Types

Table 1. Baseline characteristics

Characteristic	Integrated dataset (N=159)
Sex, n (%)	
Male	77 (48)
Female	82 (52)
Age, median (range), years	43.0 (<0.1–84.0)
Paediatric (<18), n (%)	52 (33)
Adult (≥18), n (%)	107 (67)
ECOG performance status, n (%)	
0	76 (48)
1	61 (38)
2	19 (12)
3	3 (2)
Known brain metastasis at enrolment, n (%)	13 (8)
Prior cancer treatments[a]	
Surgery	122 (77)
Systemic therapy	122 (77)
Radiotherapy	74 (47)
No. of prior systemic regimens, n (%)	
0	35 (22)
1	48 (30)
2	34 (21)
≥3	42 (26)
NTRK gene fusion, n (%)	
NTRK1	64 (40)
NTRK2	4 (3)
NTRK3[b]	88 (55)
Not confirmed[c]	3 (2)

[a]Patients may be counted in more than one row. [b]Directly demonstrated or inferred (8 of 88 patients) by *ETV6* break-apart fluorescence *in situ* hybridisation in patients with infantile fibrosarcoma. [c]Molecular profiling test used not certified by CLIA (or other similar accrediting body). CLIA, Clinical Laboratory Improvement Amendments; ECOG, Eastern Cooperative Oncology Group; *NTRK*, neurotrophic tyrosine receptor kinase.

Figure 2. Diversity of cancers treated.



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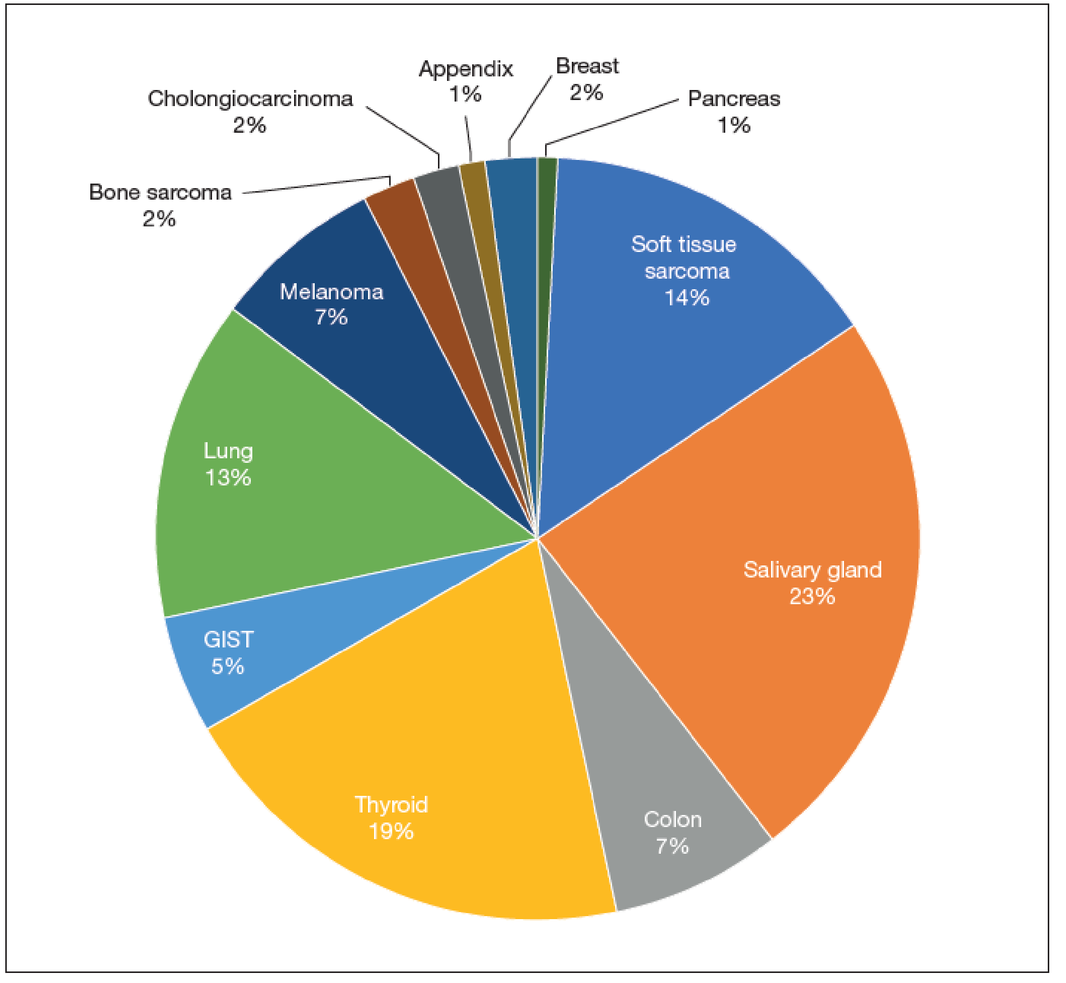
Patient Characteristics and Tumor Types - Adults

Table 1. Patient characteristics at baseline

Characteristic	All patients (N=83)
Age, years	
Median	57.0
Range	19.9–80.0
Sex, n (%)	
Male	41 (49%)
Female	42 (51%)
ECOG performance status, n (%)	
0	27 (33%)
1	47 (57%)
2	9 (11%)
NTRK fusions, n† (%)	
1	33 (40%)
2	2 (2%)
3	47 (57%)
Prior anticancer therapies, n (%)	
Systemic therapy	64 (77%)
Surgery	76 (92%)
Radiotherapy	53 (64%)
Number of prior systemic therapies, n (%)	
0	17 (20%)
1–2	41 (49%)
≥3	25 (30%)

†*NTRK* fusion was not determined for one patient
ECOG, Eastern Cooperative Oncology Group; NTRK, neurotrophic tyrosine receptor kinase

Figure 2. Patient population by tumor type (N=83)



One patient had cancer of unknown primary origin
GIST, gastrointestinal stromal tumor

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Efficacy

Table 2. Efficacy assessments

	Integrated dataset (N=159)
Response	
Evaluable patients, n	153[a]
ORR (95% CI)	79% (72–85)
Best overall response, n (%)	
Complete response	24 (16)[b]
Partial response	97 (63)[c]
Stable disease	19 (12)
Progressive disease	9 (6)
Not determined	4 (3)
Duration of response	
Median, months (95% CI)[d]	35.2 (22.8–NE)
Range, months	1.6+ to 44.2+
Rate of ongoing response at 12 months, % (95% CI)[e]	80%
Median follow-up, months	12.9
Progression-free survival	
Median, months (95% CI)	28.3 (22.1–NE)
PFS rate at 12 months, % (95% CI)[e]	67 (58–76)
Median follow-up, months	11.1
Overall survival	
Median, months (95% CI)	44.4 (36.5–NE)
OS rate at 12 months, % (95% CI)[e]	88 (83–94)
Median follow-up, months	13.9

[a]Six patients not evaluable because post-baseline assessments were not yet done at data cut-off. Best response percentages are calculated from the evaluable patient population. [b]Including three patients with pathological complete response; two patients had complete responses pending confirmation. [c]13 partial responses pending confirmation. [d]In patients with confirmed responses (n=108). [e]Kaplan–Meier estimates. CI, confidence interval; DOR, duration of response; NE, not estimable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

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Efficacy - Adults

Table 2. Efficacy of larotrectinib in adult patients with TRK fusion cancer

Patients, n (%)	Independent review-assessed patients (n=65)	Investigator-assessed patients (n=74)*
Best overall response		
Complete response	11 (17%)	7 (9%)
Partial response	33 (51%)	49 (66%)†
Stable disease	10 (15%)	9 (12%)
Progressive disease	8 (12%)	8 (11%)
Not determined	–	1 (1%)
Non-evaluable	3 (5%)	–
Overall response rate	44 (68%)	56 (76%)

Data presented are as of July 30, 2018

*Nine patients non-evaluable due to lack of post-baseline assessment; TRK, tyrosine receptor kinase

†Includes seven patients with a partial response pending confirmation

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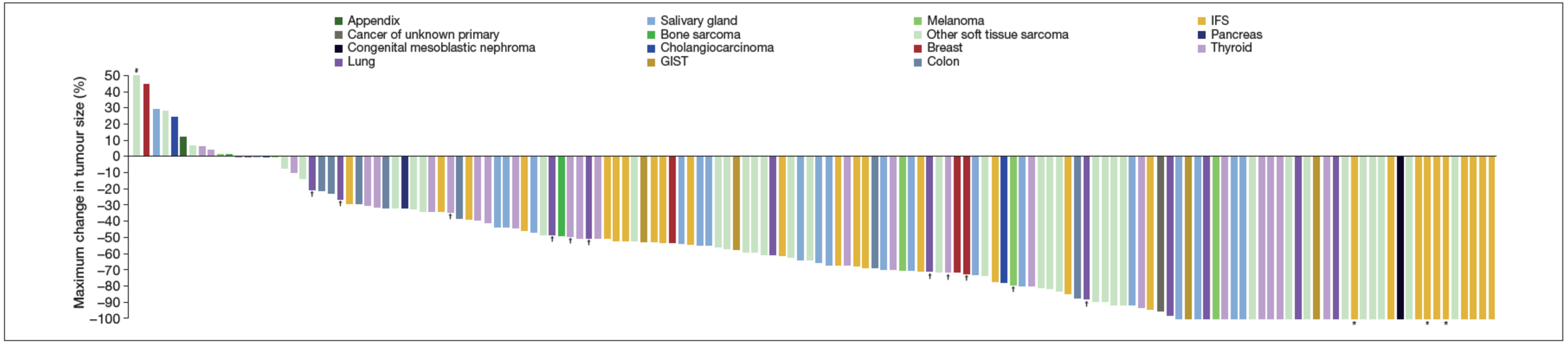
Efficacy

Figure 3. **Maximum change in tumour size.**



Excludes four patients who had clinical deterioration prior to an initial response assessment and six patients who were not evaluable due to insufficient time on therapy. *Patients with a pathological complete response. #Maximum change in tumour size of +93.2%. †Patients with brain metastases. GIST, gastrointestinal stromal tumour; IFS, infantile fibrosarcoma.

Median time to response was 1.8 months (range 0.9 to 6.1) and median treatment duration was 8.0 months (range 0.03+ to 47.2+)

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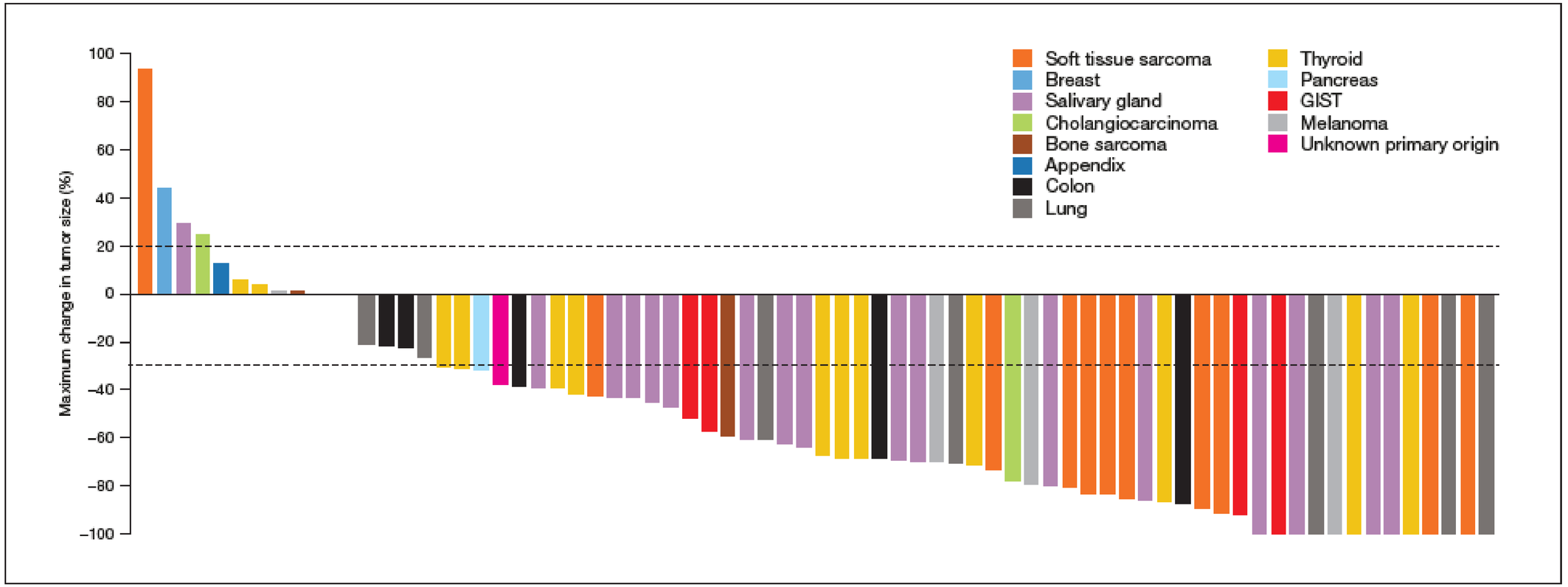
Efficacy - Adults

Figure 3. Best change in tumor size in adult patients with *NTRK* fusion cancer (n=72†)



Best change in tumor size, per investigator assessment. Data cut-off: July 30, 2018. Three patients with 0% change in tumor size: colon, thyroid, and salivary gland
†11 patients had no available tumor measurements. GIST, gastrointestinal stromal tumor; NTRK, neurotrophic tyrosine receptor kinase

ORR per investigator assessment was 76% (95% CI 64–85). Responses were observed irrespective of tumor type.

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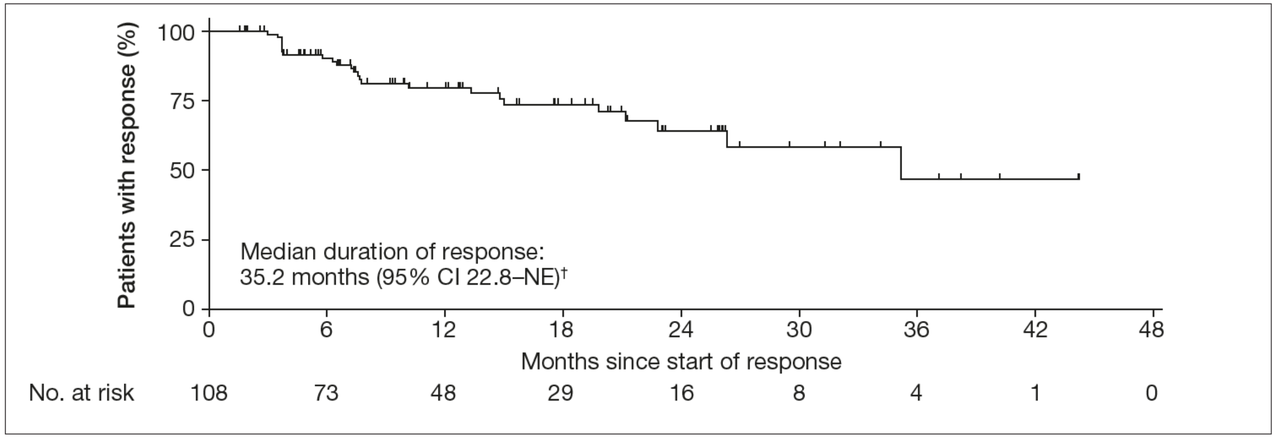
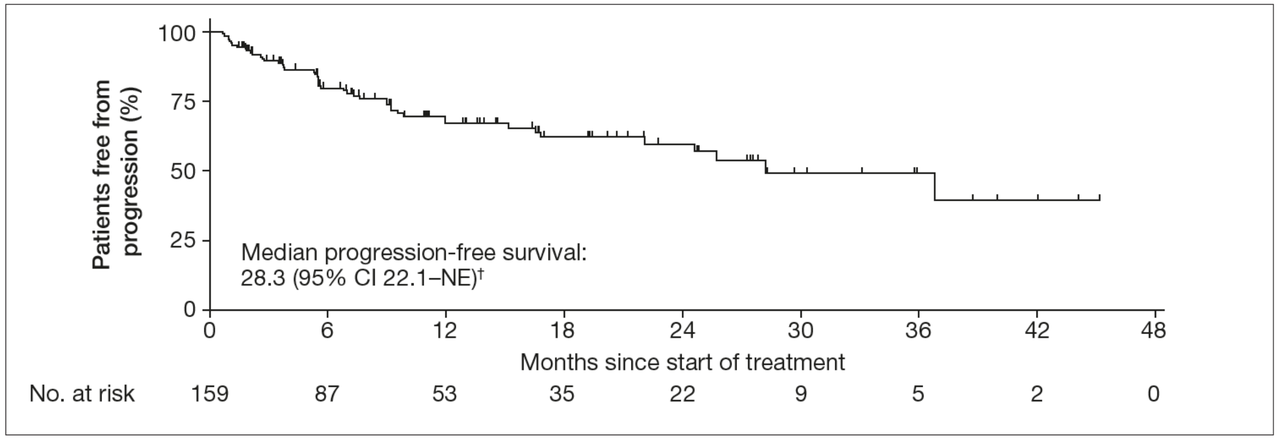
DOR - PFS

Figure 4. **Duration of response among all patients with confirmed responses.**



In 108 patients with confirmed responses. Tick marks indicate censored patients. †Median follow up of 12.9 months. CI, confidence interval; NE, not estimable.

Figure 5. **Progression-free survival among all patients.**



Tick marks indicate censored patients. †Median follow up of 11.1 months. CI, confidence interval; NE, not estimable.

Median OS was 44.4 months (95% CI 36.5–NE), with a median follow-up of 13.9 months. The estimated OS rate at 12 months was 88% (95% CI 83–94). Median OS in the primary dataset was similar (44.4 months, 95% CI 36.5–NE; median follow-up 28.5 months).

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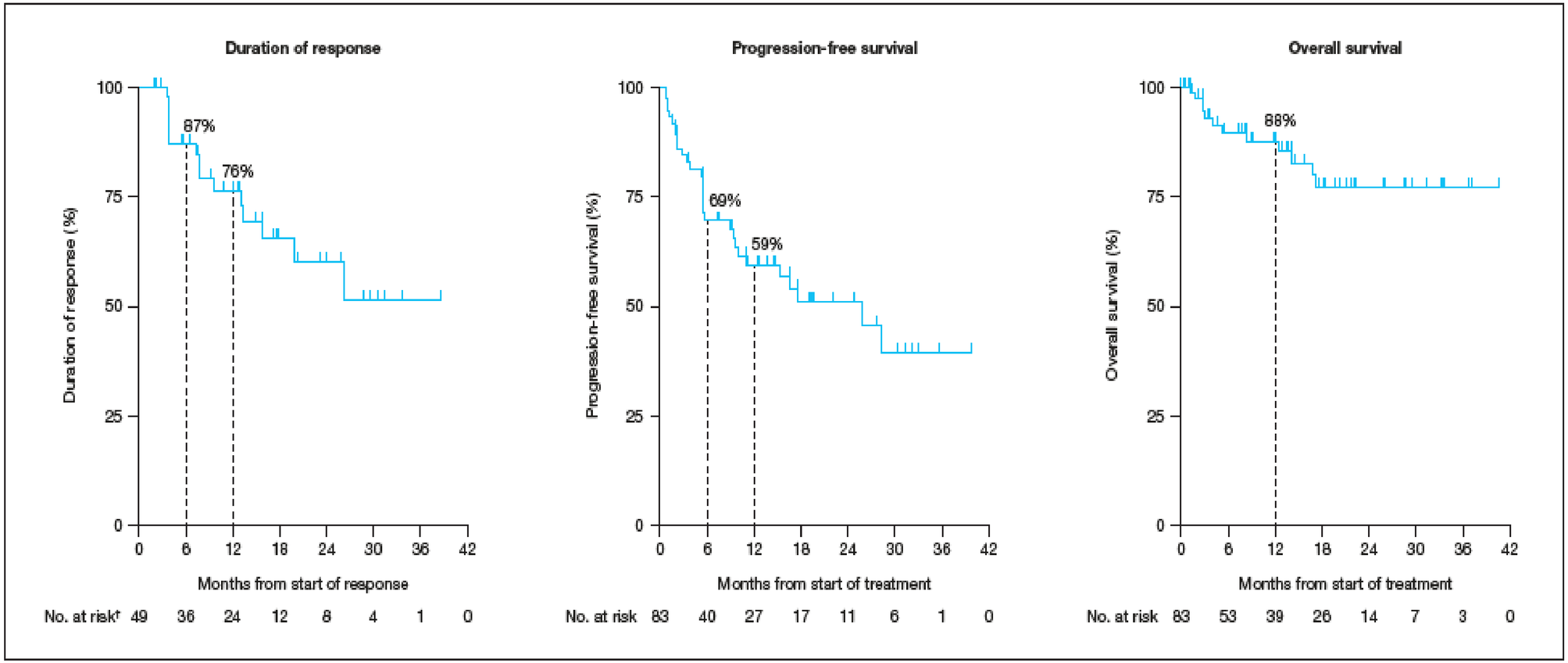
DOR - PFS Adults

Figure 4. Secondary efficacy endpoints (investigator assessed)



†Excludes seven patients with partial response pending confirmation. Data cut-off: July 30, 2018

At median follow-up of 17.2 months, median duration of response was not reached; At a median follow-up of 13.6 months, median progression-free survival was 25.8 months and median overall survival was not reached

The median duration of treatment was 7.4 months;
at data cut-off, 63% remained on treatment and 30% had discontinued due to disease progression

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Safety

Table 3. Adverse events in the expanded safety dataset (N=260)[a]

	Treatment-emergent AEs (%)				Treatment-related AEs (%)		
	Grade 1 or 2	Grade 3	Grade 4	Any grade	Grade 3	Grade 4	Any grade
Fatigue	30	2	0	33	<1	0	17
ALT increased	25	3	<1	28	3	<1	22
Cough	27	<1	0	28	0	0	1
Constipation	27	<1	0	27	0	0	11
Anaemia	17	10	0	27	2	0	10
AST increased	24	2	<1	27	<1	0	20
Dizziness	25	<1	0	25	<1	0	18
Nausea	24	<1	0	25	<1	0	13
Vomiting	24	<1	0	25	0	0	9
Diarrhoea	23	1	0	24	0	0	6
Pyrexia	19	<1	<1	20	0	0	2
Dyspnoea	13	2	0	16	0	0	<1
Myalgia	15	1	0	16	<1	0	8
Oedema peripheral	15	<1	0	16	0	0	6
Headache	15	<1	0	15	<1	0	5
Neutrophil count decreased	7	5	<1	12	2	<1	7
Lymphocyte count decreased	8	3	<1	12	<1	0	5
Hypokalaemia	5	3	<1	8	0	0	<1
Hypophosphataemia	2	3	0	5	0	0	<1

[a]The AEs listed here are those that occurred at any grade in at least 15% of patients, or at grade 3 or 4 in at least 3% of patients, regardless of attribution. AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

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Safety - Adults

Table 3. Adverse events in ≥15% of adult patients in the overall larotrectinib safety database (n=152)

	Treatment-emergent AEs (%)					Treatment-related AEs (%)		
	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 3	Grade 4	Total
Fatigue	17	19	4	–	40	1	–	20
Dizziness	31	5	1	–	36	1	–	28
Nausea	24	4	1	–	29	1	–	16
Anemia	8	8	12	–	28	3	–	9
Constipation	21	4	1	–	26	–	–	12
Cough	20	3	1	–	24	–	–	1
Dyspnea	11	7	3	-	22	–	–	1
AST increased	14	4	4	–	22	1	–	15
ALT increased	13	4	3	1	20	3	1	16
Peripheral edema	15	5	–	–	20	–	–	9
Diarrhea	12	5	2	–	19	–	–	5
Myalgia	14	5	1	–	19	–	–	11
Vomiting	13	3	1	–	17	–	–	9
Headache	13	3	–	–	15	–	–	4

AE, adverse event; ALT, alanine transaminase; AST, aspartate transaminase

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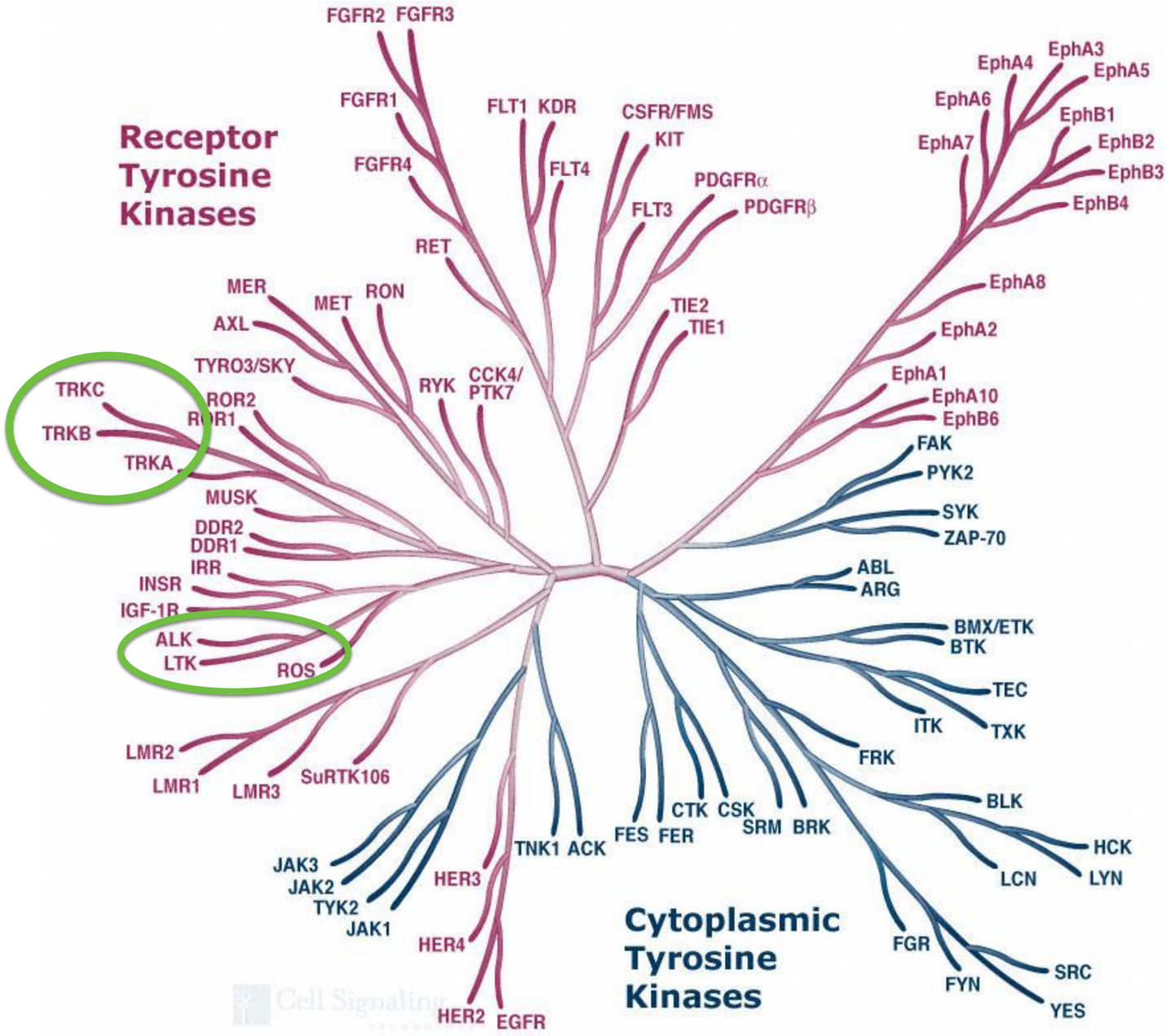

Receptor Tyrosine Kinases
FGFR2
FGFR3
FGFR1
FGFR4
FLT1
KDR
CSFR/FMS
KIT
FLT4
PDGFRα
FLT3
PDGFRβ
RET
EphA4
EphA3
EphA5
EphA6
EphB1
EphA7
EphB2
EphB3
EphB4
MER
MET
RON
AXL
TIE2
TIE1
EphA8
EphA2
TYRO3/SKY
RYK
CCK4/ PTK7
EphA1
EphA10
EphB6
TRKC
ROR2
ROR1
TRKB
TRKA
FAK
PYK2
SYK
ZAP-70
MUSK
DDR2
DDR1
IRR
ABL
ARG
INSR
IGF-1R
BMX/ETK
BTK
ALK
LTK
ROS
TEC
ITK
TXK
FRK
LMR2
LMR1
LMR3
SuRTK106
BLK
HCK
LCN
LYN
JAK3
JAK2
TYK2
JAK1
HER3
TNK1
ACK
FES
FER
CTK
CSK
SRM
BRK
HER4
FGR
SRC
FYN
YES
HER2
EGFR
Cytoplasmic Tyrosine Kinases
Cell Signaling

Entrectinib: doses

Table 1 Entrectinib clinical trials

Study	Patient population	Study design	Dose and schedule
ALKA-372-001[2]	Locally advanced or metastatic cancer targeting *NTRK1*, *NTRK2*, *NTRK3*, *ROS1*, or *ALK* molecular alterations	Phase I basket	100–1,800 mg/m^2 Schedule A (n=19): fasted, 4 days on and 3 days off for 21 of 28 days Schedule B (n=29): fed, continuous daily dosing for 28 days Schedule C (n=6): fed, 4 days on and 3 days off for 28 days
STARTRK-1[2]	Locally advanced or metastatic cancer targeting *NTRK1/2/3*, *ROS1*, or *ALK* molecular alterations	Phase I basket	100–1,800 mg/m^2 Fed, continuous daily dosing for 28 days (n=65)
STARTRK-2[36]	Solid tumors that harbor an *NTRK1/2/3*, *ROS1*, or *ALK* gene fusion	Phase II basket	600 mg Fed, continuous daily dosing for 28 days
STARTRK-NG[26]	Children with recurrent or refractory solid tumors and primary CNS tumors, with or without *TRK1/2/3*, *ROS1*, or *ALK* fusions	Phase I/Ib	250 mg/m^2 Fed, continuous daily dosing for 28 days

Liu Therap and Clinica Risk Man 2018

Entrectinib: ALKA-372-001 / STARTRK-1

	ALKA-372-001 (n=54)	STARTRK-1 (n=65)	TOTAL (n=119)
Age, years, median (range)	53 (22–77)	57 (18–80)	55 (18–80)
Sex, male/female (%)	44/56	48/52	46/54
ECOG performance status, n (%)			
0	30 (56)	22 (34)	52 (44)
1	21 (39)	41 (63)	62 (52)
2	2 (4)	2 (3)	4 (3)
Unknown	1 (2)	0	1 (1)
Prior Systemic Therapies, n (%)			
0	0	6 (9)	6 (5)
1–2	0	15 (23)	15 (13)
3 – 4	3 (6)	25 (39)	28 (24)
> 4	51 (94)	19 (29)	70 (59)
Prior ROS1/ALK Inhibitors, n (%)	10 (19)	22 (34)	32 (27)
Prior Immunotherapy, n (%)	0	4 (6)	4 (3)
Tumor type, n (%)			
NSCLC	35 (65)	36 (56)	71 (60)
Gastrointestinal Tract	9 (17)	9 (14)	18 (15)
CNS	4 (7)	1 (2)	5 (4)
Head & Neck	1 (2)	4 (6)	5 (4)
Other *	5 (9)	15 (23)	20 (17)

No.	Gene	Tumor Type	Molecular Alteration	Diagnostic Method
1	NTRK	NSCLC	*SQSTM1-NTRK1*	NGS
2	NTRK	Glioneuronal	*BCAN-NTRK1*	NGS
3	NTRK	MASC	*ETV6-NTRK3*	NGS
4	NTRK	mCRC	*LMNA-NTRK1*	NGS
5	ROS1	NSCLC	*ROS1+*	FISH
6	ROS1	NSCLC	*ROS1+*	FISH
7	ROS1	NSCLC	*CD74-ROS1*	NGS
8	ROS1	NSCLC	*ROS1+*	FISH
9	ROS1	NSCLC	*ROS1+*	FISH
10	ROS1	NSCLC	*EZR-ROS1*	NGS
11	ROS1	NSCLC	*ROS1+*	FISH
12	ROS1	Melanoma	*GOPC-ROS1*	NGS
13	ROS1	NSCLC	*ROS1+*	FISH
14	ROS1	NSCLC	*ROS1+*	FISH
15	ROS1	NSCLC	*ROS1+*	FISH
16	ROS1	NSCLC	*ROS1+*	FISH
17	ROS1	NSCLC	*ROS1+*	FISH
18	ROS1	NSCLC	*SDC4-ROS1*	NGS
19	ALK	NSCLC	*ALK+*	FISH
20	ALK	NSCLC	*ALK+*	FISH
21	ALK	RCC	*VCL-ALK*	NGS
22	ALK	NSCLC	*ALK+*	FISH
23	ALK	mCRC	*CAD-ALK*	NGS
24	ALK	NSCLC	*ALK+*	FISH
25	ALK	Unknown Primary	*D5F3-ALK*	NGS

Drilon Cancer Discovery 2017

Entrectinib: ALKA-372-001 / STARTRK-1

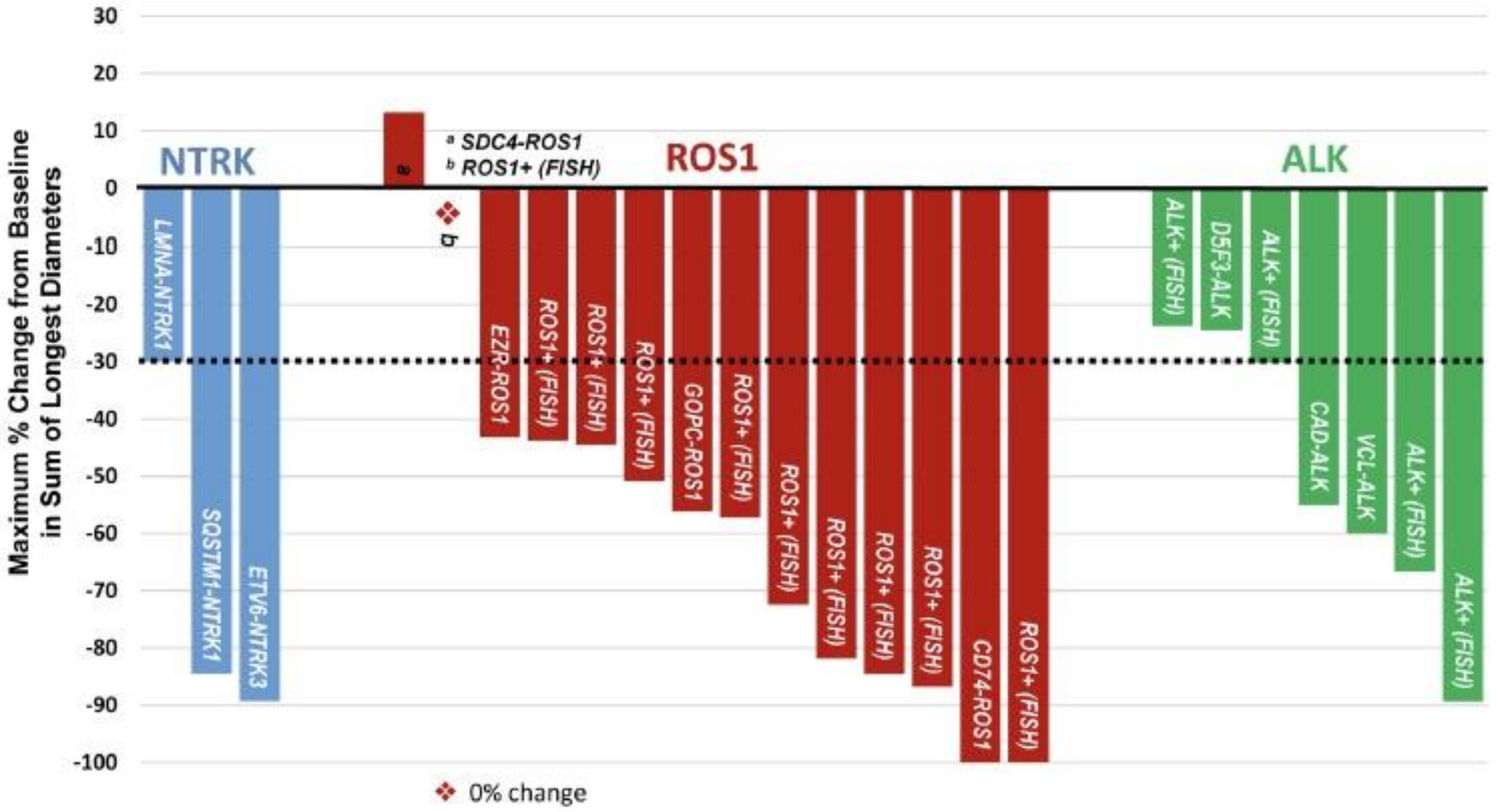
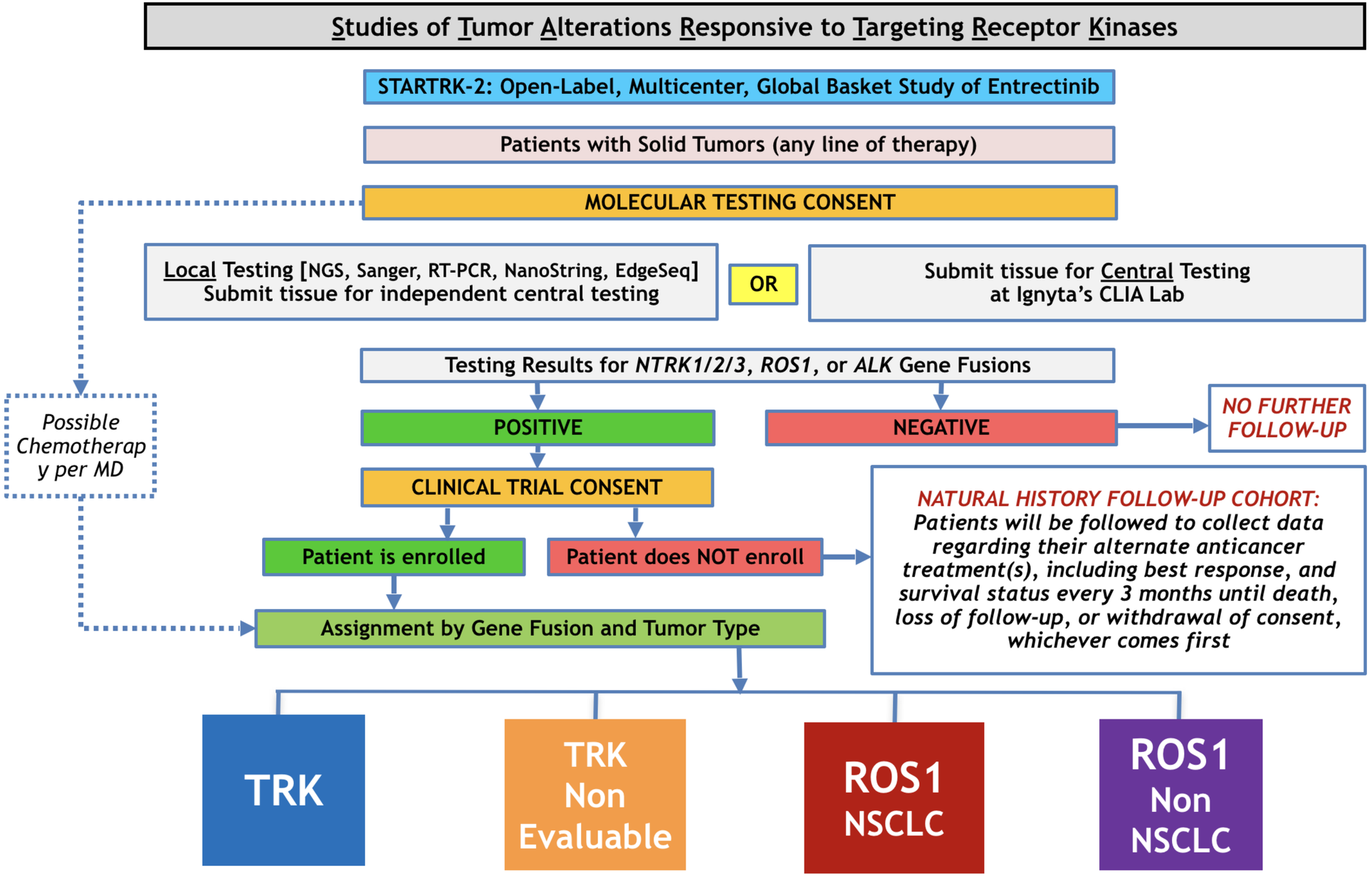


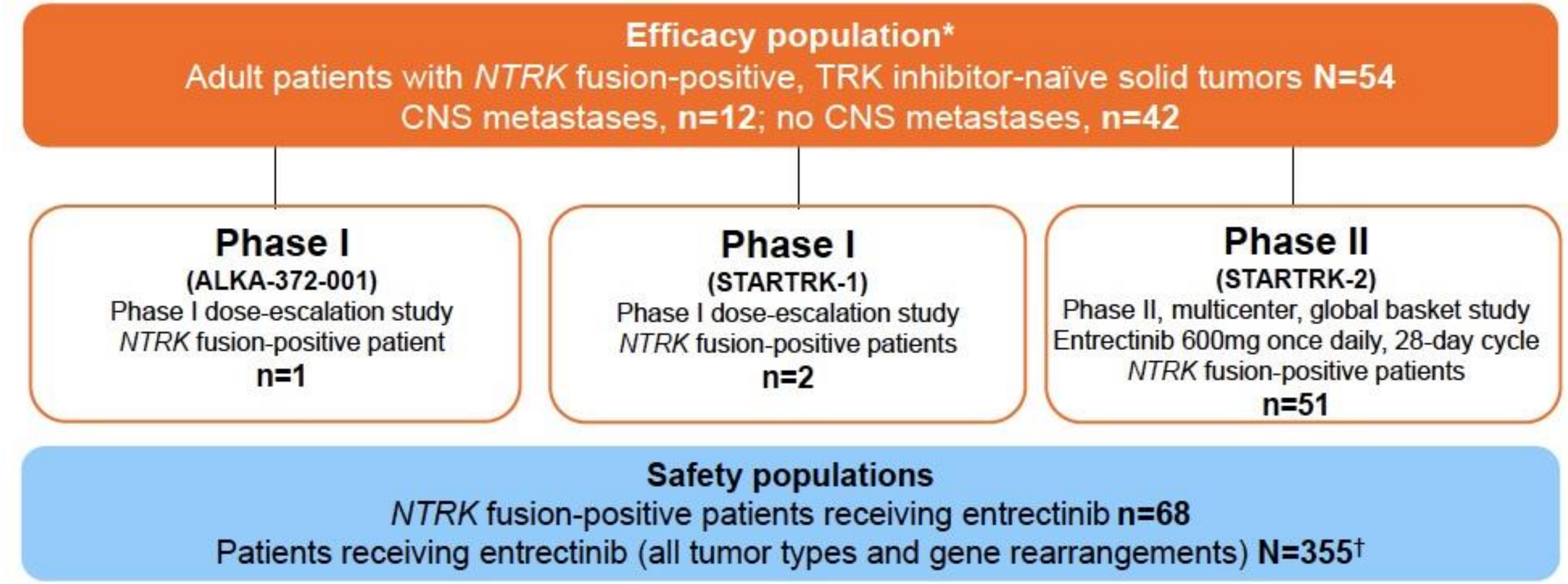
Figure 2. Best Response to Entrectinib in TKI Treatment-Naïve Extracranial Solid Tumor Patients

Drilon Cancer Discovery 2017

STARTRK-2


Studies of Tumor Alterations Responsive to Targeting Receptor Kinases
STARTRK-2: Open-Label, Multicenter, Global Basket Study of Entrectinib
Patients with Solid Tumors (any line of therapy)
MOLECULAR TESTING CONSENT
Local Testing [NGS, Sanger, RT-PCR, NanoString, EdgeSeq]
Submit tissue for independent central testing
OR
Submit tissue for Central Testing
at Ignyta's CLIA Lab
Testing Results for NTRK1/2/3, ROS1, or ALK Gene Fusions
POSITIVE
NEGATIVE
NO FURTHER FOLLOW-UP
Possible Chemotherapy per MD
CLINICAL TRIAL CONSENT
Patient is enrolled
Patient does NOT enroll
NATURAL HISTORY FOLLOW-UP COHORT:
Patients will be followed to collect data regarding their alternate anticancer treatment(s), including best response, and survival status every 3 months until death, loss of follow-up, or withdrawal of consent, whichever comes first
Assignment by Gene Fusion and Tumor Type
TRK
TRK Non Evaluable
ROS1 NSCLC
ROS1 Non NSCLC

Entrectinib integrated analysis across phase I/II



Data cut-off: 31 May 2018

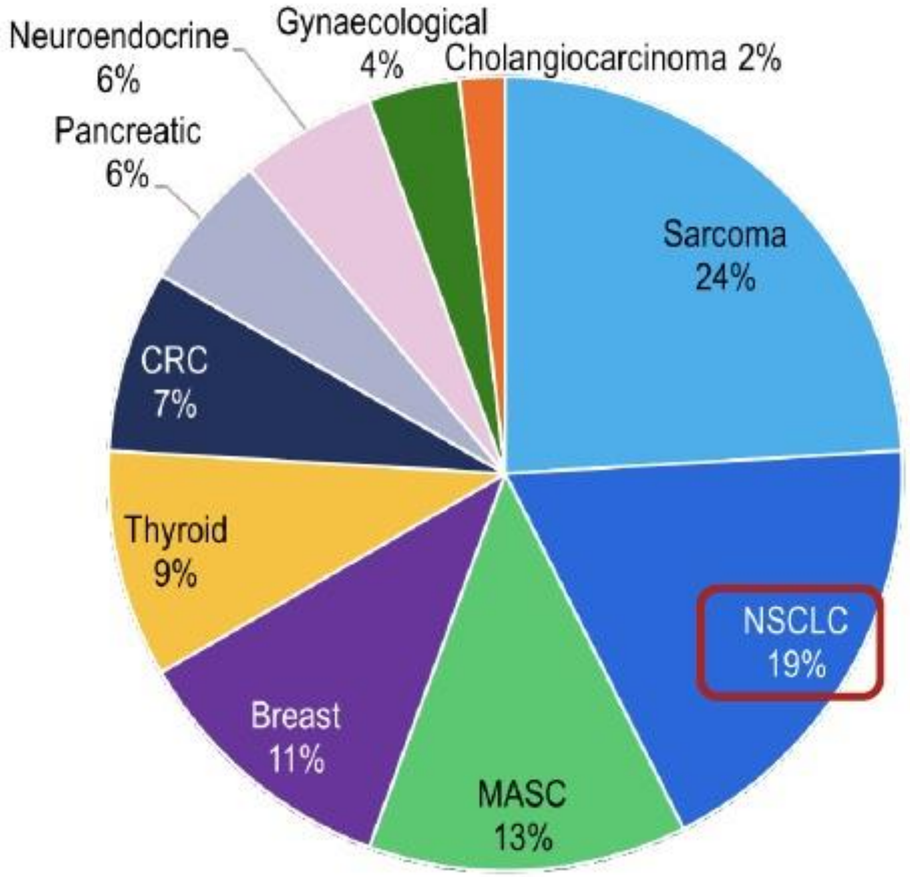
- Primary endpoints‡
  - ORR
  - DoR
- Secondary endpoints‡
  - PFS and OS
  - intracranial ORR and DoR§
  - safety and tolerability

Doebele AACR 2019

Entrectinib integrated analysis across phase I/II

Patient Characteristics and Tumor Types

Baseline characteristics		*NTRK*+ patients (n=54)	*NTRK*+ NSCLC patients (n=10)
Age, years	Median (range)	57.5 (21–83)	62.5 (46–76)
Sex, %	Female Male	59.3 40.7	50.0 50.0
Race, %	White Asian	79.6 13.0	70.0 30.0
ECOG PS, %	0 1 2	42.6 46.3 11.1	30.0 50.0 20.0
Prior lines of systemic therapy, %	0 1 ≥2	37.0 20.4 42.6	30.0 30.0 40.0
CNS mets at baseline, %		22.2	60.0



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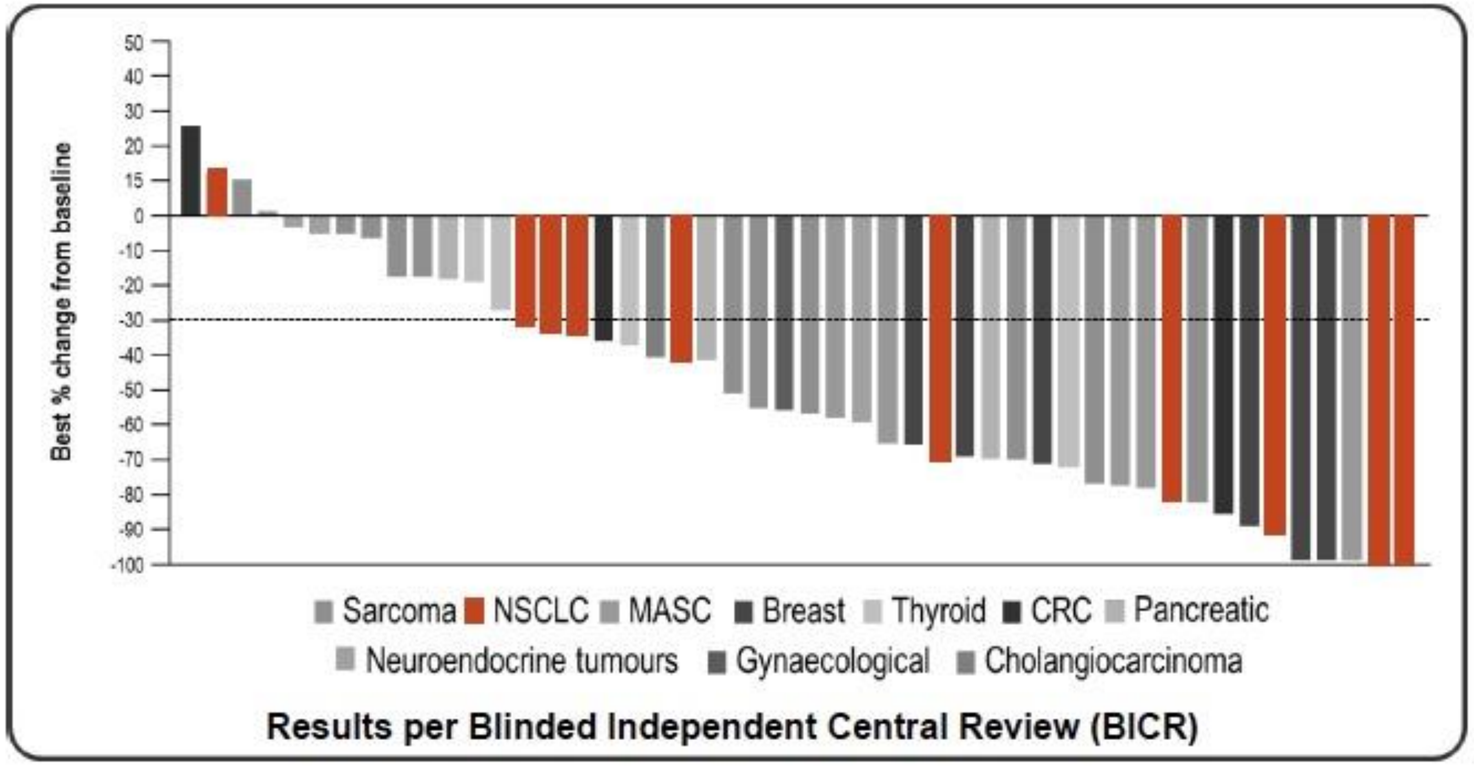
Entrectinib integrated analysis across phase I/II

Efficacy



Efficacy outcomes	*NTRK*+ patients (n=54)	*NTRK*+ NSCLC patients (n=10)
ORR*, % (95% CI)	**57.4** (43.2–70.8)	**70.0** (34.75–93.33)
CR* n (%)	4 (7.4)	1 (10.0)
Median DoR,* months (95% CI)	10.4 (7.1–NR)	NE (10.4–NE)
Median PFS,* months (95% CI)	11.2 (8.0–14.9)	14.9 (4.7–NE)
Median OS, months (95% CI)	20.9 (14.9–NR)	NE (5.9–NE)

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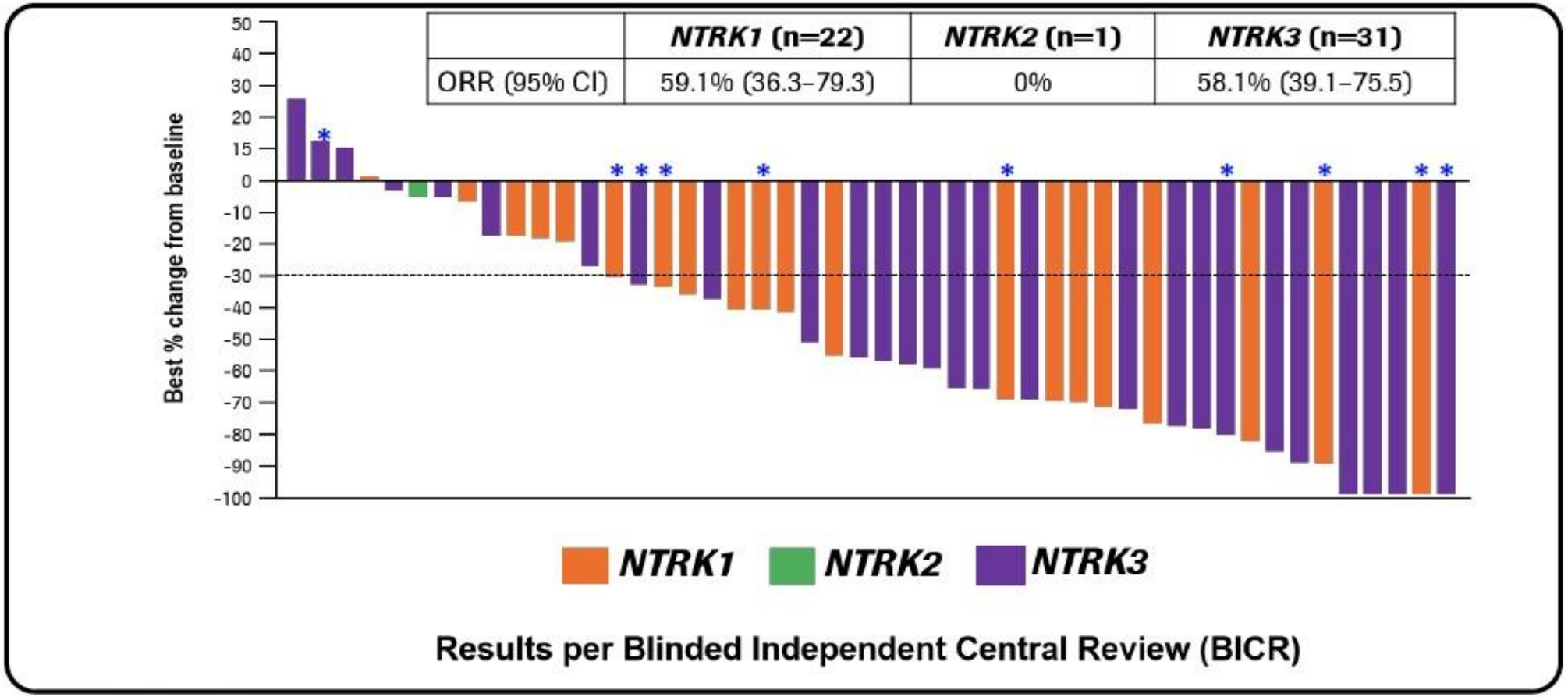
Entrectinib integrated analysis across phase I/II

Efficacy by NTRK gene



*NSCLC patients

Data cut-off date: 31 May 2018
Note: Patients (n=6) without matched pre/post therapy scans were excluded from the plot
ORR: overall response rate

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Entrectinib integrated analysis across phase I/II

Safety

Treatment-related AEs reported in ≥10% of patients	*NTRK* fusion-positive safety population (n=68)*†	
Patients, n (%)	Grade 1/2	Grade 3
Dysgeusia	32 (47.1)	0
Constipation	19 (27.9)	0
Fatigue	19 (27.9)	5 (7.4)
Diarrhea	18 (26.5)	1 (1.5)
Edema peripheral	16 (23.5)	1 (1.5)
Dizziness	16 (23.6)	1 (1.5)
Blood creatinine increased	12 (17.7)	1 (1.5)
Paresthesia	11 (16.2)	0
Nausea	10 (14.7)	0
Vomiting	9 (13.2)	0
Arthralgia	8 (11.8)	0
Myalgia	8 (11.8)	0
Weight increased	8 (11.8)	7 (10.3)
Aspartate aminotransferase increased	7 (10.3)	0
Anemia	5 (7.4)	8 (11.8)

- Most AEs were grade 1/2 and reversible
- Treatment-related AEs leading to
  - dose reduction: 39.7%
  - dose interruption: 30.9%
  - discontinuation from treatment: 4.4%
- No grade 5 treatment-related events were reported
- Treatment-related AEs reported in the *NTRK* fusion-positive and the overall safety populations were comparable

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CNS Disease

Entrectinib integrated analysis across phase I/II

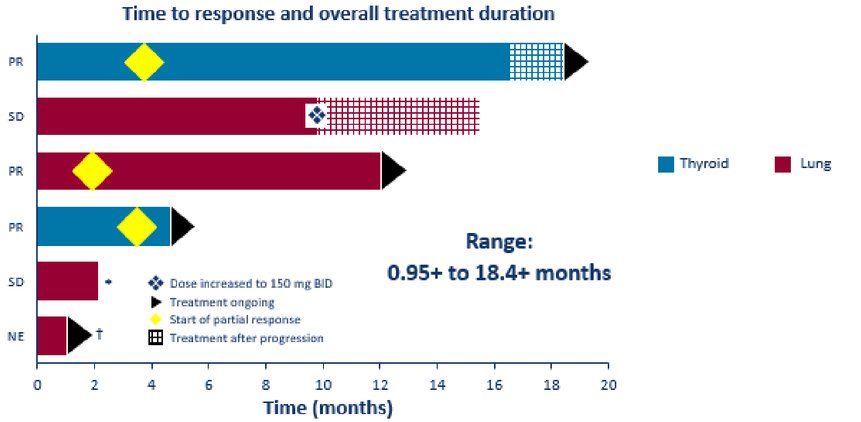
CNS Activity

Overall Response to Larotrectinib in TRK Fusion-Positive Solid Tumors with Brain Metastases

Overall efficacy	n=5 evaluable patients‡
Objective response rate*	60% (95% CI: 15–95)
Best overall response†, n (%)	
Partial response	3 (60%)§
Stable disease	2 (40%)
Progressive disease	0 (0%)

Data cutoff date July 30, 2018. *Overall (systemic) response by RECIST 1.1 including intracranial and extracranial disease when applicable. †Investigator assessment based on RECIST 1.1.
‡1 patient not shown here initiated treatment with larotrectinib but has not yet had an on-treatment scan to evaluate response. §One patient pending confirmation. RECIST, Response Evaluation Criteria in Solid Tumors.

Larotrectinib in TRK Fusion-Positive Solid Tumors with Brain Metastases: Treatment Duration



Data cutoff date July 30, 2018. Disease assessments were performed by investigators. Intracranial target tumor responses in patients with measurable disease, based on RECIST 1.1 sum of longest diameter. *Nontarget PD in asymptomatic leptomeningeal focus. †Update of this patient case presented in subsequent slide.
NE, not evaluable; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

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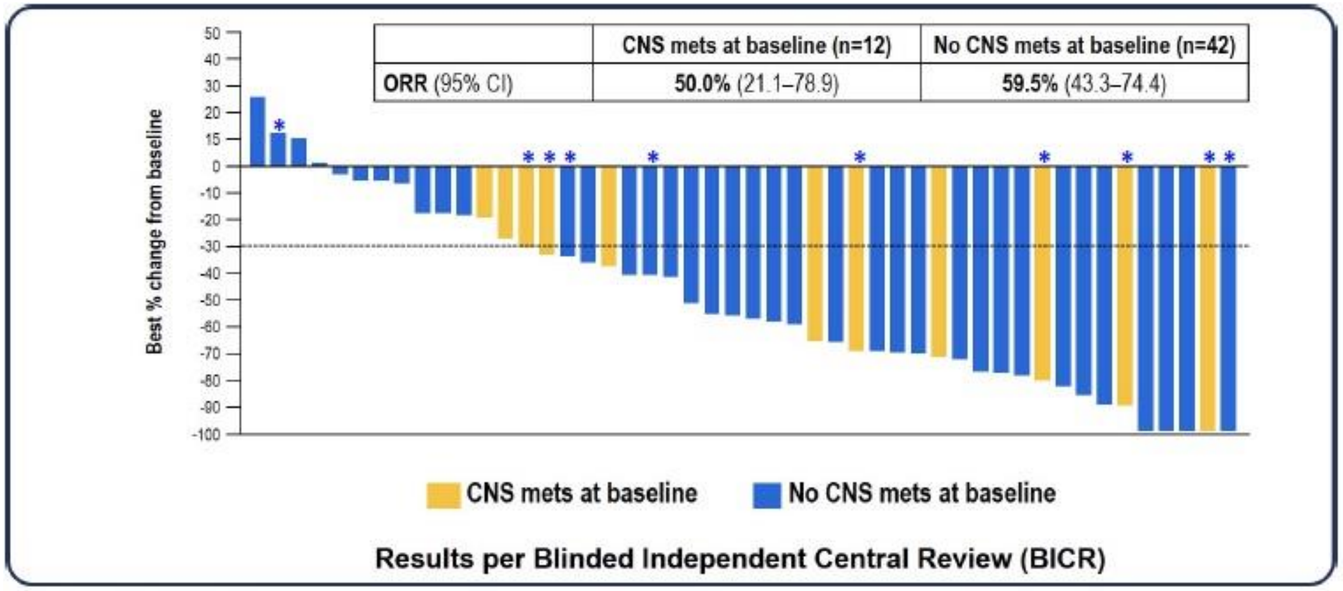
Entrectinib integrated analysis across phase I/II

CNS Activity



*NSCLC patients

Intracranial response – CNS metastases at baseline by BICR		
	***NTRK*+ patients (n=11*)**	***NTRK*+ NSCLC patients (n=6†)**
Intracranial ORR, n (%) (95% CI)	**6 (54.5)** (23.4–83.3)	**4 (66.7)**
CR	**3 (27.3)**	**2 (33.3)**
PR	3 (27.3)	2 (33.3)
SD	1 (9.1)	1 (16.7)
PD	3 (27.3)	0
Non CR/PD, Missing or unevaluable	**NE** (5.0–NE)	**1 (16.7)**
Intracranial median DoR, months (95% CI)	14.3 (5.1–NE)	NE

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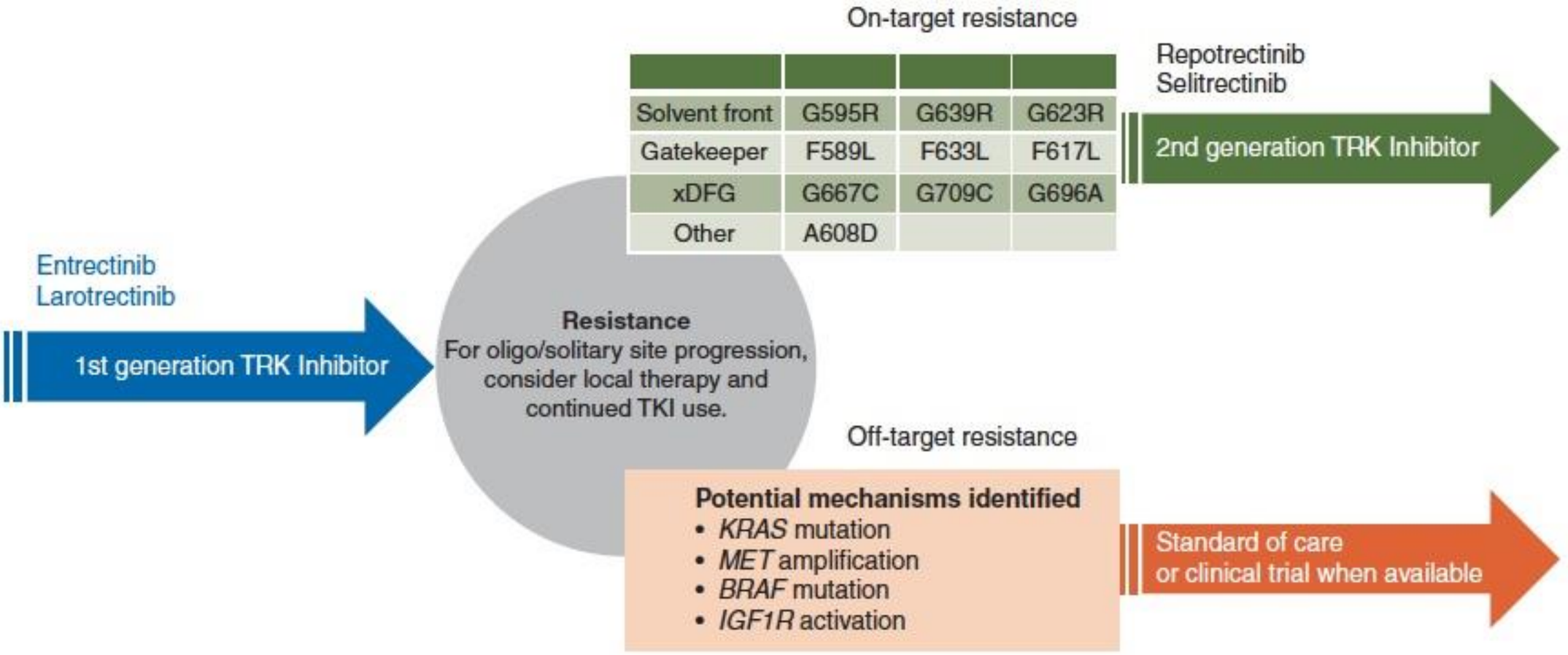
Resistance

Sequential approach



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TRK inhbitors

Table 1. TRK inhibitors

	Larotrectinib	Entrectinib	Selitrectinib	Repotrectinib
Generation				
First	✓	✓		
Second			✓	✓
Inhibits				
TRKA/B/C	✓	✓	✓	✓
ROS1		✓		✓
ALK		✓		✓
Resistance				
Inhibits most *NTRK* mutations			✓	✓

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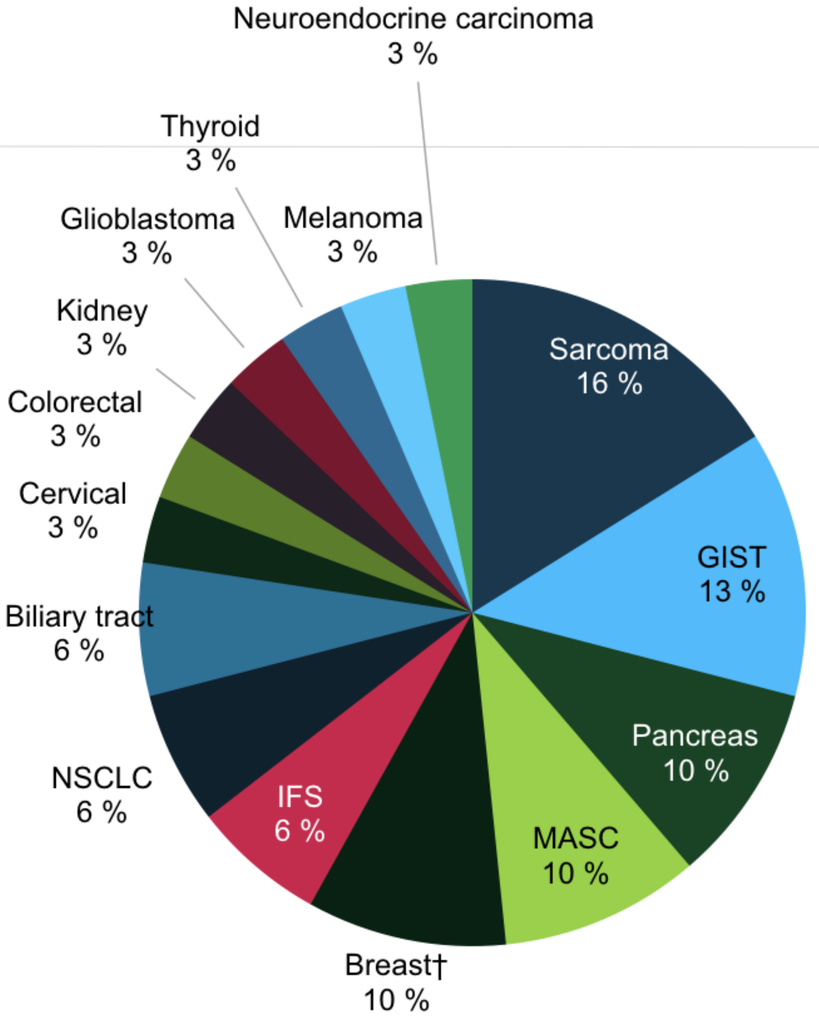
Selitrectinib phase I and expanded access

Patients characteristics

Characteristic	Total (N=31)
Gender, n (%) Female Male	 22 (71) 9 (30)
Median age (range), years Pediatric (≤18), n (%) Adult (>18), n (%)	37 (1.25–72) 7 (23) 24 (77)
Prior TKI‡, n (%) Larotrectinib Entrectinib PLX7486	31 (100) 21 (69) 9 (28) 1 (3)
Median duration* of prior TRK TKI, months (range)	11 (2–30)
TRK fusion, n (%) *NTRK1* *NTRK2* *NTRK3*	 15 (48) 1 (3) 15 (48)
Enrollment, n (%) Phase I SPP	 20 (65) 11 (35)



Tumor types (n=15)

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Selitrectinib phase I and expanded access

ORR by Resistance mechanism

Patient cohort	Patients, N	CR/PR, n	SD, n	PD, n	NE†	ORR, % (n/N)
TRK kinase mutation	20	9	6	2	3	45 (9/20)
Solvent front	14	7	4	2	1	50 (7/14)
Gatekeeper	4	1	1	0	2	25 (1/4)
xDFG	2	1	1	0	0	50 (1/2)
Identified bypass	3	0	0	3	0	0 (0/3)
Other/unknown	6	1‡	3	0	2	17 (1/6)
Total	29*	10	9	5	5	34 (10/29)

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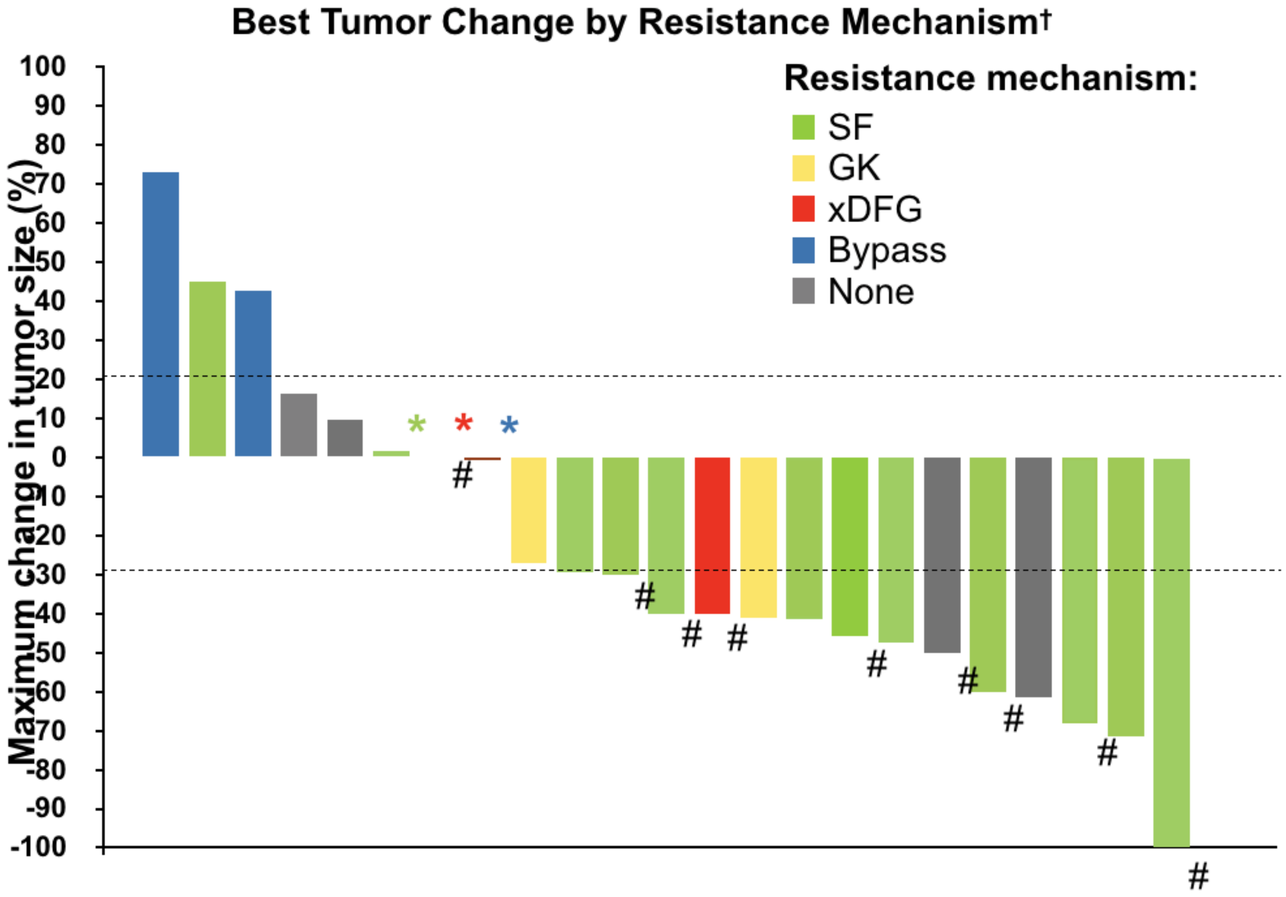
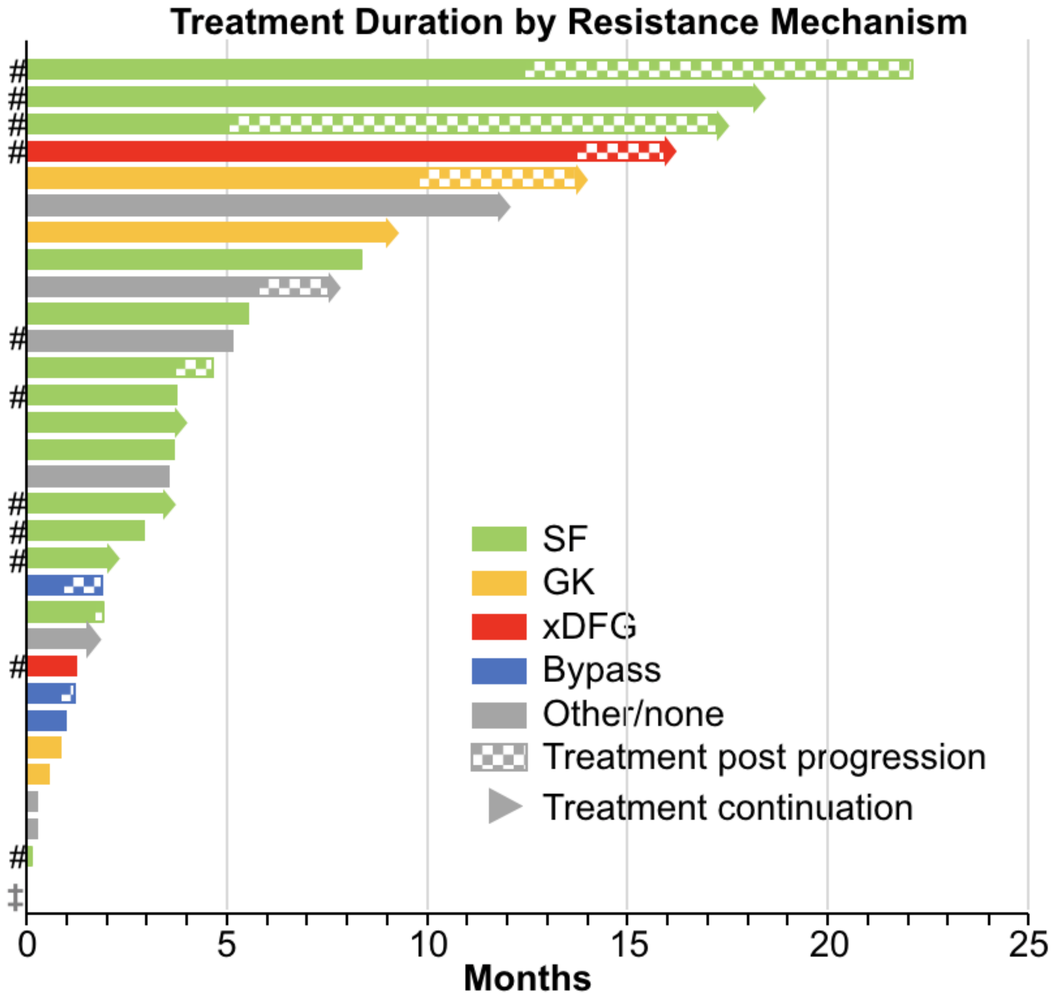
Selitrectinib phase I and expanded access

Treatment duration by Resistance mechanism





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