

Übersicht
Klinische Studien der Mitglieder
der
Projektgruppe
Tumoren der Lunge und des
Mediastinum

Stand: 18. Oktober 2016

Klinikum Rechts der Isar

NSCLC, lokal fortgeschritten, nach Radiochemotherapie

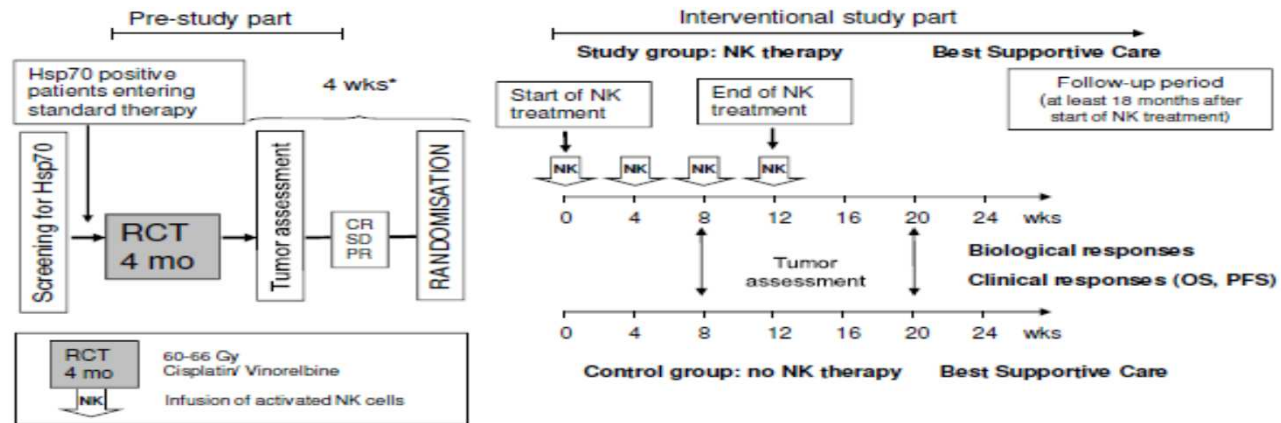
Clinical phase II trial:

Targeted Natural Killer (NK) cell based adoptive immunotherapy for the treatment of patients with Non-Small Lung Cell Carcinoma (NSCLC) after radiochemotherapy (RCT)

Screeningstudie für Hsp70



Study setup



* Immunological assessment: 4 weeks after last treatment day of RCT
Tumor assessment: 4 weeks after last treatment day of RCT
Eligible patients will be randomised to either study or control group after tumor assessment

Klinikum Rechts der Isar (Stand Oktober 2016)

NSCLC: GO29537 Abraxane/Carbo +/- Atezolizumab für Nicht Platte 1st line

SCLC: Trinity- Rovalpituzumab Tesirine für SCLC 3rd line

Klinikum Bogenhausen Stand- Stand Juli 2016 - 1

Studie	IP	Indikation
NSCLC Stadium IB – IIIA, Adjuvanz:		
GO29527 Roche (Ph III) geplant	- Atezolizumab (PD-L1 positiv) - Erhaltung nach adjuvanter Chemo - offene Studie	
NSCLC Stadium IIIA/IIIB, 1st line:		
NK-Immuntherapie (Ph II)	- TKD/IL-2 aktivierte autologe NK-Zellen - Erhaltung nach Erstlinie - offene Studie	- PECA, HSP-70 Positivität (Blutprobe) - vorherige Radiochemo (mind. 4 Gaben)
NSCLC Stadium IV, 1st line:		
Flaura AstraZeneca (Ph III) keine Rekrutierung	- AZD9291 (3.Generations-TKI) im Vergleich mit Erlotinib oder Gefitinib	- ADC, Stadium IIIB-IV - EGFR-Mutation (Exon-19-Del oder L858R)
A782 Amgen (Ph III)	- Darbepoetin bei Anämie (Hb<11g/dl) Begleitend zur Erstlinie	- NSCLC - mind. 2 Zyklen Chemo müssen noch gegeben werden
GO29436 Roche (Ph III)	- Atezolizumab (anti-PD-L1 AK) mit Carbo/Pac +/- Beva - offene Studie	- ADC - Testung auf PD-L1 Status
GO29437 Roche (Ph III)	- Atezolizumab (anti-PD-L1 AK) mit Carbo/Pac oder Nabpaclitaxel - offene Studie	- PECA - Testung auf PD-L1 Status
CA209227 BMS (Ph III)	- Nivolumab +/- Ipilimumab (anti-CTLA-4 AK) im Vergleich zu Platindoublette - offene Studie	- ADC , PECA - Testung auf PD-L1-Status

Klinikum Bogenhausen Stand- Stand Juli 2016 - 2

NSCLC Stadium IV, 2nd line:		
TH-CR-415 Threshold Pharma (PH II) keine Rekrutierung	- Th-302 (Aktivierung im hypoxischen Milieu, interkaliert mit DNA) in Kombination mit Pemetrexed	- ADC, Stadium IIIB-IV
Select-1 AstraZeneca (PH III) keine Rekrutierung	- Selumetinib (MEK-Inhibitor) in Kombination mit Docetaxel	- Stadium IIIB-IV - KRAS Mutation
HER-3-LUNG Daichii - on hold-	- Patritumab (anti-HER3 AK) in Kombination mit Erlotinib - Stadium IIIB-IV	- <u>1. Stufe (abgeschlossen)</u> : Einschluss unabh. vom HER3-Status (high oder low) - <u>2. Stufe (folgt)</u> : Einschluss nur bei HER3 high Status
OSE-2101 OSE-Pharma (Ph III) geplant	- OSE-2101 (Vakzin, 10 synthetisierte Peptide) im Vergleich zu Docetaxel oder Pemetrexed - offene Studie	- HLA-A2 positiv
NSCLC Stadium IV, 2nd / 3rd line:		
CINC280A Novartis (Ph II)	- INC280 (cMET-Inhibitor in Tablettenform) - offene Studie	- Testung auf cMET Status (Amplifikation, Mutation)
CINC280B Novartis (Ph II) geplant	<u>Phase II:</u> - INC280 (cMET-Inhibitor) +/- Erlotinib im Vergleich mit Platin/Pemetrexed - offene Studie	- cMET Amplifikation - EGFR Mutation (Exon-19-Del oder L858R) - EGFR TKI-Resistenz (<u>exakt 1</u> vorausgehende TKI-Therapie mit Erlotinib, Gefitinib oder Afatinib)
SCLC limited disease, 1st line:		
Stimuli ETOP (Ph II) geplant	- Nivolumab + Ipilimumab	<u>Studieneinschluss:</u> - max. 1 Zyklus Chemotherapie <u>Randomisierung:</u> - abgeschlossene Radiochemo nach Protokoll (4 Zyklen Cis-/Carboplatin + Etoposid, 2 thorakale und 1 prophylaktische Ganzhimbstrahlung)

Klinikum Bogenhausen Stand- Stand Juli 2016 - 3

SCLC limited/extensive disease, 2nd line:		
CA209331 BMS (Ph III)	- Nivolumab (anti-PD-1 AK) im Vergleich zu Topotecan	- Testung auf PD-L1 Status - mind. 4 vorausgehende Zyklen Chemo
SCLC, ab 3rd line:		
SCRX001-002 Stemcentrx (Ph II) geplant	- Rovalpituzumab tesirine (anti-DLL3 AK-Konjugat) - offene Studie	- DLL3 positiv
Nicht-interventionelle Studien:		
LUMINIST AstraZeneca		- Beobachtungsstudie - alle Screening Failure Patienten der Select-1 Studie
AVAdeno (Roche)	Avastin (Bevacizumab) in Kombination mit einer platinhaltigen Chemo	ADC, Stadium IIIB-IV - Erstlinie
GIDEON	Giotrif (Afatinib)	- NSCLC, Stadium IV - Erstlinie - Patienten mit akt. EGFR Mutation
RePneu	Lungenvolumen-reduktionsspirale	- Emphysem mit Überblähung - FEV1<45%, RV>175%
Insights IPF		- idiopathische Lungenfibrose - Neudiagnose oder bestehend
FOCUS FOCUS bioSeq		- akute Lungenarterienembolie - Ausschluss: Zufallsbefund

Klinikum Innenstadt Stand 14.10.2016 - 1

<i>Histo, stage</i>	<i>Mutation</i>	<i>Linie</i>	<i>Protokoll</i>	<i>Eudract Nr.</i>	<i>Sponsor</i>	<i>Studientitel</i>	<i>Status</i>
<i>ongoing</i>							
NSCLC,	EGFR+	2nd line TKI	TIGER-2 CO-1686-019	2013-005532-23	Clovis oncology	Oral CO-1686 as 2nd line EGFR-directed TKI in patients with mutant EGFR NSCLC with T790M resistance mutation, auch ohne Mutation	Closed Pat ongoing
NSCLC	ALK+	Nach Crizotinib	ALTA AP26113-13-201	2013-002134-21	ARIAD pharmaceuticals	AP26113 in patients with ALK-positive NSCLC, previously treated with Crizotinib	Closed Pat ongoing
NSCLC IIIB, IV	Heregulin positive	2nd line	Merrimack Sherlock	2014-003673-42	Merrimack	MM-121 in Combination with Docetaxel or Pemetrexed versus Docetaxel or Pemetrexed alone in patients with Heregulin positive locally advanced or metastatic NSCLC	open
sNSCLC	Squamous	2nd line	Primus	2015-001123-22	AIO-Studien	Pembrolizumab maintenance following first-line platinum based chemotherapy in patients with metastatic sNSCLC	open
NSCLC, IIIa, IIIb	HSP 70 present	Erhalt nach Radiochemo	Killercell NSCLC-TKD/IL-2	2008-002130-30	TU München	Zielgerichtete adjuvante Immuntherapie mittels aktivierter NK-Zellen bei Patienten mit einem NSCLC im Anschluss an Radiochemotherapie	open
NSCLC	Alk+	Ceritinib	Food Effect CLDK378A2 112	2014-004001-32	Novartis	Exposure, efficacy and safety of different doses of ceritinib taken with a low-fat meal or in fasted state in patients with NSCLC Alk+	open

Klinikum Innenstadt Stand 14.10.2016 - 2

NSCLC IIIA/B	Not defined	Consolid after firstline	Nicolas ETOP 6-14	2014-005097-11	ETOP Schweiz	Anti-PD1 Nivolumab Consolidation after firstline chemo and radiotherapy in NSCLC Stage IIIA/B	open
NSCLC	EGFR+	Firstline Giotrif	GIDEON 1200.205	NIS	Boehringer Ingelheim	Giotrif in der Erstlinientherapie des fortgeschrittenen NSCLC mit aktivierenden EGFR-Mutationen	open
SCLC	-	Limited maintenance	STIMULI ETOP IFCT 4-12	2013-002609-78	ETOP Schweiz	Phase II Studie mit Nivolumab und Ipilimumab zur Erhaltungstherapie beim SCLC limited nach Radio/Chemo	Open
NSCLC inoperable	EGF>250	inoperable	BIOVEN2 BV NSCLC002	2013-005335-25	Bioven Aberdeen UK	EGF Cancer vaccine in inoperable, late stage biomarker positiv NSCLC patients	on hold
Adv. NSCLC after firstline wih Afatinib	EGFR+	after firstline wih Afatinib	MARBLE AIO-TRK-0114	2014-001983-36	AIO Studien	Phase II Studie of maintaining pan-ERBB blockade following platinum-based induction chemotherapy in patients with advanced NSCLC after firstline with Afatinib	open

Klinik Gauting – Stand Oktober 2016 – 1 (laufende Studien)

NSCLC	1st	alle	alle	advanced	3	Splendour	ETOP	2013-003156-21	NCT02129699	ETOP		1st line SOC + Denosumab	
Meso	1st	Meso	unresectable		2	MORAb-009-201	009-021	2014-004489-85	NCT02357147	Morphotek		Amaxutimab + Pem + Cis	Monoklonaler Antikörper anti mesothelin
NSCLC	1st	Platte	maint. nach NAB Pacli+Carbo	IIIb/IV	3	ABI-007-NSCLC-003	Abi007	2014-003804-66	NCT02027428	Celgene		NAB-Paclitaxel	
NSCLC	ab 1st	alle	ALK pos mit brain mets		2	CLDK378A2205	CLDK	2014-000578-20	NCT02336451	Novartis	1201	Ceritinib oral	ALK Inhibitor
NSCLC	adjuvant	Adeno	EGFR positiv nach Kompletresektion	Ib-IIIa	3	D5164C00001	Adaura	2015-000662-65	NCT02511106	Astra Zeneca	2603	AZD9291/Placebo	EGFR + T790M Inhibitor
NSCLC	adjuvant	alle	mit + ohne PD L1, vorher Test	Ib, II, IIIa	3	MK-3475-091 EORTC-1416-LCG	Pearls	2015-000575-27	NCT02504372	Merck		Pembrolizumab/Placebo	Monoklonaler Antikörper anti PD-1
NSCLC	3rd	Crizo vorbeh.	ALK pos.	advanced	3	MO29750	Alur	2015-000634-29	NCT02604342	Roche		Alecitinib oral vs. Alimta oder Doce	ALK Inhibitor
NSCLC	recurrent	alle	brain mets		2	AIO-ZNS-0113	CaBaMet	2013-005545-37	NCT02166658	AIO		Cabacitaxel	
NSCLC	1st	Adeno	EGFR positiv	IIb/IV	3	8273-CL-0302	Solar	2015-002894-39	NCT02588261	Astellas	49003	ASP8273 vs. Gefitinib	EGFR+ T790M inhibitor
ED-SCLC	maint after 1st line	ED-SCLC		ED	3	CA 209-451	BMS Kleinzeller	2015-002441-61	NCT02538666	BMS	0166	Nivolumab, Nivolumab + Ipi/Placebo	
solid tumors	Start neue Therapie	alle	hohes Thromboserisiko	IIB-IV		39039039STM4001	Riva	2015-001631-21	NCT02555878	Janssen		Rivaroxaban vs Placebo	Thromboseprophylaxe
NSCLC	3rd	Adeno	EGFR wild	IIIb/IV	2	CINC280A2201	Geometry mono	2014-003850-15	NCT02414139	Novartis	1314	INC280 oral	cMET Inhibitor
SCLC	2nd	SCLC			2	CESAR C-II-011	Veliparib	---	---	Cesar	01	Veliparib + Topotecan	PARP1 inhibitor
NSCLC	1st	Adeno		IV		GO29537	IMPowor130	2014-003206-32	NCT02367781	Roche		Atetolizumab in combination with Carbo + Nab-Pacli	anti PD-L1 Antikörper
NSCLC			min. SD nach 4 mts Nivo Vorbehandlung	IIIB/IV		CA209-384		2015-004633-27	NCT02713867	BMS		Nivolumab dose frequency Optimierung	

Klinik Gauting – Stand Oktober 2016 – 2 (kommend)

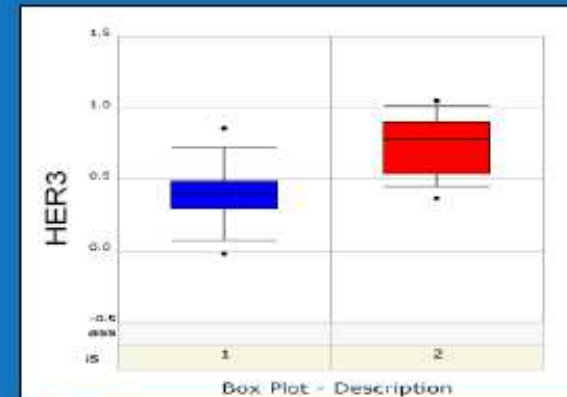
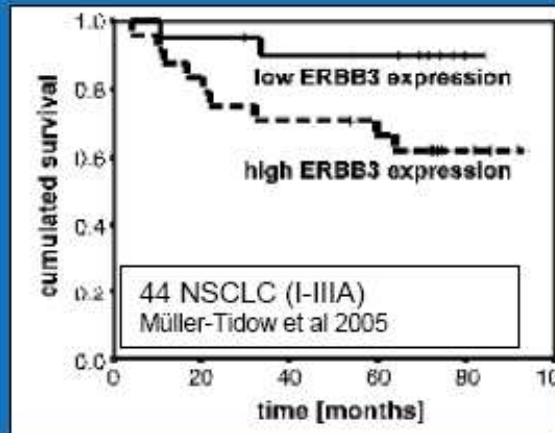
SCLC	ab 3rd	SCLC	mit DLL3 expr.	relapsed/ refractory	2	SCRX001-002	Trinity	2015-004506-42	NCT02674568	Stemcentrx		Rovalpituzumab Tesirine	DLL3 Antikörper
kommend													
NSCLC	2nd	Adeno	EGFR pos Cmet apfliziert		3	CINC280B2201	Geometry duo	2015-001241-84	NCT02468661	Novartis		INC280 oral + Erlo/Chemo	cMET Inhibitor
SCLC	2nd	SCLC			3	PM1183-C-003-14	Atlantis	2015-001641-89	NCT02566993	Pharma Mar SA		Lurbinectedin + Doxorubicin vs Toptecan	Chemoalternative bei Platinresistenz
SCLC		refraktär				D419QC00002	AZ SCLC	2016-001202-42	--	Astra Zeneca			
NSCLC	2nd			IV	2	I4T-MC-JVDN		2016-001317-25	NCT02831491	Eli-Lilly		Ramucirumab + weekly Doce	
SCLC	1st	ED-SCLC		advanced	3	GO30081	IMPower133	2015-004861-97	NCT02763579	Roche		Carbo/Etoposid +/- Atezolizumab	
NSCLC	ab 2nd	Adeno	Exxon 14 skipping alteration		2	MS200095-0022	Project blue	2015-005696-24	NCT02864992	Merck KGaA		Tepotinib single arm	cMET Inhibitor
NSCLC	ab 2nd	alle	EGFR + ALK negativ, MET Mutation vorh.	IIIb/IV	2	265-109	Mirati	2015-002070-21	NCT02544633	Mirati		MGCD265 oral	RTK Inhibitor, targets: Axl + MET Rezeptoren
NSCLC	egal	alle	mit NTRK1, NTRK2, NTRK3 or ROS1 Rearrangements; naive to crizotinib, ceritinib, and other NTRK and ROS1 inhibitors.	IIIb/IV	2	Strtrk2		2015-003385-84	NCT02568267	Ignyta		Entrectinib	Pan-Trk, ROS1, and ALK inhibitor
NSCLC			Heregulin pos.	advanced	2	MM-121-01-02-09	Sherloc	2014-003673-42	--	Merrimack		MM-121+ Doce or Pem vs. Doce or Pem	
NSCLC	ab 2nd	Adeno				CanStem43L		2016-002718-32	NCT02826161	Boston Biomedical		Napabucasin + weekly Pacli vs. Weekly Pacli	
NSCLC	2nd	ohne Alk TKI Vorbeh.	ALK pos	advanced	3	AP26113-13-301	Ariad	2015-003447-19	NCT02737501	Ariad		Brigantinib vs Crizotinib	
NSCLC	ab 3rd		ohne Mutation	IIIb/IV	1b/2	54767414LUC2001	LUC2001	2016-002579-83		Janssen		Daratumumab +/- Atezolizumab	
NSCLC						2016/01	NEOLung		--	NewOncology			
NSCLC	1st	Adeno		IV	2	M18-007	Denali	2014-003356-30	NCT02259582	Oncomed		Carbo, Pemetrexed + Placebo vs Carbo, Pem + 1 or 2 Truncated Courses of Demcizumab	monoklonaler Antikörper, target: DLL4
NSCLC	1st		ALK pos	advanced	3	B9991008			--	Pfizer		Lorlatinib mono vs. Lorlatinib + Avelumab vs. Crizotinib	
NSCLC	2nd/3rd			advanced		AIO-YMO/TRK-0415	FORCE	2015-005741-31	--	AIO		Nivolumab + radiotherapy	
NSCLC	1st			IV	3	GO29431	IMPower110	2014-003083-21	NCT02409342	Roche		Atezolizumab vs. Cis/Carbo + Pem	
NSCLC						D5160R00005	Panorama		NCT02777658	Astra-Zeneca		Beobachtung, Datendoku	
SCLC	je nach Kohorte!			advanced	1	VX12-970-001		2012-003126-25	NCT02157792	Vertex		VX970 + Chemo 1st in human	
NSCLC		Adeno		IV		AIO-TRK-0215		--	--	AIO			
NSCLC	1st			IIIb/IV	3	MO29872		--	--	Roche		Atezolizumab vs.Chemo	

Klinik Gauting – Stand Juli 2016

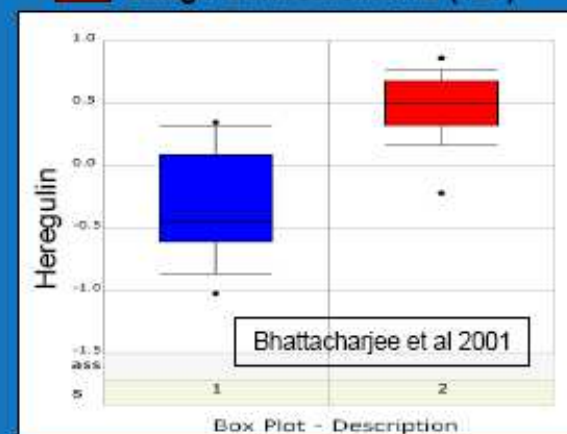
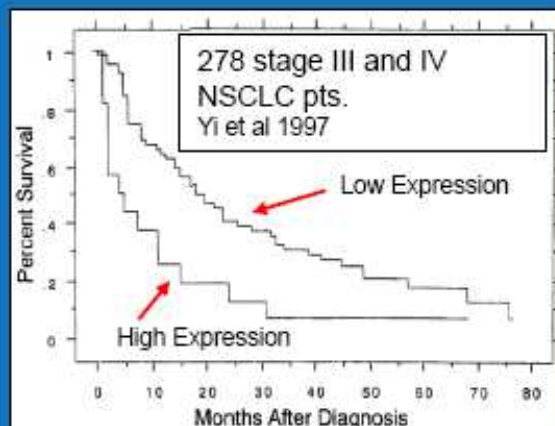
Lurbinectedin: synthet. Tetrahydropyrrolo-[4, 3, 2-de]quinolin-8(1H)-1 Alkaloid Analog [with potential antineoplastic activity. Lurbinectedin covalently binds to residues lying in the minor groove of DNA, which may result in delayed progression through S phase, cell cycle arrest in the G2/M phase and cell death.]

Duratumumab (Darzalex): monoklon. CD38-AK, zugel. für vorbeh+refrakt Myelom [CD38 molecule is highly expressed on the surface of multiple myeloma cells. It is believed to induce rapid tumor cell death through programmed cell death, or apoptosis, and multiple immune-mediated mechanisms, including complement-dependent cytotoxicity, antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity.]

Die prognostische Bedeutung der Expression von HER3 und Heregulin beim NSCLC

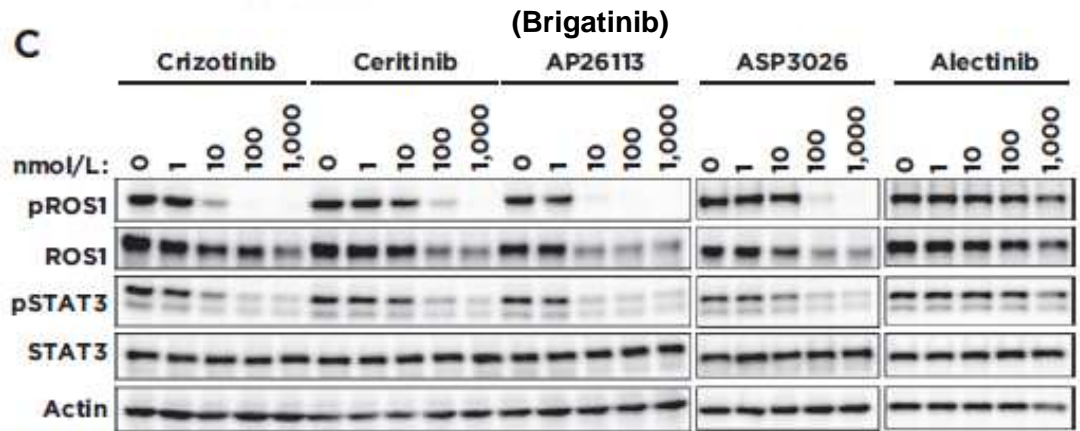


- Normal Lung (17)
- Lung Adenocarcinoma (127)



Next-generation ROS1/ALK-inhibitors

Drugs	Targets other than ALK	Activity against G2032R mutation	Activity
Ceritinib	IGF-1R, InsR, ROS1	NO	
Alectinib	LTK, GAK	---	
Brigatinib	ROS1, EGFR	?	
Entrectinib	TrkA, TrkB, TrkC, ROS1	?	
PF-06463922	ROS1	YES!	
TSR-011	TrkA, TrkB, TrkC	---	
ASP3026	ROS1, ACK	?	
X-396	MET	---	
CEP-37440	FAK	---	
Cabozantinib	RET, MET, VEGFR	Yes!!!	



C, inhibition of phospho-ROS1 by various ALK inhibitors in Ba/F3 models. CD74-ROS1-expressing Ba/F3 cells were exposed to increasing concentrations of crizotinib, ceritinib, AP26113, ASP3026, or alectinib for 3 hours. Cell lysates were immunoblotted to detect the indicated proteins.

Sullivan/Planchard; ALK inhibitors in NSCLC: the latest evidence and developments. Ther Adv Med Oncol 8, 32-47, 2016
 Katayama et al. Cabozantinib overcomes Crizo resistance in ROS1-positive cancer. Clin Cancer Res 21: 166-174, 2015
 Zou et al. PF-0643922 is a potent ROS1/ALK inhibitor blocking CRZ-resistant ROS1 mutations. PNAS 112: 3493-98, 2015