Oncolines

Webinar – 10 a.m. EDT

Comparative Cancer Cell Panel Profiling of Recently Approved Kinase Inhibitors

Comparative cancer cell panel profiling of kinase inhibitors

Webinar presenters

Guido Zaman, Ph.D.
Managing Director &
Head of Biology

Jeffrey Kooijman, M.Sc.
Bioinformatician

Overview of webinar contents

- Introduction to:
  - NTRC Oncolines™ and available services
  - Kinase inhibitors
- Overview
  - Recently approved kinase inhibitors
- Comparative analysis:
  - 1st, 2nd, and 3rd generation EGFR inhibitors
  - ALK inhibitors

NTRC Oncolines Introduction

- NTRC Oncolines is a precision medicine services company in oncology and cancer immunotherapy
- We offer a set of complimentary services to enable clients to characterize their compounds, determine activities, selectivities, and mechanism of action
- Our clients are biopharma companies, and academics that seek differentiation for their drugs and drug candidates

Combining cancer cell biology with genomics and bioinformatics

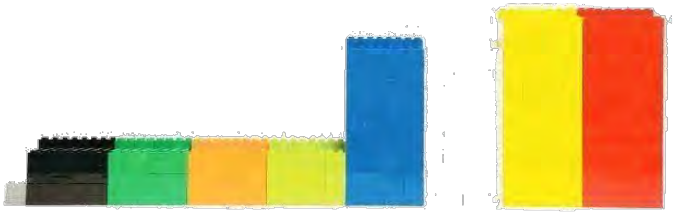
How we differentiate

- We generate, process, analyze, visualize, and interpret complex data

DATA

SORTED

ARRANGED



MEANINGFUL

- We present meaningful data and discuss them with our clients

Our Services

- **Oncolines™ Profiling** is the parallel dose-response testing of compounds on a large panel of genetically characterized human cancer cell lines

- We analyze the correlation between cell line sensitivity and the mutation status of more than 100 cancer genes, to identify drug response biomarkers for selecting patient populations for clinical trials

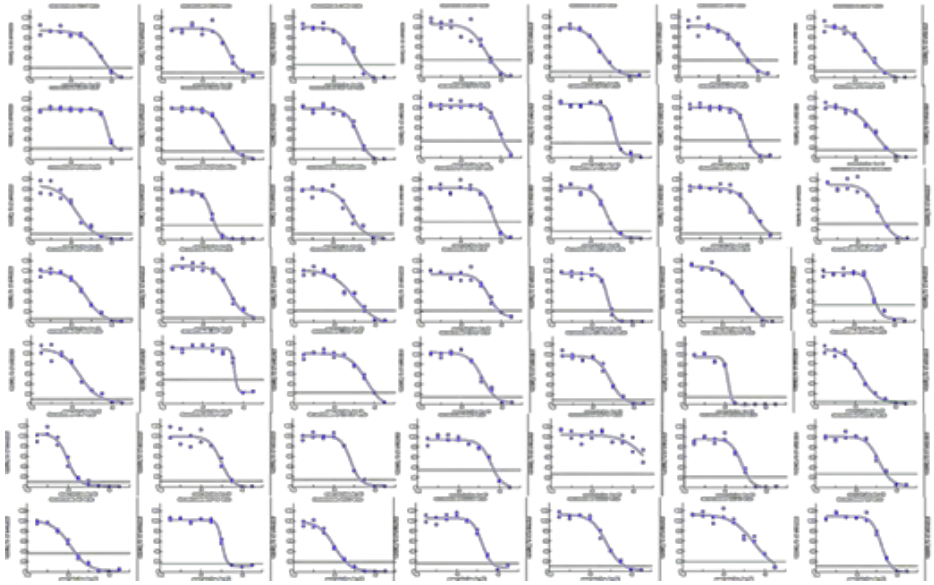
Oncolines™ Profiling

SynergyFinder™

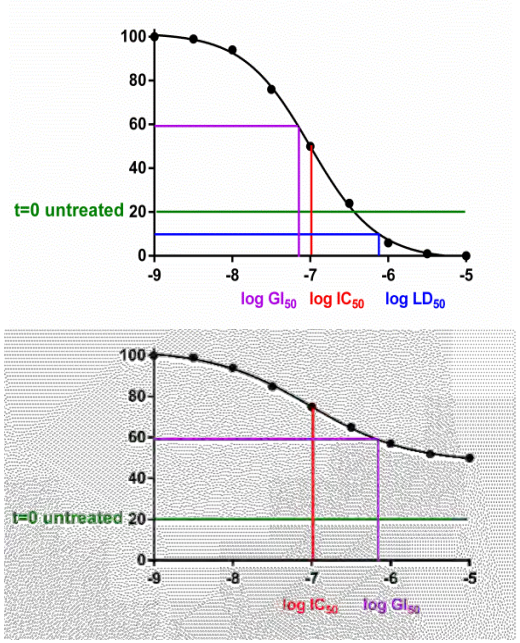
Mechanism of Action

Oncolines™ Profiling introduction

- Cell proliferation assays: measurement of intracellular ATP content as an indirect readout of cell number (ATPLite™)
- Low passage numbers and cultured at ATCC recommended culture conditions
- 9-point duplicate dose response curves
- Determination of half-maximal inhibitory concentration (IC_{50}) for bioinformatic analyses



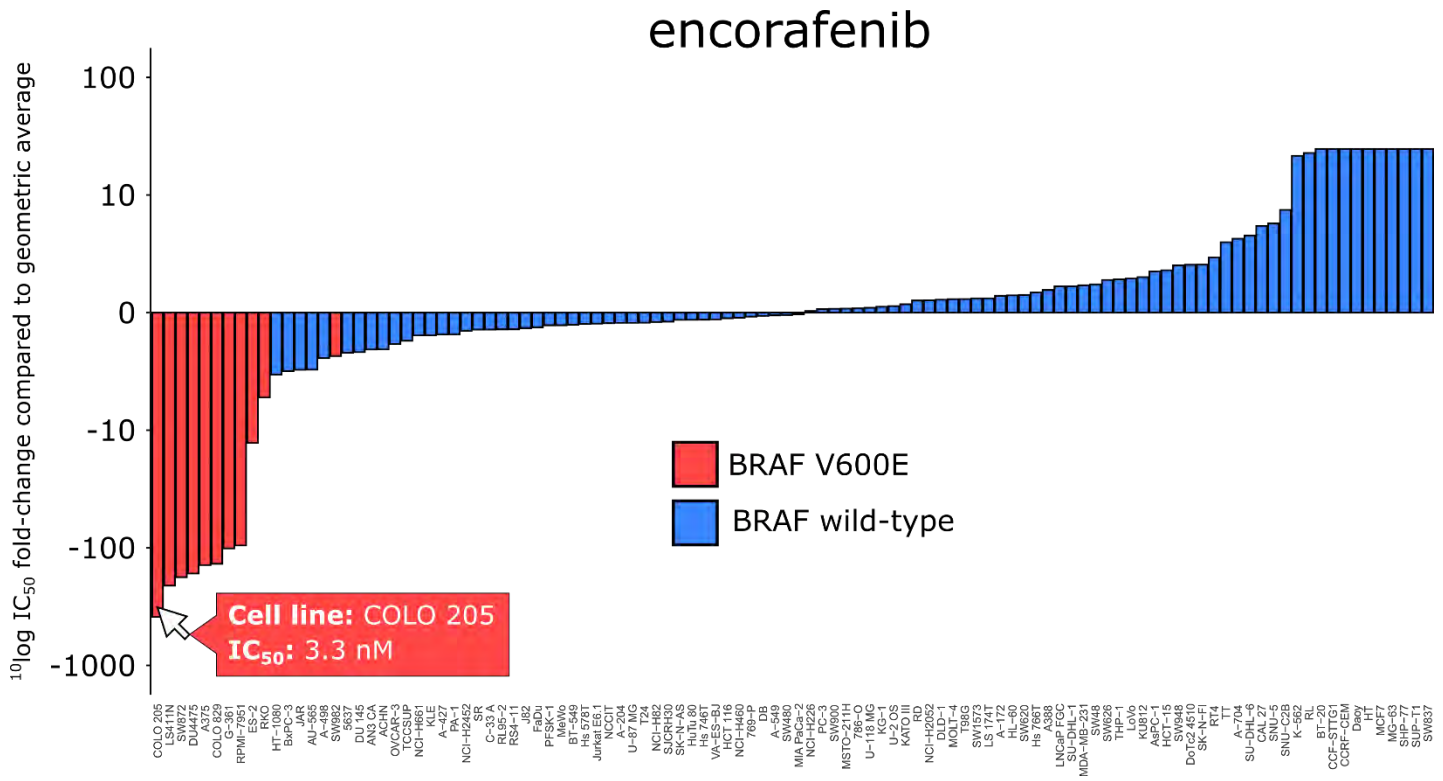
Oncoline panel profiling: 102 dose-response curves



Graphic display of IC_{50}, GI_{50} and LD_{50}

Oncolines™ Profiling powerful interactive reports

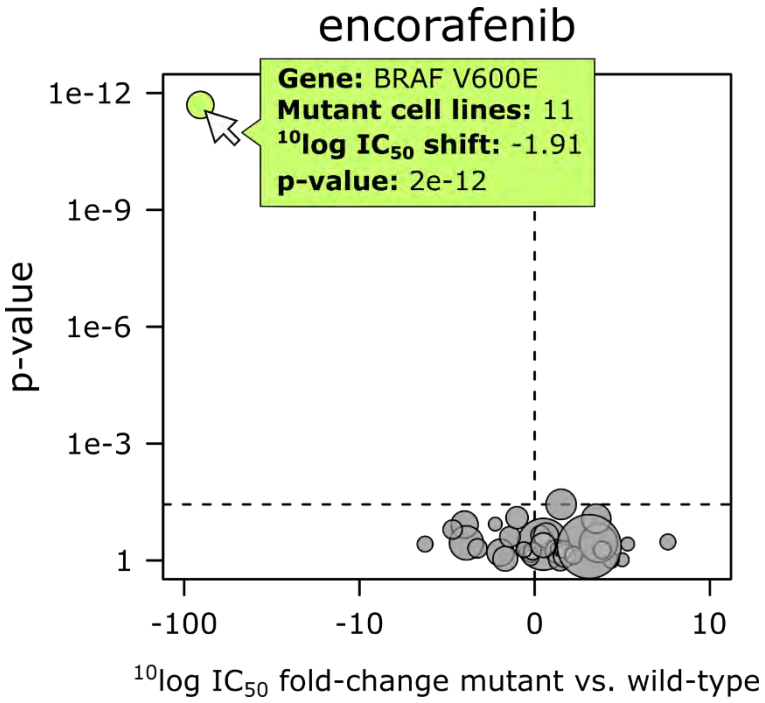
- Our unique interactive reports facilitate easier and faster interpretation of results



Waterfall plot showing the ranking, from left to right, of cancer cell lines with low IC_{50} to high IC_{50} in cell proliferation assays with the BRAF kinase inhibitor encorafenib. Cell lines harboring the *BRAF(V600E)* mutation are indicated in red. Cancer cell lines not having this mutation ('wild-type') are indicated in blue.

Oncolines™ Profiling genomic biomarker analysis

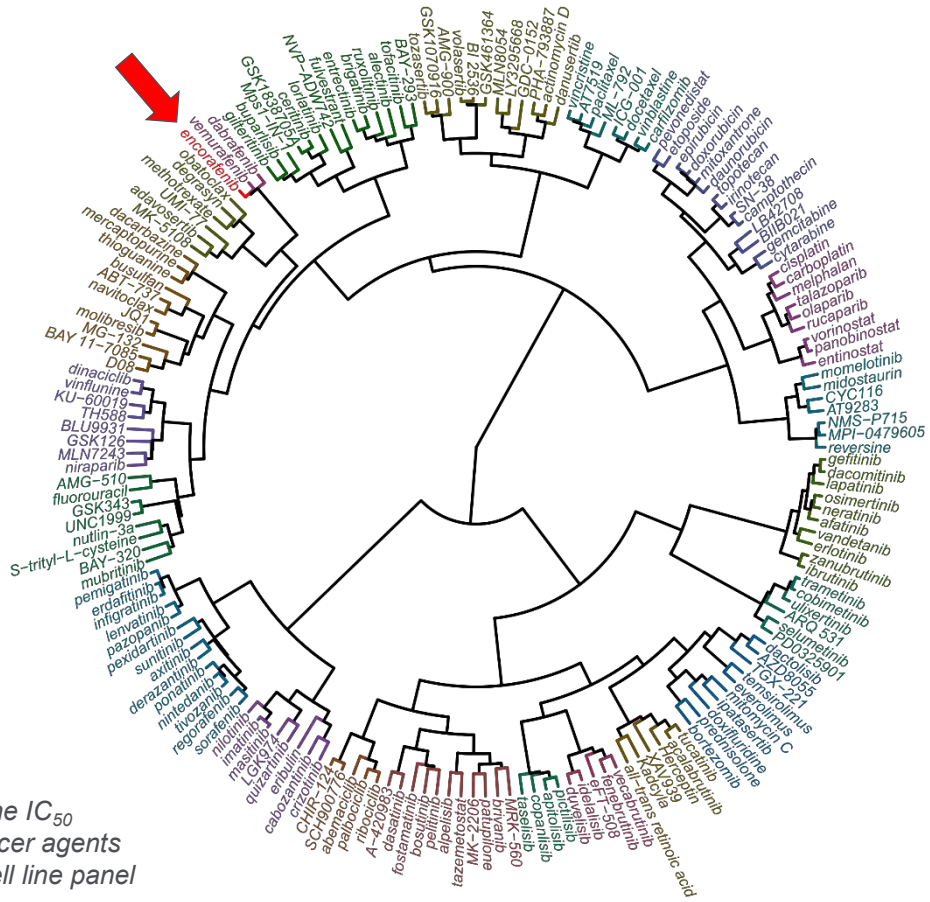
- Identification of cancer gene mutations that correlate with drug sensitivity or resistance



Volcano plot showing the result of an Analysis Of Variance (ANOVA). Cell lines were grouped according to the mutation status of 38 well-known cancer genes. Cell lines harbouring different cancer gene mutations are represented by circles. Sensitivity (IC_{50}) is plotted on the x-axis. Statistical significance on the y-axis. The volcano plot shows that cell lines harbouring mutant *BRAF(V600)* are on average 80-fold more sensitive to encorafenib than cell lines not harbouring this mutation.

Comparative profiling

- Comparison of the Oncolines™ Profiling IC_{50} fingerprint with those of 178 reference anti-cancer agents to identify differentiation or mechanism of action



Hierarchical clustering of the IC_{50} fingerprints of 178 anti-cancer agents profiled in the Oncolines cell line panel

Additional cell-based services

- **SynergyFinder™** is the profiling of combinations of drugs, to identify new synergistic drug combinations

- We perform gene and protein expression analysis, DNA and RNA sequencing, and flow cytometry, to investigate the **Mechanism of Action** of drug candidates

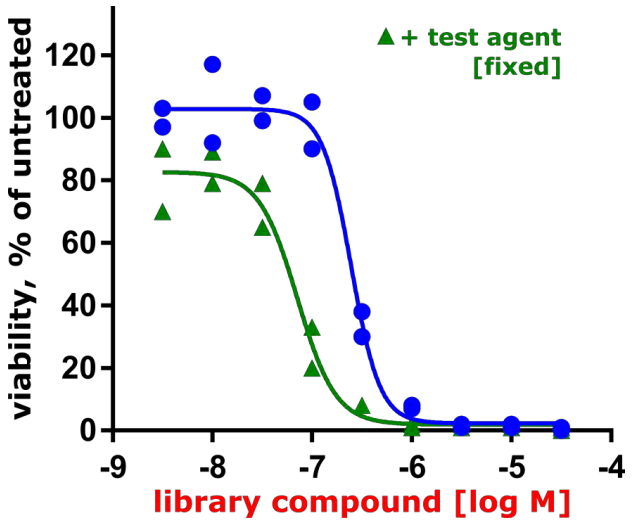
Oncolines™ Profiling

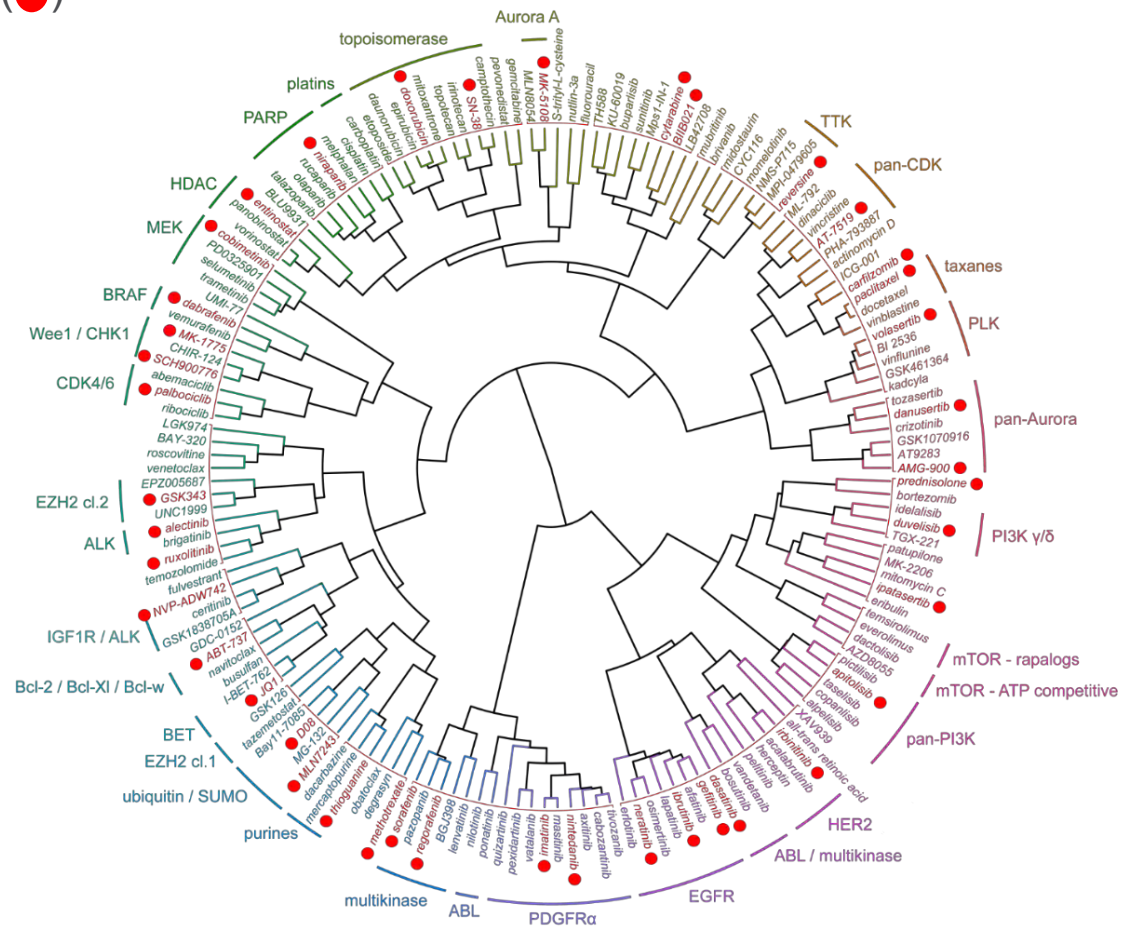
SynergyFinder™

Mechanism of Action

SynergyScreen™

- High-throughput drug combination testing against a set of 42 representative reference anti-cancer agents (●)





Biochemical kinase assays

- **ResidenceTimer™** is the determination of binding kinetics of compound – target interactions using Biacore T200 (> 100 kinase assays available)
- Enables precise determination of kinase inhibitor affinity and selectivity

- **QuickScout™** is kinase inhibitor profiling in enzyme activity assays at Carna Biosciences, Inc. (represented in Europe and Israel by NTRC Oncolines)
- 326 wild-type and mutant kinases (% inhibition and IC_{50}) are available for profiling

ResidenceTimer™

QuickScout™

Molecular interactions

Published kinase inhibitor profiling studies by NTRC

Nearly sixty small molecule kinase inhibitors have been approved for clinical use

PLOS ONE

Comparison of the Cancer Gene Targeting and Biochemical Selectivities of All Targeted Kinase Inhibitors Approved for Clinical Use

Joost C. M. Uitdehaag[1], Jeroen A. D. M. de Roos[1], Antoon M. van Doornmalen[1], Martine B. W. Prinsen[1], Jos de Man[1], Yoshinori Tanizawa[2], Yusuke Kawase[2], Kohichiro Yoshino[2], Rogier C. Buijsman[1], Guido J. R. Zaman[1]*

1 Netherlands Translational Research Center B.V., Oss, The Netherlands, **2** Carna Biosciences Inc., Kobe, Japan

until October 2013

PLoS ONE 9(3): e92146; 2014

Companion Diagnostic, Pharmacogenomic, and Cancer Biomarkers

Molecular Cancer Therapeutics

Combined Cellular and Biochemical Profiling to Identify Predictive Drug Response Biomarkers for Kinase Inhibitors Approved for Clinical Use between 2013 and 2017

Joost C.M. Uitdehaag[1], Jeffrey J. Kooijman[1], Jeroen A.D.M. de Roos[1], Martine B.W. Prinsen[1], Jelle Dylus[1], Nicole Willemsen-Seegers[1], Yusuke Kawase[2], Masaaki Sawa[2], Jos de Man[1], Suzanne J.C. van Gerwen[1], Rogier C. Buijsman[1], and Guido J.R. Zaman[1]

from November 2013 until May 2018

Molecular Cancer Therapeutics 18(2) 470-481; 2019

Comparative profiling of recently approved kinase inhibitors

New case studies from recently approved inhibitors

- Between 2018 and 2020, twenty novel small molecule kinase inhibitors have been approved by the U.S. Food & Drug Administration (FDA) for treatment of diverse cancer indications

- We studied:
  - Twenty newly approved inhibitors
  - Nineteen previously approved or clinical stage competitor drugs
  - Biochemical profiling on 255 wild-type and select mutant kinases (at Carna)
  - Cellular profiling on 134 cancer cell lines*

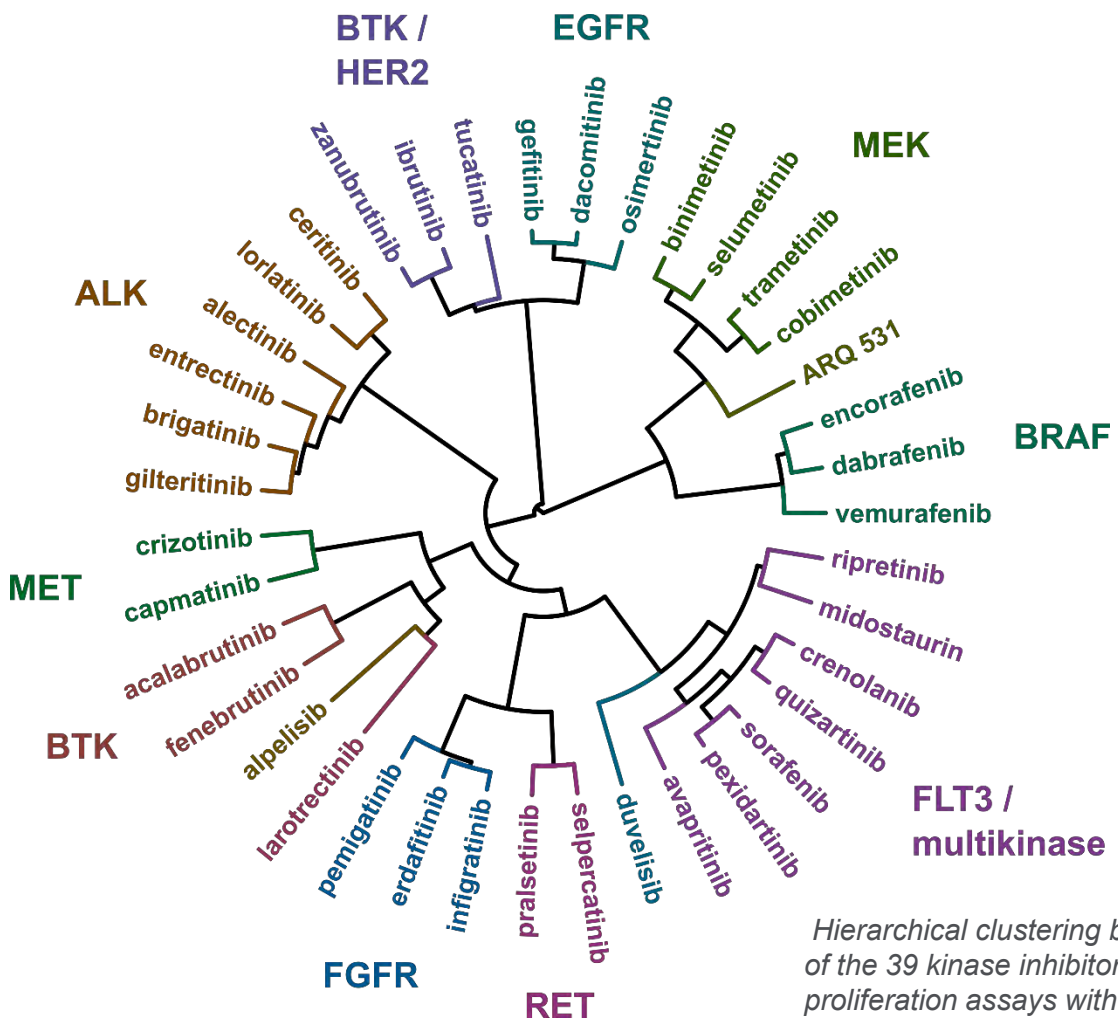
** 102 Oncolines cell line panel + 32 additional cell lines*

Overview of compounds profiled in the current study

Generic Name	Trade Name	Clinical Use	First approval
dacomitinib	Vizimpro	EGFR L858R or exon 19 mutant non-small cell lung cancer	September 2018
gefitinib	Iressa	EGFR L858R or exon 19 mutant non-small cell lung cancer	May 2003
osimertinib	Tagrisso	EGFR L858R, exon 19 or T790M mutant non-small cell lung cancer	November 2015
erdafitinib	Balversa	FGFR2 or FGFR3 altered urothelial carcinoma	April 2019
infigratinib	Truseltiq	FGFR2-positive cholangiocarcinoma	May 2021
pemigatinib	Pemazyre	FGFR2-positive cholangiocarcinoma	April 2020
entrectinib	Rozlytrek	NTRK-positive solid tumors and ROS1-positive NSCLC	August 2019
larotrectinib	Vitrakvi	NTRK-positive solid tumors	November 2018
alectinib	Alecensa	ALK-positive non-small cell lung cancer	December 2015
brigatinib	Alunbrig	ALK-positive non-small cell lung cancer	April 2017
ceritinib	Zykadia	ALK-positive non-small cell lung cancer	April 2014
crizotinib	Xalkori	ALK- or ROS1-positive non-small cell lung cancer or anaplastic large cell lymphoma	August 2011
lorlatinib	Lorbrena	ALK-positive non-small cell lung cancer	November 2018
ARQ 531			Phase 2
fenebrutinib			Phase 3 (non-oncology)
ibrutinib	Imbruvica	various hematological inidications	November 2013
zanubrutinib	Brukinsa	mantle cell lymphoma	November 2019
dabrafenib	Tafinlar	BRAF V600E or V600K mutant melanoma or non-small cell lung cancer	May 2013
encorafenib	Braftovi	BRAF V600E or V600K mutant melanoma or colorectal cancer	June 2018
vemurafenib	Zelboraf	BRAF V600E mutant melanoma	August 2011
midostaurin	Rydapt	FLT3 mutant acute myeloid leukemia	April 2017
gilteritinib	Xospata	FLT3 mutant acute myeloid leukemia	November 2018
quizartinib	Vanflyta	FLT3 mutant acute myeloid leukemia	June 2019 (Japan)
pexidartinib	Turalio	tenosynovial giant cell tumor	August 2019
tucatinib	Tukysa	HER2-positive breast cancer	April 2020
ripretinib	Qinlock	gastrointestinal stromal tumor	May 2020
binimetinib	Mektovi	BRAF V600E or V600K mutant melanoma	June 2018
cobimetinib	Cotellic	BRAF V600E or V600K mutant melanoma	November 2015
selumetinib	Koselugo	neurofibromatosis	April 2020
trametinib	Mekinist	BRAF V600E or V600K mutant melanoma or non-small cell lung cancer	May 2013
capmatinib	Tabrecta	MET mutant non-small cell lung cancer	May 2020
avapritinib	Ayvakit	PDGFRA mutant gastrointestinal stromal tumor	January 2020
pralsetinib	Gavreto	RET-positive non-small cell lung cancer or thyroid cancer	September 2020
selpercatinib	Retevmo	RET-positive non-small cell lung cancer or thyroid cancer	May 2020
alpelisib	Piqray	PIK3CA mutant, HR-positive, HER2-negative breast cancer	May 2019
duvelisib	Copiktra	various lymphoma indications	September 2018
sorafenib	Nexavar	hepatocellular cancer, renal cancer, or thyroid cancer	December 2005
ripretinib	Qinlock	gastrointestinal stromal tumor	May 2020
crenolanib			Phase 3

Hierarchical clustering of cell panel IC_{50} profiles

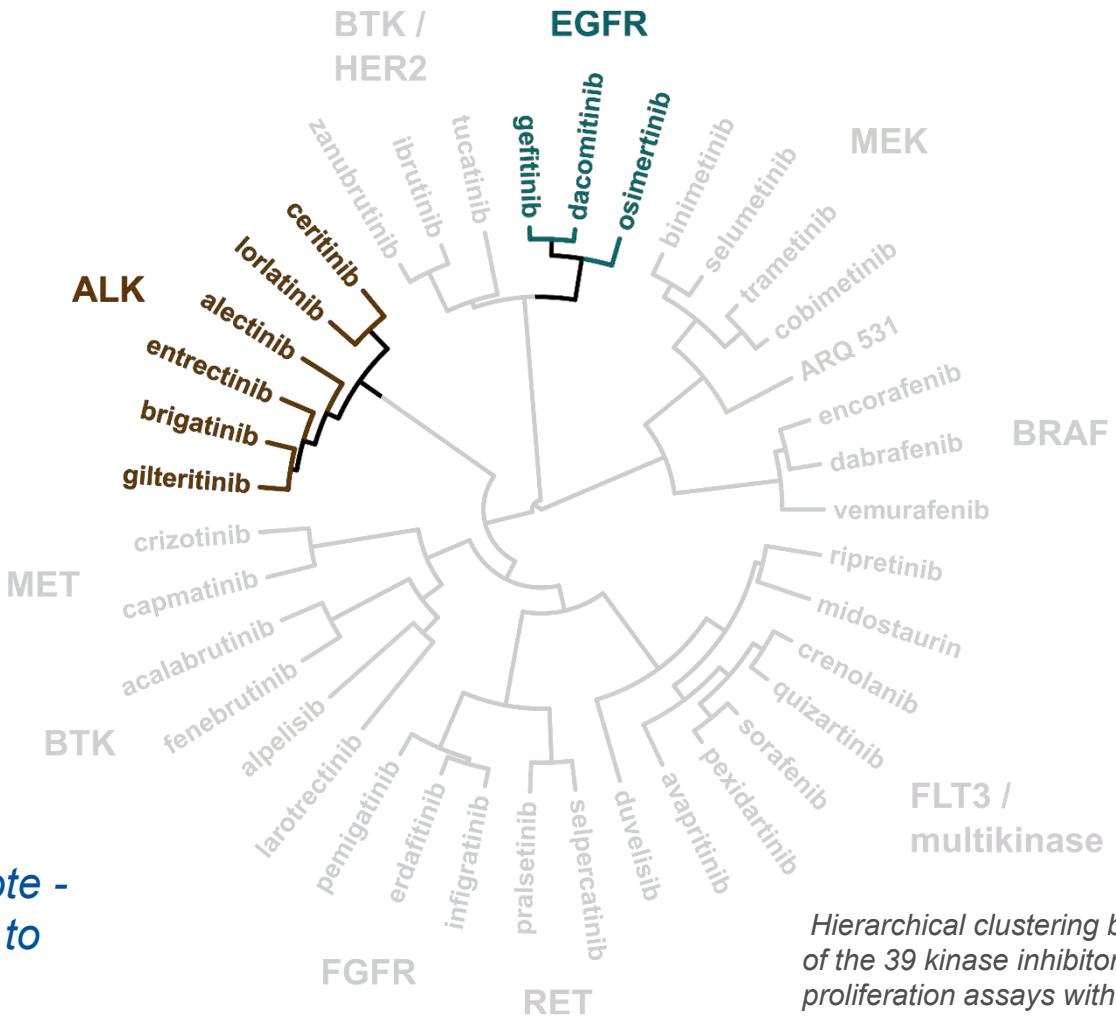
Distinct clusters are formed based on compound mechanism of action



Hierarchical clustering based on the IC_{50} fingerprints of the 39 kinase inhibitors, as determined in proliferation assays with 134 cancer cell lines

Hierarchical clustering of cell panel IC_{50} profiles

*Comparative analyses of EGFR and ALK inhibitor clusters overview**



Hierarchical clustering based on the IC_{50} fingerprints of the 39 kinase inhibitors, as determined in proliferation assays with 134 cancer cell lines

**Make a mental note - we will come back to this data later.*

Comparative analysis of 1st, 2nd, and 3rd generation EGFR inhibitors

To identify differences in targeting of specific EGFR mutations by various generations of EGFR inhibitors

Overview of FDA approved EGFR inhibitors

- Drug resistance frequently occurs after treatment with first- and second-generation EGFR inhibitors
  - Commonly via the T790M gatekeeper mutation
- Osimertinib is specifically designed to target the EGFR T790M mutant form

Generic Name	Trade Name	Generation	Clinical Use	First Approval
gefitinib	Iressa	First	EGFR L858R or exon 19 mutant non-small cell lung cancer	May 2003
erlotinib	Tarceva	First	non-small cell lung cancer or pancreatic cancer	November 2004
afatinib	Gilotrif	Second	non-resistant EGFR mutant non-small cell lung cancer	July 2013
dacomitinib	Vizimpro	Second	EGFR L858R or exon 19 mutant non-small cell lung cancer	September 2018
osimertinib	Tagrisso	Third	EGFR L858R, exon 19 or T790M mutant non-small cell lung cancer	November 2015

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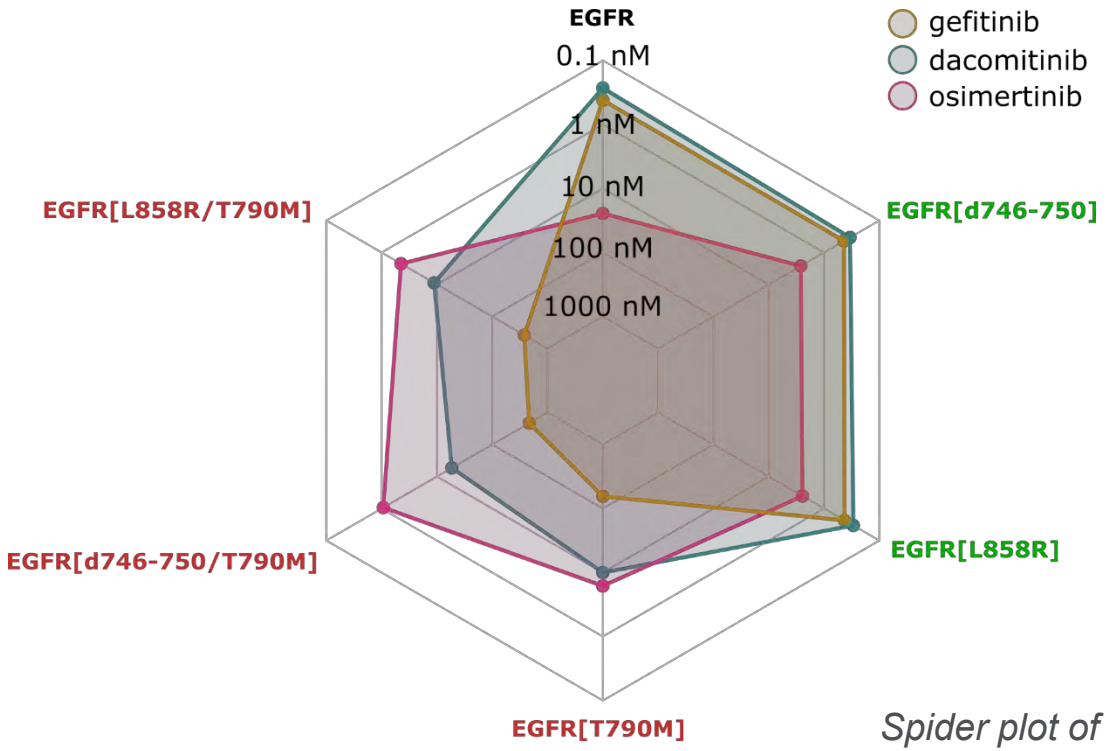
afatinib	Gilotrif	Second	non-resistant EGFR mutant non-small cell lung cancer	July 2013
dacomitinib	Vizimpro	Second	EGFR L858R or exon 19 mutant non-small cell lung cancer	September 2018
osimertinib	Tagrisso	Third	EGFR L858R, exon 19 or T790M mutant non-small cell lung cancer	November 2015

Biochemical potency of EGFR inhibitors

EGFR inhibitors show large differences in biochemical targeting of EGFR mutant forms

- Gefitinib potency is strongly reduced by the T790M resistance mutation
- Dacomitinib is most active on the sensitizing EGFR mutations
- Osimertinib spares wild-type EGFR and is most active on the T790M resistance mutation



Spider plot of IC_{50} values, as determined in biochemical assays

Overview of EGFR mutant cell lines

Cell lines of clinically relevant indications were included in the cell line panel

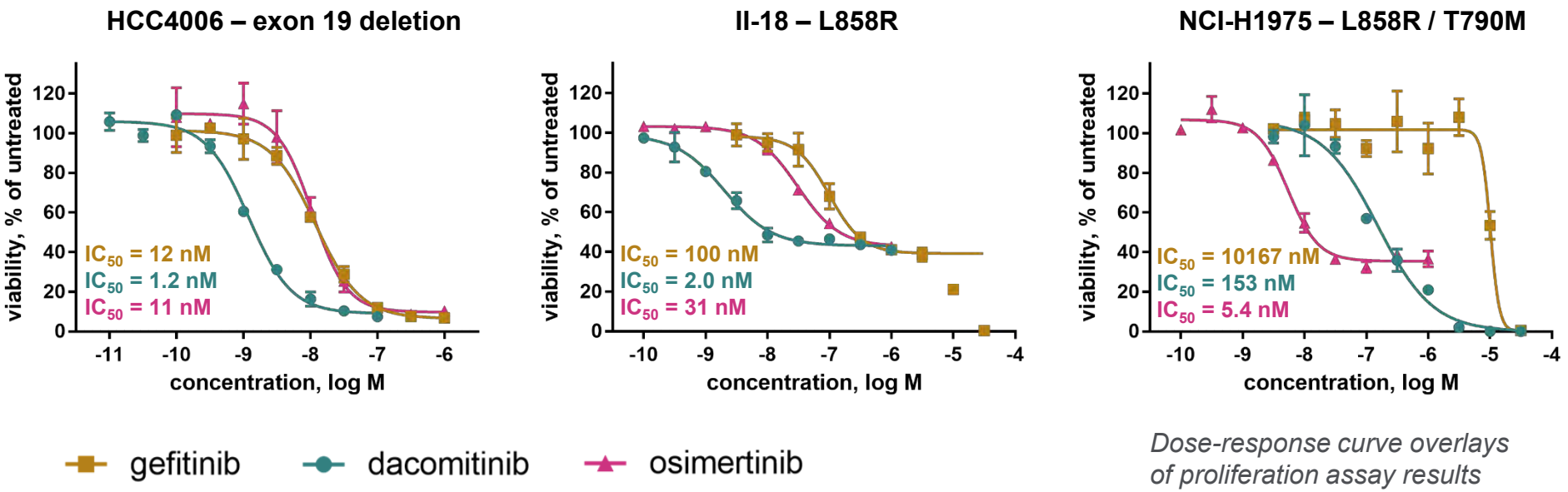
- The panel contained four cell lines that had sensitizing *EGFR* mutations which are included in the FDA labels of the three profiled inhibitors
- The T790M resistance mutation was present in one cell line
- A total of five cell lines had mutations other than those included in the FDA label

Cell line	Disease	EGFR mutation	FDA label
HCC4006	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
HCC827	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1650	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
II-18	Non-small cell lung cancer	L858R	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1975	Non-small cell lung cancer	L858R + T790M	osimertinib
SW48	Colon adenocarcinoma	G719S	afatinib (broadened)
HEC-6	Endometrial adenocarcinoma	A289V	none
RL95-2	Endometrial adenosquamous carcinoma	A289V	none
HEC-1-B	Endometrial adenocarcinoma	A864V	none
SNU-C2B	Colon adenocarcinoma	R165Q	none

Cellular potencies of EGFR inhibitors

The different biochemical potencies translate to cell lines

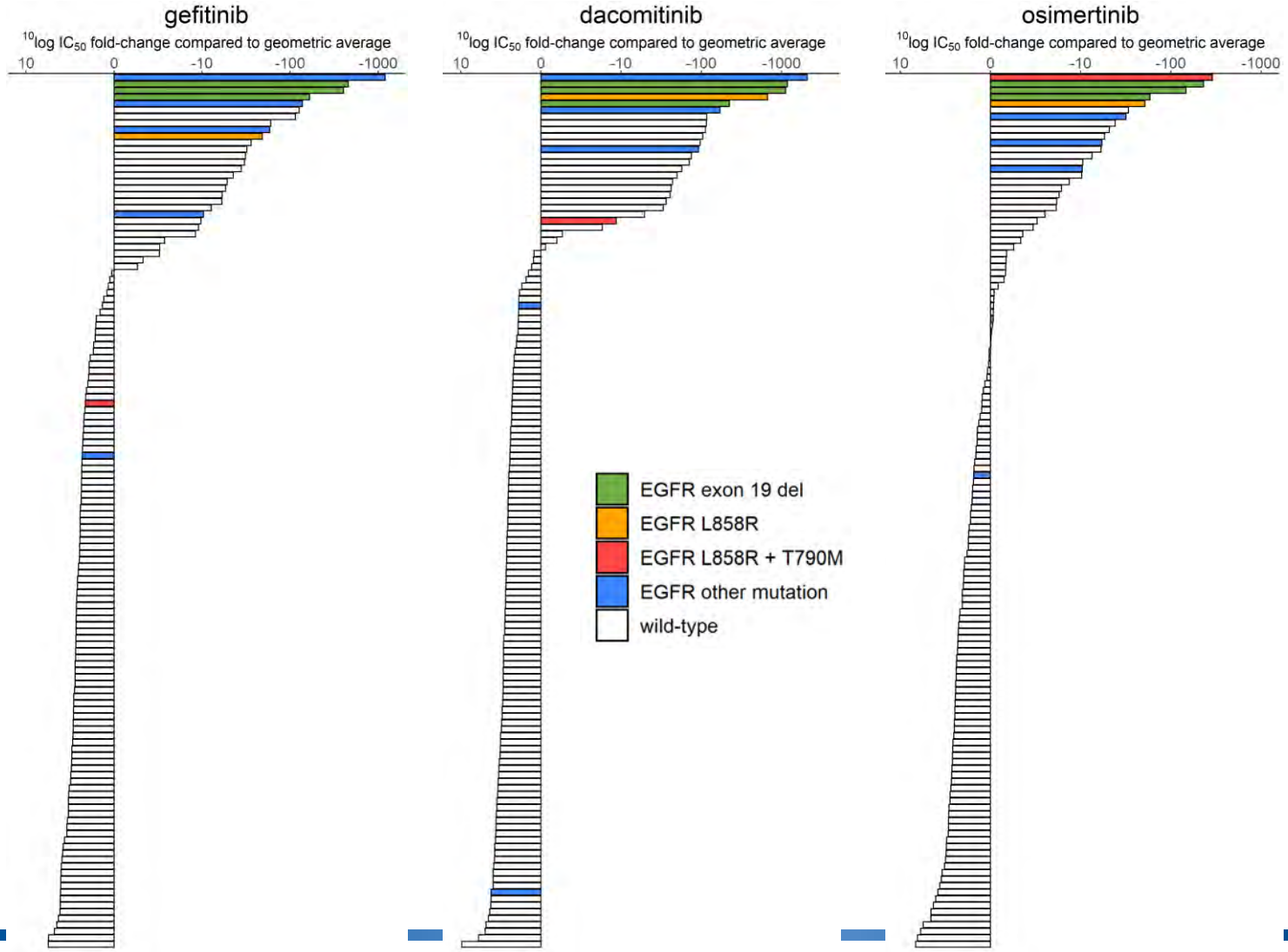
- Also in cell lines, dacomitinib is the most potent inhibitor in sensitizing mutants
- The double mutant cell line is most sensitive to osimertinib



Dose-response curve overlays of proliferation assay results

Cell panel targeting of EGFR inhibitors

EGFR mutant cell lines are among the most sensitive of the complete panel

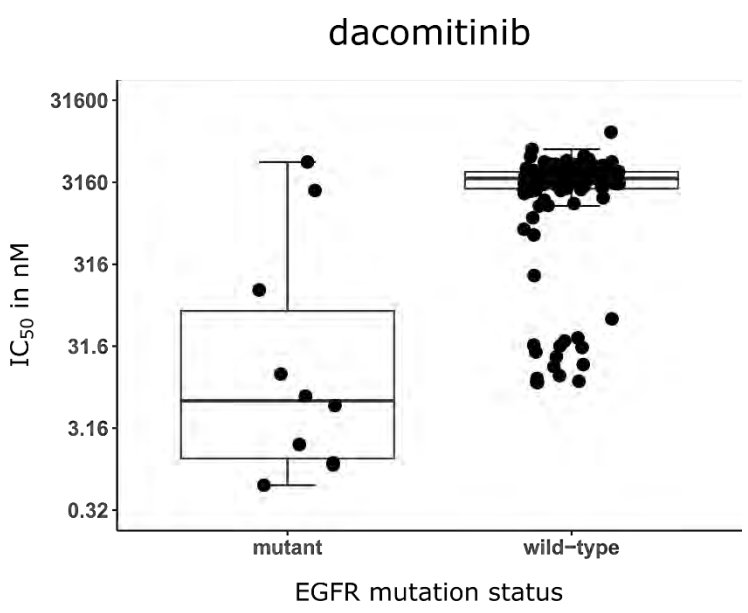


Waterfall plots relating IC$_{50}$s to the panel average. Cell lines harbouring relevant genomic alterations are highlighted

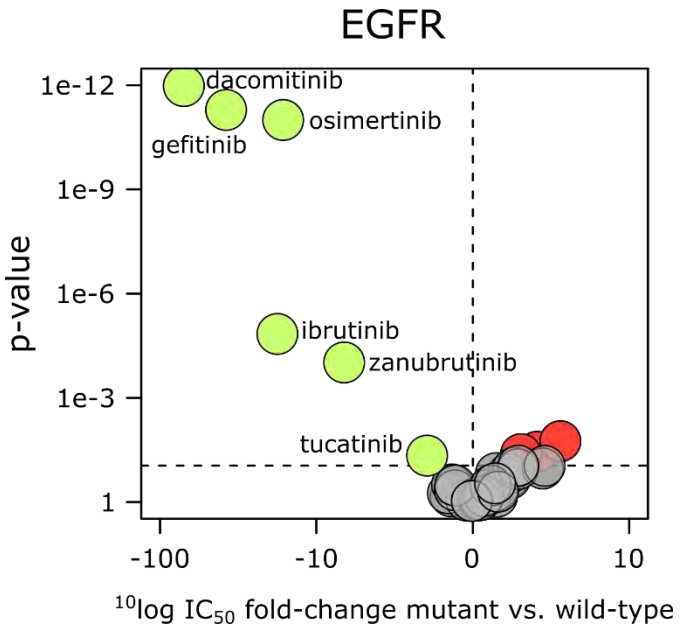
EGFR mutations as biomarker for kinase inhibitors

The three EGFR inhibitors significantly target EGFR mutant cell lines

- Dacomitinib shows the largest preference for EGFR mutant cell lines (70-fold), followed by gefitinib (38-fold) and osimertinib (16-fold)
- Several other kinase inhibitors show significant activity in EGFR mutant cell lines



Boxplot of the IC_{50} distribution across EGFR mutant- and wild-type groups



Volcano plot comparing IC_{50} fold-changes and biomarker significance for all 39 inhibitors

Overview of EGFR mutant cell lines

Non-FDA label EGFR mutations might induce drug sensitivity

- Exon 19 deletion, L858R, and T790M mutations are known to induce sensitivity for either of the inhibitors
- However, the significant associations also included other mutations

Cell line	Disease	EGFR mutation	FDA label
HCC4006	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
HCC827	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1650	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
II-18	Non-small cell lung cancer	L858R	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1975	Non-small cell lung cancer	L858R + T790M	osimertinib
SW48	Colon adenocarcinoma	G719S	afatinib (broadened)
HEC-6	Endometrial adenocarcinoma	A289V	none
RL95-2	Endometrial adenosquamous carcinoma	A289V	none
HEC-1-B	Endometrial adenocarcinoma	A864V	none
SNU-C2B	Colon adenocarcinoma	R165Q	none

Overview of EGFR mutant cell lines

Non-FDA label EGFR mutations might induce drug sensitivity

- Exon 19 deletion, L858R, and T790M mutations are known to induce sensitivity for either of the inhibitors

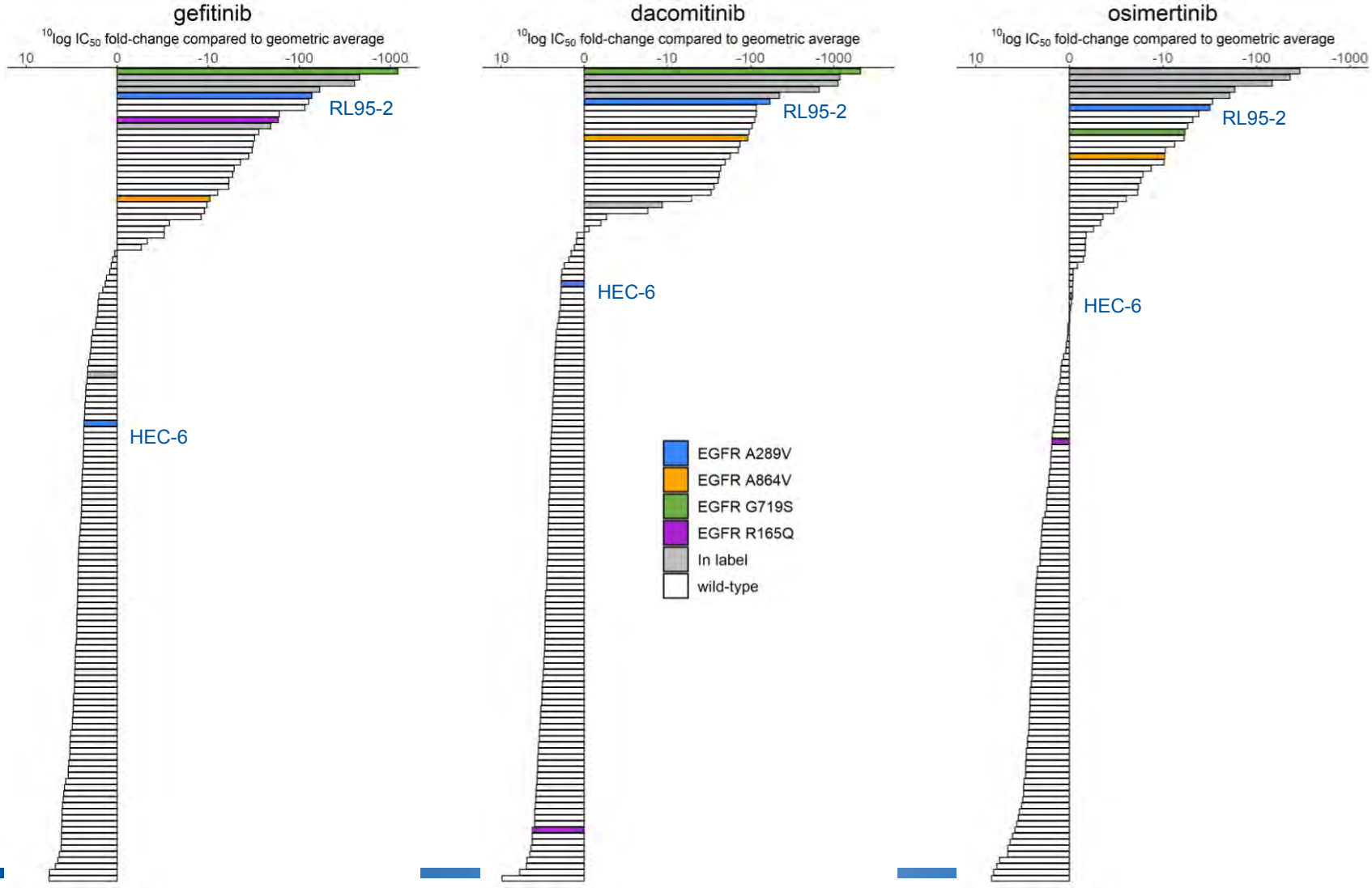
- However, the significant associations also included other mutations
  - G719S → kinase domain
  - A864V → kinase domain
  - A289V → extracellular domain, frequently observed in glioblastoma[1]
  - R165Q → extracellular domain

Cell line	Disease	EGFR mutation	FDA label
HCC4006	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
HCC827	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1650	Non-small cell lung cancer	Exon 19 deletion	gefitinib, afatinib, dacomitinib, osimertinib
II-18	Non-small cell lung cancer	L858R	gefitinib, afatinib, dacomitinib, osimertinib
NCI-H1975	Non-small cell lung cancer	L858R + T790M	osimertinib
SW48	Colon adenocarcinoma	G719S	afatinib (broadened)
HEC-6	Endometrial adenocarcinoma	A289V	none
RL95-2	Endometrial adenosquamous carcinoma	A289V	none
HEC-1-B	Endometrial adenocarcinoma	A864V	none
SNU-C2B	Colon adenocarcinoma	R165Q	none

[1]Binder et al. 2018. Cancer Cell. 34:163-177

Cell panel targeting of EGFR inhibitors

Other EGFR mutations have variable predictive power of EGFR inhibitor sensitivity



Waterfall plots relating IC_{50}s to the panel average. Cell lines harbouring relevant genomic alterations are highlighted

Conclusions EGFR inhibitor comparison

- The differences in biochemical activity between various generations of EGFR inhibitors translate well to cellular models

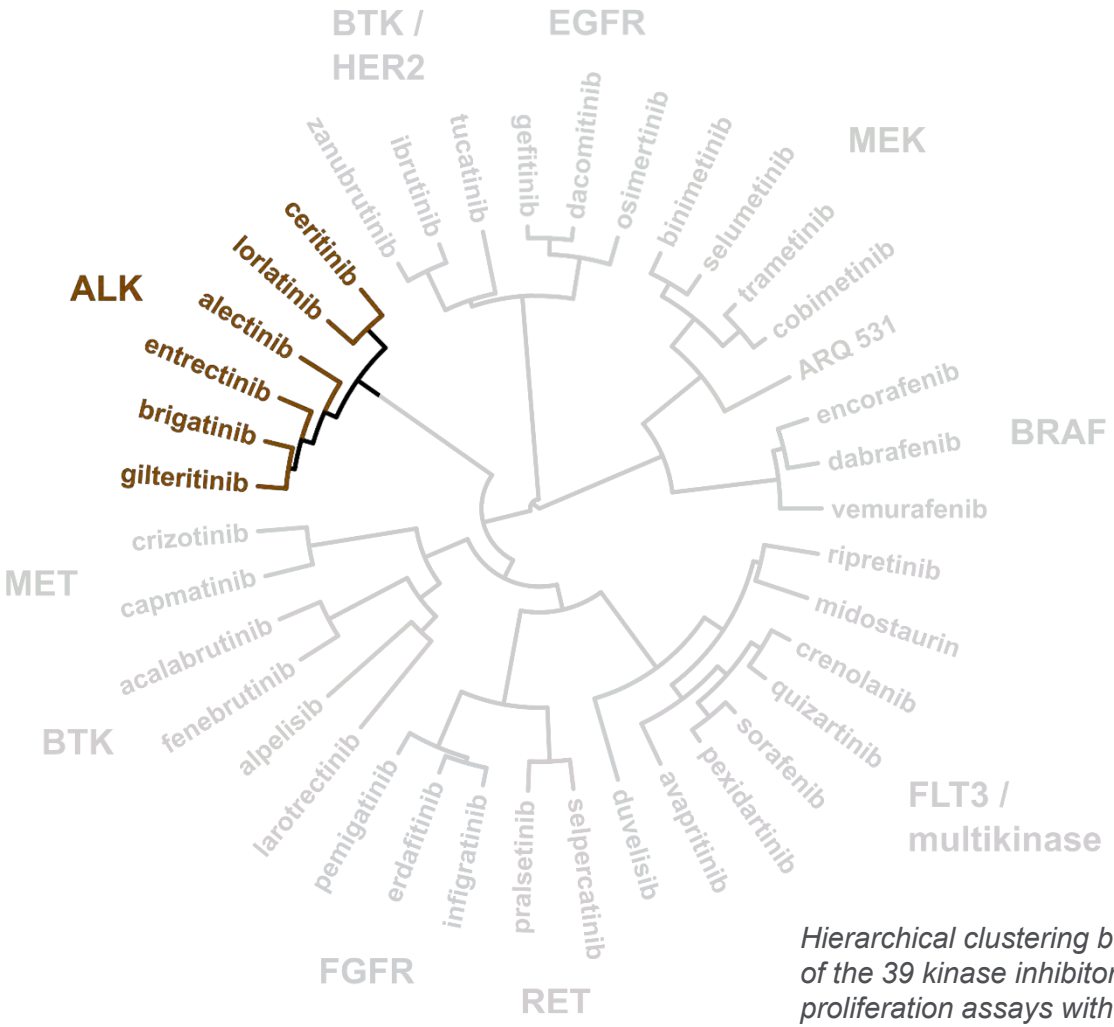
- The targeting of ‘uncommon’ EGFR mutations suggests relevance of indication broadening
  - *A phase 2 study is initiated for osimertinib in NSCLC with uncommon EGFR mutations, including G719X (NCT03434418)*

ALK inhibitor comparison

To determine differences in potency and selectivity between ALK targeting inhibitors

Hierarchical clustering of cell panel IC_{50} profiles

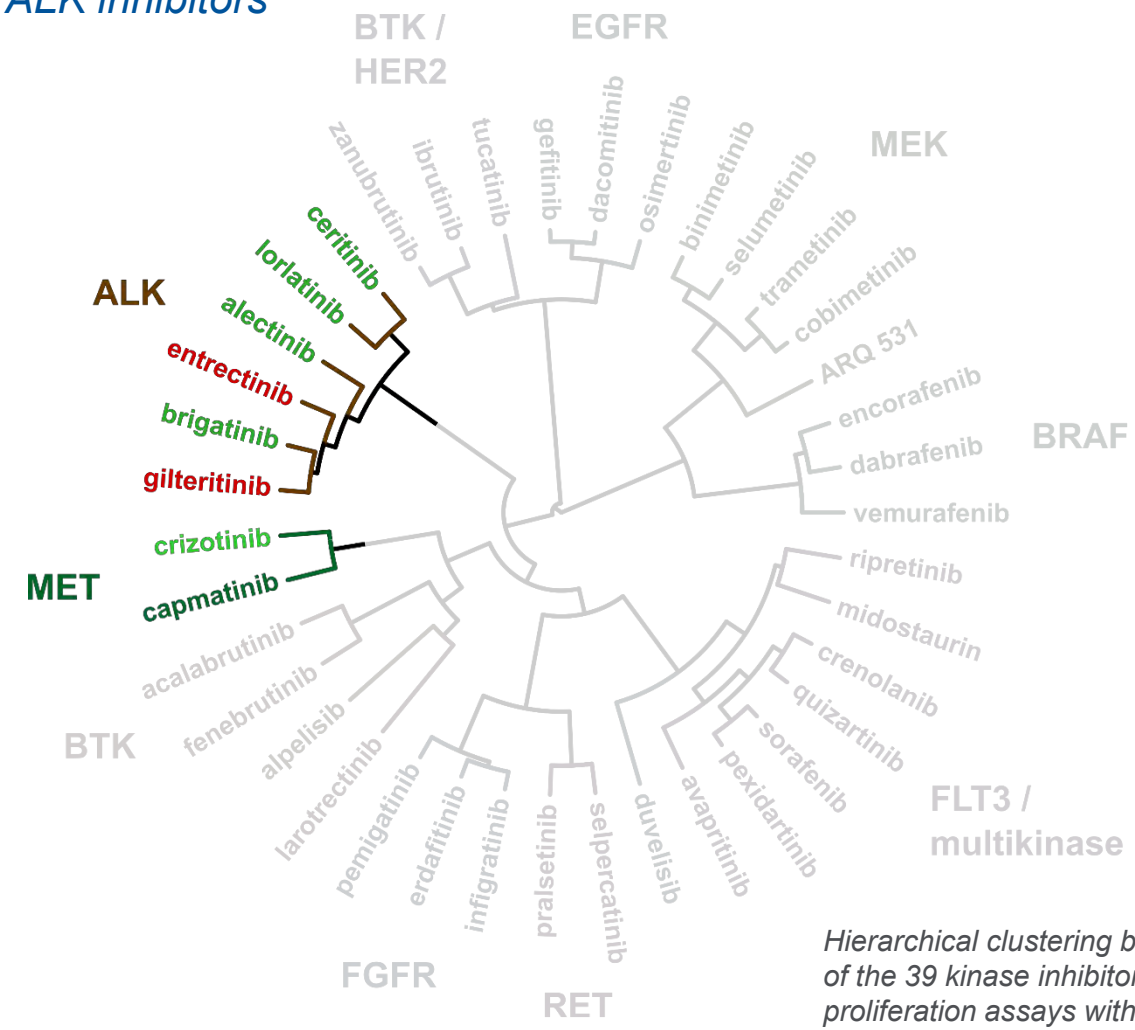
A distinct cluster is formed of ALK-targeted inhibitors



Hierarchical clustering based on the IC_{50} fingerprints of the 39 kinase inhibitors, as determined in proliferation assays with 134 cancer cell lines

Hierarchical clustering of cell panel IC_{50} profiles

Crizotinib clusters with a MET inhibitor. Entrectinib (NTRK) and gilteritinib (FLT3) cluster with approved ALK inhibitors



Hierarchical clustering based on the IC_{50} fingerprints of the 39 kinase inhibitors, as determined in proliferation assays with 134 cancer cell lines

ALK and co-clustered inhibitor comparison

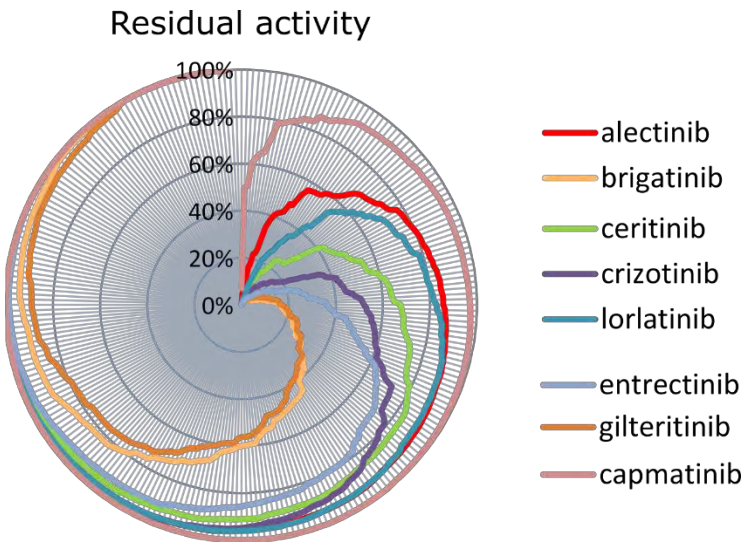
- All five ALK inhibitors are approved for ALK-positive non-small cell lung cancer
- Crizotinib was recently approved for treatment of ALK-positive anaplastic large cell lymphoma
- The co-clustered compounds entrectinib, gilteritinib, and capmatinib are not approved for ALK-related indications

Generic Name	Trade Name	Clinical Use	First Approval
alectinib	Alecensa	ALK-positive non-small cell lung cancer	December 2015
brigatinib	Alunbrig	ALK-positive non-small cell lung cancer	April 2017
ceritinib	Zykadia	ALK-positive non-small cell lung cancer	April 2014
crizotinib	Xalkori	ALK- or ROS1-positive non-small cell lung cancer or anaplastic large cell lymphoma	August 2011
lorlatinib	Lorbrena	ALK-positive non-small cell lung cancer	November 2018
entrectinib	Rozlytrek	NTRK-positive solid tumors and ROS1-positive NSCLC	August 2019
gilteritinib	Xospata	FLT3 mutant acute myeloid leukemia	November 2018
capmatinib	Tabrecta	MET mutant non-small cell lung cancer	May 2020

Biochemical selectivity of ALK- and co-clustered inhibitors

ALK inhibitors' exhibit large differences in selectivity

- Brigatinib is the least selective of the five inhibitors approved for ALK indications
- Crizotinib also inhibits MET, which might explain the clustering with the MET inhibitor capmatinib
- Entrectinib (NTRK) and gilteritinib (FLT3) inhibit ALK, besides their FDA approved target



Radar chart of the percentage residual activity of 255 wild-type kinases with 1 μM compound

Compound	Kinases >90% inhibited	Major targets >90% inhibited
alectinib	7	**ALK**, RET
brigatinib	57	**ALK**, EGFR, FGFR1/2/3, **FLT3**, FMS, PDGFRα/β, RET, **ROS**
ceritinib	19	**ALK**, **ROS**
crizotinib	28	**ALK**, FMS, **MET**, **ROS**, **TRKA/B/C**
lorlatinib	15	**ALK**, **ROS**, **TRKA/B/C**
entrectinib	51	**ALK**, FGFR1/2/3, **FLT3**, RET, **ROS**, **TRKA/B/C**
gilteritinib	40	**ALK**, **FLT3**, FMS, PDGFRα/β, RET, **ROS**, **TRKA/B/C**
capmatinib	1	**MET**

Clinically approved targets inhibited by >90% at a compound concentration of 1 μM. Targets present in the label of one of the eight inhibitors are indicated in bold.

Overview of ALK-driven cell lines

Cell lines of clinically relevant indications were included in the cell line panel

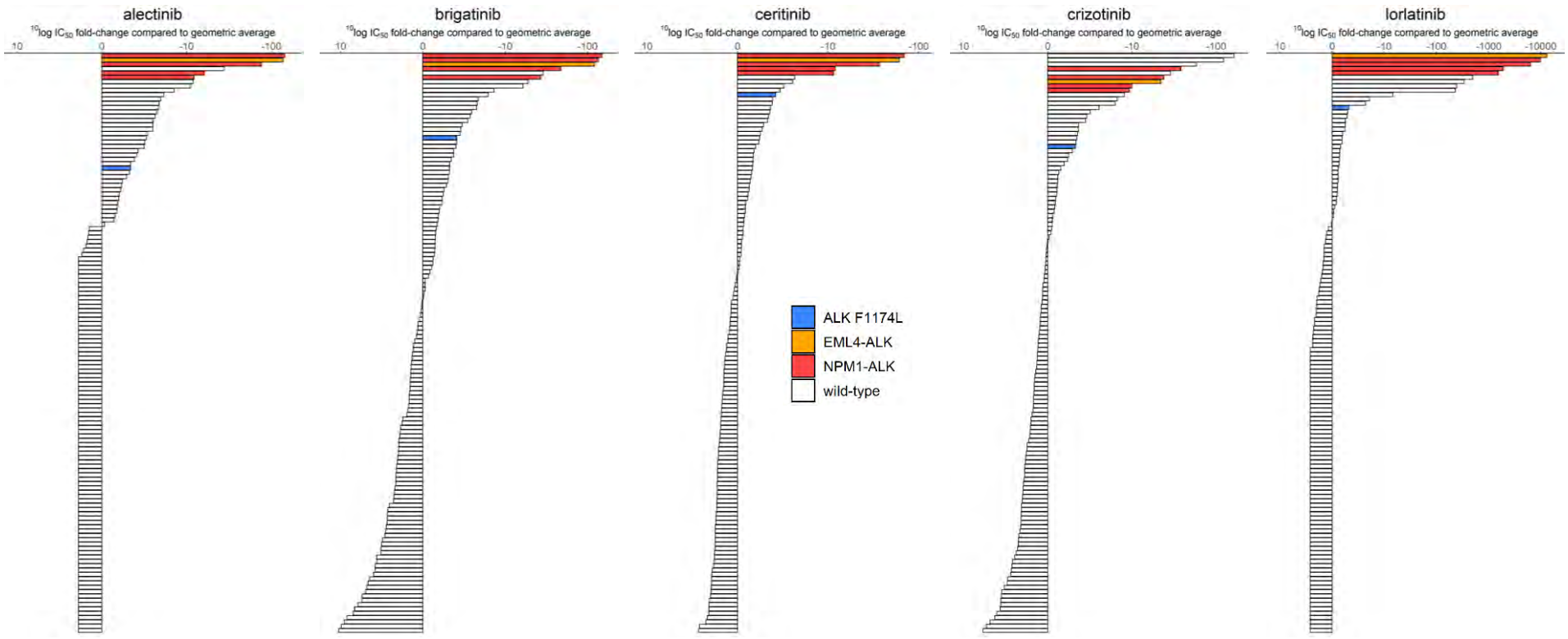
- The panel contained one ALK+ NSCLC cell line, which is an indication for all five ALK inhibitors
- Four ALK+ ALCL cell lines were included, which is an indication for crizotinib
- One cell line was of neuroblastoma origin and contained a F1174L mutation
  - *This mutation is frequently observed in ALK-mutated neuroblastoma*[1]

Cell line	Disease	ALK alteration	FDA label
NCI-H2228	Non-small cell lung cancer	EML4-ALK	alectinib, brigatinib, ceritinib, crizotinib, lorlatinib
DEL	Anaplastic large cell lymphoma	NPM1-ALK	crizotinib
L-82	Anaplastic large cell lymphoma	NPM1-ALK	crizotinib
SR	Anaplastic large cell lymphoma	NPM1-ALK	crizotinib
SU-DHL-1	Anaplastic large cell lymphoma	NPM1-ALK	crizotinib
SK-N-SH	Neuroblastoma	F1174L	none

[1]Chen *et al.*, (2008) Nature, 455: 971-974

Cell panel targeting of ALK inhibitors

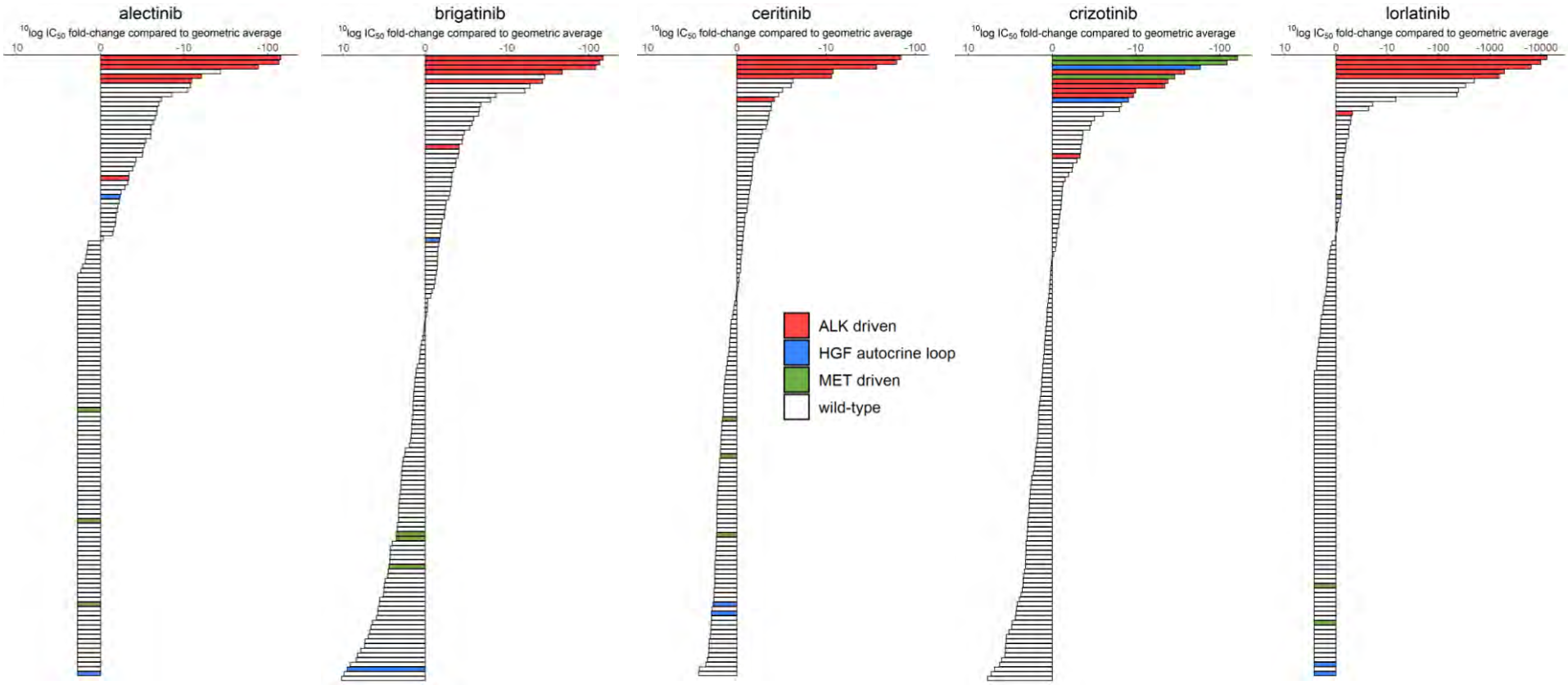
ALK inhibitors show different levels of selectivity in the cell line panel



Waterfall plots relating IC_{50}s to the panel average. Cell lines harbouring relevant genomic alterations are highlighted

Cell panel targeting of ALK inhibitors

Crizotinib also inhibits cell lines driven by MET and its ligand HGF

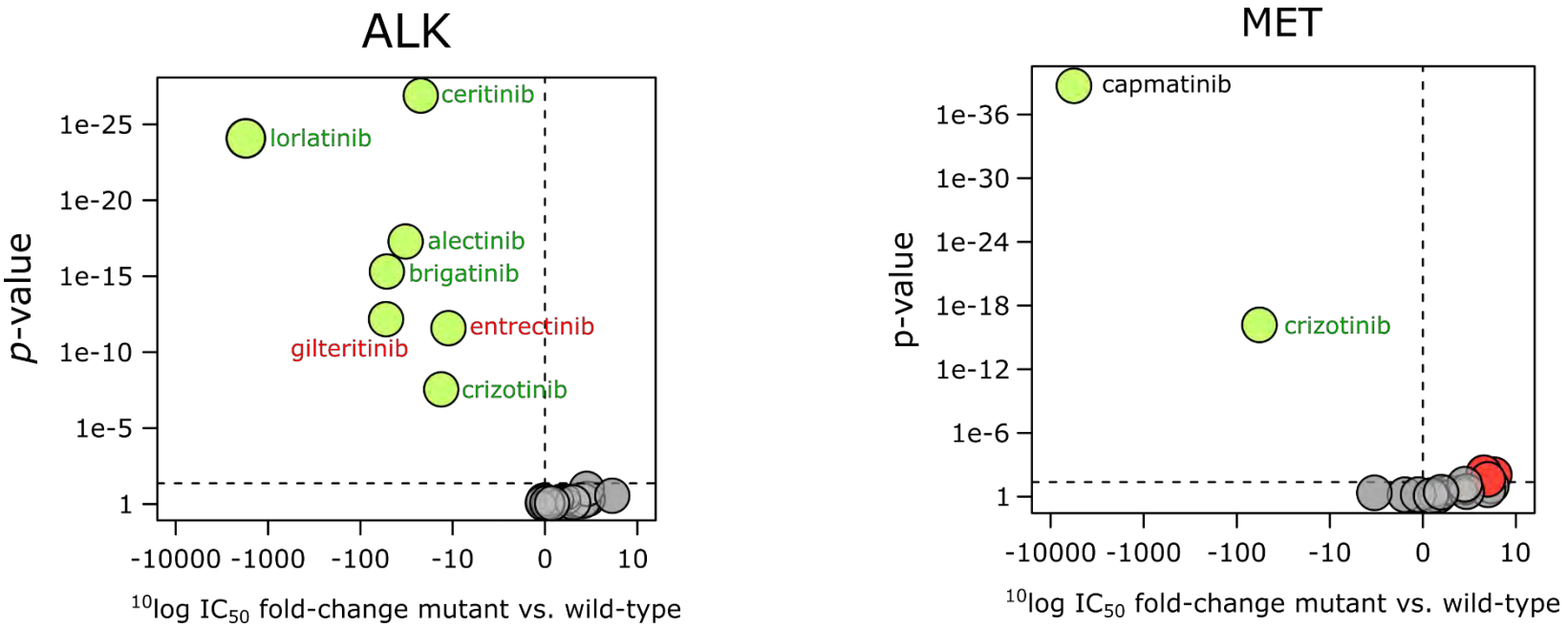


Waterfall plots relating IC_{50}s to the panel average. Cell lines harbouring relevant alterations are highlighted

ALK and MET as biomarkers for kinase inhibitors

The inhibitors have large differences in their preferential targeting of ALK and MET

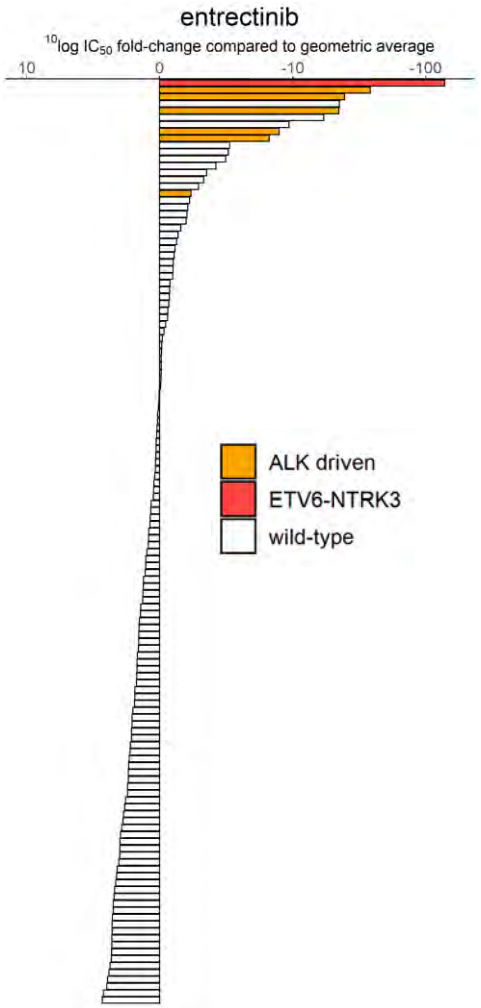
- Lorlatinib shows the strongest preference for ALK-driven cell lines (> 1000-fold)
- Gilteritinib and entrectinib show significant preference for ALK-driven cell lines
- Crizotinib significantly targets both ALK and MET-driven cell lines

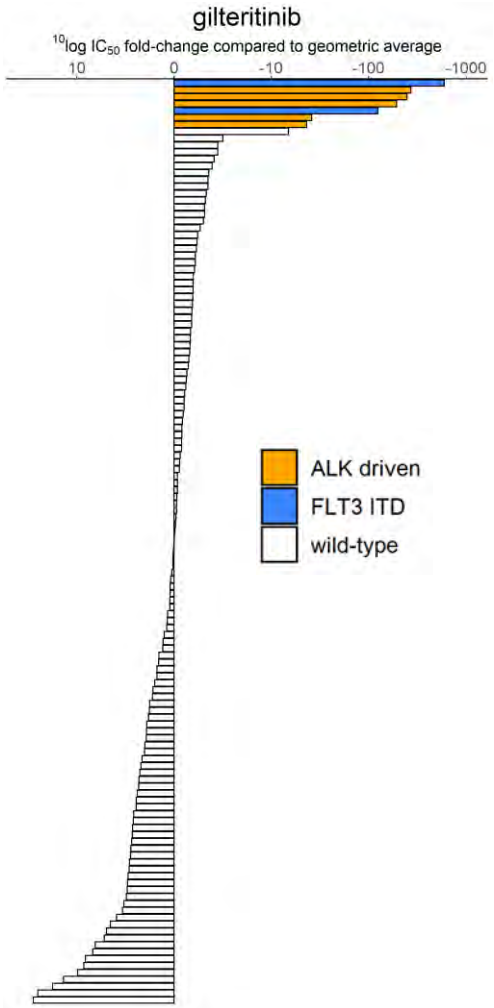


Volcano plots comparing IC_{50} fold-changes and biomarker significance for all 39 inhibitors. Inhibitors approved for ALK-related indications are highlighted in green

Cell panel targeting of co-clustered compounds

Besides their approved target, entrectinib (NTRK) and gilteritinib (FLT3) preferentially target ALK-driven cell lines





Waterfall plots relating average IC$_{50}$s to the panel average. Cell lines harbouring relevant genomic alterations are highlighted

Conclusions comparative analyses of ALK inhibitors

- ALK inhibitors show large differences in biochemical and cellular selectivity

- Besides ALK, crizotinib significantly targets MET-driven cell lines, suggesting repurposing of crizotinib for MET-driven cancer
  - Crizotinib was tested in a clinical trial for MET-driven NSCLC[1]

- The co-clustered inhibitors entrectinib (NTRK) and gilteritinib (FLT3) significantly targeted ALK-driven cell lines
  - Entrectinib was evaluated in trials for ALK-related indications, including neuroblastoma[2]
  - Gilteritinib was preclinically evaluated in NPM1-ALK ALCL[3]

[1]Drilon *et al.* (2020) Nat Med. 26: 47-51
[2]Pacenta *et al.* (2018) Drug Des Devel Ther. 12: 3549-3561
[3]Kuravi *et al.* (2021) Mol Cancer Res. 19: 913-920

Summary

- Recently approved kinase inhibitors and competitors
  - Compared selectivity and potency by biochemical and cellular profiling
- Comparative analyses of
  - EGFR inhibitors
  - ALK inhibitors
- Biochemical profiling and Oncolines™ Profiling of kinase inhibitors can aid in biomarker identification, development of next-generation inhibitors, and drug repurposing

Comparative cancer cell panel profiling of kinase inhibitors

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