CHI-MED

HUTCHISON CHINA MEDITECH

(AIM/Nasdaq: HCM)

R&D Briefing

London, UK & New York, NY

March 29 & 30, 2017

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All references to "Chi-Med" as used throughout this presentation refer to Hutchison China MediTech Limited and its subsidiaries. This presentation should be read in conjunction with Chi-Med's final results for the year ended December 31, 2016, copies of which are available on Chi-Med's website (www.chi-med.com).

Agenda

09:30	INTRODUCTION: Mr Christian Hogg, Chief Executive Officer
09:40	THE FUTURE OF TARGETED CANCER THERAPY IN LUNG CANCER: Susan Galbraith, Senior Vice President and Head of Oncology Innovative Medicines & Early Development, AstraZeneca
10:10	1ST WAVE – POST-POC PORTFOLIO, PART 1: Fruquintinib, Sulfatinib
10:45	*Coffee Break*
10:55	1ST WAVE – POST-POC PORTFOLIO, PART 2: Savolitinib, Epitinib
11:20	2ND WAVE – PRE-POC PORTFOLIO: Theliatinib, HMPL-523, HMPL-689, HMPL-453
11:50	RESEARCH STRATEGY: The 3rd Wave
12:10	TRANSFORMING INTO A FULLY INTEGRATED GLOBAL BIOPHARMA: Manufacturing & Commercialization
12:25	Wrap-Up / Q&A
12:30	*Buffet Lunch*

Introduction

Christian Hogg, Chief Executive Officer

A risk-balanced global-focused BioPharma

Innovation Platform

Broad late-stage pipeline

- ✓ 8 oncology drug candidates in 30 studies worldwide.
- ✓ 1st positive Ph.III result - fruquintinib - Launch 2018.
- ✓ 7 further Phase III trials; 3 underway & 4 in-planning.
- ✓ ~330-person Scientific Team.

Commercial Platform

Solid cash flow from operations

- ✓ >3,300-person China Sales Team (~2,200 med. reps).
- ✓ To commercialise Innovation Platform drugs in China.
- ✓ 2016 sales[1] up 21% to $627.4 million.
- ✓ 2016 net income[2] up 180% to $70.3 million.[3]

[1] Aggregate sales of consolidated subsidiaries ($180.9 million) and non-consolidated joint ventures ($446.5 million); [2] Net income attributable to Chi-Med;
[3] Includes the share of gain from land compensation of Shanghai Hutchison Pharmaceuticals Limited in Prescription Drugs Business ($40.4 million).

Exceptional scale for pre-approval biotech

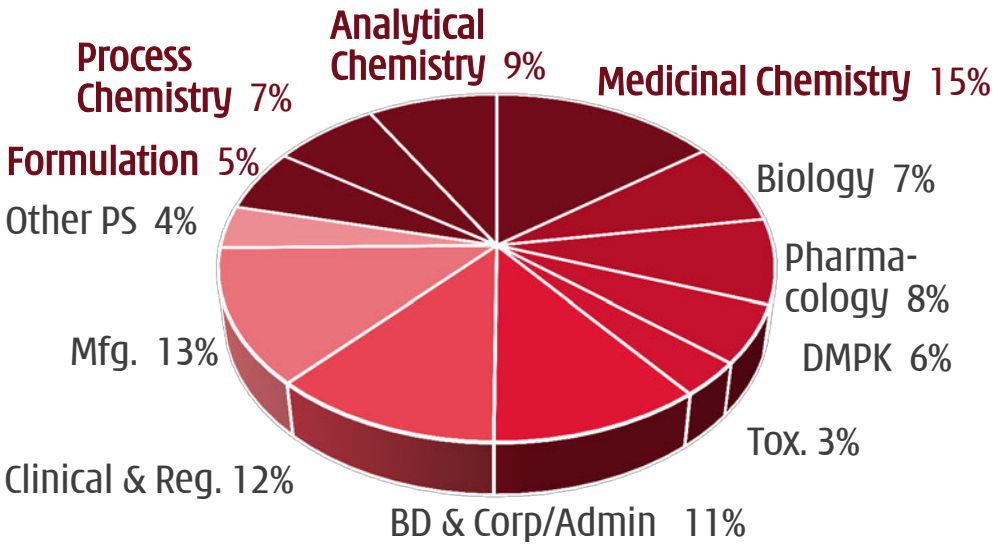
>15 years. Well over $400 million invested to date

CHI-MED

One of the leading China-based innovators in oncology & immunology

~330 SCIENTISTS & STAFF[1]

- ✓ 208 with advanced technical degrees
- ✓ 26 M.D.s
- ✓ 54 doctorate degrees



OUR ADVANTAGES

- ✓ **Fully integrated in-house platform**
  chem, biol, pharmacol, DMPK, tox, CMC, clin & reg, and translational orgs working together seamlessly
- ✓ **China clinical speed**
  major unmet medical needs (3.4m new cancer pts/yr[2]), rapid dev & reg support. Can study multiple indications and POC in China
- ✓ **Competitive costs**
  Clinical costs, esp. pre-PoC, fraction of US/Europe
- ✓ **Constancy of purpose**
  15+ years with continuous financial support

[1] Headcount as of December 31, 2016; Chem. = Chemistry; DMPK = Drug, Metabolism, & Pharmacokinetics; Tox. = Drug Safety Evaluation; PS = Pharmaceutical Science (CMC); Mfg = Manufacturing; Reg. = Regulatory; C&R = Clinical & Regulatory; BD = Business Development; [2] Frost & Sullivan.

Chemistry is our edge

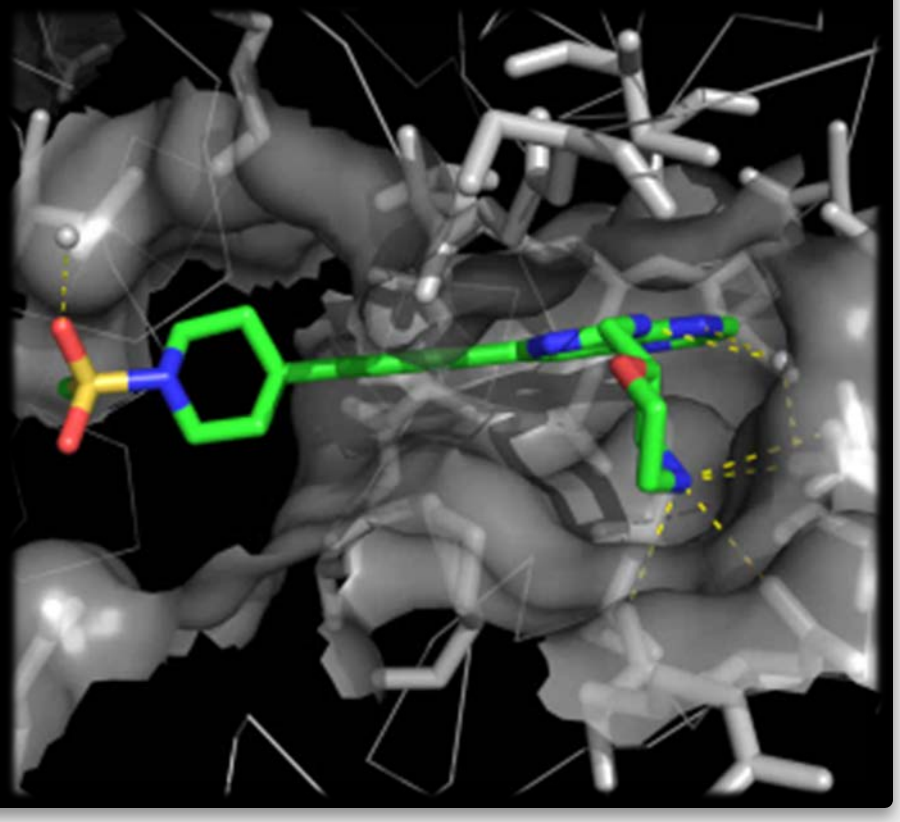
Targeted, selective small molecules

Fragment-based design of NCEs.

- **Designed all 8 clinical drug candidates in-house.**
- Use of co-crystal structures.
- Focus on small molecule interactions with tyrosine kinases (Proteins/enzymes involved in cell signaling).

Use of co-crystal structures.

- Focus on small molecule interactions with kinases.
- ✓ Optimize binding to on-target protein, for potency.
- ✓ Minimize binding to off-target proteins for selectivity.



Superior selectivity = Better tolerability

More use = prolonged target coverage = better efficacy

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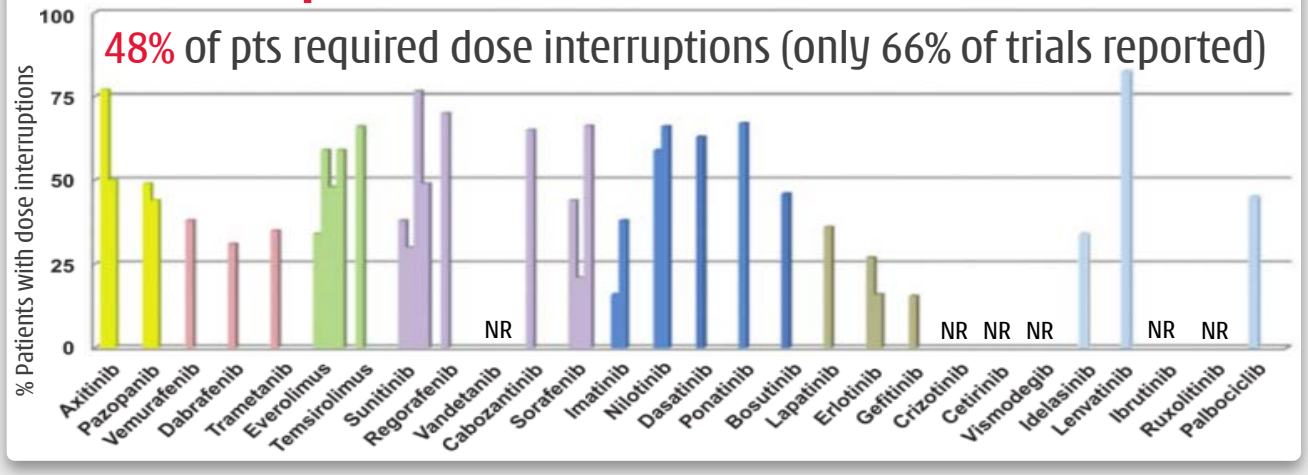
Better tolerability for sustained usage

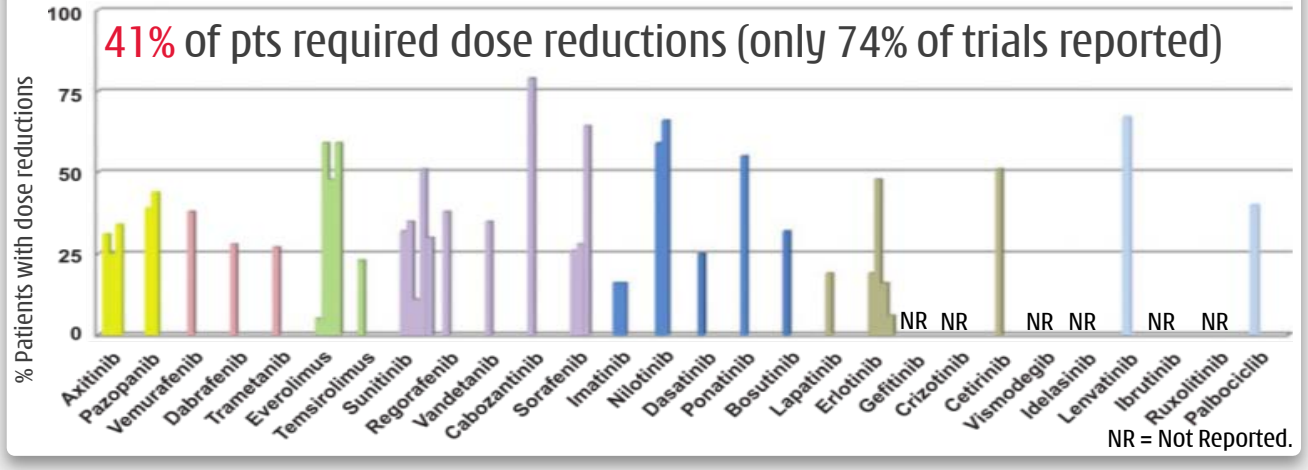
Review of 28 FDA approved small molecule oncology targeted therapies revealed high incidence of toxicity[1]

- Pronounced in drugs with narrow therapeutic index (i.e. efficacious dose at or near MTD)
- Combination trials even harder - 64% with grade 3-4 toxicities vs. 37% in monotherapy trials

Dose interruptions in Phase III studies



Dose reductions in Phase III studies



[1] FDA approved btw Jan '02 to Feb '15. Roda D et al. "*Are Doses and Schedules of Small-Molecule Targeted Anticancer Drugs Recommended by Phase I Studies Realistic?*" Clinical Cancer Research 2016 May 1;22(9):2127-32.

30 active clinical trials on 8 drug candidates

1st positive pivotal readout – 4 lead candidates all in pivotal Ph.III in 2017

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Program	Target	Partner	Study number/Indication	Latest Status	Line	Target patient	Combo therapy	Site	Preclin.	Ph.I	Proof-of-concept	Pivotal/Ph.III
Savolitinib (AZD6094)	c-MET	AstraZeneca	1. Papillary renal cell carcinoma	Report Ph.II Feb. 2017; **Ph.III start H12017**	1st	c-MET-driven		Global				*
			2. Papillary renal cell carcinoma	NCI Ph.II – savo vs. sunitinib vs. cabozan. vs. crizot.	All	c-MET-driven		US				
			3. Papillary renal cell carcinoma	Ph.Ib enrolling (dose finding)	-	All	**durvalumab** (PD-L1)	UK				*
			4. Clear cell renal cell carcinoma	Start when Study 2/4 begin Ph.Ib expansion stage	2nd	VEGF TKI refractory		UK				*
			5. Clear cell renal cell carcinoma	Ph.Ib enrolling (dose finding)	2nd	VEGF TKI refractory	**durvalumab** (PD-L1)	UK				*
			6. Non-small cell lung cancer	Ph.IIb expans'n enrolling; **Pivotal decision 2017**	2nd	EGFR TKI refractory	**Tagrisso®** (T790M)	Global				*
			7. Non-small cell lung cancer	Ph.II enrolling	3rd	EGFR/T790M TKI	**Tagrisso®** (T790M)	Global				*
			8. Non-small cell lung cancer	Ph.II enrolling	2nd	EGFR TKI refractory	**Iressa®** (EGFR)	China				*
			9. Non-small cell lung cancer	Ph.II enrolling	1st	c-MET+/Ex.14skip		China				*
			10. Pulmonary sarcomatoid ca.	Ph.II enrolling	1st	c-MET+/Ex.14skip		China				*
			11. Gastric cancer	Ph.Ib enrolling	3rd/All	c-MET+		SK/PRC				*
			12. Gastric cancer	Ph.Ib enrolling	2nd	c-MET+	**docetaxel** (chemo)	SK				*
			13. Gastric cancer	Ph.Ib enrolling	2nd	c-MET O/E	**docetaxel** (chemo)	SK				*
Fruquintinib	VEGFR 1/2/3	Lilly (in China only)	14. Colorectal cancer	**Ph.III met all endpoints; NDA mid 2017** ✓	3rd	All		China				
			15. Non-small cell lung cancer	**Ph.III enrolling**	3rd	All		China			n/a	*
			16. Non-small cell lung cancer	Ph.Ib enrolling (dose finding)	1st	All	**Iressa®** (EGFR)	China				*
			17. Caucasian bridging	Ph.I dose escalation start 2017	-	All comers		US				
			18. Gastric cancer	**Ph.III (w/ interim analysis) start 2017**	2nd	All	**paclitaxel** (chemo)	China				*
Sulfatinib	VEGFR/ CSF-1R/ FGFR1		19. Pancreatic NET	**Ph.III enrolling**	1st	All		China				*
			20. Non-pancreatic NET	**Ph.III enrolling**	1st	All		China				*
			21. Caucasian bridging	Ph.I dose escalation enrolling	-	All comers		US				
			22. Medullary thyroid ca.	Ph.II enrolling	2nd	Radiotherapy ref.		China				*
			23. Differentiated thyroid ca.	Ph.II enrolling	2nd	Radiotherapy ref.		China				*
			24. Biliary tract cancer	Ph.II enrolling	2nd	Gemcitabine ref.		China				*
Epitinib	EGFRm+		25. Non-small cell lung cancer	**Ph.III start 2017**	1st	EGFRm+ brain mets		China				*
			26. Glioblastoma	Ph.II start 2017	-			China				*

4 pivotal Phase III studies active & 4 more to start in 2017

Oncology | Immunology

Notes: * = when an NDA submission is possible based on the receipt of favorable clinical data; Proof-of-concept = Phase Ib/II study (the dashed lines delineate the start and end of Phase Ib); combo = in combination with; brain mets = brain metastasis; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; EGFR = epidermal growth factor receptor; NET = neuroendocrine tumors; ref = refractory, which means resistant to prior treatment; T790M= EGFR resistance mutation; EGFRm+ = epidermal growth factor receptor activating mutations; EGFR wild-type = epidermal growth factor receptor wild-type; 5ASA = 5-aminosalicyclic acids; chemo = chemotherapy; c-MET+ = c-MET gene amplification; c-MET O/E = c-MET over-expression; MS = Multiple Sclerosis; RA = Rheumatoid Arthritis; Aus = Australia; SK = South Korea; PRC = People's Republic of China; UK = United Kingdom; US = United States; EU = Europe; Global = >1 country.

Next wave of innovation now in proof-of-concept

4 novel 2nd wave drug candidates in Phase Ib/II studies or about to start

Program	Target	Partner	Study number/Indication	Latest Status	Line	Target patient	Combo therapy	Site	Preclin.	Ph.I	Proof-of-concept	Pivotal/Ph.III
Theliatinib	EGFR WT		27. Solid tumors	Ph.I dose escalation enrolling (continuing)	-	All comers		China				*
			28. Esophageal cancer	Ph.Ib expansion enrolling	1st	EGFR WT		China				*
HMPL-523	Syk		29. Rheumatoid arthritis	Ph. I complete; preparing for Ph.II in 2017	-	Methotrexate ref.		Aus				*
			30. Immunology	Ph.I dose escalation start 2017	-	Healthy volunteers		China				*
			31. Hematological cancers	Ph.I enrolling; target complete Ph.I 2017	2nd/3rd	All comers		Aus			*	
			32. Lymphoma	Ph.I dose escalation enrolling	-	All comers		China			*	
HMPL-689	PI3Kδ		33. Hematological cancers	Ph.I dose escalation (PK analysis)	-	Healthy volunteers		Aus				*
			34. Lymphoma	Ph.I dose escalation start 2017	2nd/3rd	All comers		China				*
HMPL-453	FGFR 1/2/3		35. Solid tumors	Ph.I dose escalation	-	All comers		Aus			*	
			36. Solid tumors	Ph.I dose escalation start 2017	-	All comers		China			*	
HM004-6599	NF-κB (TNF-α)	Nestlé Health Science	Ulcerative colitis (Induction)	HMPL-004 reformulation; Re-submit IND 2017	2nd	5ASA refractory		China				*
			Ulcerative colitis (Maintenance)	Await positive Ph.II in Ulcerative Colitis (Induction)	2nd	5ASA refractory		China				*
NSP DC2	TBD	Nestlé Health Science	Immunology	Preclinical complete end 2017				China				*
Multiple	TBD		Oncology	Four small molecule/antibody programs in preclin.				TBD			*	

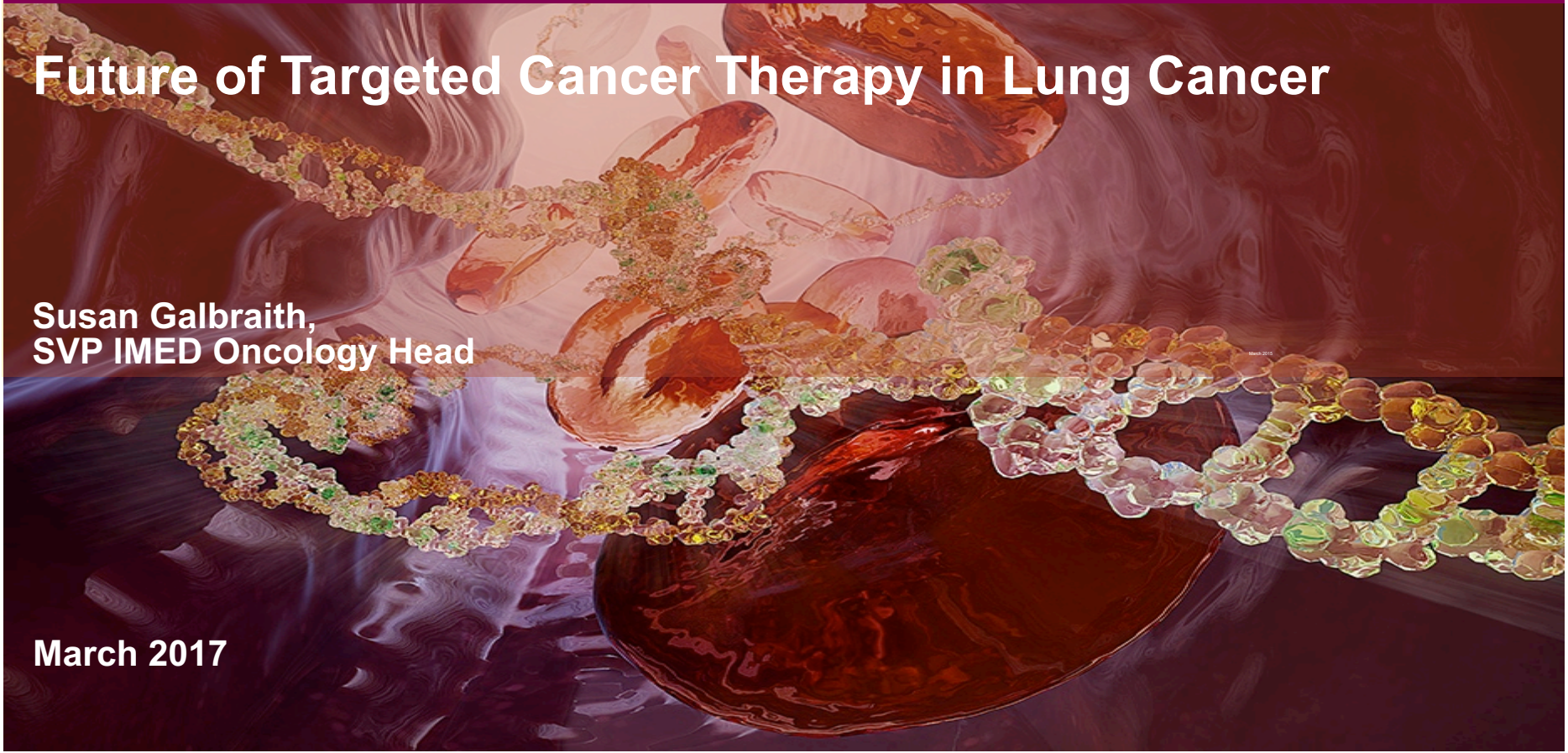
Oncology | Immunology

~2,900 patients/subjects treated in studies to date on our drug candidates, with about 711 dosed in 2016 (2015: 705).

Notes: * = when an NDA submission is possible based on the receipt of favorable clinical data; Proof-of-concept = Phase Ib/II study (the dashed lines delineate the start and end of Phase Ib); combo = in combination with; brain mets = brain metastasis; VEGFR = vascular endothelial growth factor receptor; TKI = tyrosine kinase inhibitor; EGFR = epidermal growth factor receptor; NET = neuroendocrine tumors; ref = refractory, which means resistant to prior treatment; T790M= EGFR resistance mutation; EGFRm+ = epidermal growth factor receptor activating mutations; EGFR wild-type = epidermal growth factor receptor wild-type; 5ASA = 5-aminosalicyclic acids; chemo = chemotherapy; c-MET+ = c-MET gene amplification; c-MET O/E = c-MET over-expression; MS = Multiple Sclerosis; RA = Rheumatoid Arthritis; Aus = Australia; SK = South Korea; PRC = People's Republic of China; UK = United Kingdom; US = United States; EU = Europe; Global = >1 country; MTC = Medullary Thyroid Cancer; DTC = Differentiated Thyroid Cancer.

AstraZeneca
IMED Biotech Unit

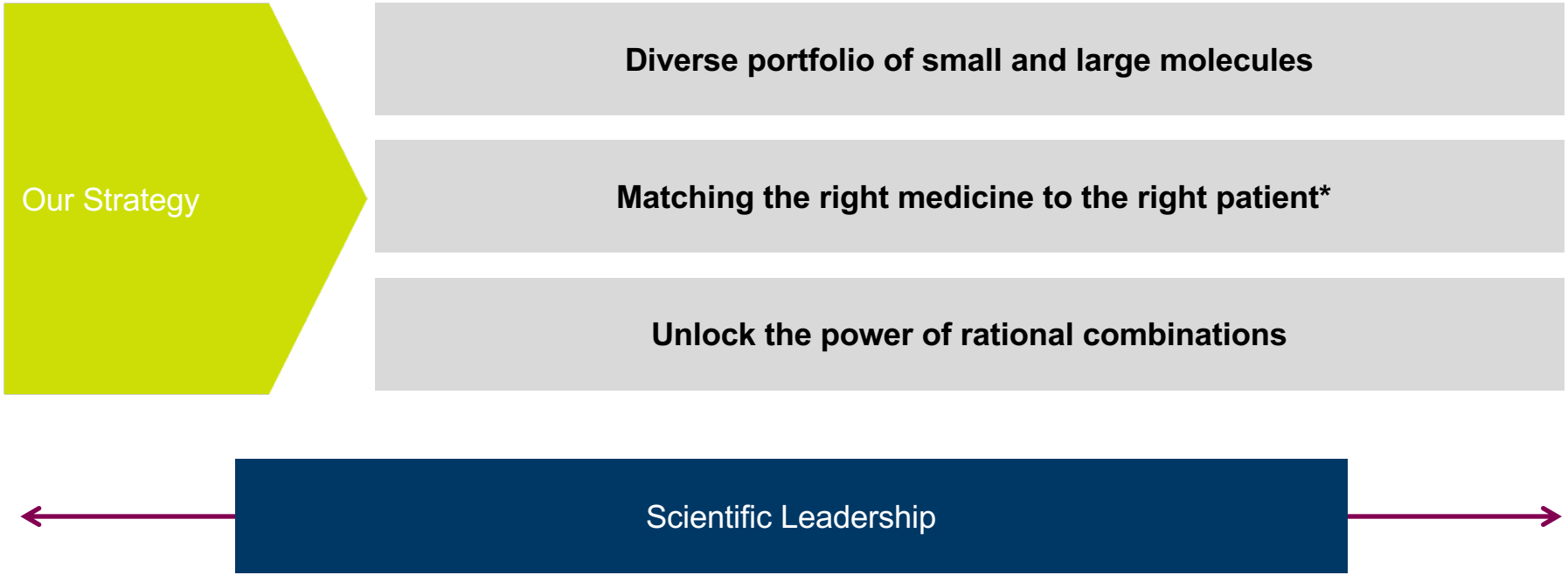
Future of Targeted Cancer Therapy in Lung Cancer



Susan Galbraith,
SVP IMED Oncology Head

March 2017

AZ Oncology - Patient and science driven

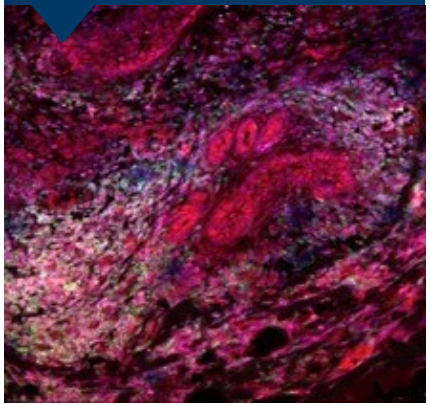


**Patient segmentation through Personalised Healthcare (PHC)*

AZ science drives transformation across our four oncology leadership platforms

Tumour Drivers and Resistance

Next-generation targeted medicines which overcome resistance mechanisms

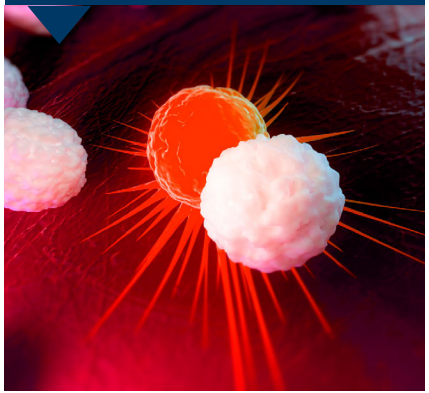


DNA Damage Response (DDR)

Targeting DDR and cell cycle control deficiencies to selectively kill cancer cells

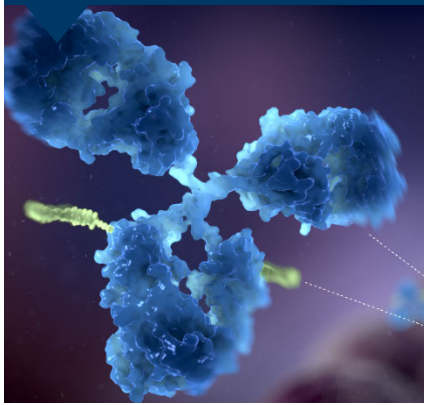
Immuno-Oncology (IO)

Applying multiple approaches to activate the immune system to search and destroy cancer



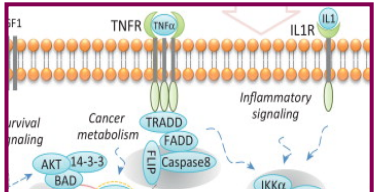
Antibody-Drug Conjugates (ADCs)

Eliminating cancer by delivering highly-potent warheads directly to the tumour cell



Personalised healthcare as a key driver

AZ Scientific leadership: Four mechanisms of action

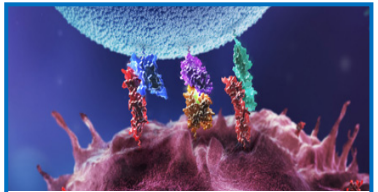


Tumour drivers and resistance

- Osimertinib (EGFRm)
- Selumetinib (MEK)
- Acalabrutinib (BTK)
- **Savolitinib (cMET)**
- Vistusertib (TORC1/2)
- AZD4547 (FGFR)
- AZD5363 (AKT)
- AZD8186 (PI3Kβ)
- AZD9496 (SERD)
- AZD5991 (MCL1)
- AZD4573 (CDK9)
- AZD5153 (BRD4)
- AZD0466 (Bcl2/xL)
- AZD4205 (JAK1)
- AZD4785 (KRas ASO)
- AZD0364 (ERK)

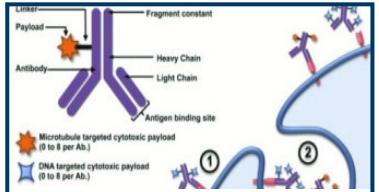
DNA damage repair

- Olaparib (PARP)
- Cediranib (VEGFR)
- AZD1775 (Wee1)
- AZD6738 (ATR)
- AZD0156 (ATM)
- AZD1390 (ATM-BBB)
- AZD2811 (Aurora B nanoparticle)



Immunotherapy

- Durvalumab (PD-L1)
- Tremelimumab (CTLA-4)
- MEDI0680 (PD-1)
- MEDI0562 (OX40 hz mAb)
- MEDI9447 (CD73)
- MEDI1873 (GITRL)
- MEDI9197 (TLR7/8)
- MEDI565 (CEA-BITE)
- AZD9150 (STAT3 ASO)
- AZD5069 (CXCR2)
- AZD4635 (A2aR)

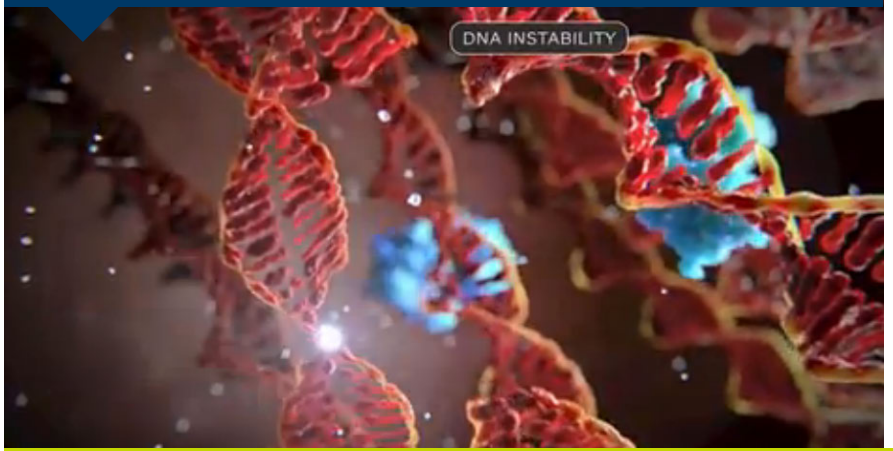


Antibody drug conjugates

- Moxetumomab (CD22)
- Medi4276 (Her2 ADC)
- ADC-Bispecifics

Tumour drivers and resistance mechanisms play a key role in cancer pathology

Genetic instability gives cancer cells an advantage



Mutations can alter signalling pathways controlling cell growth and survival

Identifying genes that exhibit a growth or survival advantage offer targeted therapeutic approaches

Lung cancer kills more people than colon, breast, and prostate cancer *combined*

•Lung cancer is the biggest cancer killer in the world: someone somewhere dies of lung cancer every 20 seconds

•Lung cancer 5 year survival rate is <10%, much lower than many other major cancers.

•Only 15% of patients have their lung cancer diagnosed while still localised in the lung. For over half of patients, their lung cancer is already metastatic at first diagnosis.

•Prevalence of smoking has declined in the West, but high levels in many developing nations (notably China) will deliver an epidemic in lung cancer in the next 2 or 3 decades.

•25% of lung cancer patients never smoked: Never-smoker Lung Cancer is the 7th most common cancer in the world

Note: Other includes head & neck, pancreatic, gastric, thyroid, ovarian, SCLC, mesothelioma, bladder, neuroendocrine, actinic keratosis, soft tissue, and other cancers with <$100M in 2012 global sales
Source: EvaluatePharma

Non-Small Cell Lung Cancer Today

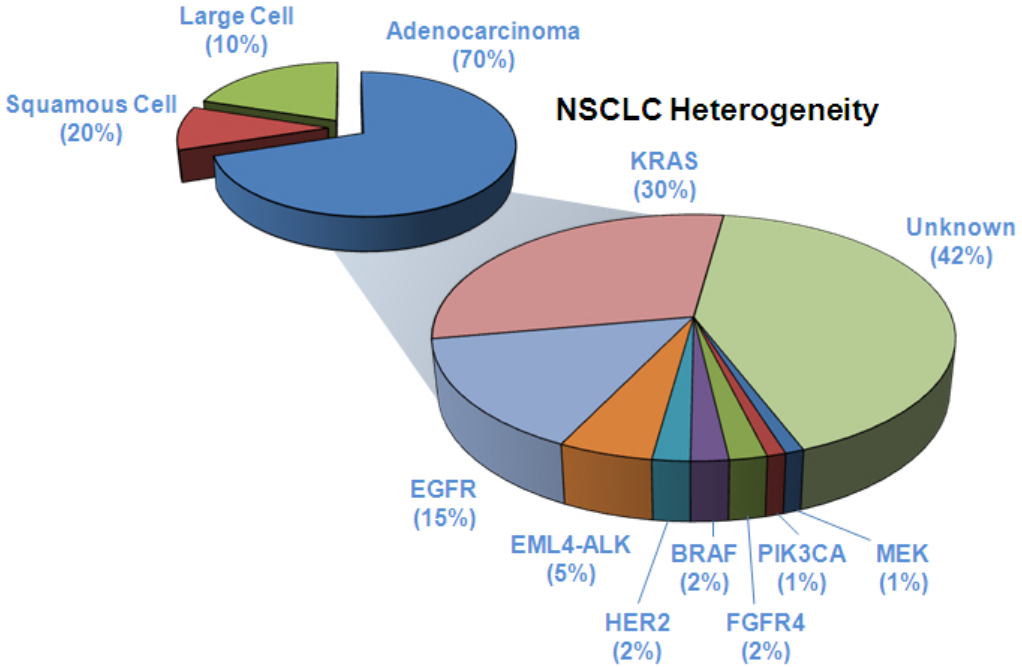
Increasingly sub-divided by molecular markers

EGFR and ALK inhibitors produce high response rate and durable responses in selected patient populations

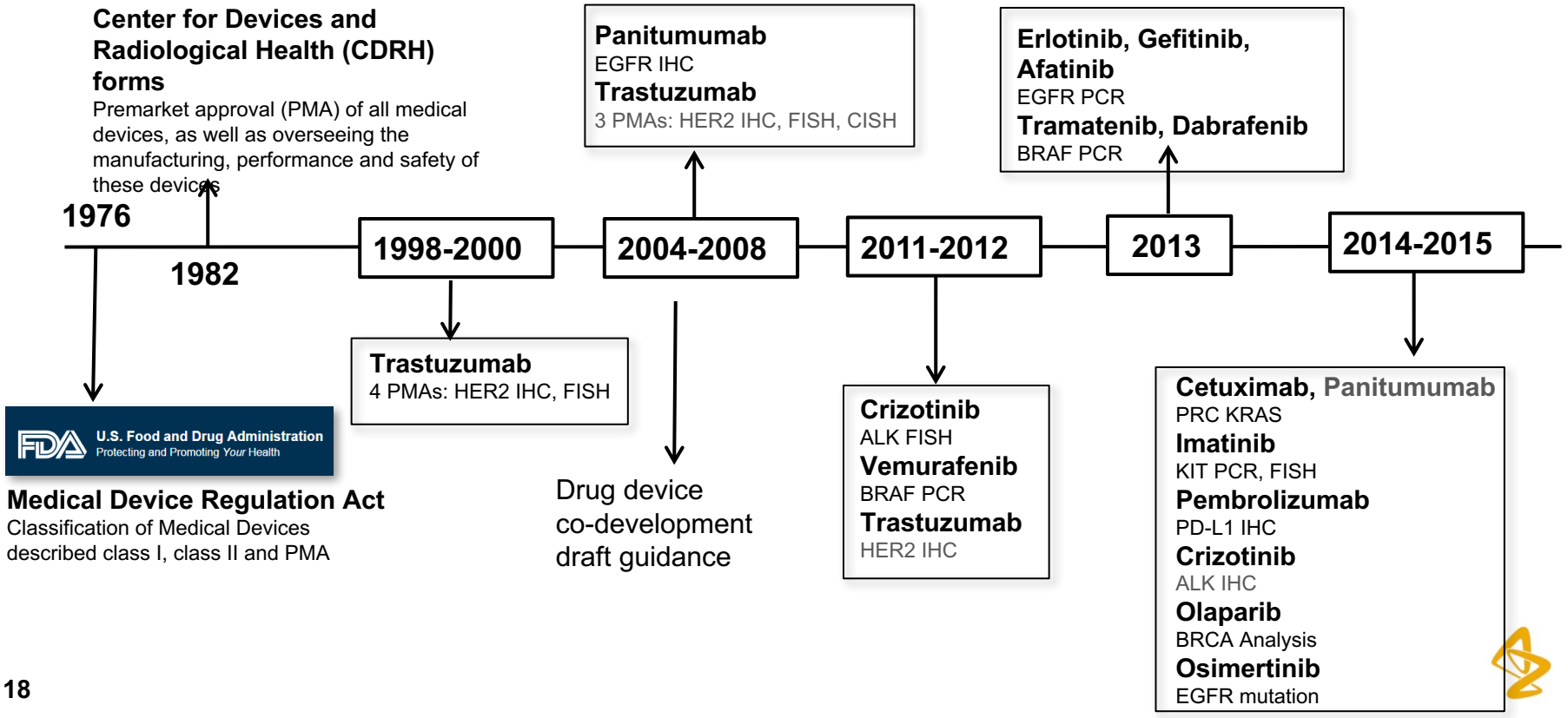
EGFR mutant NSCLC represents ~40 and 15% of adenocarcinomas in Asian and Western patients respectively.

The most common activating EGFR mutations are
Exon 19 deletions (Ex19del)
and
L858R substitution.

The activating mutations decrease the affinity of the receptor for ATP.

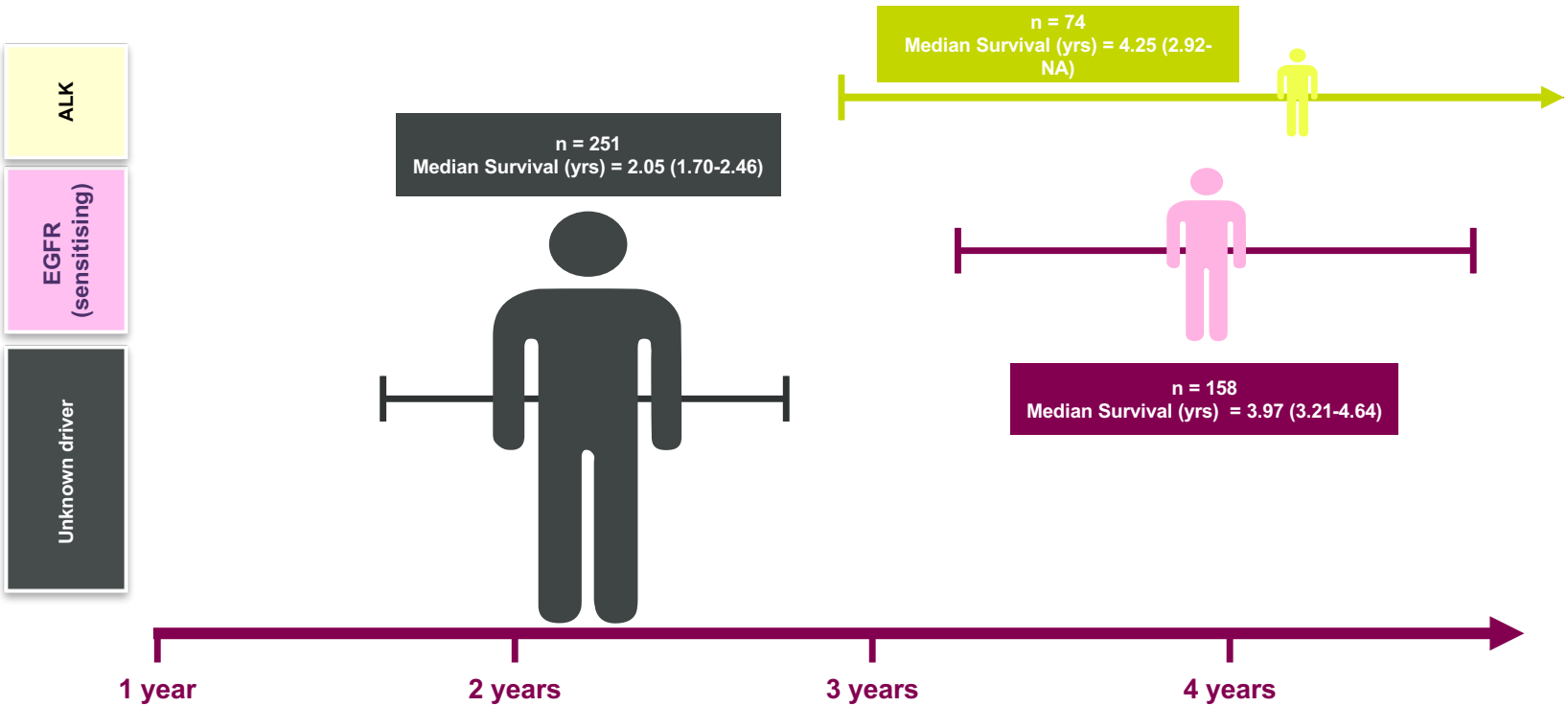


Personalised Medicine is already here – growing number of FDA CDx PMA approvals (1998-2015)



Science is driving a change in survival; patients who receive therapies matched to their tumour live longer

Immuno-oncology potentially transformative across multiple segments



JAMA. 2014;311(19):1998-2006. doi:10.1001/jama.2014.3741.

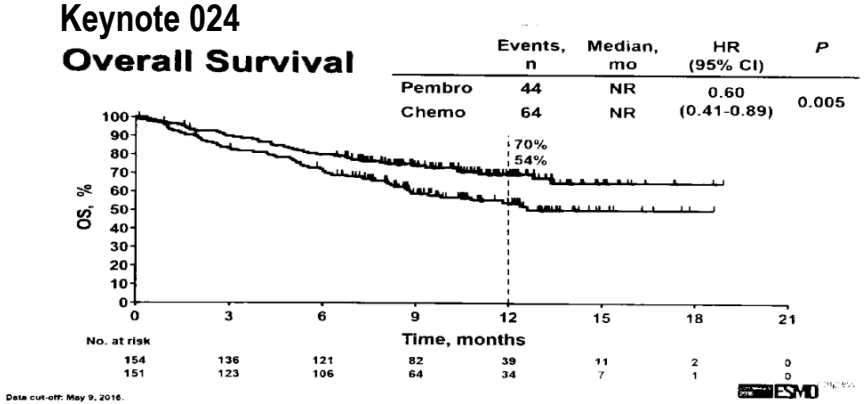
PD1/PDL1 agents have improved OS in 1st and 2nd line NSCLC – but many questions remain

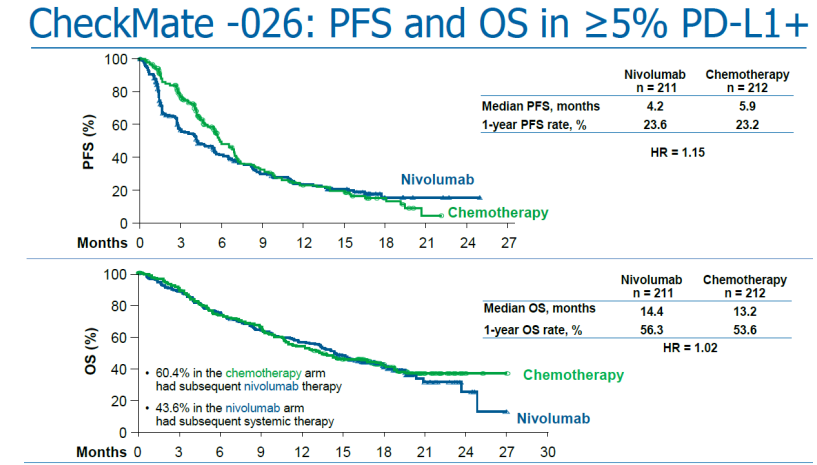
- Nivolumab, Pembrolizumab and Atezolizumab all now approved in 2nd line NSCLC based on randomised OS improvement vs docetaxel

- In 1st line Checkmate 026 trial, in patients with ≥5% PDL1+ tumours, nivolumab did not improve OS or PFS[1]

- In 1st line Keynote 024 trial, in patients with high ≥50% PDL1+ tumours pembrolizumab showed impressive OS benefit (HR 0.60)[2]

- In 1st line Phase 2 Keynote 021, pembrolizumab plus chemotherapy showed improved response rate vs chemotherapy alone (55% vs 29%) and improved PFS but dataset immature

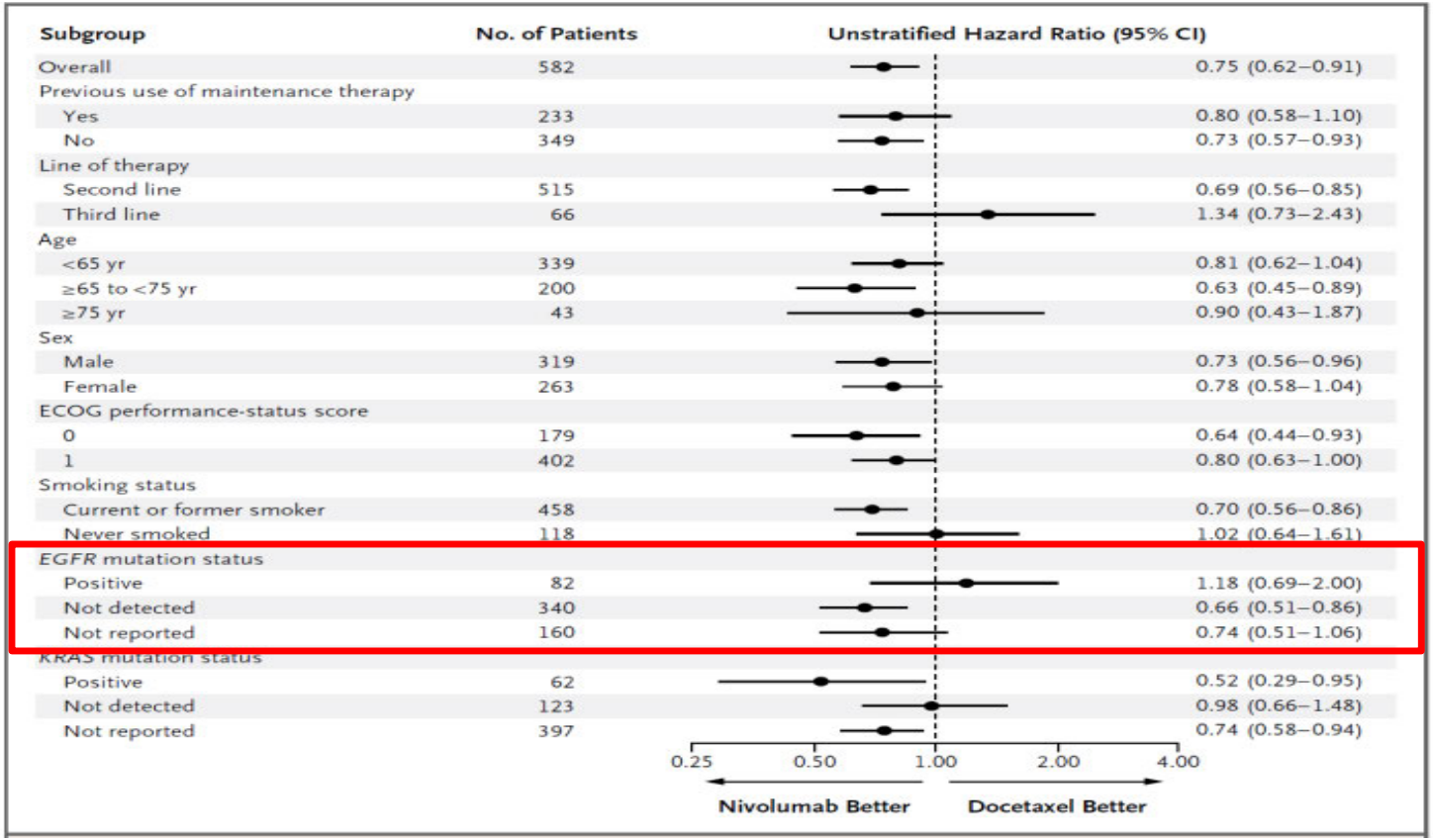




[1]ESMO 2016 Socinski et al
[2]ESMO 2016 Reck et al

Nivolumab Checkmate CM057 - reduced IO efficacy in EGFRm

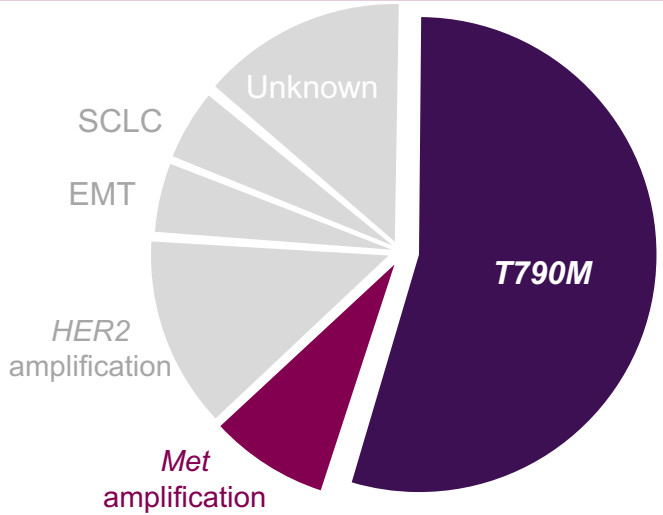
CM057 Ph2/3 2L N.Sq NSCLC (EGFR n = 82, HR = 1.18, NS)



NEJM 2015, 373:1627-39 Borghaei et al

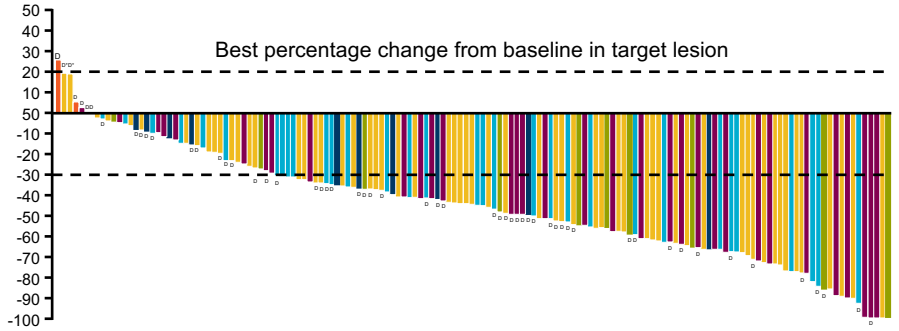
Next-generation drugs to overcome resistance in EGFRm

Main mechanisms of acquired resistance to first generation EGFR targeted drugs[1]



Compound	Activating-mutant	Double-mutant	Wild-type
Gefitinib	Active	Inactive	Active
Erlotinib	Active	Inactive	Active
Afatinib	Highly active	Active	Highly active
Project goal	**Highly active**	**Highly active**	**Low activity**

Response rate in Osimertinib Phase I *T790M* positive cohorts



Janne et al NEJM 2015;372:1689-99

Figure adapted from Cortot A et al. Eur Resp Rev 2014

1. Cortot A et al. Eur Resp Rev 2014; 2. Kobayashi et al. NEJM 2005; 3. Pao W et al. PLoS MED 2005; 4. Ma C et al. J Thorac Dis 2011; 5. Sequist L et al. Sci Transl Med 2011; 6. Yu H et al. Clin Canc Res 2013

Osimertinib: Fastest development time

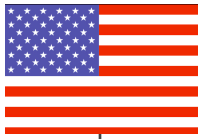
Rationally-designed and targeted treatment

First in human

March 2013

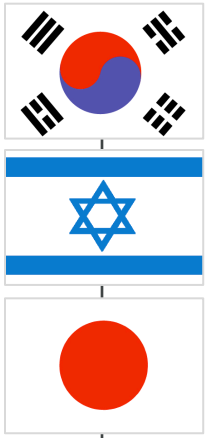
>>

32 months from first in human to first approval



November 2015

February 2016



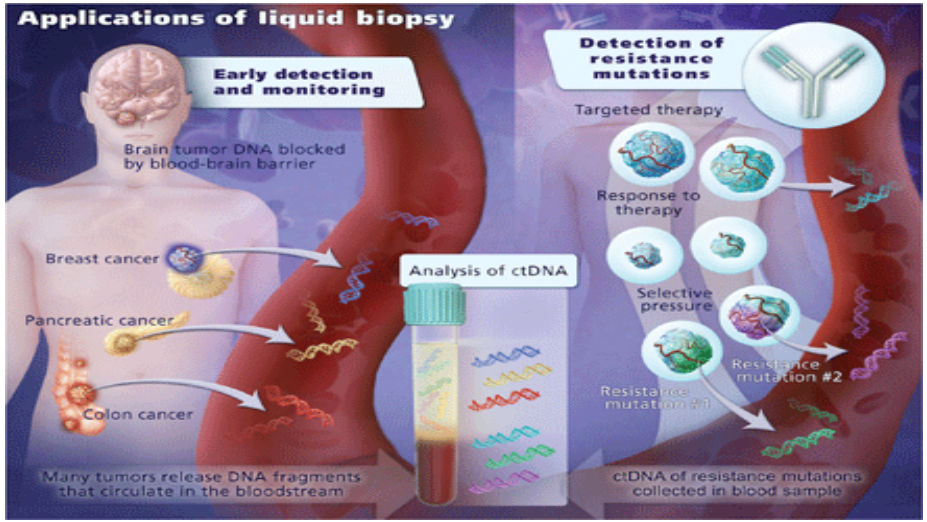
March 2016

USA, EU and Japan approved within six months

H1 2017

Now approved in 42 countries including China

Potential of plasma-based ‘liquid biopsies’



Chetan Bettegowda et al. *Sci Transl Med* 6, February 19, 2014

- Patient Selection
- Monitoring of response, early detection of relapse
- Identification of resistance mechanisms

Minimally invasive, low risk, & allows more frequent sampling

But challenging DNA source to work with:

- Dilute / low amounts of tumour DNA, germline contamination.
- Highly fragmented
- Short half-life (until purified)
- Sampling methods immature / variable

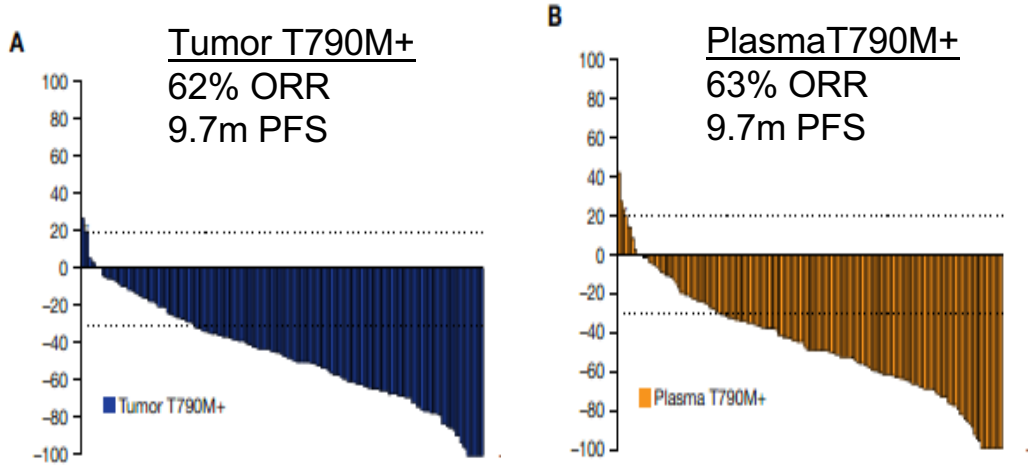
Assays must be highly specific and highly sensitive

Osimertinib: Plasma T790M test predicts clinical response

- Across the AURA trials, plasma was collected for analysis
- Key differences in patient population, dose, and plasma assay utilized

	AURA Phase I	Phase II studies: AURA extension and AURA2
Treatment / dosing	Osimertinib dose escalation and dose expansion cohorts (20–240mg QD)	Osimertinib 80 mg QD
T790M status	T790M positive and negative	Only T790M positive
Analysis	Exploratory post-hoc analysis	Intention to treat for regulatory submission
Plasma assay	BEAMing	cobas
Method of comparison	ddPCR or cobas	NGS

- BEAMing dPCR plasma analysis (n=271 patients) for T790M, Del19, & L858R at all tested Tagrisso doses (20-240mg)



- Plasma T790M positive by BEAMing predicts for a high ORR and a prolonged PFS, identical to that predicted by a tumor T790M positive result (Cobas)

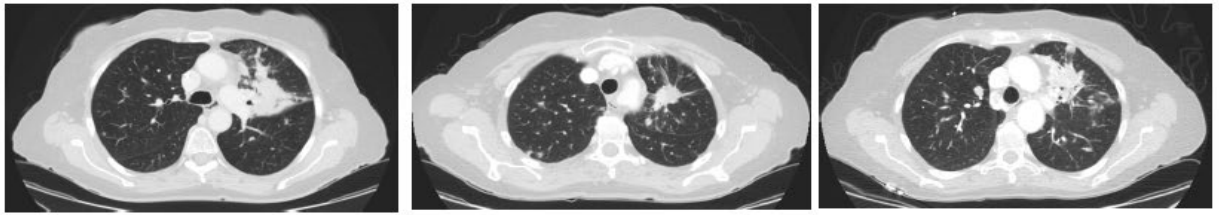
*Oxnard G, Thress K, et al *Journal of Clinical Oncology 2016;34:3375-3382*

Met amplification as a driver of resistance to osimertinib

Case report: osimertinib resistant MET amp

- 69-year-old female with EGFR-mutant NSCLC metastatic to liver, adrenal, bones who had progression after first-line chemotherapy and subsequent erlotinib
- Resistance biopsy was inadequate for genotyping, but plasma genotyping positive for L858R (26%) and T790M (4%)
- Initiated osimertinib and responded on the first scan (-40%) but progressed after 24 weeks
- Resistance biopsy undergone for targeted NGS:
  - Positive for L858R, negative for T790M, positive for MET amplification
  - MET protein overexpression also seen on IHC

Pre-osimertinib plasma genotype:
L858R (26%)
T790M (4%)



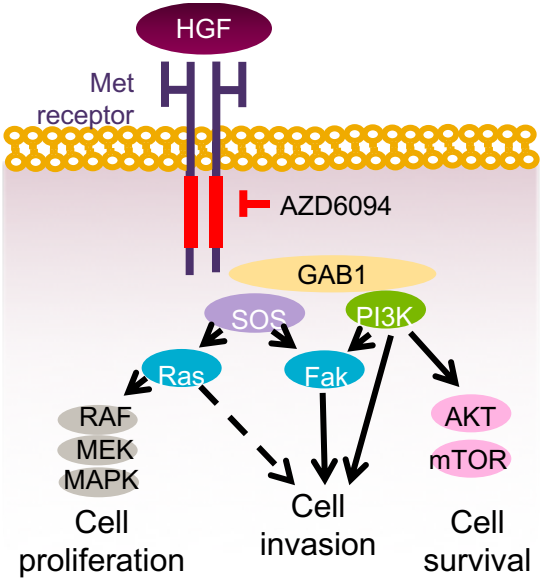
Progression tumor genotype:
L858R
T790M negative
MET amplified

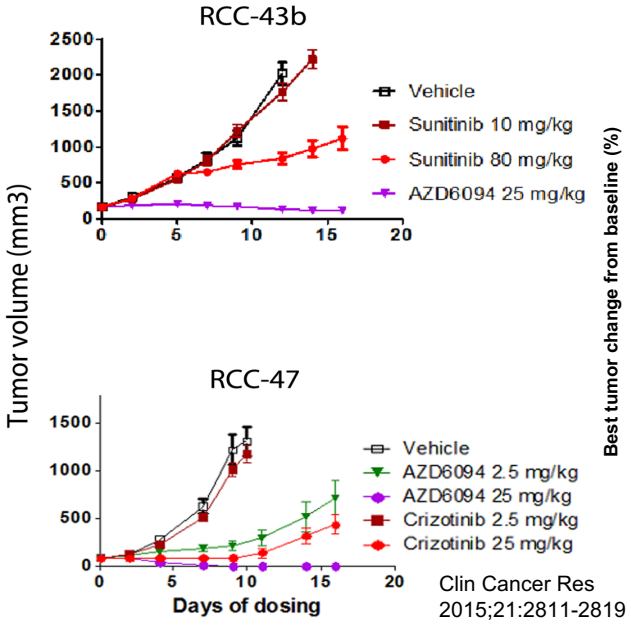
Baseline | **4 months** | **6 months**

Data source: R. Pillai; S. Ramalingam
IHC, immunohistochemistry; NSCLC, non-small cell lung cancer

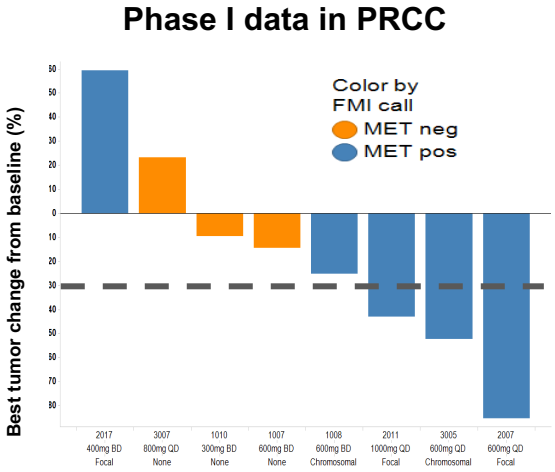
Presented by GR Oxnard at the World Conference on Lung Cancer 2015. ***Journal of Thoracic Oncology*** **2015; 10(9, Suppl 2): S207, abstract Oral 17.07**

Savolitinib is a highly potent and selective inhibitor of MET





Clin Cancer Res 2015;21:2811-2819



J Clin Oncol 32:5s 2014 (suppl; abstr 11111)

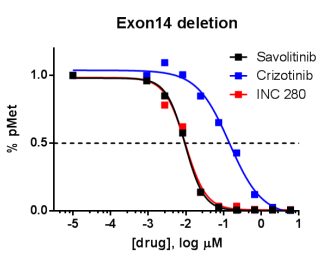
- Savolitinib is a highly potent inhibitor of MET with an IC50 of 4 nM,
- >650 fold selectivity demonstrated vs 265 other kinases
- Active in 2 papillary renal cancer patient derived explants with met copy number gain
- Phase I responses seen in 3 of 8 patients with papillary renal cancer

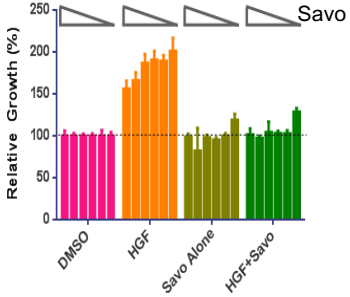
Savolitinib

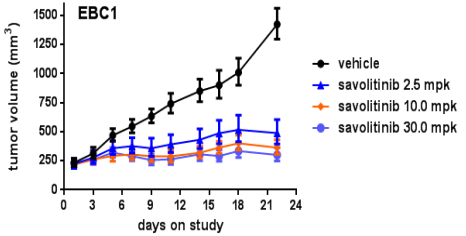
- **Savolitinib Hypothesis:**
- ~4% NSCLC tumours have MET exon14 deletion, driving addiction to MET signalling
- MET inhibitors have demonstrated PoC in this patient population
- Savolitinib shows efficacy in relevant preclinical models

- **Clinical status**
- Phase 2 dose identified
- PoC demonstrated as monotherapy in pRCC; activity in EGFRm+ MET+ NSCLC in combination with osimertinib and gefitinib

Savolitinib inhibits MET+ signaling leading to in vivo efficacy







Exon14 del - MET signalling blocked by savolitinib

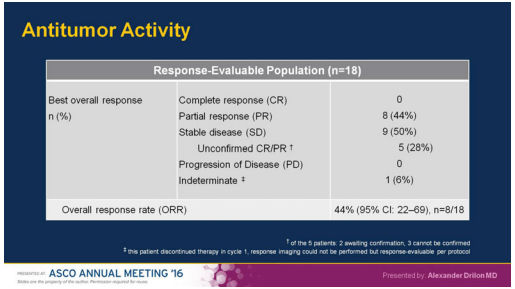
AACR 2016 Barry et al Abstract 1150

Exon14 deletion cell line

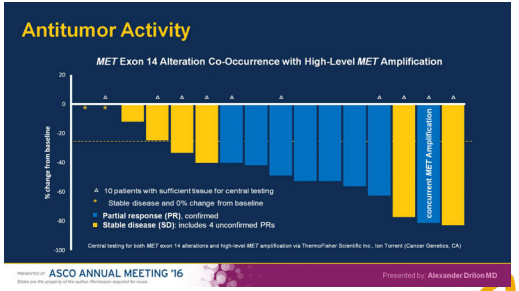
HGF-driven proliferation blocked by savolitinib

MET-amplified tumour growth blocked in vivo by savolitinib

MET inhibitors show PoC in MET exon14 deleted NSCLC

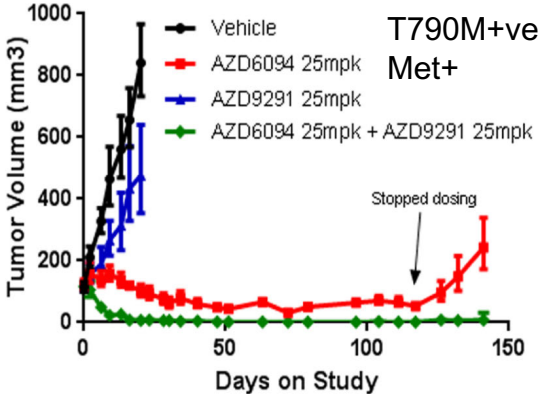


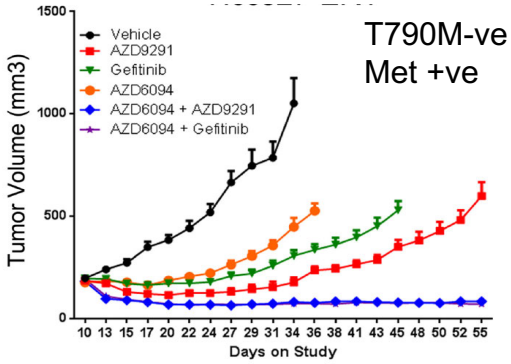
Crizotinib ($PFE): 44% (8/18)

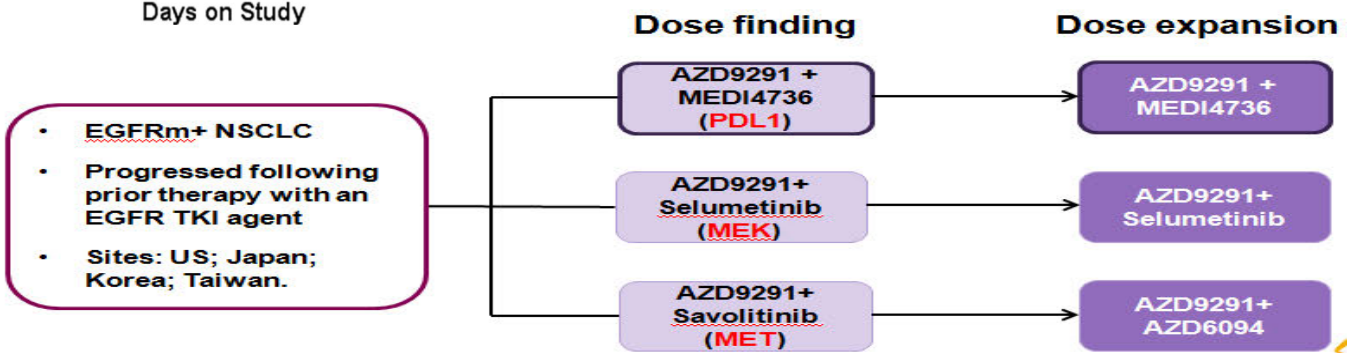


Capmatinib (INC280 $NVS): 47% (7/15)

Savolitinib and Osimertinib efficacious in combination





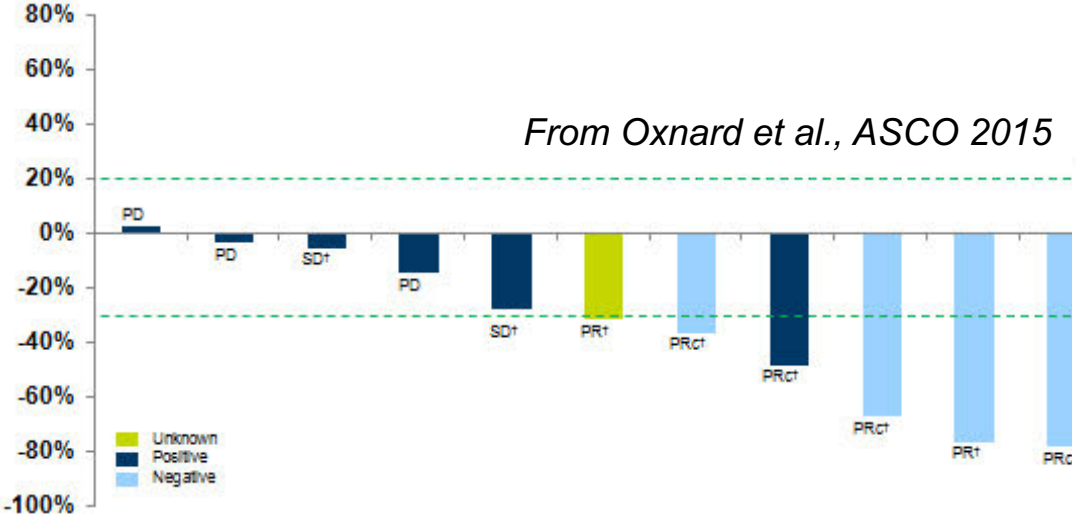


Savolitinib and Osimertinib combination tolerated at full monotherapy doses of each drug

Oxnard, et al; Preliminary results of TATTON, a multi-arm Phase Ib trial of AZD9291 combined with MEDI4736, AZD6094 or selumetinib in EGFR-mutant lung cancer. ASCO Annual Meeting, Chicago, May 2015

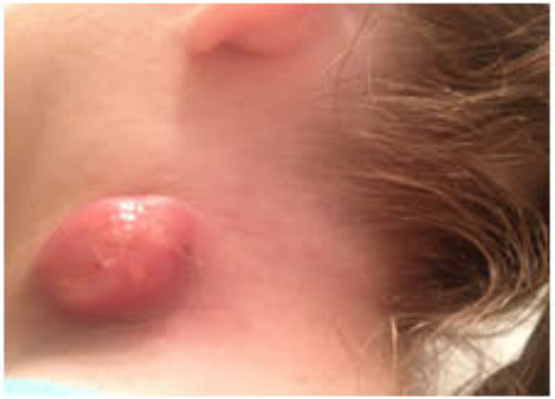
Osimertinib / Savolitinib clinical combination

- 32-year-old female with aggressive tumour with exon 19 deletion and high MET amplification
- Metastases to neck and brain and 5th line of therapy
- Tumour responds to osimertinib / savolitinib 800 mg (qd)

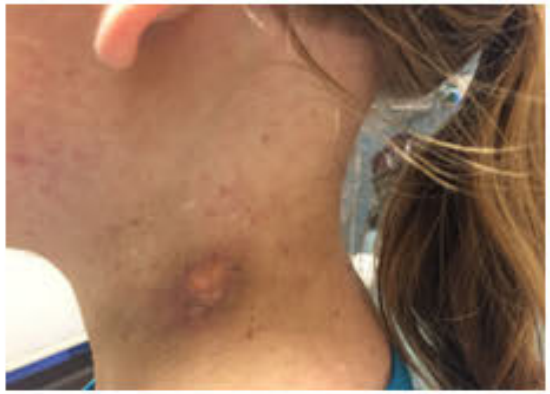


From Oxnard et al., ASCO 2015

*Population: All patients dosed who had a baseline and 6-week RECIST assessment
†Patients ongoing treatment at data cut off
PD, progressive disease; PR, partial response; PRc, confirmed partial response; RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease

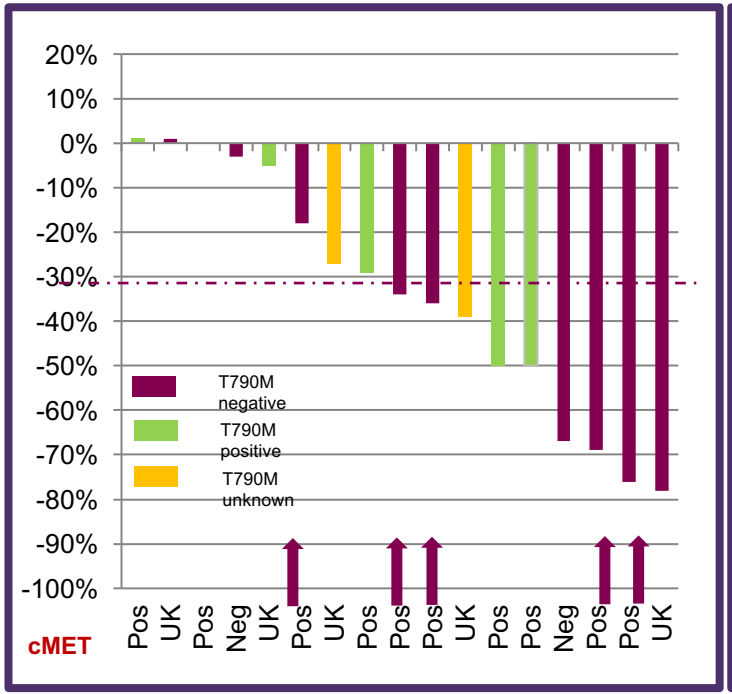


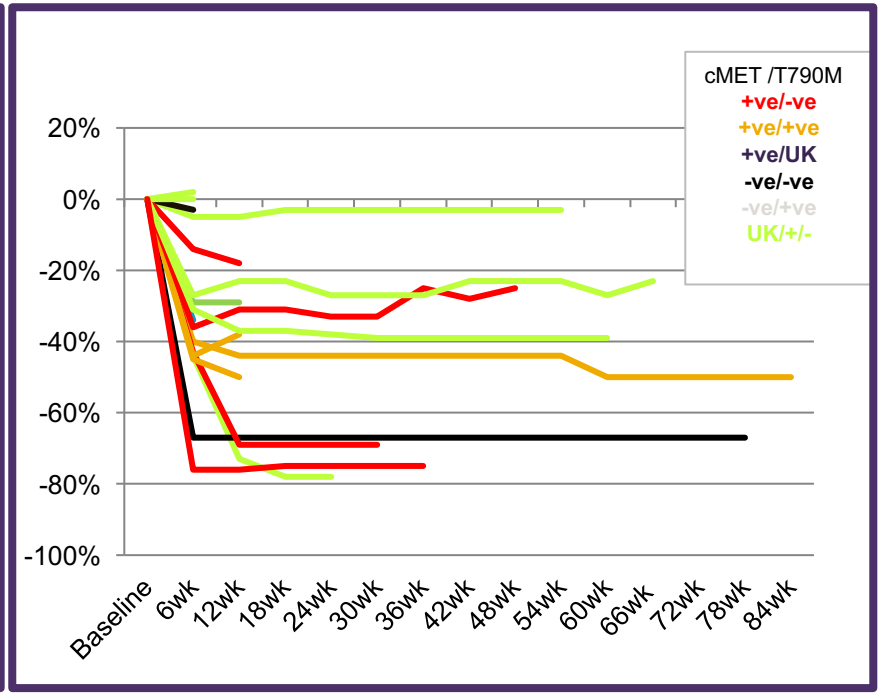
Pre-treatment



4 weeks

Savolitinib + Osimertinib: Tatton Study Tumour Response and Duration





ESMO 2016 Galbraith - Novel Clinical Trials for Precision Medicine

Savolitinib builds upon Osimertinib value in EGFRm Lung Cancer

Combination could extend benefit to patients across different lines in Met+ disease

Activity of combination seen in T790M negative and positive patients

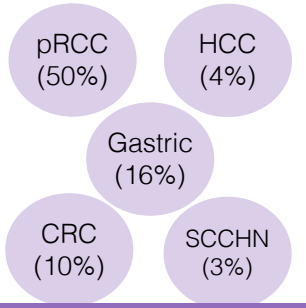
Ability to understand and overcome resistance mechanisms to Osimertinib enables use in earlier lines of therapy

Met inhibitor targeted therapy potential

Tatton trial

NSCLC	
EGFR (resistance driver)	EGFR WT (disease driver)
10-15% of 1 gen TKI patients who progress have cMET amplification or other MET resistance drivers[1]	3-6% of EGFR WT patients have de novo MET aberrations
Savolitinib combination with Osimertinib	Monotherapy opportunity

MET driven diseases



~Potential beyond NSCLC[2]

1- Camidge et al. Acquired resistance to TKIs in solid tumours: learning from lung cancer. Nature Reviews 2014
2. G7: from Garajova et al, Translational Oncogenomics 2-15: 7 (S1)

Summary

- Combinations of tolerable targeted therapies are important to overcome resistance mechanisms

- AZ/Hutchison collaboration is building value in both organisations
  - AZ has track record of development in EGFRm lung cancer and personalised healthcare with delivery of ctDNA testing
  - Hutchison has important relationships in Asia where EGFRm lung cancer is more common

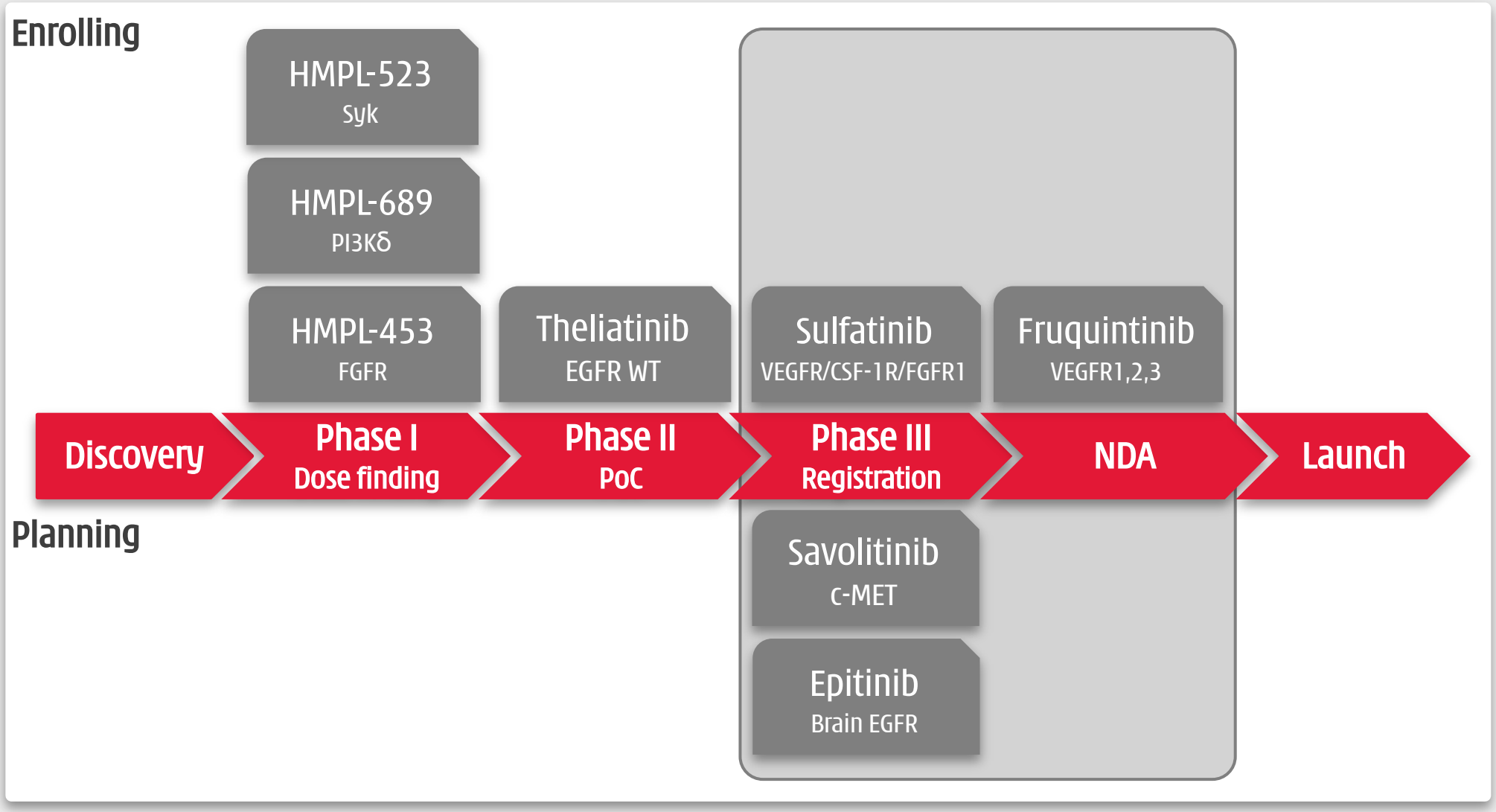
- Savolitinib/Osimertinib combination early data are encouraging and could help to improve the potential of both drugs in EGFRm Lung Cancer

- Targeted therapies are complementary to the use of IO therapies in lung cancer
  - EGFRm tumours less responsive to IO therapy
  - Combinations with IO therapy under exploration

1st Wave - Post-POC Portfolio

Dr Weiguo Su, Chief Scientific Officer

8 clinical candidates – current status



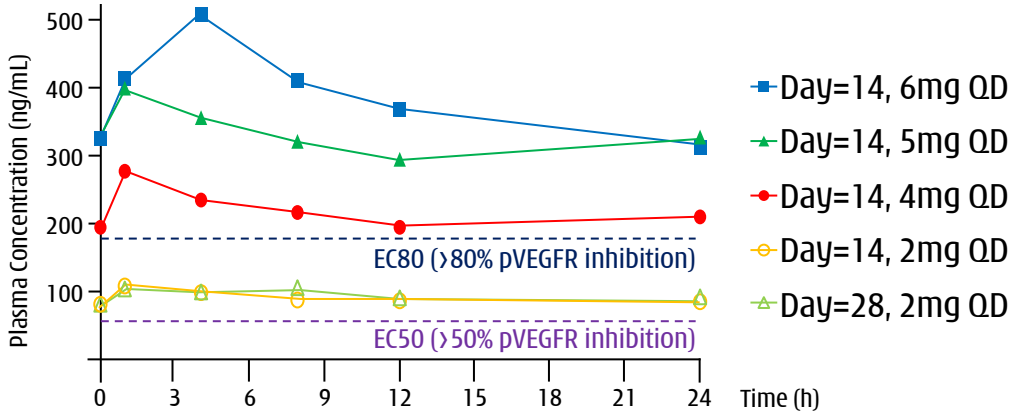
Fruquintinib

Highly selective anti-angiogenesis inhibitor

Fruquintinib: key differentiation features

- High kinase selectivity, low off-target toxicity
- Potent anti-VEGFR3 activity: lymph angiogenesis critical for breast & lung cancers:
  - ↗ Both bevacizumab and ramucirumab failed in breast cancer hypothesized due to lack of lymph angiogenesis control
- Expected full target coverage at clinical dose
- Clean DDI profile suitable for combination

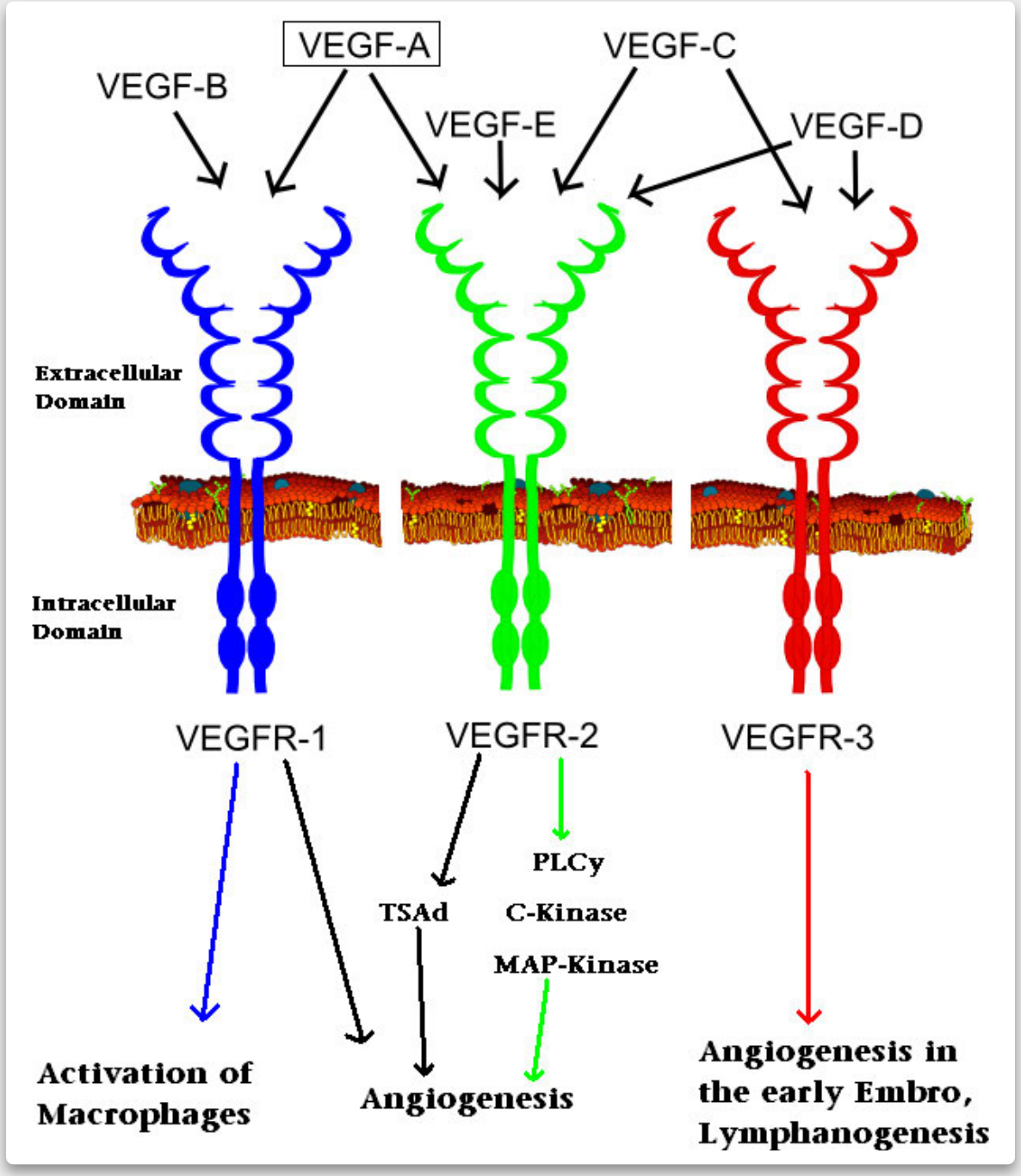
Full & sustained target inhibition above 4 mg dose



FRUQUINTINIB KINASE PROFILE

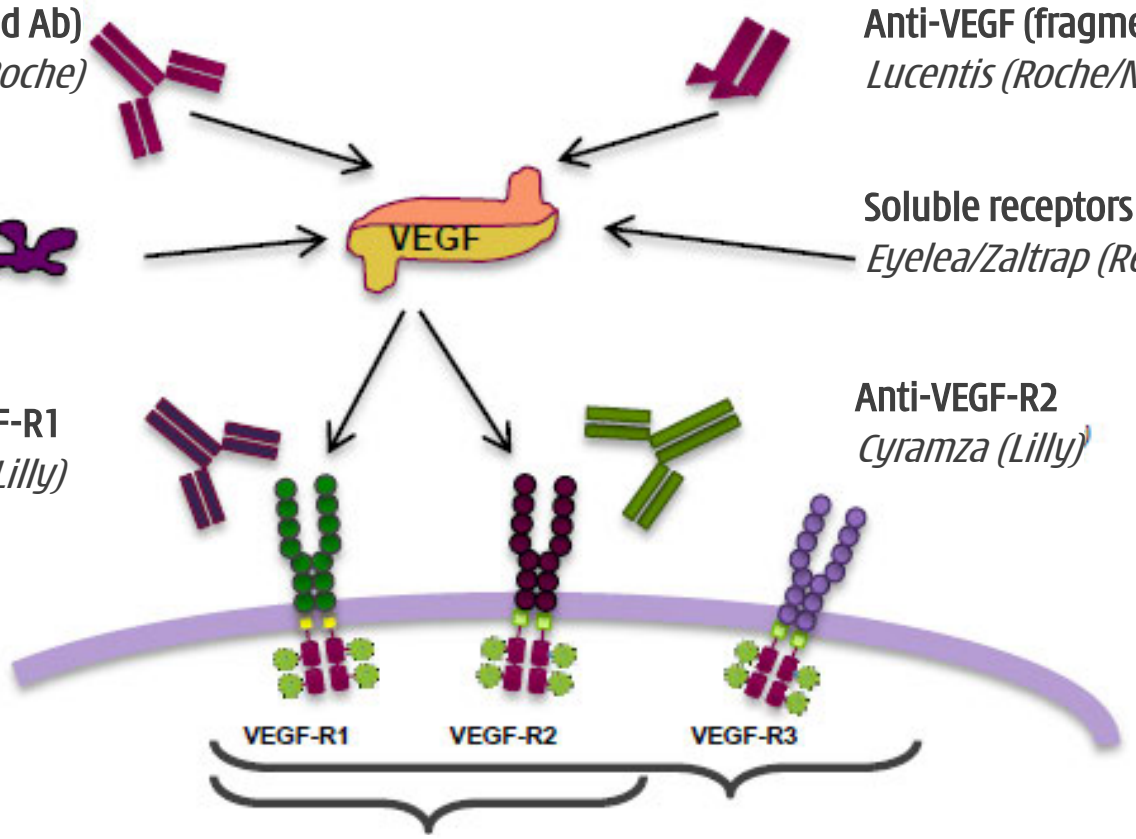
Kinase assay	IC50 (nmol/L) or Inhibition rate (%)
BIOCHEMICAL ACTIVITY	
VEGFR2 (KDR)	35* (25)
VEGFR3 (Flt4)	0.5*
VEGFR1 (Flt1)	33*
Ret	128*
FGFR1	181*
c-kit	458*
Flt3	›10,000
PDGFRβ	›10,000
EGFR	›30,000
Tie2	›10,000
c-MET	›10,000
EphB4	›3,000
Akt	›3,000
CHK1	›10,000
CDK1	›10,000
CDK2	›10,000
CDK5	›10,000
CELL-BASED ACTIVITY	
bFGF stimulated p-FGFR1 in HUVEC	›1000
VEGF-A stimulated p-KDR in HEK293-KDR	0.6 ± 0.2, n = 3
VEGF-C stimulated p-VEGFR3 in HLEC	1.5
VEGF-A dependent HUVEC proliferation	1.7
VEGF-C dependent HLEC proliferation	4.2
HUVEC tube formation	94% at 300 nmol/L
ANTI-ANGIOGENESIS ACTIVITY: Chorioallantoic Membrane (CAM)	strong inhibition at 0.1 & 1 nmol/egg

Cancer Biol & Therapy, 15:12, 1635-1645 (2014)



http://www.cancerpublications.com/newsletter/colorectal/AIO/v2n3/Article2/a2f1.gif

Fruquintinib: covers VEGFR1, 2 and 3 equally well



Anti-VEGF (humanized Ab)
Avastin (Roche)

Anti-VEGF (fragment of human Ab)
Lucentis (Roche/Novartis)

Aptamer (oligonucleotides)
Macugen (OSI/Pfizer)

Soluble receptors
Eyelea/Zaltrap (Regeneron/Bayer)

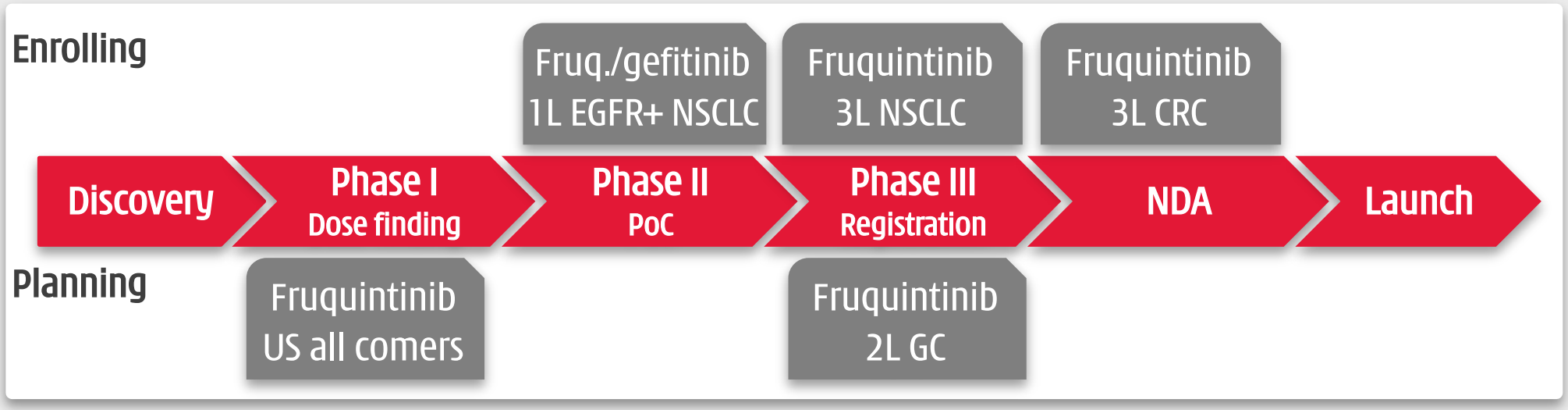
Anti-VEGF-R1
Icrucumab (Lilly)

Anti-VEGF-R2
Cyramza (Lilly)

TKIs incl. VEGFR 1 or 2
Nexavar (Bayer)
Sutent (Pfizer)
Vatalanib (Bayer/Novartis)

VEGFR 1, 2 and 3 TKIs
Fruquintinib (Chi-Med)
Ofev (BI) - also targets PDGFR and FGFR
Stivarga (Bayer) - also targets Raf, Ret, PDGFR, c-Kit

Fruquintinib: ongoing trials

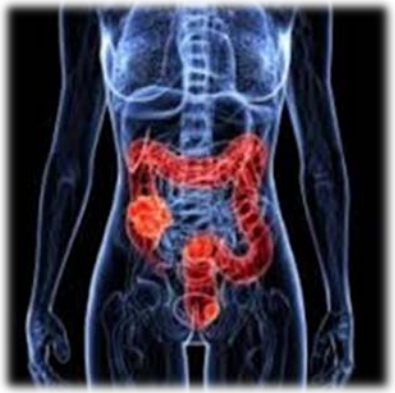


Colorectal cancer (CRC)

3rd in incidence and 4th in deaths globally

	new cases/year	deaths/year
Global	1.36 million	694,000
U.S.	135,430	50,260
China	376,300	191,000

Symptoms



- Blood in or on your stool (bowel movement)
- Pains, aches, or cramps in your stomach that do not go away
- Losing weight and you don't know why

Risk factors

- Age: 90% of CRC in patients >50 years old
- Family history of CRC
- Genetic syndromes such as familial adenomatous polyposis (FAP) or hereditary non-polyposis CRC (a.k.a. Lynch syndrome)
- History of inflammatory bowel disease, Crohn's disease, or ulcerative colitis
- High risk lifestyle: lack of physical activity, diet (low fruit/veg, fiber, high fat/protein), alcohol/tobacco, high BMI

Sources: Ferlay J et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015; 136:E359-386. Chen W et al. Cancer statistics in China, 2015. CA Cancer J Clin. 2016; 66:115-132.

Fruquintinib: Phase II PoC in 3L mCRC[1]

- ✓ 71 patients, 3rd line or above, randomized in 2:1 for fruquintinib or placebo
- ✓ **Clearly met** Ph.II primary endpoint: **70% reduction** in risk of progression
- ✓ Well tolerated; **safety profile consistent with VEGFR inhibition**
  - ★ Hypertension & HFS are **on-target** VEGFR AEs
  - ★ Weak patients – 73% of patients 4th line or above

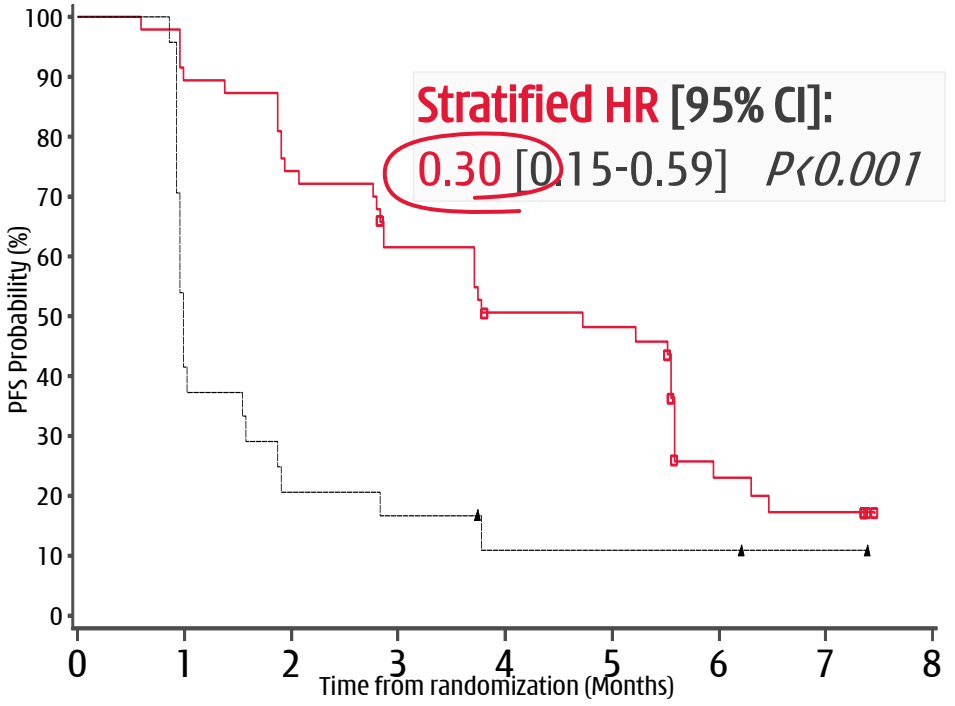
Patients, %	Fruquintinib (n=47)	Placebo (n=24)
All AEs, any grade	47 (100%)	20 (83.3%)
All AEs, grade ≥3	31 (66.0%)	6 (25.0%)
Hypertension, grade ≥3	11 (23.7%)	0
Hand-foot syndrome ("HFS"), grade ≥3	7 (14.9%)	0
All other AEs, grade ≥3 (each)	≤2 (≤4.3%)	≤1 (≤4.2%)
Leading to dose interruption	14 (29.8%)	4 (16.7%)
Leading to dose reduction	13 (27.7%)	0
Leading to treatment discontinuation	6 (12.8%)	3 (12.5%)

[1] J. Hematol. Oncol., 2017 10 (1), 22.

Fruquintinib: Phase II PoC in 3L mCRC[1]

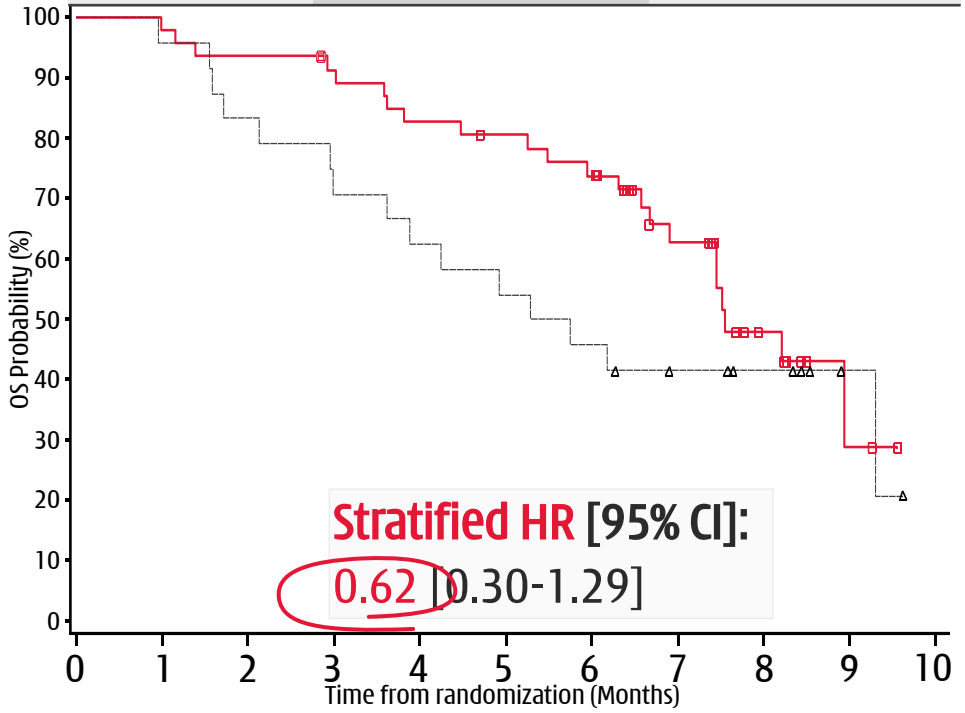
Progression Free Survival [2]

	Fruquintinib (n=47)	Placebo (n=24)
Events, n	36 (76.6%)	21 (87.5%)
Median, mo.	4.7 (2.9, 5.6)	1.0 (1.0, 1.6)



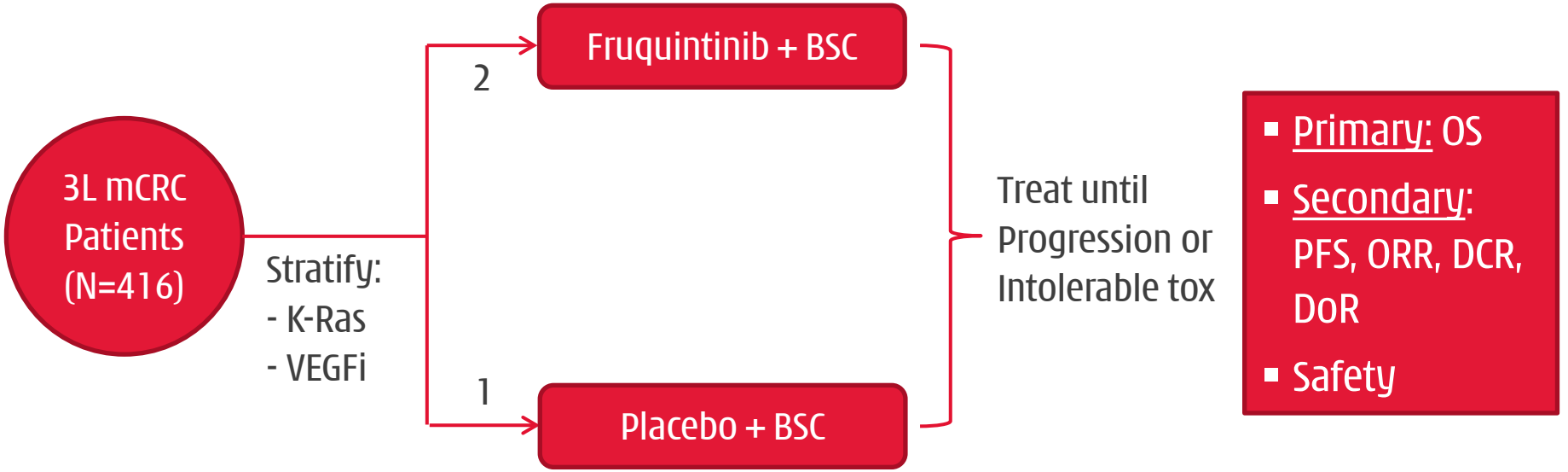
Overall Survival

	Fruquintinib (n=47)	Placebo (n=24)
Events, n	22 (46.8%)	15 (62.5%)
Median, mo.	7.6 (6.9, -)	5.5 (3.6, -)



[1] J. Hematol. Oncol., 2017 10 (1), 22; [2] Median PFS = Local Physician Assessment - mPFS under Blinded Independent Clinical Review 3.8 mo. vs. 1.1 mo.

Fruquintinib: Phase III in 3L mCRC (FRESCO)



- 416 patients. 28 centers. Enrollment from Dec 2014 to May 2016
- Database closed on Jan 17, 2017
- **Positive** topline results announced on March 3, 2017
- Full data to be presented at **ASCO 2017**

Non-Small Cell Lung Cancer (NSCLC)

Lung cancer 1st in both incidence and in deaths globally

	new cases/year	deaths/year
Global	1.82 million	1.59 million
U.S.	222,500	155,870
China	733,300	610,200

Risk factors

- Smoking: 80-90% of linked to smoking, including second-hand smoking
- Family history of lung cancer
- Radon
- Other substances including air pollution
- Radiation therapy to the chest

Symptoms

- Coughing
- Chest pain
- Shortness of breath
- Wheezing
- Coughing up blood

Sources: Ferlay J et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015; 136:E359-386. Chen W et al. Cancer statistics in China, 2015. CA Cancer J Clin. 2016; 66:115-132.

Fruquintinib: Phase II PoC in 3L NSCLC (2016 WCLC)

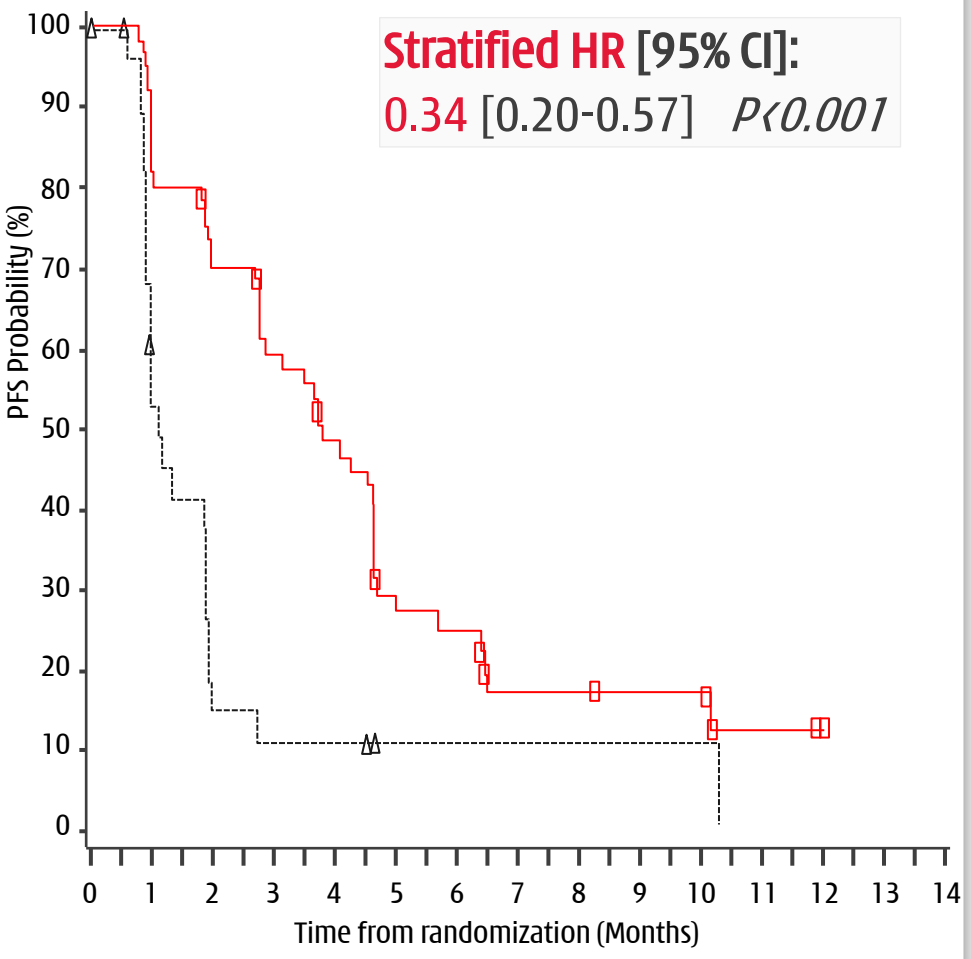
- ✓ 91 patients, 3rd line, **enrolled in ~9 months** (Jun'14-Mar '15)
- ✓ **Met primary endpoint** of progression free survival ($p<0.001$)
- ✓ Generally well tolerated with known AEs

Patients, %	Fruquintinib (n=61)	Placebo (n=30)
All AEs, any grade	61 (100%)	27 (90.0%)
All AEs, Gr ≥3	20 (32.8%)	6 (20.0%)
Hypertension, Gr ≥3	5 (8.2%)	1 (3.3%)
Hand-foot syndrome ("HFS"), Gr ≥3	3 (4.9%)	0
All other AEs, Gr ≥3 (each)	≤2 (≤3.3%)	0
Leading to dose interruption	9 (14.8%)	0
Leading to dose reduction	8 (13.1%)	0
Leading to treatment discontinuation	6 (9.8%)	1 (3.3%)

Lu S et al. OA11.03 A Randomized, Multi-Center, Double-Blind Phase II Study of Fruquintinib in Patients with Advanced Non-Small Cell Lung Cancer. Journal of Thoracic Oncology , Volume 12 , Issue 1 , S286 .

Fruquintinib: Phase II PoC in 3L NSCLC (2016 WCLC)

Progression Free Survival



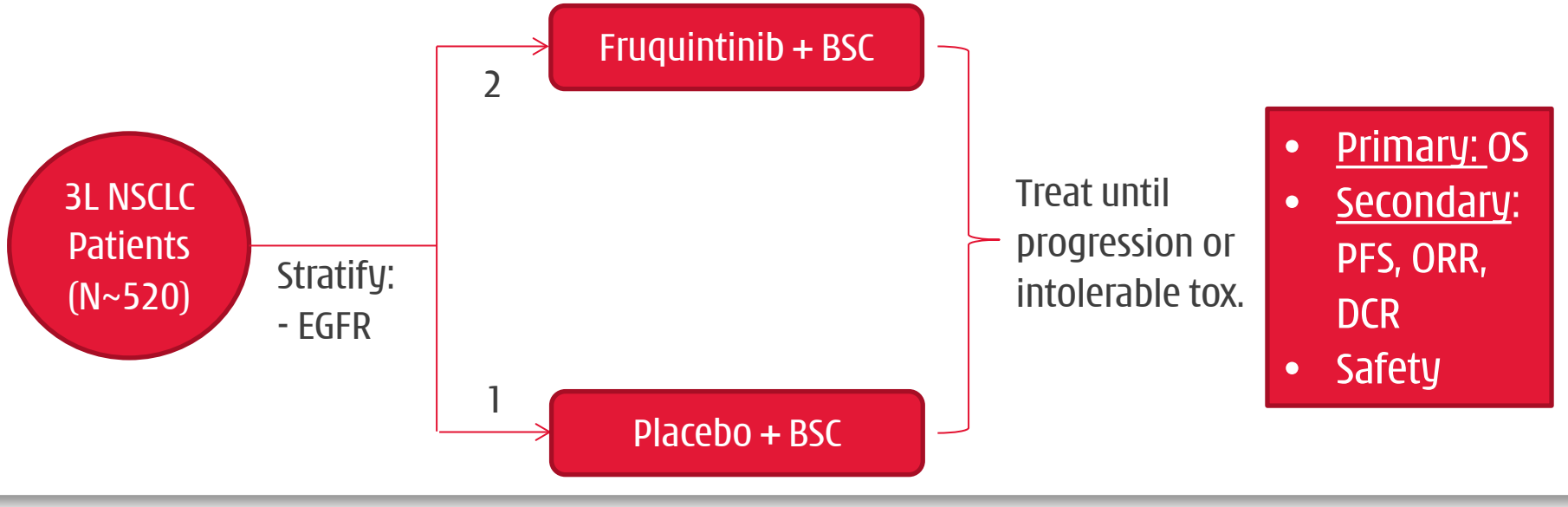
	Fruquintinib (n=61)	Placebo (n=30)
Events, n	40 (65.6%)	21 (70.0%)
Median, mo.	3.8 (2.8, 4.6)	1.1 (1.0, 1.9)

Response Rate	Fruquintinib (N=61) n (%)	Placebo (N=30) n (%)
Complete response (CR)	0	0
Partial response (PR)	10 (16.4)	0
Stable disease (SD)	33 (54.1)	5 (16.7)
Progressive disease (PD)	14 (23.0)	20 (66.7)
Objective response rate (ORR)*	10 (16.4)	0
Disease control rate (DCR)**	43 (70.5)	5 (16.7)

* p=0.021; **p<0.001

Lu S et al. OA11.03 A Randomized, Multi-Center, Double-Blind Phase II Study of Fruquintinib in Patients with Advanced Non-Small Cell Lung Cancer. Journal of Thoracic Oncology , Volume 12 , Issue 1 , S286 .

Fruquintinib: Phase III in 3L NSCLC (FALUCA)

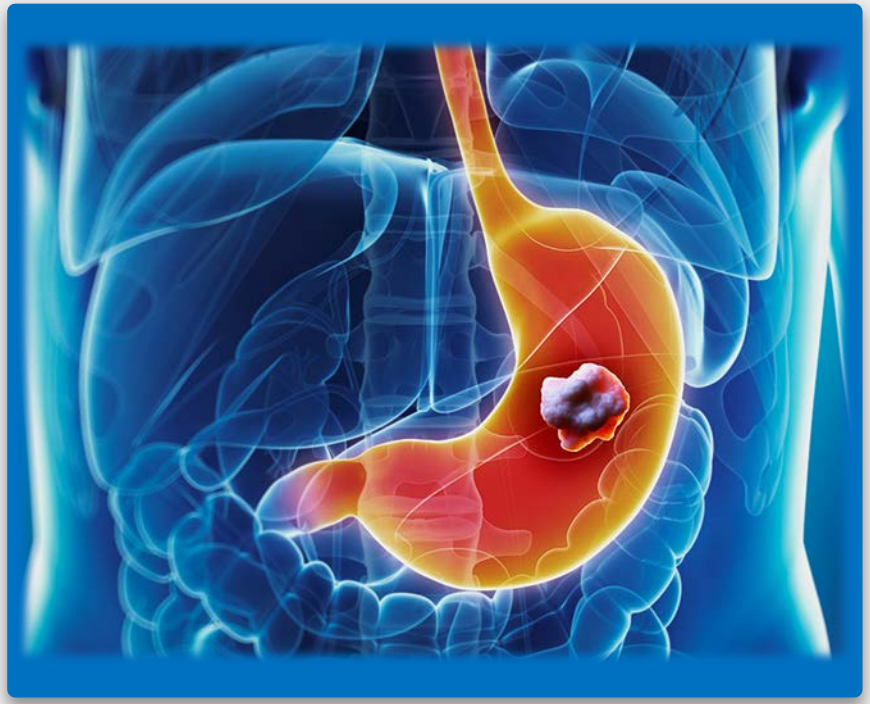


- Approximately 520 patients to be enrolled
- Expect full enrollment by 3Q 2017
- Database close anticipated by mid-2018

Gastric Cancer (GC)

5th in incidence and 2nd in deaths globally

	new cases/year	deaths/year
Global	951,000	723,000
U.S.	28,000	10,950
China	679,100	498,000



Risk factors

- Diet: high in salty, smoked foods, preserved foods
- Eating foods contaminated with aflatoxin fungus
- Family history of stomach cancer
- Infection with *Helicobacter pylori*
- Long-term stomach inflammation
- Smoking

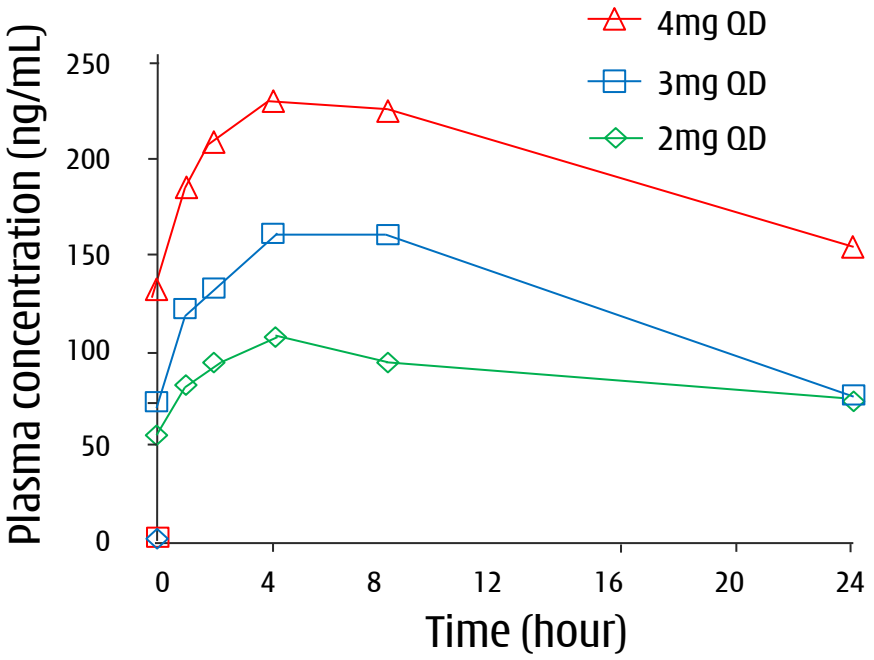
Symptoms

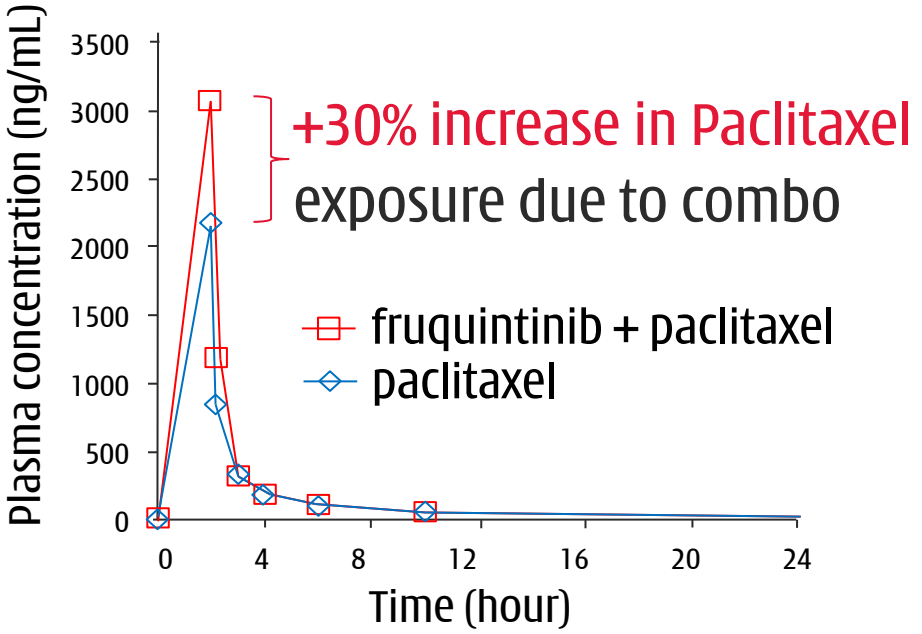
- Severe and persistent heartburn/pain
- Severe and unrelenting indigestion: bloating, full
- Persistent nausea and vomiting
- Fatigue

Sources: Ferlay J et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015; 136:E359-386. Chen W et al. Cancer statistics in China, 2015. CA Cancer J Clin. 2016; 66:115-132.

Fruquintinib: Phase Ib dose finding for combination with paclitaxel

- Dose proportional increase of fruquintinib AUC at steady state
- Over 30% increase in paclitaxel drug exposure following multiple doses of fruquintinib

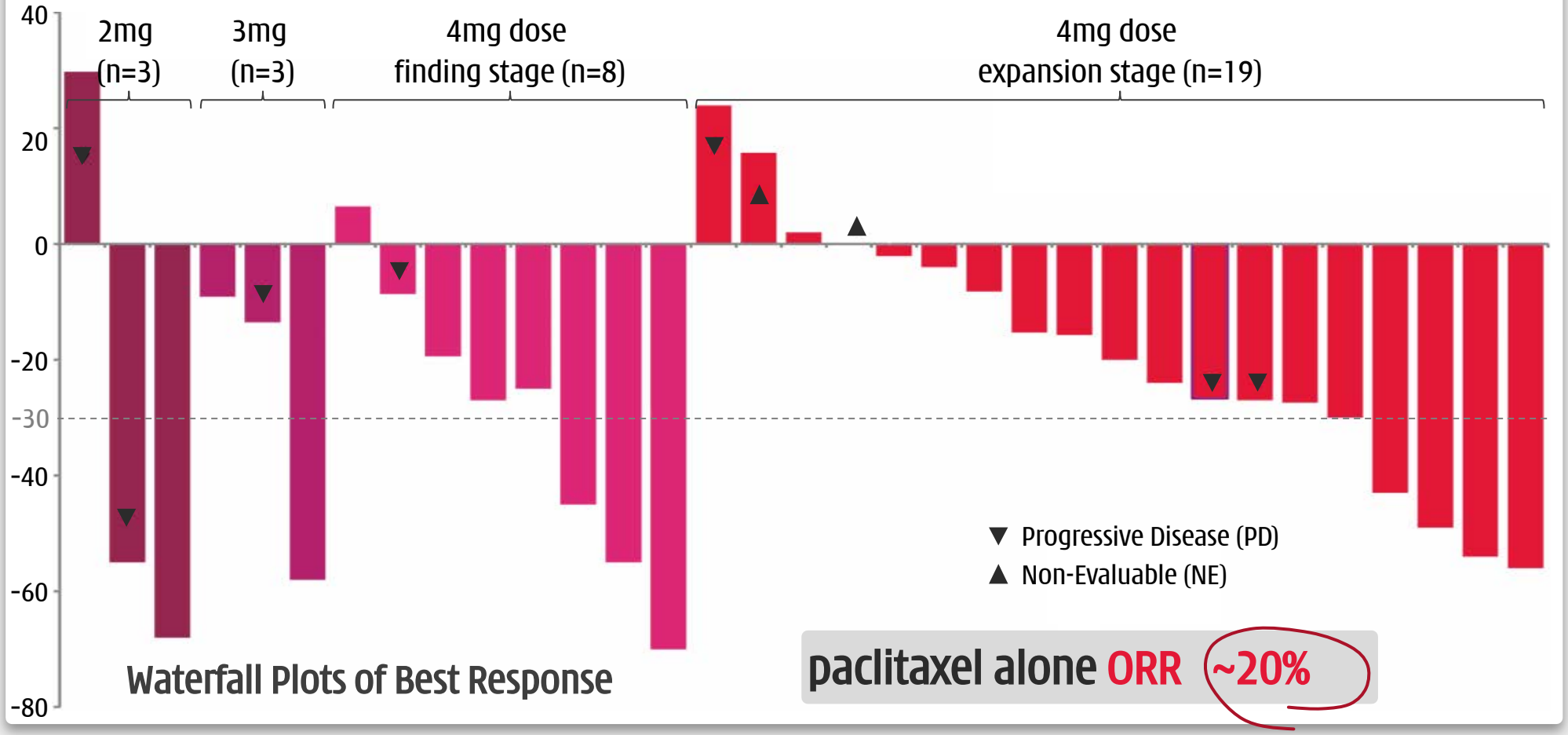




Xu R et al. A Phase I/II trial of fruquintinib in combination with paclitaxel for second-line treatment in patients with advanced gastric cancer. J Clin Oncol 35, 2017 (suppl 4S; abstract 128).

Fruquintinib: Phase Ib dose finding for combination with paclitaxel

ORR of 36% (10/32) & **DCR of 68%** in efficacy evaluable pts.
Fruquintinib 4mg, **≥16 wk. PFS of 50%** & **≥7 mo. OS of 50%.**



paclitaxel alone ORR ~20%

Xu R et al. A Phase I/II trial of fruquintinib in combination with paclitaxel for second-line treatment in patients with advanced gastric cancer. J Clin Oncol 35, 2017 (suppl 4S; abstract 128).

Fruquintinib: Phase Ib dose finding for combination with paclitaxel

- Encouragingly low level of dose reduction / interruption
- Actual mean administered dose in 1st cycle
  - ↗ 3.32mg/day for fruquintinib (83.0% planned dose)
  - ↗ 78.6 mg/m2/week for paclitaxel (98.3% planned dose)

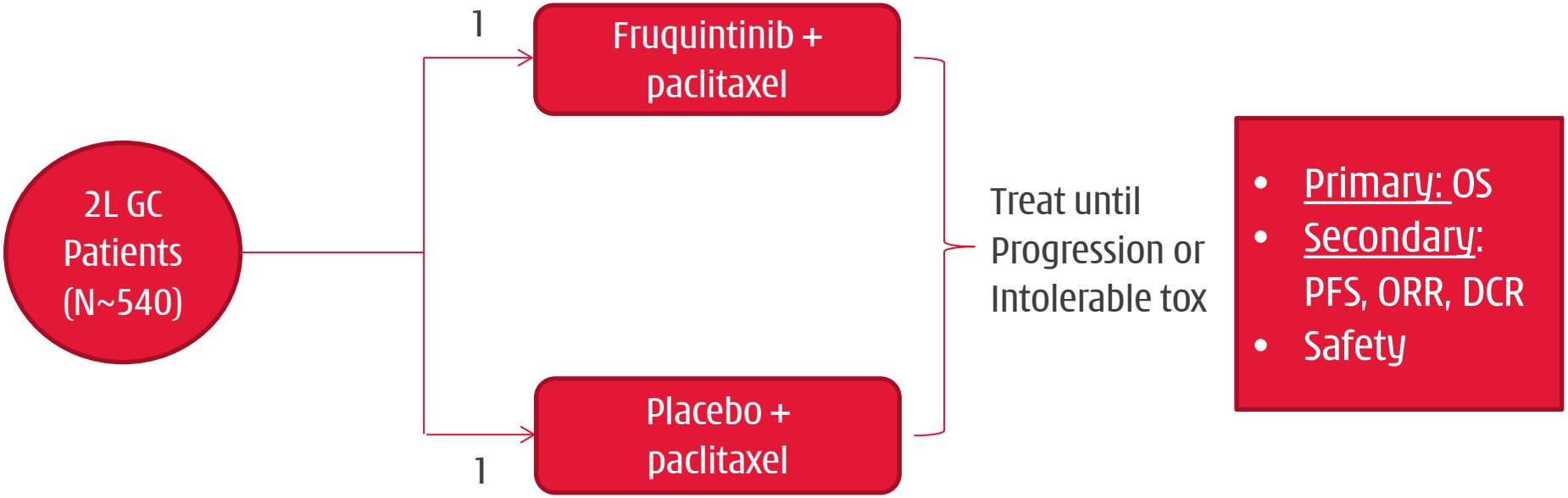
Characteristics (Unit)	Drug Expansion Stage (N=19) Fruquintinib 4 mg + paclitaxel 80 mg/m²	
	Drug interruption	Drug reduction
Dose modification with Fruquintinib N (%)	2 (10.5%)	2 (10.5%)
Dose modification with Paclitaxel N (%)	5 (26.3%)	1 (5.3%)

AE profile in-line with expectations and similar to ramucirumab in combo with paclitaxel in Asian 2L GC patients

Drug related grade 3 or 4 AEs	Fruquintinib 4 mg + paclitaxel 80 mg/m² (N=28)	Ramucirumab + paclitaxel 80 mg/m² (Asia N=109)
Hematologic AEs		
Neutropenia	57%	60%
Leukopenia	29%	34%
PLT decreased	4%	4%
Anemia	4%	12%
Non-hematologic AEs		
Hypertension	7%	8%
Hemorrhage	4%	5%
GI bleeding	4%	3%
Proteinuria	0%	4%
Mucositis	4%	NA

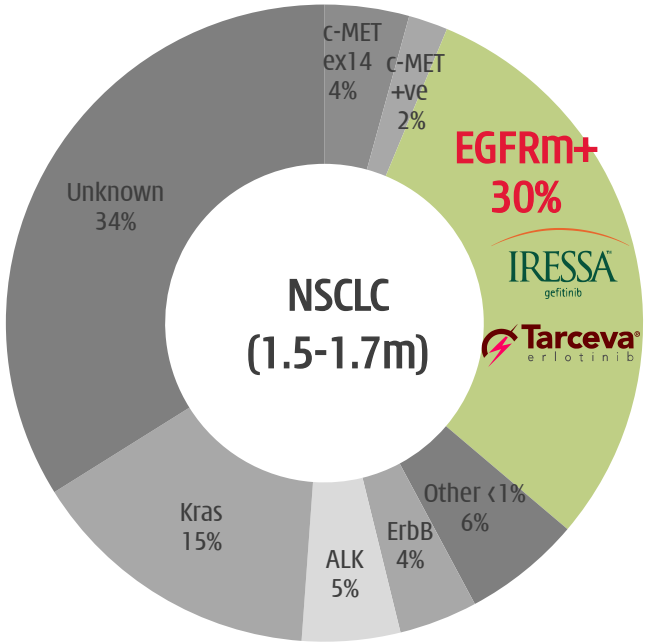
Xu R et al. J Clin Oncol 35, 2017 (suppl 4S; abstract 128); Wilke H et al. The Lancet Oncology, Volume 15, Issue 11, 1224 - 1235.

Fruquintinib: Phase II/III initiation in 2L gastric cancer expected H2 2017

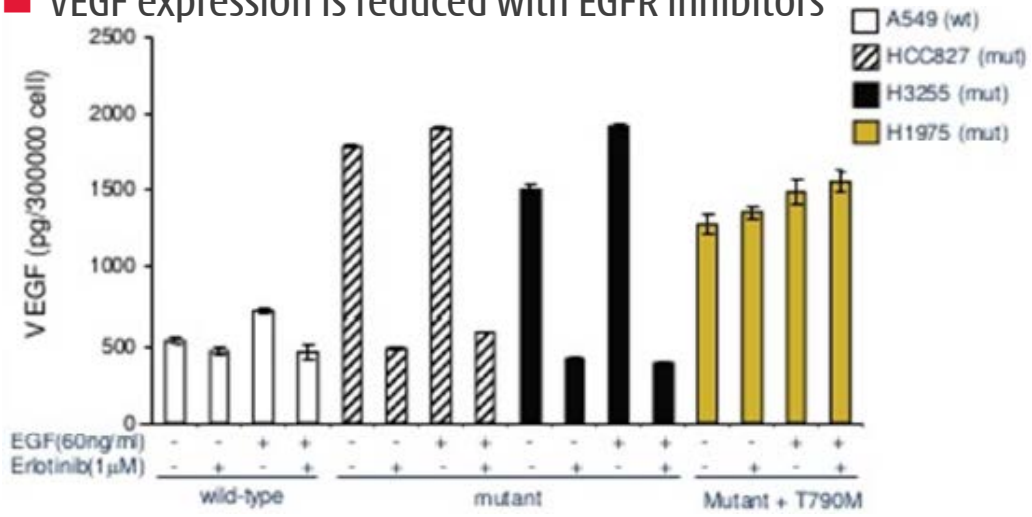


- Approximately 540 patients to be enrolled
- Interim analysis after the first 100 patients being treated
- Expect full enrollment by H2 2019
- Database close anticipated by H1 2020

Fruquintinib
Rationale for Combinations in EGFRm+ NSCLC



- EGFR mutant NSCLC cell lines express higher levels of VEGF
- VEGF expression is reduced with EGFR inhibitors

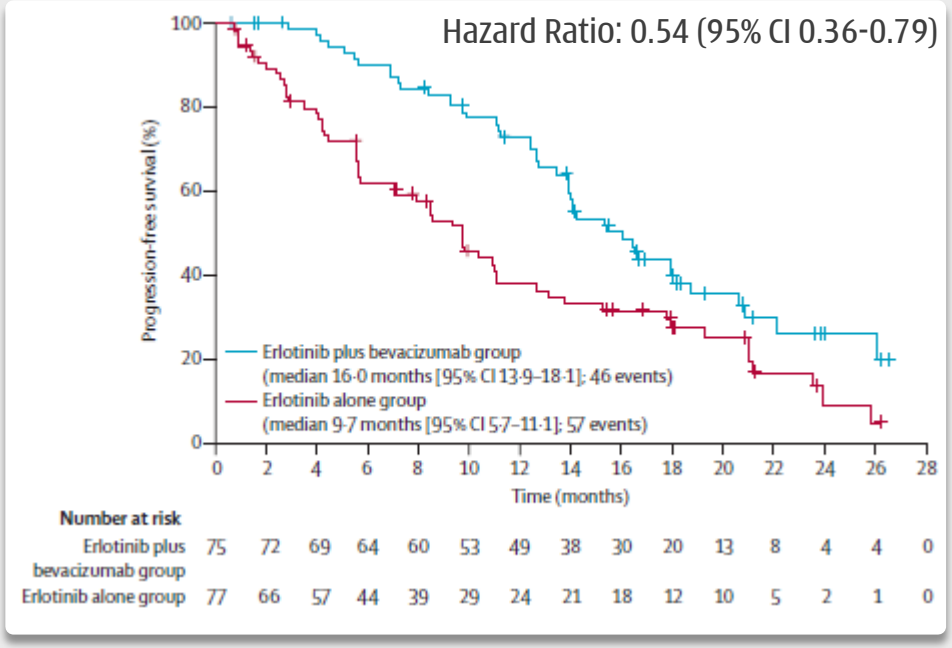


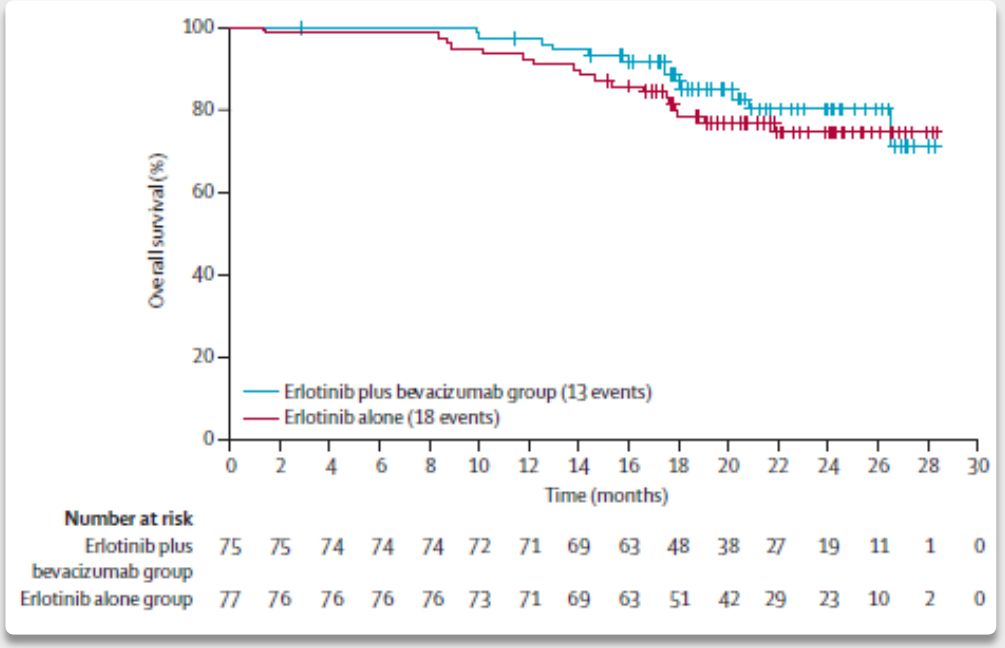
Heymach et al. ASCO 2014.

- Driver genetic alterations have been identified in nearly two thirds of NSCLC
- Tumors with driver genetic alterations, such as EGFR, secrete more VEGF and are more dependent on angiogenesis
- Blocking EGFR and VEGFR pathways simultaneously could represent a more effective treatment

EGFRm+ NSCLC

Pivotal Phase II comparing erlotinib vs erlotinib + bevacizumab (JO25567)





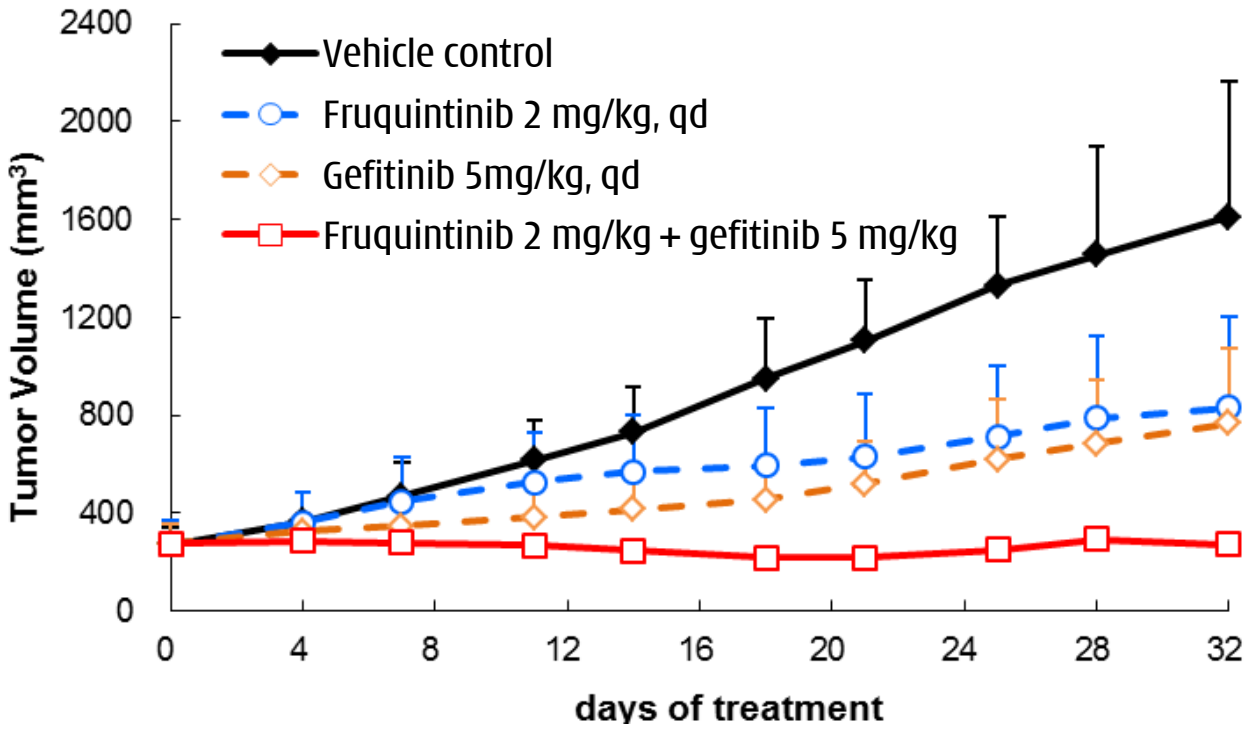
The Lancet Oncology, 2014, 15: 1236-1244

- Blocking EGFR and VEGFR simultaneously leads to significant improvement in PFS, but less clear in OS
- CHMP granted approval of erlotinib/bevacizumab combo in EU
- Toxicities are more difficult to manage with antibodies

Fruquintinib: EGFRm+ NSCLC

Targeting EGFR and VEGFR simultaneously with two oral TKIs could offer convenience and possible advantages in AE management

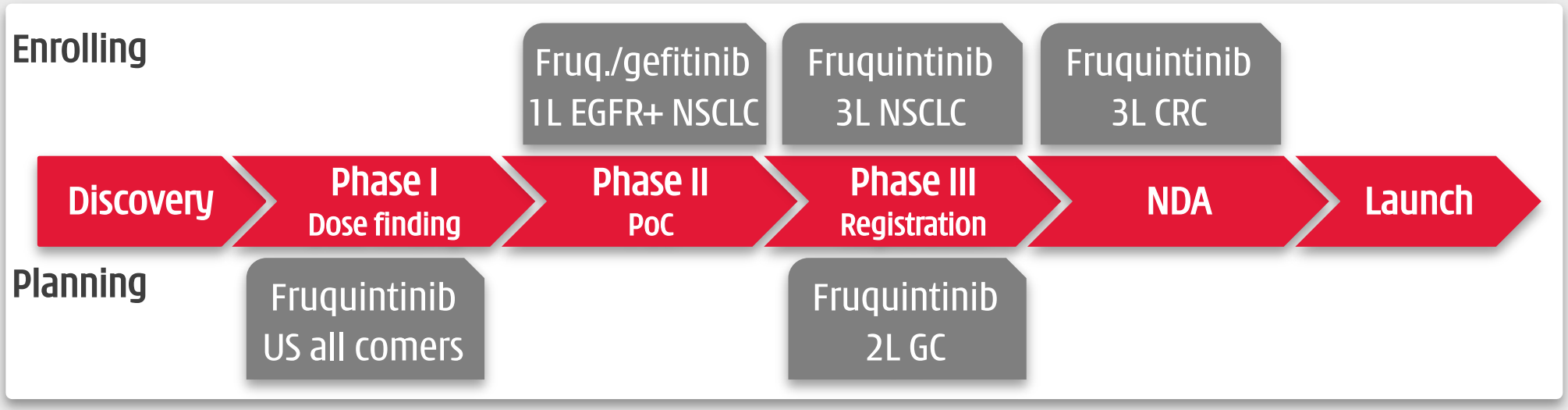
- Strong synergy was observed in animal models with fruquintinib / gefitinib combo
- Could fruquintinib / gefitinib combo be tolerated and able to provide benefit in patient?



Fruquintinib: EGFRm+ NSCLC
Summary

- Strong evidence that targeting EGFR and VEGFR simultaneously will provide significant benefit
- Using two oral TKIs could offer convenience and possibly better AE management
- Fruquintinib/gefitinib combo Phase II safety run in is in progress and expected to complete by YE 2017
- Phase II/III will follow once the safe dose has been confirmed
- Large patient population and long duration of treatment lead to significant market opportunity

Fruquintinib: what is the market potential for these indications?



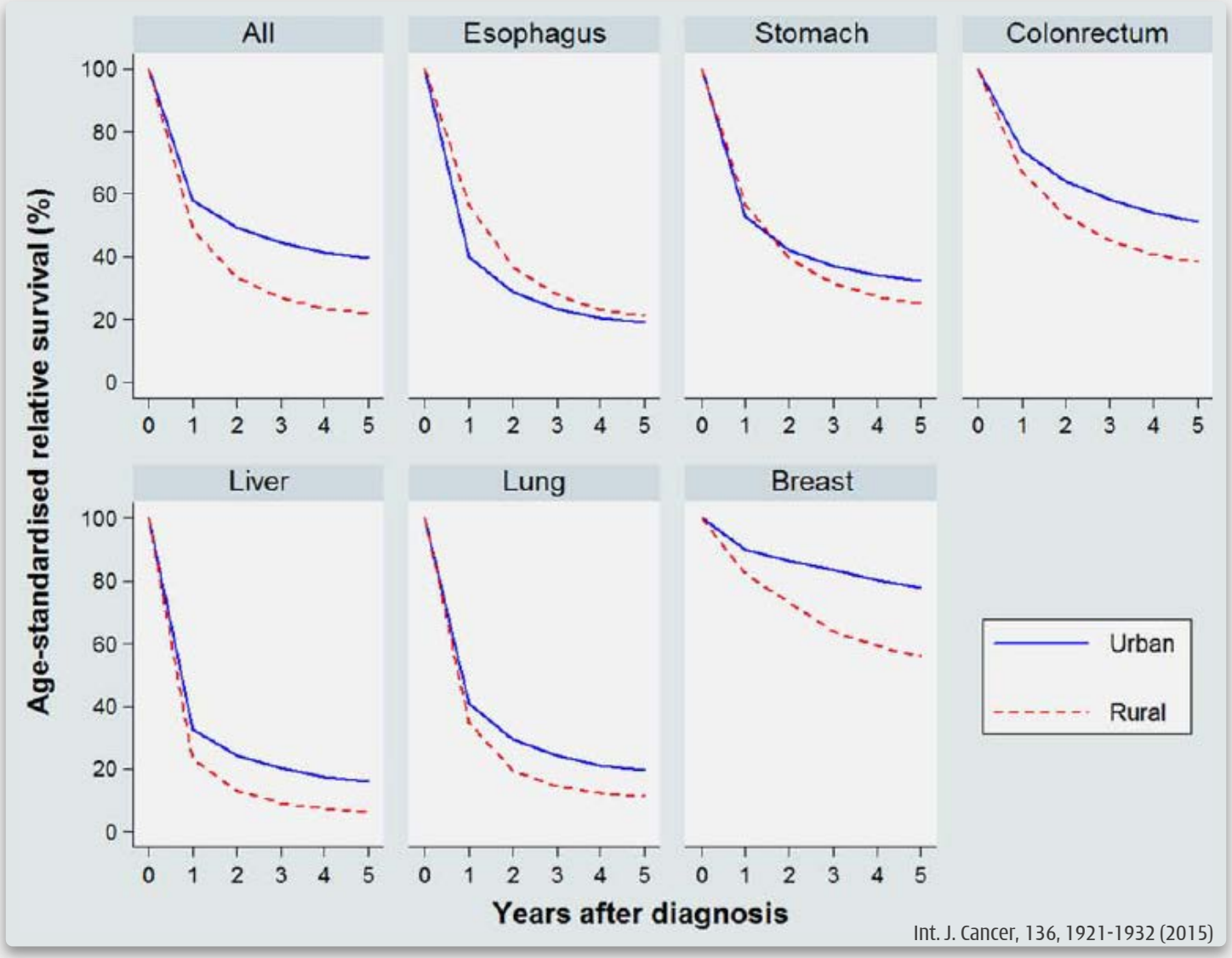
Patient population in China

TABLE 2. Estimated New Cancer Cases and Deaths (Thousands) by Sex: China, 2015*

CA Cancer J Clin 2016;66:115-132

SITE	ICD-10	INCIDENCE			MORTALITY		
		TOTAL	MALE	FEMALE	TOTAL	MALE	FEMALE
Lip, oral cavity, & pharynx (except nasopharynx)	C00-C10, C12-C14	48.1	31.1	16.9	22.1	15.3	6.8
Nasopharynx	C11	60.6	43.3	17.3	34.1	24.9	9.2
Esophagus	C15	477.9	320.8	157.2	375.0	253.8	121.3
Stomach	C16	679.1	477.7	201.4	498.0	339.3	158.7
Colorectum	C18-C21	376.3	215.7	160.6	191.0	111.1	80.0
Liver	C22	466.1	343.7	122.3	422.1	310.6	111.5
Gallbladder	C23-C24	52.8	24.5	28.3	40.7	18.8	21.8
Pancreas	C25	90.1	52.2	37.9	79.4	45.6	33.8
Larynx	C32	26.4	23.7	2.6	14.5	12.6	1.9
Lung	C33-C34	733.3	509.3	224.0	610.2	432.4	177.8
Other thoracic organs	C37-C38	13.2	8.2	5.0	6.5	4.1	2.3
Bone	C40-C41	28.0	16.4	11.6	20.7	12.4	8.3
Melanoma of the skin	C43	8.0	4.3	3.7	3.2	1.8	1.5
Breast	C50	272.4	3.8	268.6	70.7	1.2	69.5
Cervix	C53	98.9	—	98.9	30.5	—	30.5
Uterus	C54-C55	63.4	—	63.4	21.8	—	21.8
Ovary	C56	52.1	—	52.1	22.5	—	22.5
Prostate	C61	60.3	60.3	—	26.6	26.6	—
Testis	C62	4.0	4.0	—	1.0	1.0	—
Kidney	C64-C66, C68	66.8	43.2	23.6	23.4	15.2	8.2
Bladder	C67	80.5	62.1	18.4	32.9	25.1	7.8
Brain, CNS	C70-C72	101.6	52.3	49.3	61.0	35.8	25.2
Thyroid	C73	90.0	22.2	67.9	6.8	2.5	4.3
Lymphoma	C81-C85, C88, C90, C96	88.2	53.0	35.2	52.1	32.7	19.4
Leukemia	C91-C95	75.3	44.4	30.9	53.4	32.0	21.3
All other sites and unspecified	A_O	178.1	95.5	82.6	94.0	55.0	39.0
All sites	**ALL**	**4291.6**	**2512.1**	**1779.5**	**2814.2**	**1809.9**	**1004.4**

Cancer survival rates in China

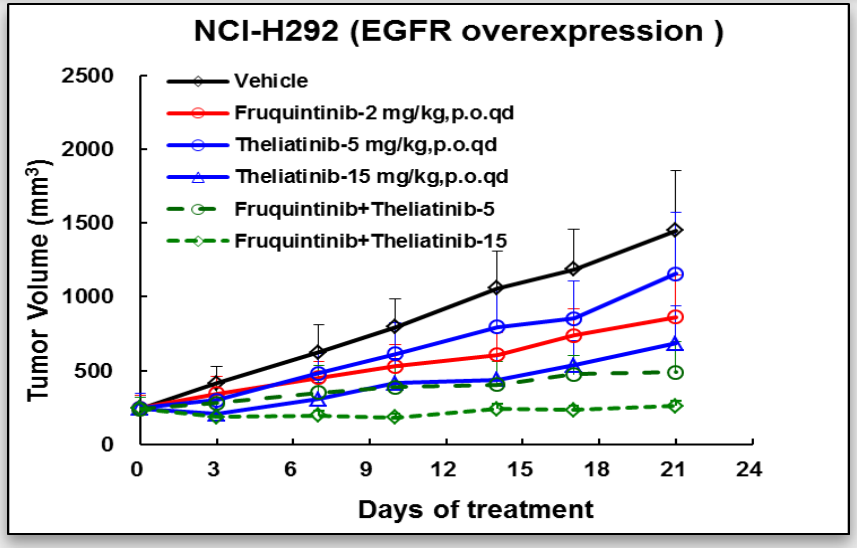


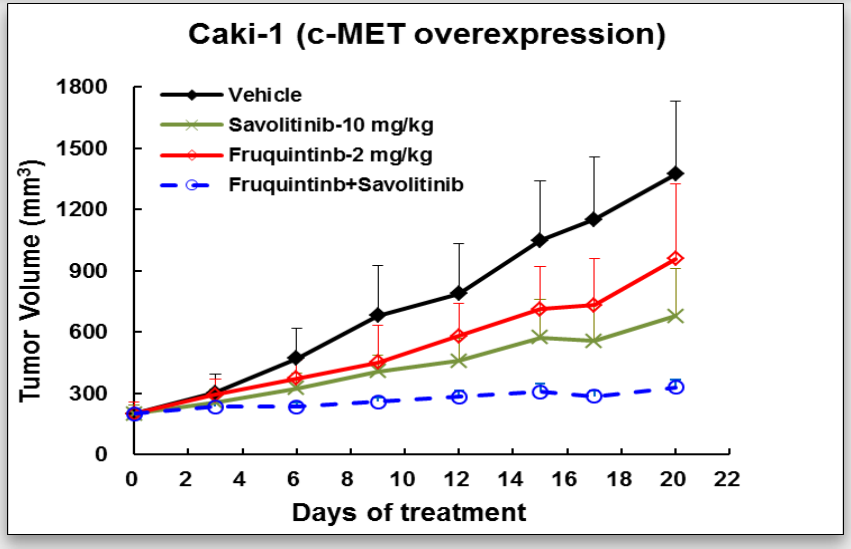
Int. J. Cancer, 136, 1921-1932 (2015)

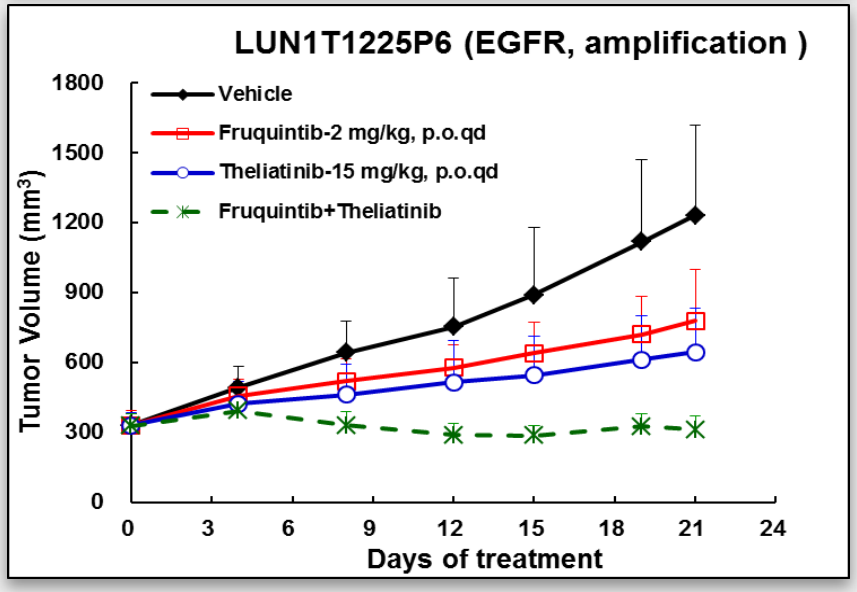
Fruquintinib: possible development opportunities

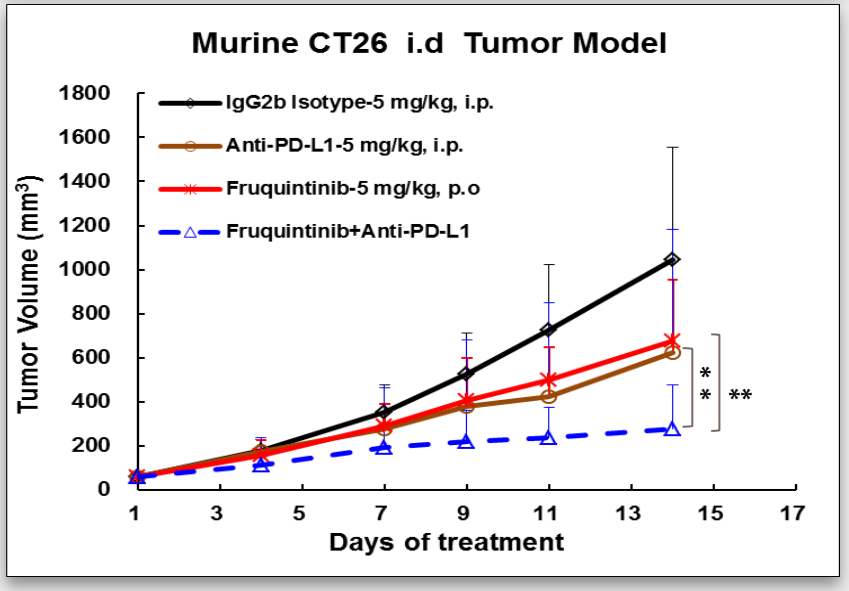
- **Leveraging on overall favorable clinical safety and tolerability**
  - 1L in high risk patient population: NSCLC, CRC, GC, etc for fast track registration potential
  - 2L monotherapy comparing to chemotherapy standard-of-care (SOC)
- **Exploring VEGFR3 activity**
  - 3L NSCLC, GC, etc behind ramucirumab as monotherapy for rapid registration potential outside China
  - Breast cancer where bevacizumab and ramucirumab both failed
- **Leveraging on ability to combine**
  - With chemotherapies
    - paclitaxel / pemetrexed in GC/BC/NSCLC
    - gemcitabine in pancreatic, biliary cancers
  - with therapies that target driver genes: EGFR, ALK, HER2, c-MET etc in 1L and 2L
  - With immuno-oncology therapies (IOs): anti-PD-1/PD-L1 in 1L and 2L
- **Overcoming VEGFR inhibitor resistance in combo with:**
  - HDAC inhibitor in RCC
  - c-MET inhibitor in RCC, NSCLC, GC, CRC

Fruquintinib as the backbone for the treatment in 1, 2 and 3L









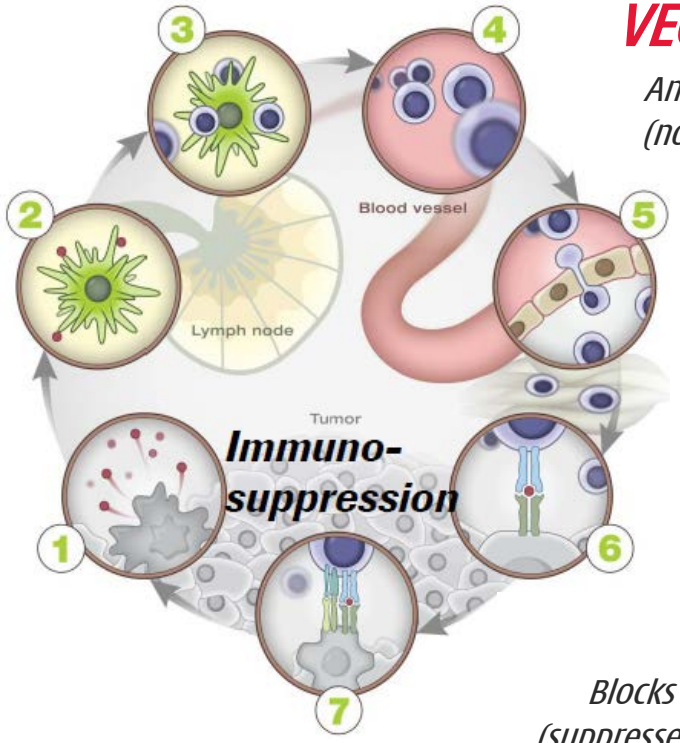
Sulfatinib

A selective angio-immunokinase inhibitor

Sulfatinib: an angio-immunokinase inhibitor

Kinase	IC_{50} (μM)
VEGFR 1	0.002
VEGFR 2	0.024
VEGFR 3	0.001
FGFR1	0.015
CSF-1R	0.004
TrkB	0.041
FLT3	0.067
278 other kinases	›0.150

Unique angio-immuno kinase profile & MoA activates & enhances the immune system (T-cells), via VEGFR/FGFR while inhibiting production of macrophages (CSF-1R) which cloak cancer cells.



VEGFR / FGFR

Anti-angiogenesis (normalizes tumor vasculature)

FGFR

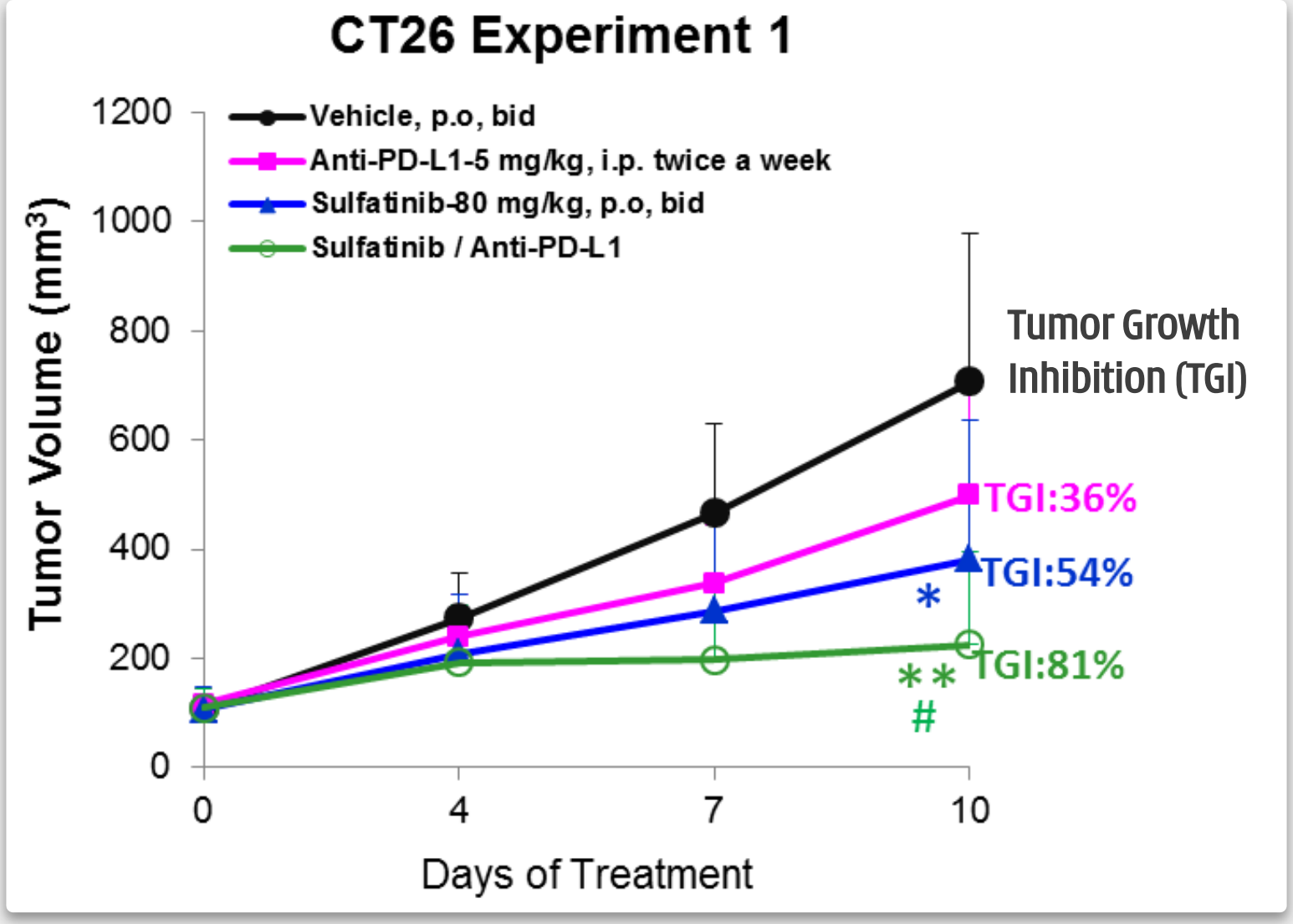
Antigen release (activation of T-cells)

CSF-1R

Blocks negative regulators (suppresses M1 to M2 conversion)

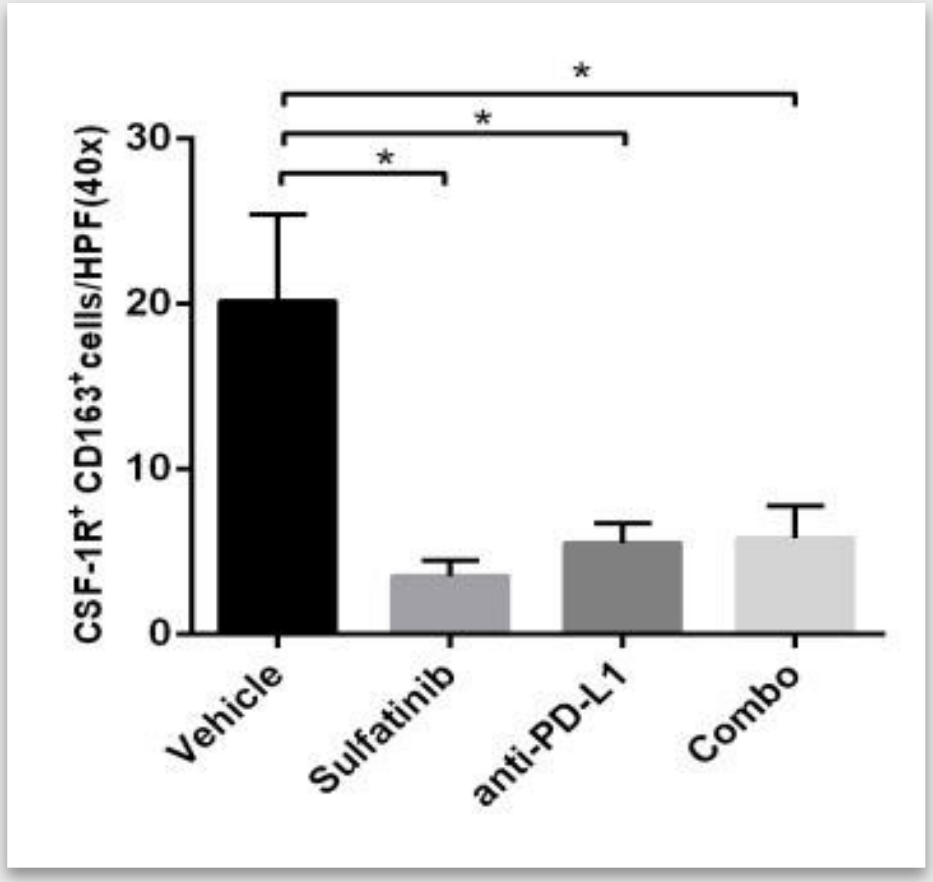
 Derived from Chen DS et al. Oncology Meets Immunology: The Cancer-Immunity Cycle. Immunity , Volume 39 , Issue 1 , 1 - 10.

Sulfatinib
Synergistic effect in combo with PD-L1 inhibitor

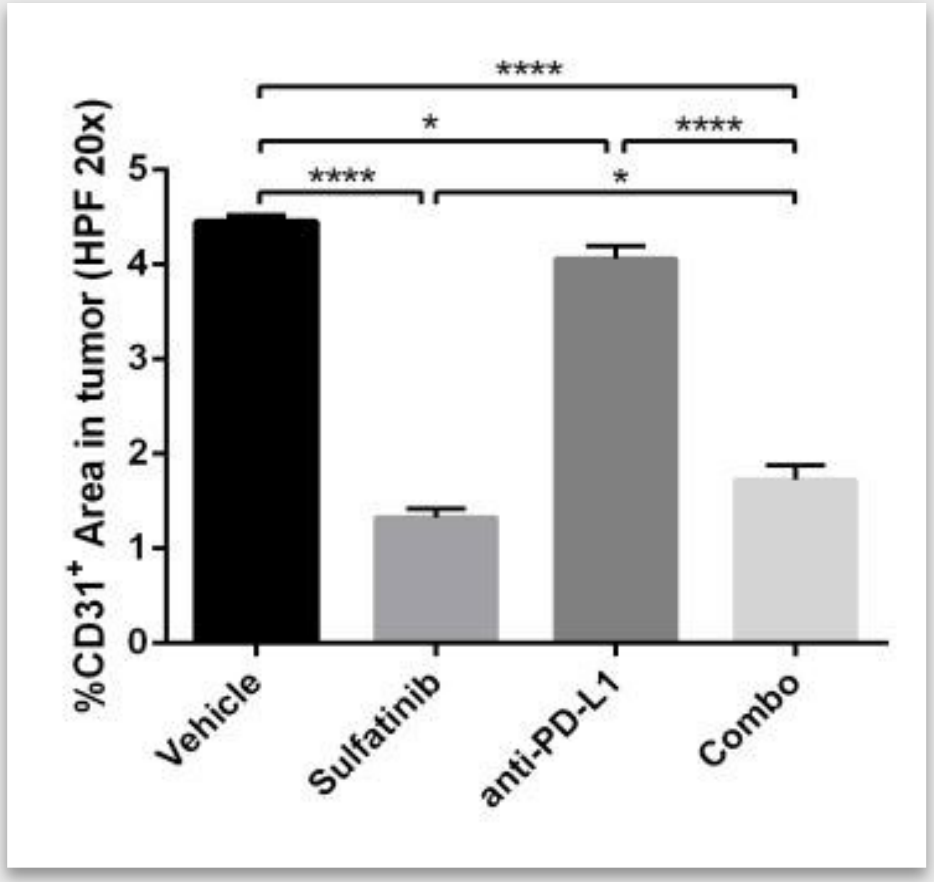


Sulfatinib
Strong effect on TAM and angiogenesis

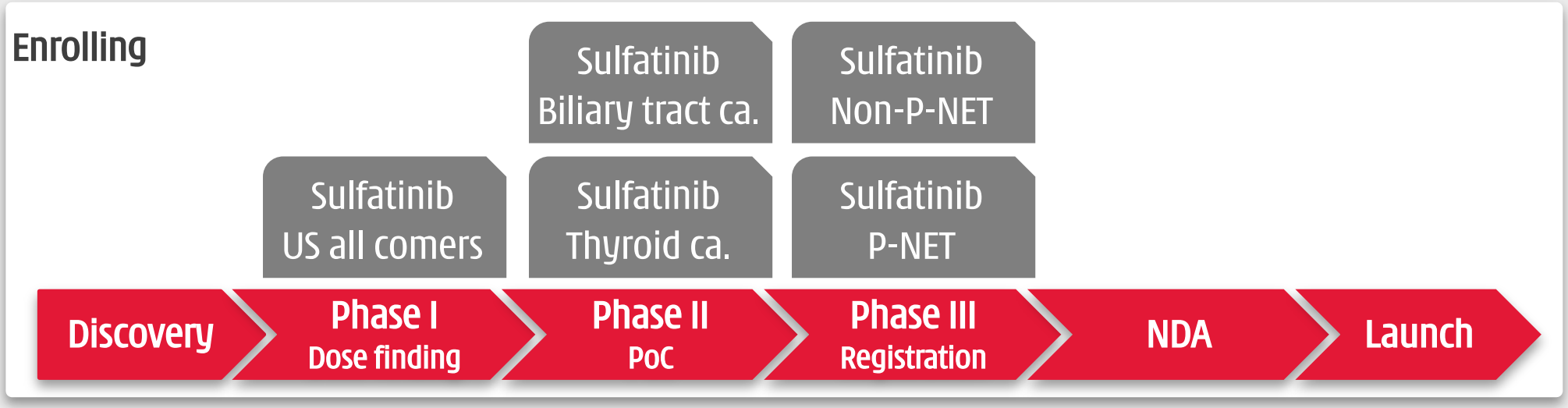
Tumor Associated Macrophages



Angiogenesis



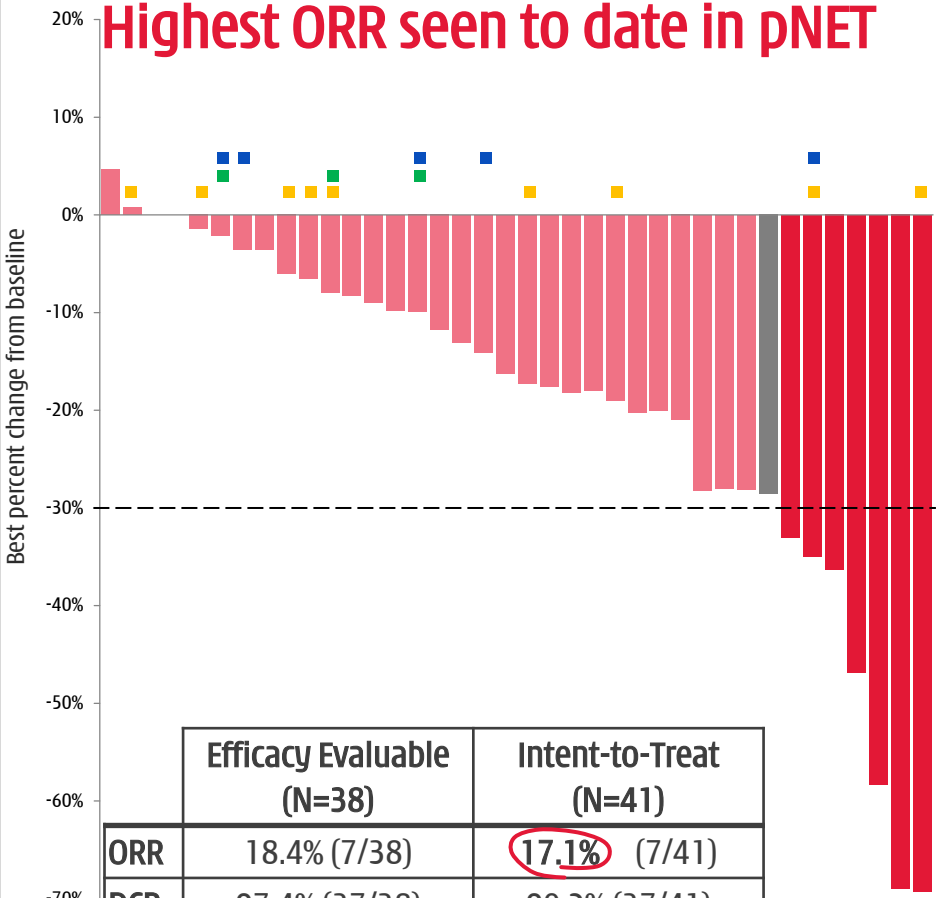
Sulfatinib: ongoing trials



Sulfatinib proof of concept in NET:
81 patients, single arm

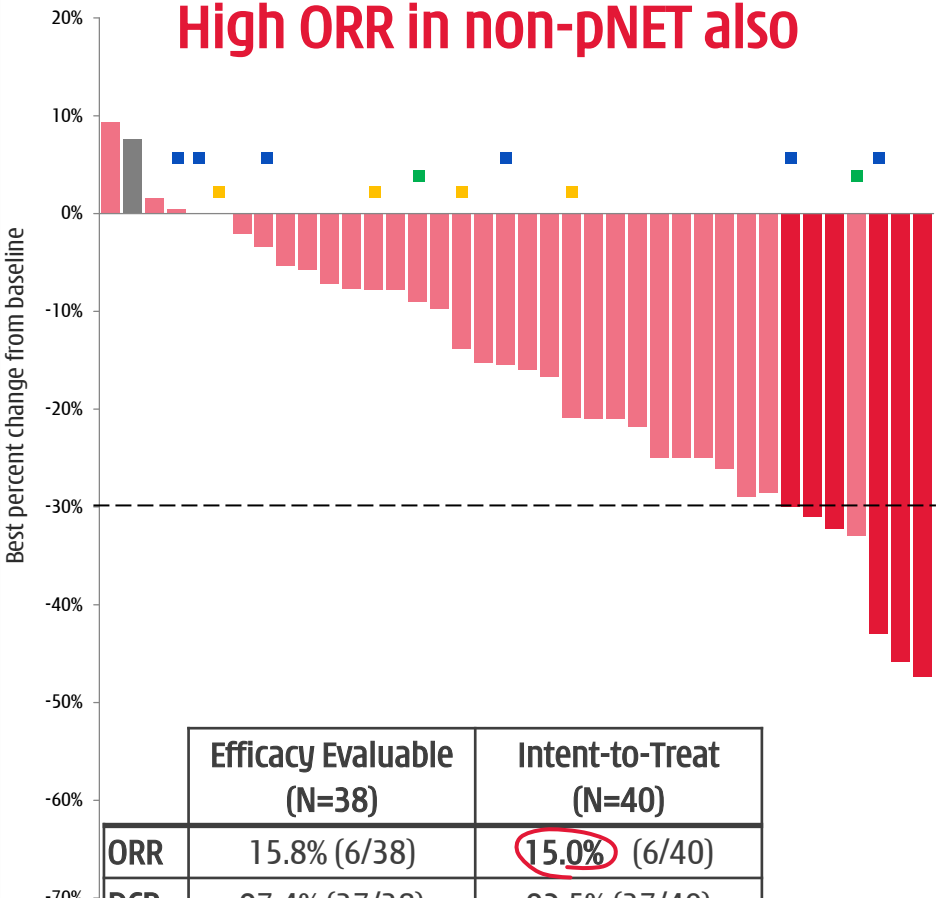
CHI-MED

Pancreatic NET –
Highest ORR seen to date in pNET



	Efficacy Evaluable (N=38)	Intent-to-Treat (N=41)
ORR	18.4% (7/38)	17.1% (7/41)
DCR	97.4% (37/38)	90.2% (37/41)

Non-Pancreatic NET –
High ORR in non-pNET also



	Efficacy Evaluable (N=38)	Intent-to-Treat (N=40)
ORR	15.8% (6/38)	15.0% (6/40)
DCR	97.4% (37/38)	92.5% (37/40)

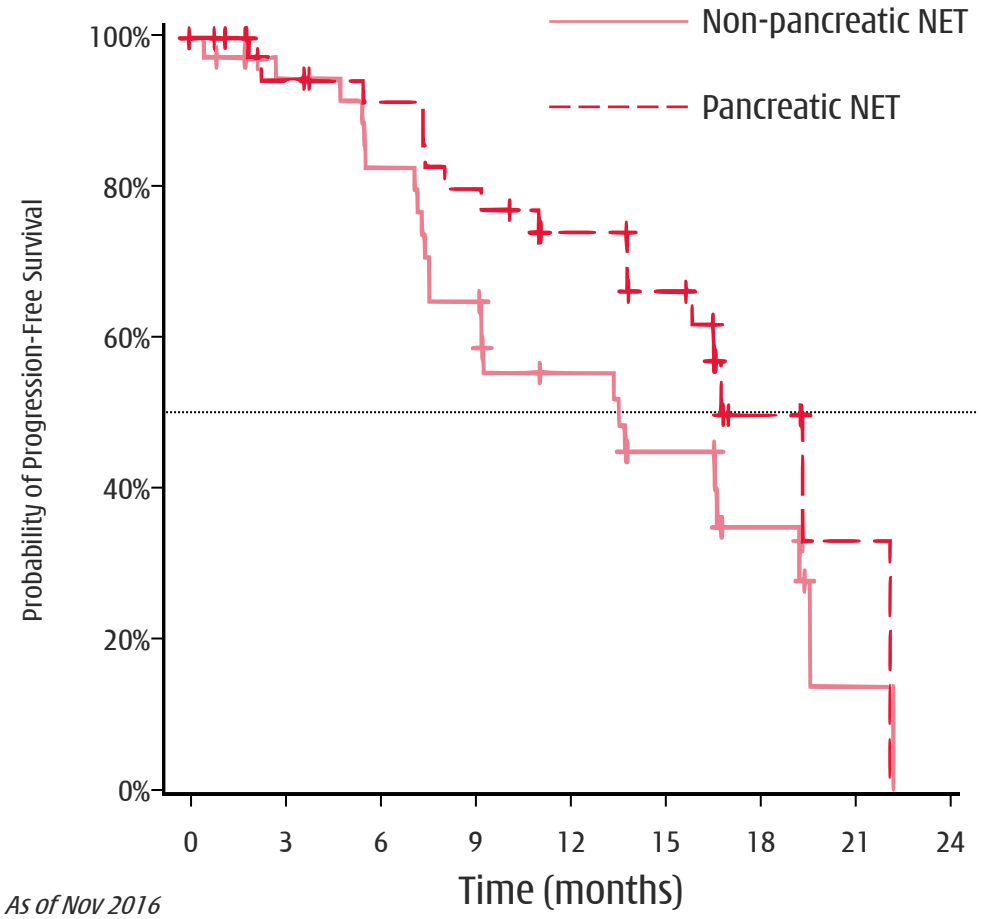
Partial Response | Stable Disease | Progressive disease | Prior Afinitor® | Prior Famitinib (VEGFR) | Prior Sutent®

European Neuroendocrine Tumour Society Conference 2017. Data cut-off as of Jan 20, 2017.

Sulfatinib proof of concept in NET:
81 patients, single arm

CHI-MED

Progression-Free Survival (PFS)



As of Nov 2016

	Median PFS (months)	PDs / Deaths (% pts)
All NET (81)	16.6m (13.6, 19.4)	48.1% (39/81)
P-NET (41)	19.4m (13.9, 22.1)	39.0% (16/41)
Non-P NET (40)	13.6m (7.6, 19.3)	57.5% (23/40)

Safety
- Well tolerated
- Adverse Events manageable

	Grade ≥3 (≥4pts) n (%)
Hypertension	25 (30.9)
Proteinuria	11 (13.6)
Hyperuricemia	8 (9.9)
Hypertri-glyceridemia	7 (8.6)
Diarrhea	6 (7.4)
ALT increased	5 (6.2)
Anemia	4 (4.9)
Hypokalemia	4 (4.9)
Hepatic function abnormal	4 (4.9)

Adverse Events ("AEs") - Regardless of causality	N=81 n (%)
Any AE	81 (100)
Grade ≥3 AE	63 (77.8)
Any SAE	21 (25.9)
Any drug-related AE	81 (100)
Any drug-related Gr ≥3 AE	58 (71.6)
Any drug related SAE	10 (12.3)
Drug related AE leading to:	
dose interruption	40 (49.4)
dose reduction	20 (24.7)
drug withdrawal	7 (8.6)

European Neuroendocrine Tumour Society Conference 2017. Data cut-off as of Jan 20, 2017.

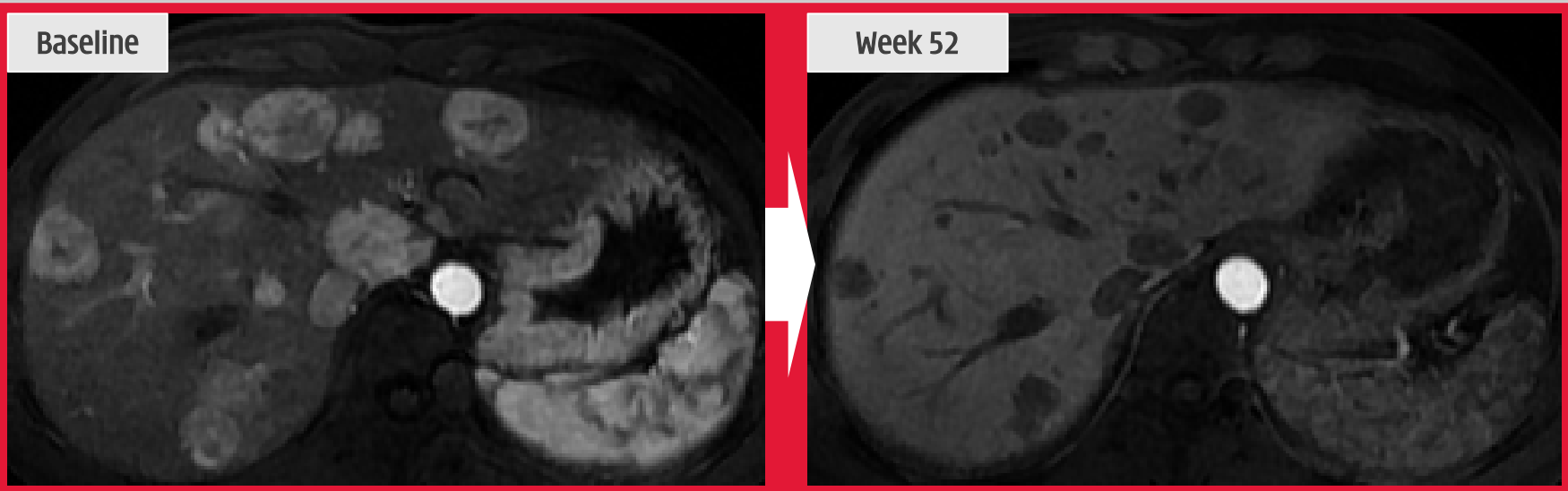
Sulfatinib proof of concept in NET

CHI-MED

Patient 1

Duodenum NET G2

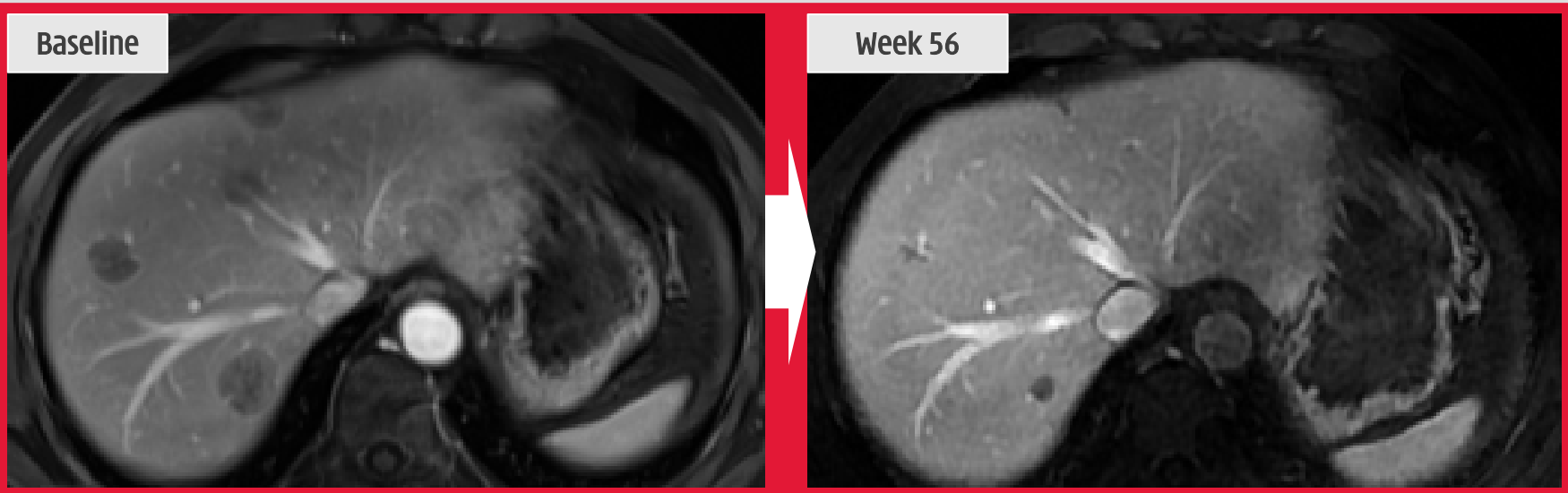
w/ multiple liver & retroperitoneal lymph node metastases



Patient 2

Rectum NET G2

w/ multiple liver metastases



Sulfatinib
Unmet medical need

- Neuroendocrine tumor therapeutic area is very fragmented
- NET incidence 7/100,000 (ENETS 2017) & prevalence rising
- No therapies approved across all NET types
- Unmet medical needs both in induction of response and maintenance
- Longer survival translates into the need for multiple therapeutic options

	Somatostatin Based Therapies			Kinase Inhibitor Therapies		
	Sandostatin® (octreotide)	Somatuline Depot® (lanreotide)	Lutathera® (^{177}Lu-Dotatate) [3]	Afinitor® (everolimus)	Sutent® (sunitinib)	Sulfatinib
PRIMARY TUMOR SITE						
Pancreas (6% NET)	×	×	×	✓	✓	✓
Entire GI tract (67% NET)	×	✓	×	✓	×	✓
with Mid-gut (20% NET)	✓	✓ *(Ki67‹10%)*	✓	✓	×	✓
Lung & Thymus (27% NET)	×	×	×	✓	×	✓
Other	×	×	×	×	×	✓
Median PFS (months)	14.3	NR	Est. ~40.0 (mid-gut)	11.0 (p) 11.0 (lung & GI)	11.4	19.4 (p) 13.6 (All non-p)
Objective Response Rate [1]	2%	NR	18% (mid-gut)	5% (p) 2% (lung & GI)	9%	17.1% (p) 15.0 % (All non-p)
Disease Control Rate [2]	69%	NR	95% (mid-gut)	73% (p) 81% (lung & GI)	72%	90.2% (p) 92.5% (All non-p)

[1] ORR = percent of patients with ›30% tumor diameter shrinkage; [2] DCR = percent of patients with tumor diameter growth ‹20%.
Sources: Prescribing Information; ENETS 2017.

Sulfatinib – Two Registration Trials
SANET-p and SANET-ep

	Pancreatic NET Phase III (SANET-p)	Non-Pancreatic NET Phase III (SANET-ep)
Primary site	Pancreas	GI, lung, other or unknown
Population	Unresectable or metastatic disease; well differentiated (G1/G2); ≤2 prior systemic drugs.	
# of Sites	20-30 (China)	
# of Patients	~195	~270
Study design	Double-blind. Randomized 2:1 to sulfatinib or placebo, treat until PD. Predefined interim analysis.	
Dosage	Sulfatinib 300mg QD, 28 days per cycle (vs. placebo)	
Primary Endpoint	Progression-Free Survival (PFS) by BICR evaluation	
Secondary Endpoints	Overall Survival (OS), ORR, safety, etc.	
First Patient In / Readout	March 2016 / 2018	December 2015 / 2018

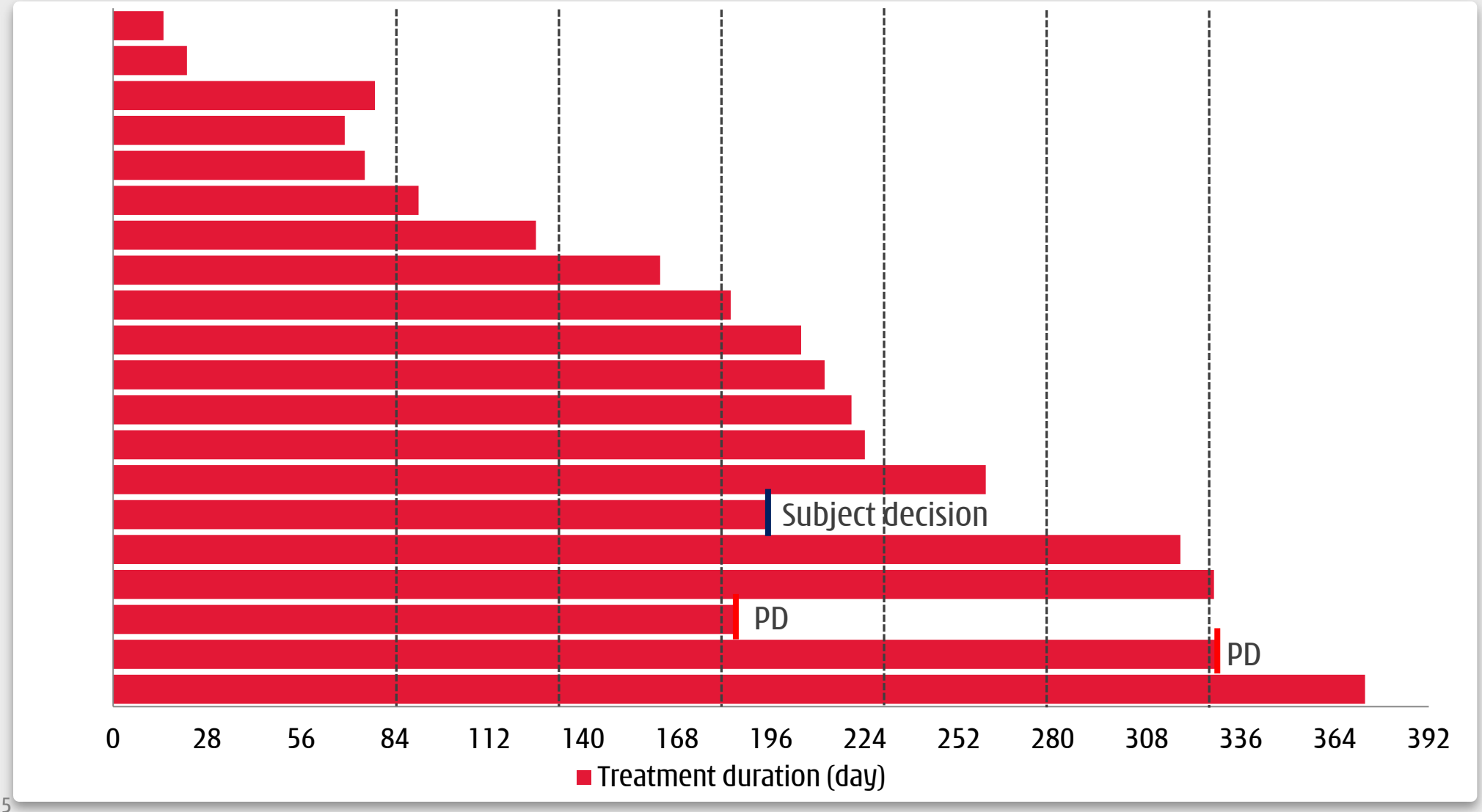
Sulfatinib: PoC study in thyroid cancer

Rapidly rising incidence and prevalence in China, major unmet medical need

Clinical trials	Phase 2, POC study
Patients	Advanced MTC and I^{131} refractory DTC
Sites	6-8 sites
Study design (Simon's two-stage design)	In the first stage, 15 subjects will be enrolled in both subgroups (advanced MTC and I131 refractory DTC), if at least 2 subjects have objective response, another 10 subjects will be enrolled in each subgroup in the second stage
Study treatment	Sulfatinib 300mg/qd, 28 days of each cycle
# of subjects	30-50
Study duration	24-28 months (enrollment: 12 months; follow up 16 months)
Primary objective	ORR
Secondary objective	DCR, DoR, PFS, TTP and safety, etc.

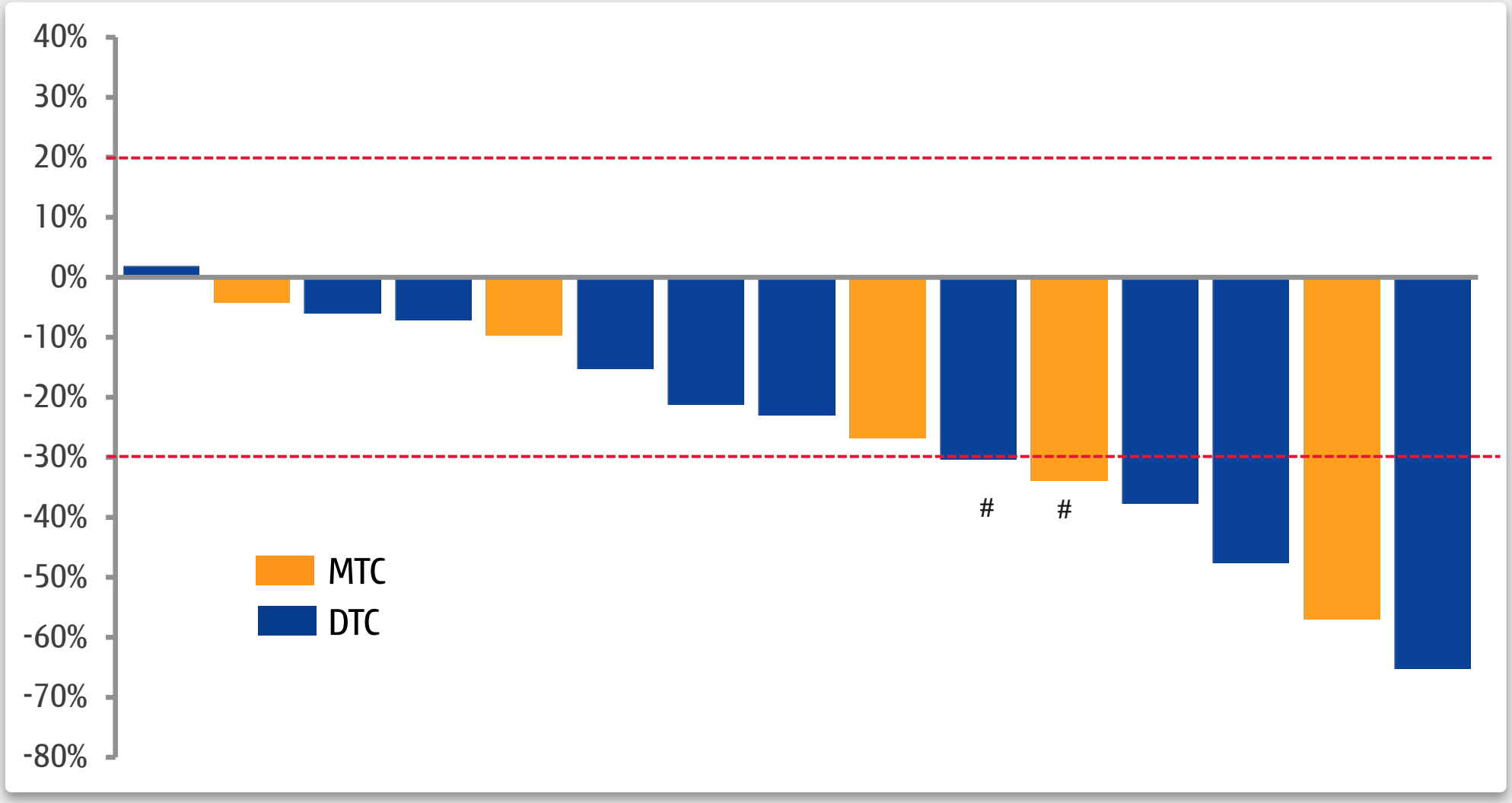
Sulfatinib: PoC study in thyroid cancer

Duration of treatment (as of March 8, 2017)



Sulfatinib: PoC study in thyroid cancer

Best tumor response



PR unconfirmed

Sulfatinib: PoC study in biliary tract cancer

few treatment options after gemcitabine, mOS ~6 months

Clinical trials	Phase 2, POC study
Patients	Unresectable, metastatic BTC who progressed after 1st line chemotherapy
Sites	5 sites
Study design (two-stage design)	First stage: 16 subjects will be enrolled Second stage: additional 16 subjects will be enrolled, if ≥ 4 subjects remain progression free in first stage *(Null hypothesis 16 week PFS rate≤16%, alternative hypothesis 16 week PFS rate ≥40%; Power 90%)*
Study treatment	Sulfatinib 300mg/qd, 28 days of each cycle
Planned # of subjects	16-32
Study duration	12-18 months (enrollment: 12 months; follow up 6 months)
Primary objective	16 Week PFS Rate

Sulfatinib
Summary and future development plans

CHI-MED

Summary

- Unique angio-immuno MOA: mainly VEGFR activity with partial contribution from FGFR1/CSF-1R
- Promising clinical efficacy in NETs, including VEGFRi and mTORi failures
- Good safety profile following once daily dosing, hypertension and proteinuria (on-target AEs) readily manageable
- 2 pivotal trials ongoing with possible first readout in 2018
- Multiple PoC trials ongoing/planned

Future development plans

- Late line therapy for NETs in the US: possibly fastest registration pathway
- Possible additional new indications: SCLC (NEC), RCC, breast cancer
- Novel combinations such as immuno-oncology therapies (IO)

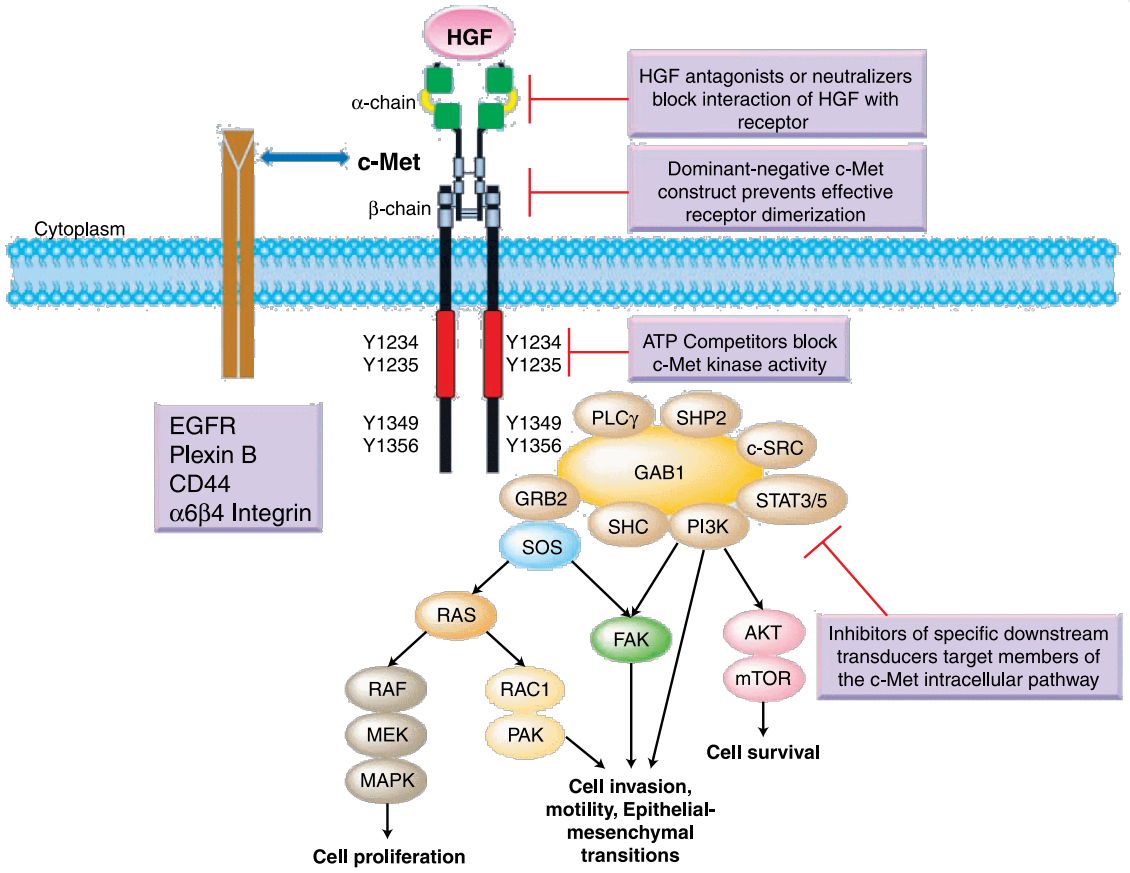
Coffee Break

10 minutes

Savolitinib

Highly selective c-MET kinase inhibitor

Savolitinib: c-MET genetic alterations drive multiple cancers



Joseph Paul Eder, et al, Novel Therapeutic Inhibitors of the c-MET Signaling Pathway in Cancer, Clin Cancer Res 2009;15(7)

- Aberrant HGF/c-MET pathway activation leads to uncontrolled tumor cell growth, invasion and survival
- Four different mechanisms of c-MET pathway activation:
  - ↗ c-MET gene amplification
  - ↗ HGF/c-MET over-expression
  - ↗ Mutations
  - ↗ Cross talk with other receptors
- Aberrant HGF/c-MET axis activation has been detected in multiple major tumor types, including lung, stomach, RCC, CRC and HCC

Savolitinib: c-MET aberrance detected in many tumor types

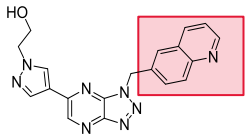
- Driver genetic alterations are often low incidence, fragmented, across multiple tumor types
- Tumors with driver genetic alterations may respond to savolitinib single agent and best chance of BTT
- Tumors with c-MET overexpression may require combination therapy, but represent much larger population

c-MET ABERRATIONS	"Driver" alterations		"Passenger" alterations
Tumor type	Ampli-fication	Mutation	Over-Expression
Gastric	5-10%	1%	42-46%
NSCLC primary	2-4%	3-4% (Exon 14)	67%
NSCLC EGFRm+ TKI resistant (co-drivers)	10-20%		
Head & Neck		11%	52%
Colorectal (Erbitux resistant)	12.5%		65%
Renal Cell Carcinoma (Papillary)	40-70%	100% (hereditary)	100%
Renal Cell Carcinoma (Clear cell)			78%
Esophagus	3.4%		92%

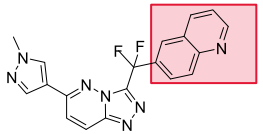
Savolitinib: key features

- Designed to eliminate the quinolone metabolite in humans that was reported to be associated with kidney toxicity
- Highly potent and selective against c-MET kinase
- Good pharmacokinetic and safety profile in preclinical evaluations

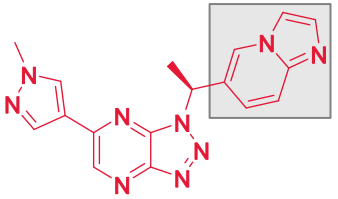
›460 patients treated to-date with no serious renal toxicity



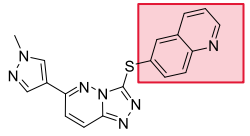
Pfizer
PF-04217903



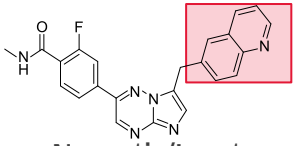
Janssen
JNJ-38877605



savolitinib

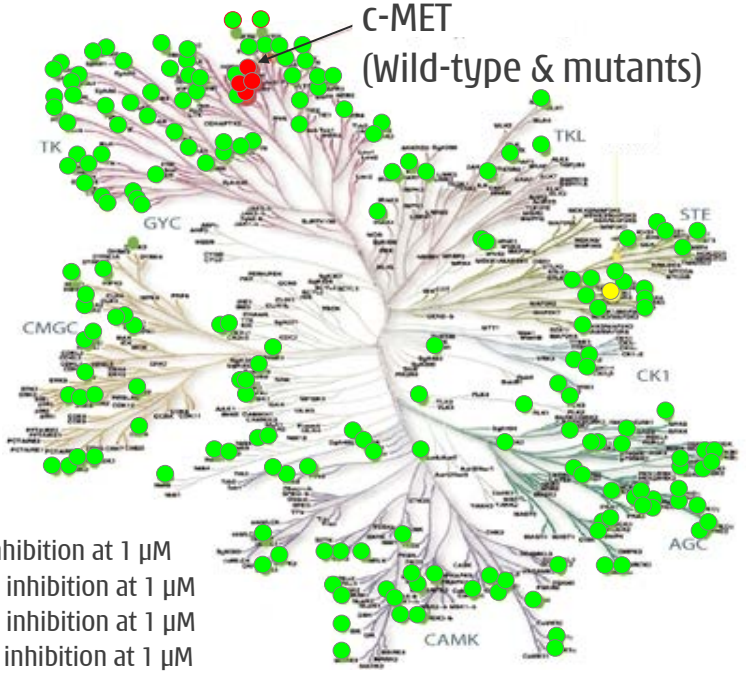


Lilly
SGX-523



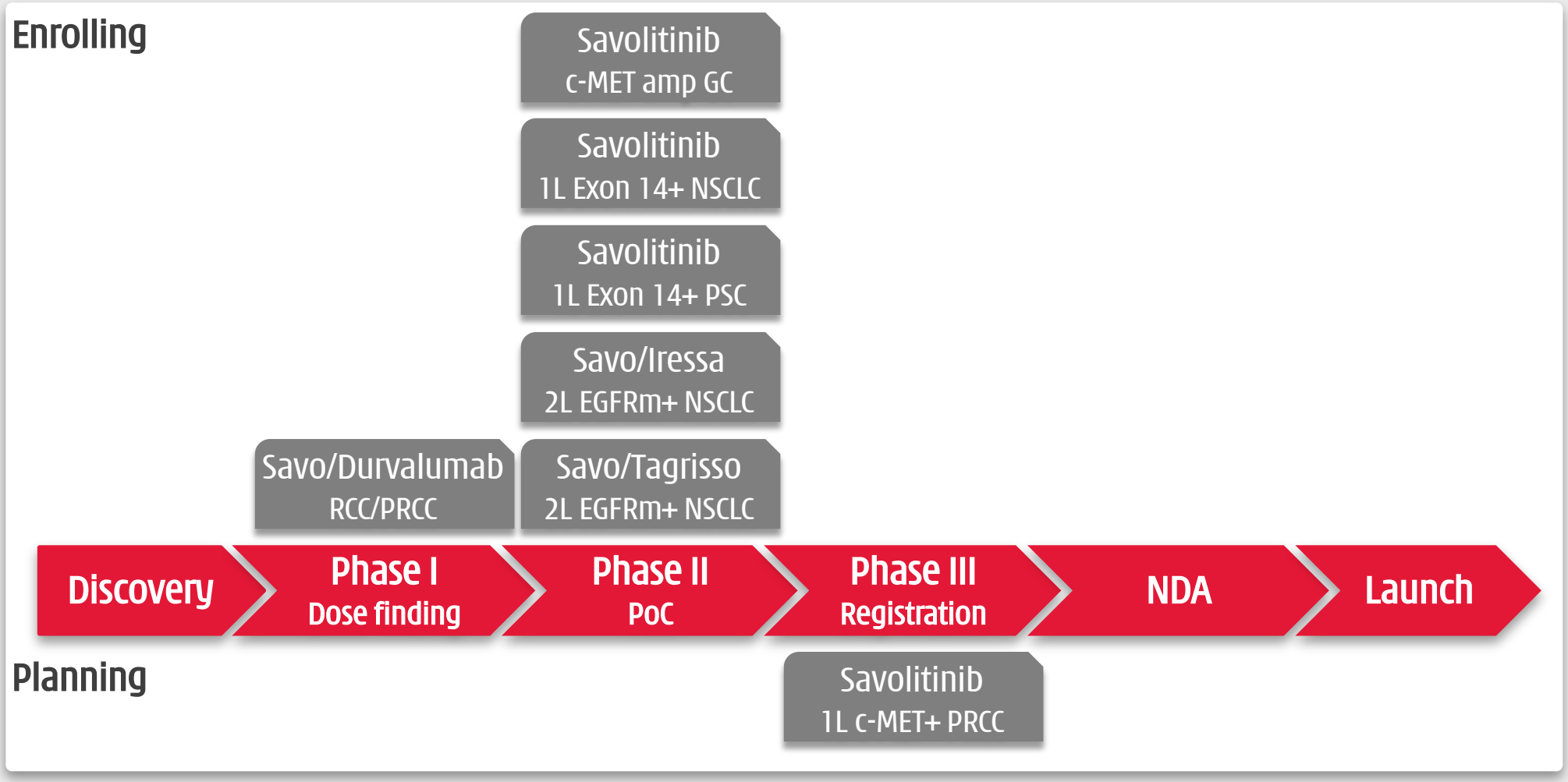
Novartis/Incyte
INC-280

2-quinolinone metabolite in humans in 1st gen c-MET compounds has dramatically reduced solubility and appeared to crystallize in the kidney resulting in obstructive toxicity.



Sources: Diamond, S.; et. al.: Species-specific metabolism of SGX523 by aldehyde oxidase, Drug Metabolism and Disposition, 2010, 38, 1277-85.. W. Su, et al, 2014 American Association of Cancer Research.

Savolitinib:
Ongoing clinical trials (key trials only)



Savolitinib: c-MET+ PRCC clear unmet medical need

CHI-MED

1. No treatment choices for non-ccRCC patients.

Approved therapies in RCC [3]

Good efficacy in ccRCC; Multiple treatment options

FIRST LINE – clear-cell RCC [4]	ORR	mPFS	mOS
Placebo (avg. multiple studies)	~2%	~3.5	~15.0
Interferon-α	6%	5.0	21.8
Sorafenib (VEGFR, multi-kinase SM) (avg. multiple studies)	~12%	~6.0	~21.0
Sunitinib (VEGFR, multi-kinase SM) (avg. multiple studies)	~28%	~10.5	~27.0
Pazopanib (VEGFR, multi-kinase SM)	31%	10.5	28.4
Axitinib (VEGFR, multi-kinase SM)	32%	10.1	21.7
SECOND LINE – clear-cell RCC			
Placebo	~0%	~2.0	~14.0
Cabozantinib (VEGFR/c-MET, multi-kinase SM). *(METEOR)*	17%	7.4	21.4
Everolimus (mTOR). *(METEOR)*	3%	3.9	16.5
Everolimus (mTOR). *(CheckMate025)*	5%	4.4	19.6
Nivolumab (PD-1 mAb). *(CheckMate025)*	25%	4.6	25.0

Nothing approved in non-ccRCC

NCCN guideline – "Patients should enter clinical trials"

FIRST LINE – non clear-cell RCC	ORR	mPFS	mOS
Sunitinib (VEGFR, multi-kinase SM) [4]	9%	6.1	16.2
Everolimus (mTOR) [4]	3%	4.1	14.9
SECOND LINE – non-clear-cell RCC			
Sunitinib (VEGFR, multi-kinase SM) [4]	10%	1.8	na
Everolimus (mTOR) [4]	9%	2.8	na

2. RCC est. ~$3.3 bln. market by 2020 [1]

Clear-cell RCC (~$2.7b)
~80% of RCC
~ 270k new patients/yr.[2]

Non-Clear-cell RCC (~$0.6b)
~20% of RCC
~ 70k new patients/yr.[2]

3. Two crucial questions:

c-MET +ve Papillary RCC (~$0.2-0.3b)
~7% of RCC
~ 25k new patients/yr.[2]

c-MET -ve Papillary RCC (~$0.2-0.3b)
~7% of RCC
~ 25k new patients/yr.[2]

Other non-ccRCC (~$0.1-0.2b)
~5% of RCC
~ 20k new patients/yr.[2]

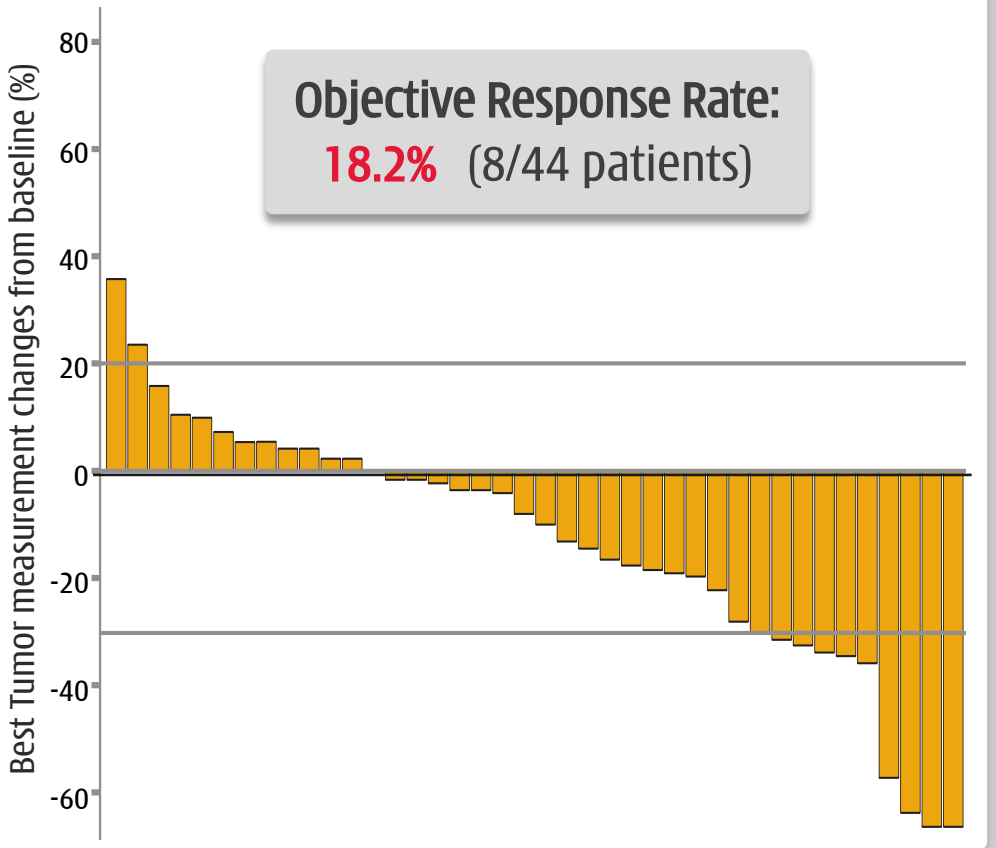
Question 1: Does savolitinib provide meaningful benefit to patients with c-MET positive PRCC?

Question 2: Is c-MET positive status predictive of worse outcome (PFS/OS) in PRCC patients?

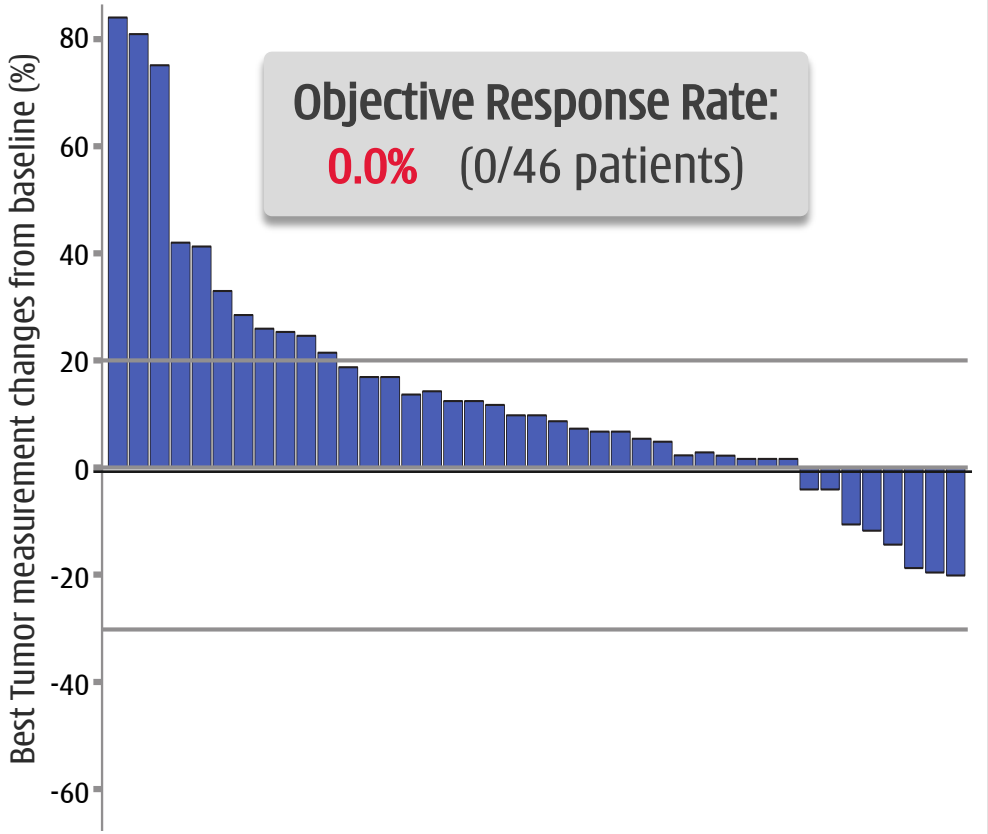
[1] Transparency Market Research, March 2015 – RCC (excl. non-RCC Kidney Cancer). [2] Frost & Sullivan, March 2016. [3] NCCN Guideline for kidney cancer. Version 3.2016, 05/26/16. ; [4] ORR = Objective Response Rate, mPFS = median Progression Free Survival, mOS = median Overall Survival; [5] ESPN study, Tannir, N. M. et al.

Savolitinib: Phase II PoC study in PRCC clear benefit in c-MET+ PRCC patients

Savolitinib clear ORR benefit in c-MET positive patients



c-MET negative patients – no response to savolitinib



Choueiri T et al. A single-arm biomarker-based phase II trial of savolitinib in patients with advanced papillary renal cell cancer (PRCC). J Clin Oncol 35, 2017 (suppl 6S; abstract 436).

Savolitinib: Phase II PoC study in PRCC clear benefit in c-MET+ PRCC patients

Big advantage in Disease Control Rate ("DCR")

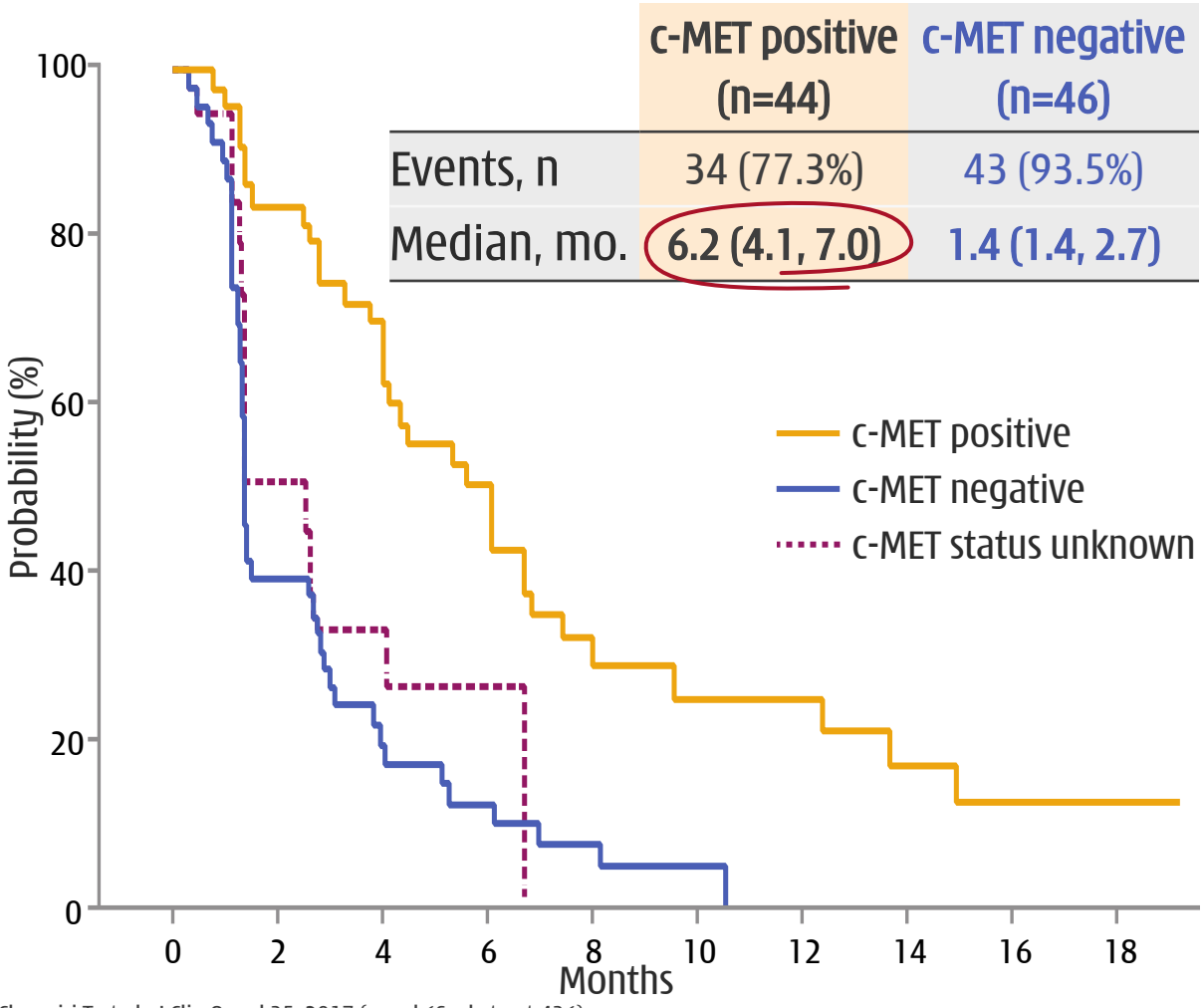
- c-MET positive DCR 73.2%
- c-MET negative DCR 28.2%

Tumor responses in the overall treatment population and by c-MET status

RECIST response, n (%)	c-MET positive (n=44)	c-MET negative (n=46)	c-MET unknown (n=19)	Total (n=109)
Partial Response†	8 (18.2%)*	0 (0.0%)	0 (0.0%)	8 (7.3%)
Stable Disease	22 (50.0%)	11 (23.9%)	5 (26.3%)	38 (34.9%)
Progressive Disease	11 (25.0%)	28 (60.9%)	9 (47.3%)	48 (44.0%)
Not Evaluable	3 (6.8%)	7 (15.2%)	5 (26.3%)	15 (13.8%)

*P=0.002 versus c-MET-independent subgroup (Fisher exact test). Responses assessed according to RECIST version 1.1.
†Unconfirmed responses excluded.

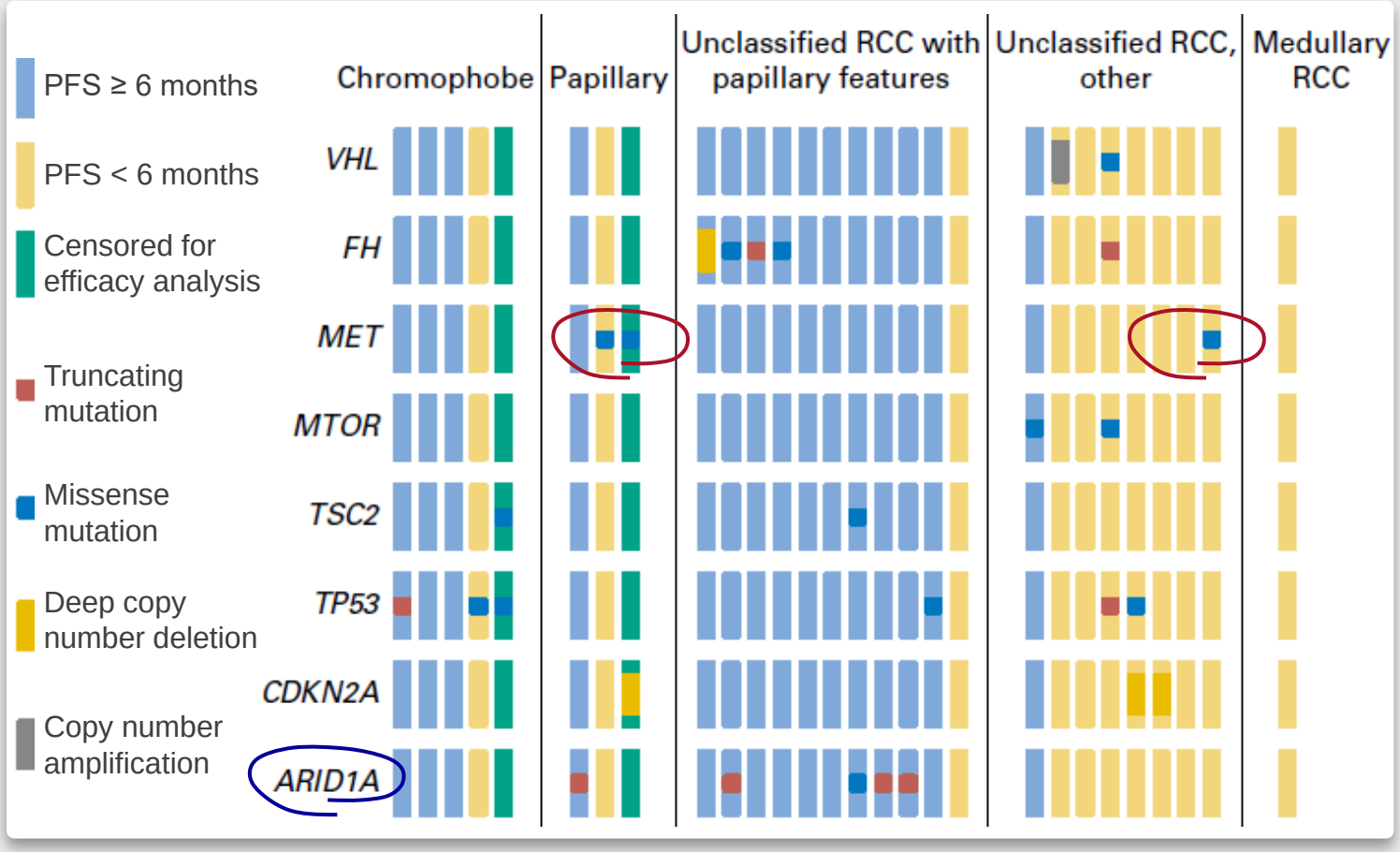
Median PFS – big advantage in c-MET +ve patients.



Choueiri T et al. J Clin Oncol 35, 2017 (suppl 6S; abstract 436).

Savolitinib: c-MET as a prognostic factor in PRCC

- No systematic study done to date on c-MET genetic alterations as a prognostic factor
- A recent study indicated that c-MET mutations in RCC/PRCC led to shorter PFS with Afinitor® / Avastin® treatment
- Larger epi study needed to better understand the effect of c-MET genetic alterations on prognosis of PRCC



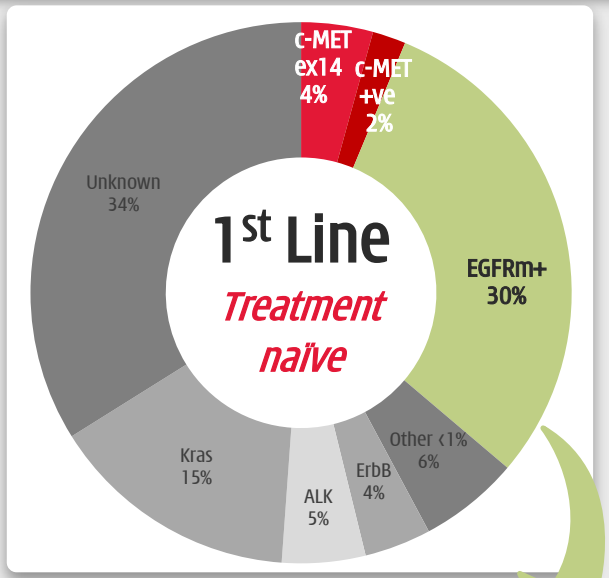
J. Clin Oncol., 32 (34), 3846 (2016)

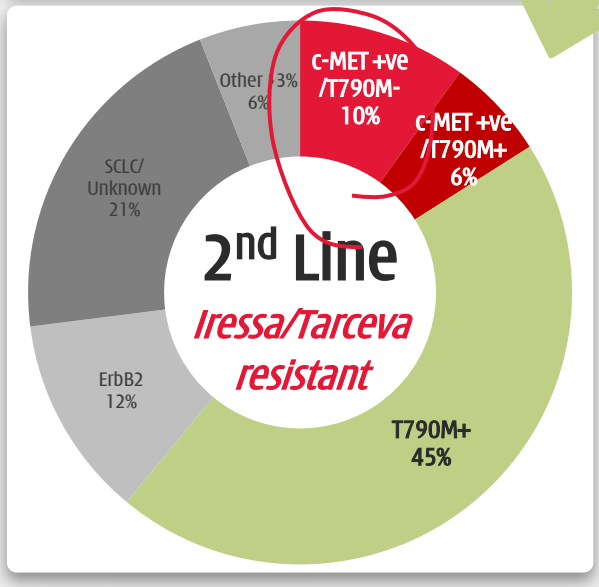
Savolitinib: PRCC registration strategy

- US breakthrough therapy possibility
  - ↗ Global epidemiology study on 300+ PRCC patient samples ongoing, expecting data by YE2017
  - ↗ If c-MET genetic alterations proven a poor prognostic factor, then the positive Phase II data might support a BTT application in the US
- Global registration
  - ↗ Global pivotal Phase III expected to be kicked off Q2 2017
  - ↗ Topline data 2019

Savolitinib: targeting c-MET+ lung cancer
multiple studies ongoing, targeting different patient populations

- 1L NSCLC with c-MET Exon 14 skipping or c-MET gene amplification: 4-6% of NSCLC, similar size of opportunity for ALK+
- 1L PSC with Exon 14 skipping: PSC only 1% of lung cancer, but 20-30% Exon 14+, orphan drug / fast track approval potential
- 2L EGFR TKI resistant EGFRm+ NSCLC: combination with Iressa® or Tagrisso®

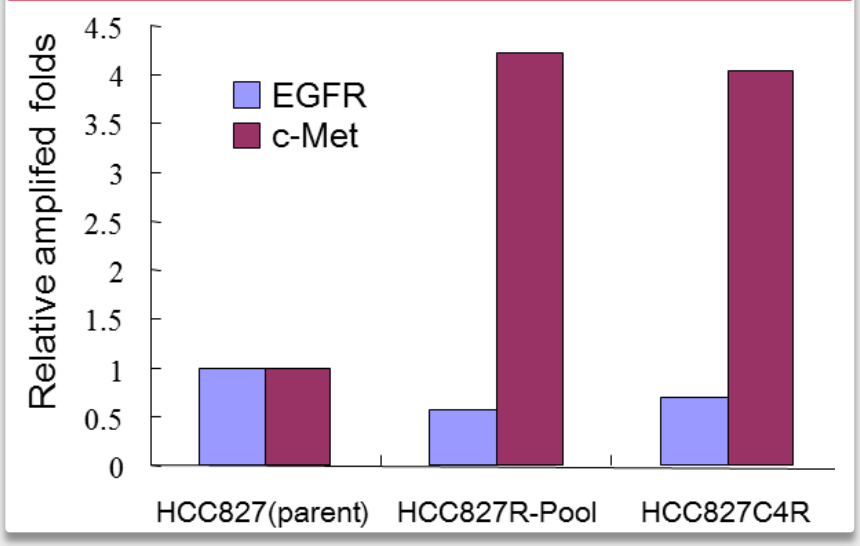




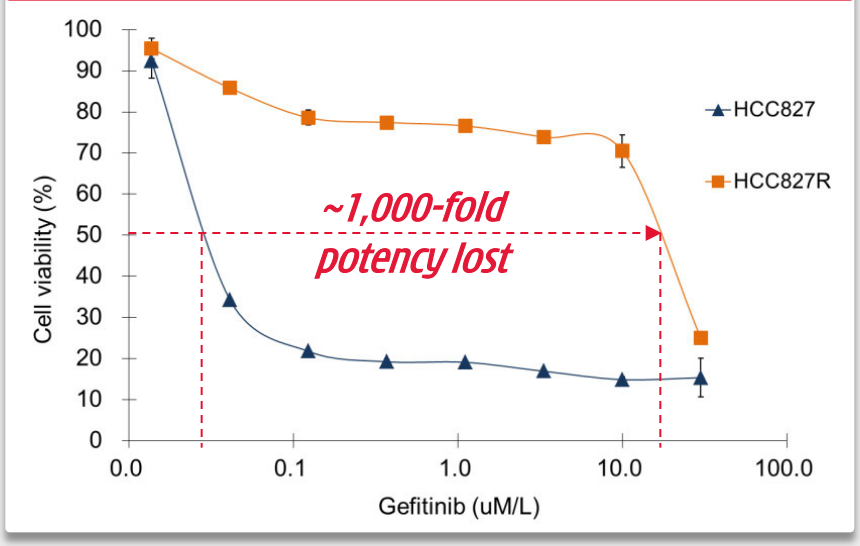
Savolitinib: targeting c-MET+ lung cancer

c-MET gene amplification is induced by EGFR TKI treatment

Gene copy numbers of *c-MET* in HCC827 resistant cells



Iressa® (gefitinib) effect on cell viability

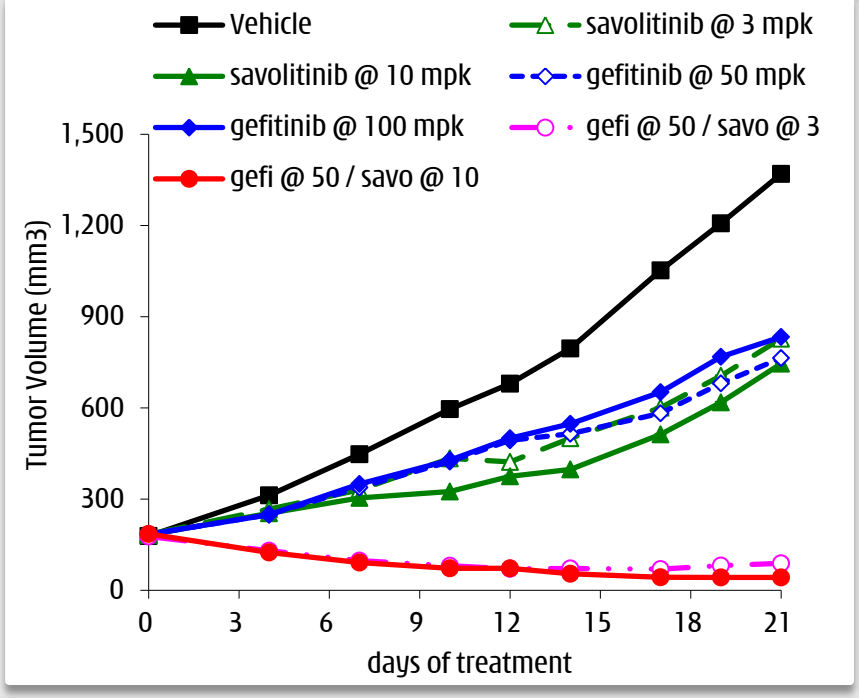


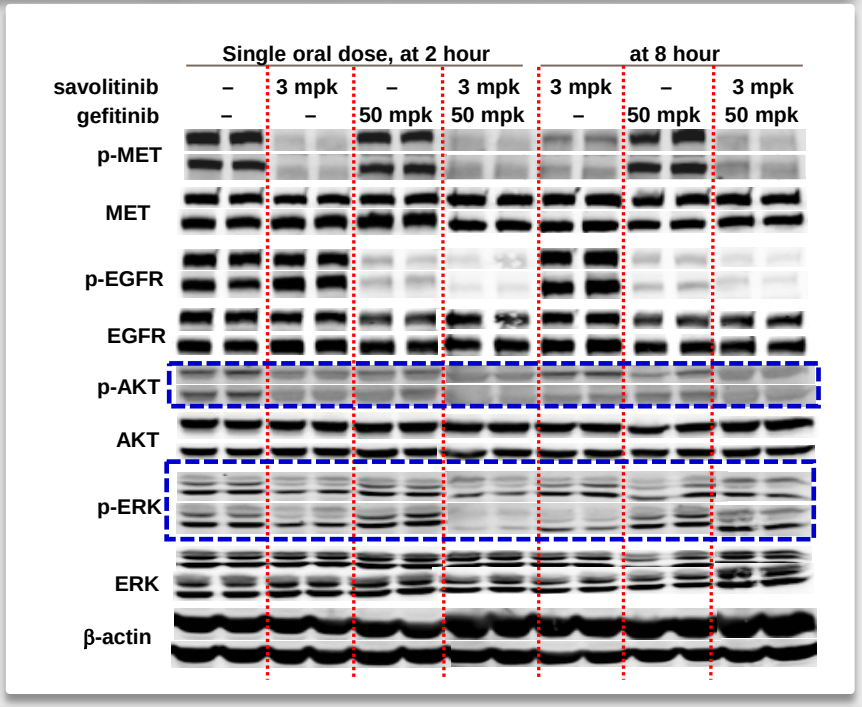
- HCC827 is a NSCLC cell line with exon 19 deletion, highly sensitive to EGFR TKIs
- After multiple passages in the presence of increasing concentrations of TKI, HCC827C4R was selected with 4-fold c-MET gene copies and resistant to EGFR TKIs

Savolitinib: targeting c-MET+ lung cancer

In c-MET amplified EGFR TKI resistant EGFRm+ cancer cells, both pathways are activated

Savolitinib in combination with Iressa® (gefitinib) in HCC827C4R





- High levels of p-EGFR and p-MET are present in the EGFRm+/c-MET+ cells, indicating both pathways are activated
- Inhibiting either pathway is ineffective in stopping tumor cell growth
- Blocking the two pathways simultaneously results in profound & sustained efficacy

Savolitinib: targeting c-MET+ lung cancer

TATTON study (Part A) Demographics: savolitinib arm – dose escalation

Characteristic	Osimertinib (Tagrisso®) + savolitinib (N=12)
Sex: male/female, n (%)	2/10 (17/83)
Median age, years	64
Region: Japan/Asia/US, n (%)	0/8/4 (0/67/33)
Smoking status*: never/current/former, n (%)	8/0/3 (67/0/25)
Prior treatment, n (%)	
≥2 prior TKIs	7 (58)
Prior T790M directed treatment#	2 (17)
≥2 prior chemotherapy	6 (50)
Prior radiotherapy	6 (50)

Oxnard et al J Clin Oncol 33, 2015 (suppl; abstr 2509)

Population: all dosed patients

*Smoking status unknown: selumetinib n=5, savolitinib n=1, MEDI4736 n=3

#All patients received osimertinib except one patient in the selumetinib combination who received CO-1686

Savolitinib: targeting c-MET+ lung cancer

TATTON study - All-causality adverse events: osimertinib + savolitinib

- Most common AEs were vomiting, nausea and rash
- 3 DLTs: fatigue (Gr 3 at 600 mg), neutropenia (Gr 4 at 800 mg), and nausea (Gr 3 at 800 mg)
- Phase II savolitinib dose confirmed as 600 mg QD with osimertinib 80 mg QD

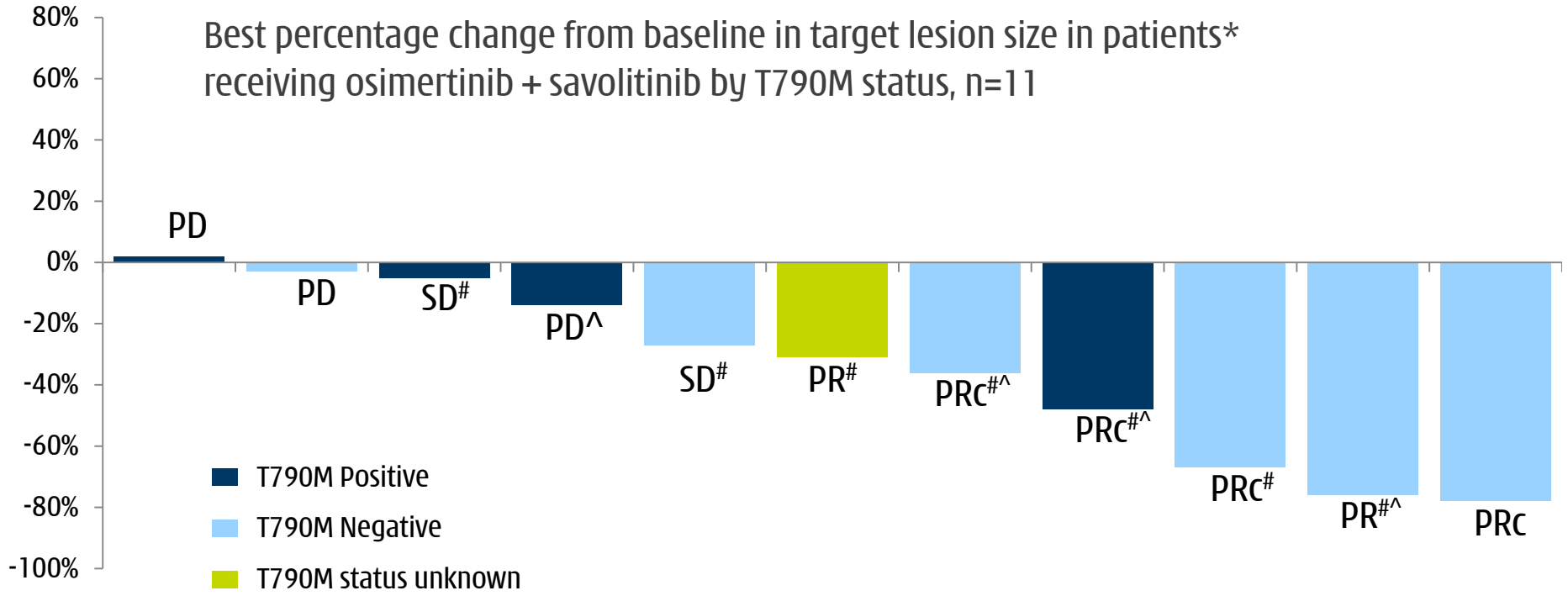
Number of events, n AE occurring in ≥3 instances at any dose	600 mg N=6		800 mg N=6	
	Any Gr	Gr ≥3	Any Gr	Gr ≥3
Vomiting	7	0	3	0
Nausea	3	0	6	1
Rash	4	0	3	0
Pyrexia	3	0	3	0
WBC count decreased	4	0	1	1
Decreased appetite	1	0	3	0

AE, adverse event; DLT, dose-limiting toxicity; Gr, grade; QD, once daily; WBC, white blood cell

Oxnard et al J Clin Oncol 33, 2015 (suppl; abstr 2509)

Savolitinib: targeting c-MET+ lung cancer

Dose-finding stage



Partial responses reported in 6/11 patients°, or 2/2 in c-MET+/T790M- population

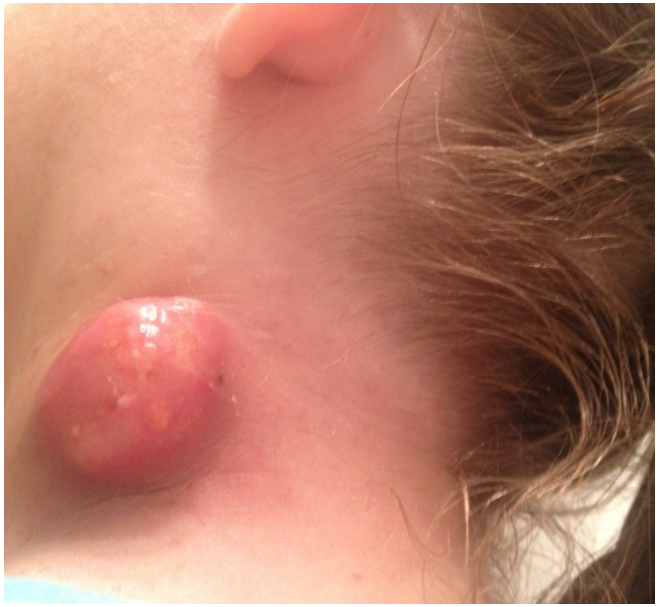
*Population: all patients dosed who had a baseline and 6-week RECIST assessment i.e. 11/12 patients
#Patients ongoing treatment at data cut-off
^Patients c-MET +ve
°including unconfirmed and confirmed PRs
PD, progressive disease; PR, partial response; PRc, confirmed partial response;
RECIST, Response Evaluation Criteria In Solid Tumors; SD, stable disease

Oxnard et al J Clin Oncol 33, 2015 (suppl; abstr 2509)

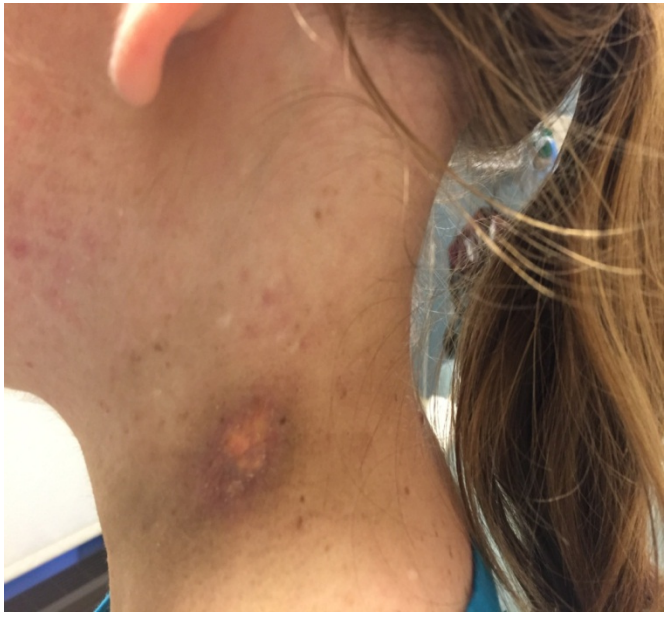
Savolitinib: targeting c-MET+ lung cancer

Tumor response to treatment with osimertinib + savolitinib

32-year-old female with a tumor harboring *EGFR* exon 19 deletion and high *c-MET* amplification responds to osimertinib + savolitinib



Pre-treatment



4 weeks later

Oxnard et al J Clin Oncol 33, 2015 (suppl; abstr 2509)

Savolitinib: targeting c-MET+ lung cancer

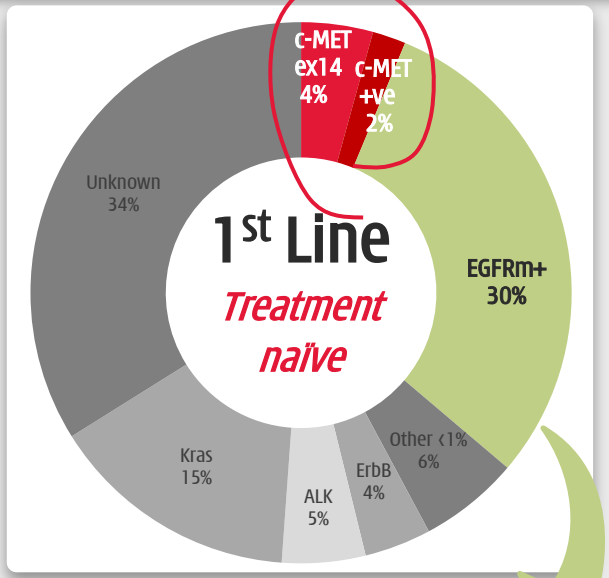
Targeting EGFR TKI resistant c-MET+/T790M- patients

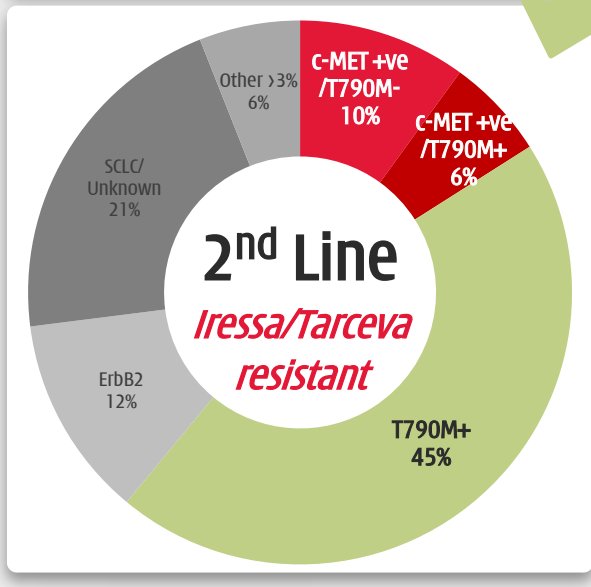
- In EGFR TKI resistant EGFRm+ patients, c-MET gene amplification accounts for 10-20%
- Strong preclinical and early clinical data support the combination of savolitinib and Tagrisso® or Iressa® for this patient population
- Based on the promising early clinical efficacy & safety data, AZ/HCM progressed the combo into Phase II in 2016; enrollment is ongoing
- Breakthrough designation likely given the promising early clinical efficacy and clear understanding of the molecular pathways
- Decision for global registration trial targeted for YE 2017

Savolitinib: targeting c-MET+ lung cancer

Targeting c-MET Exon 14+ NSCLC or gene amplification

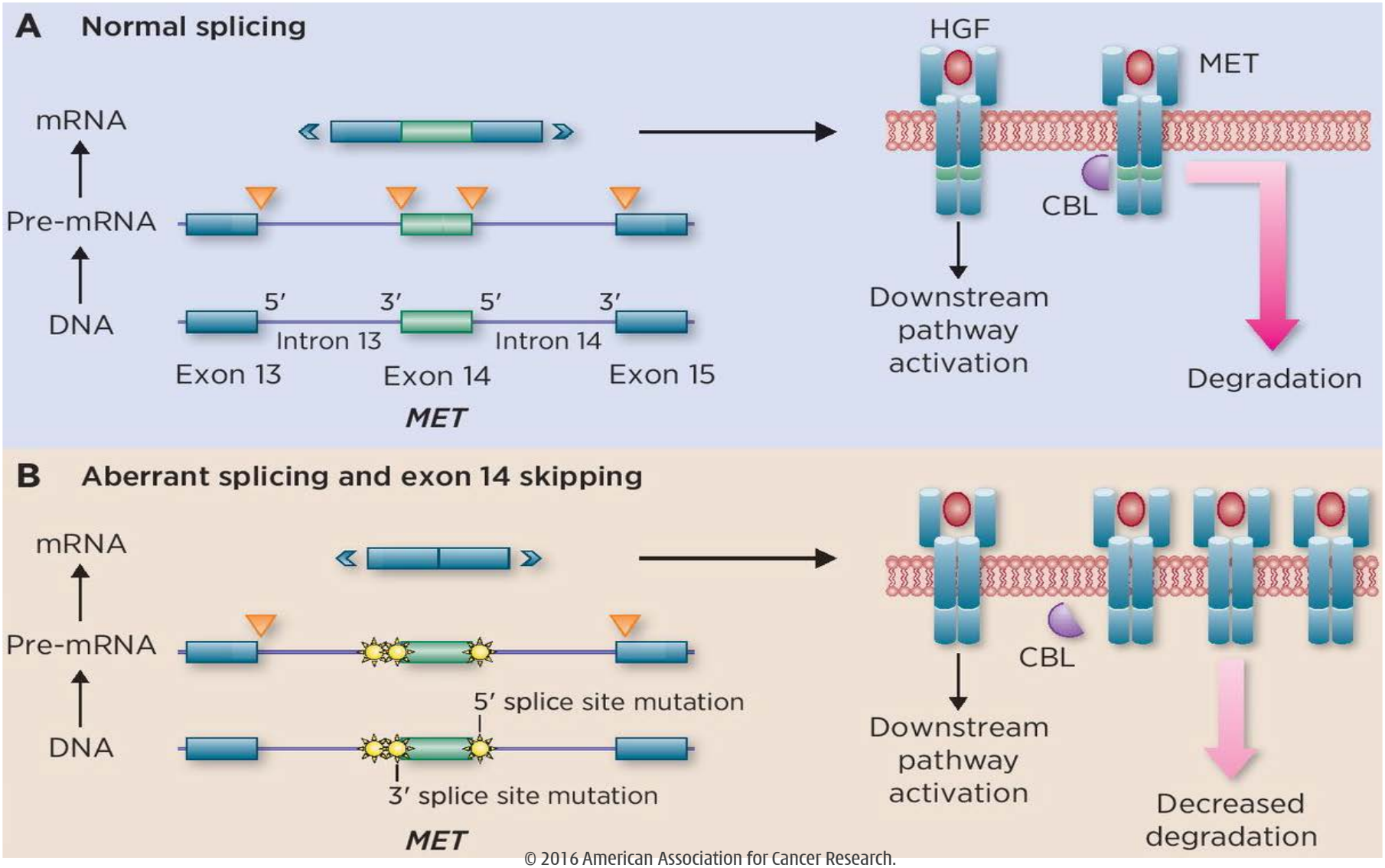
- 1L NSCLC with c-MET Exon 14 skipping or c-MET gene amplification: 4-6% of NSCLC, similar size of opportunity for ALK+
- 1L PSC with Exon 14 skipping: PSC only 1% of lung cancer, but 20-30% Exon 14+, orphan drug / fast track approval potential
- 2L EGFR TKI resistant EGFRm+ NSCLC: combination with Iressa® or Tagrisso®





What is c-MET Exon 14?

Encodes CBL-binding protein which is responsible for c-MET degradation

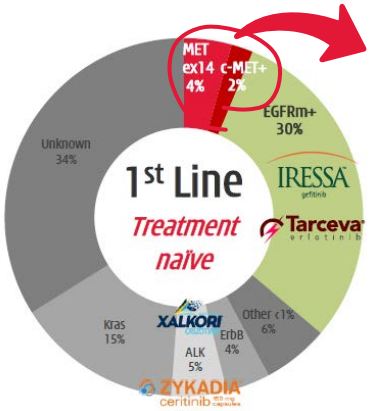


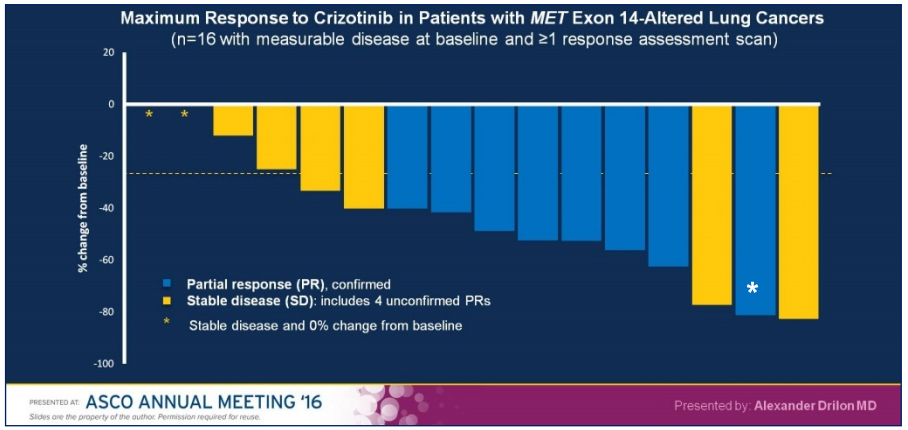
Savolitinib: targeting c-MET+ lung cancer

c-MET Exon 14 skipping or gene amplification are "driver" alterations that are targetable

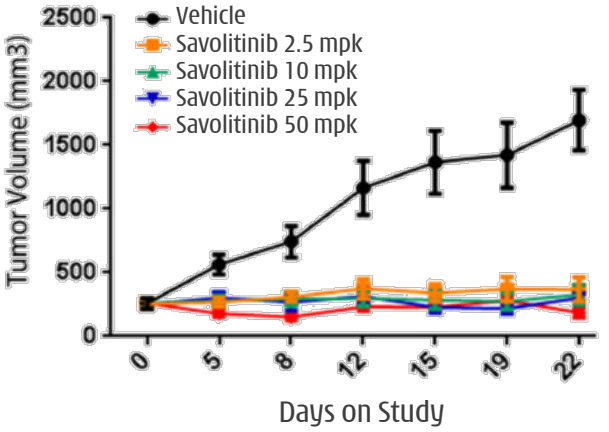
CHI-MED

Crizotinib shown good activity in c-MET Exon14 skipping NSCLC with or without c-MET gene amplification – 2016 ASCO [2]





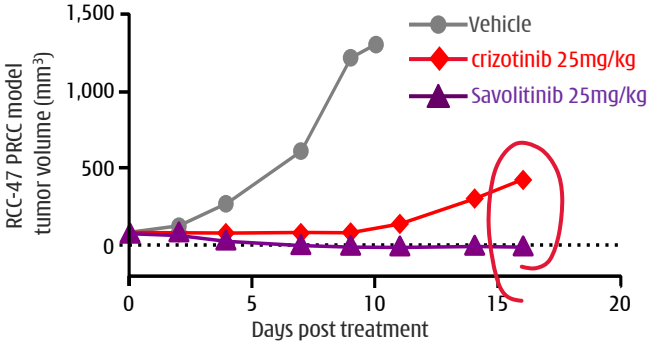
Savolitinib potently inhibits growth of NSCLC w/ c-MET gene amplification



Crizotinib is a multi-kinase inhibitor with ALK, ROS1, & c-MET, savolitinib is uniquely selective and more potent against c-MET+ NSCLC [1]

IC_{50} (nM)	Savolitinib	Crizotinib	Savolitinib vs. Crizotinib
EBC1 Viability (gene amp)	2	19	10x
EBC1 pMET (gene amp)	1	39	39x
293T pMET (wild type)	7	79	11x
293T pMET (Ex14del)	9	140	16x

Savolitinib may be more durable than crizotinib [3]



[1] Drilon A, Abstract 108 Efficacy and safety of crizotinib in patients with advanced c-MET Exon 14-altered non-small cell lung cancer; [2] Paik, P.K., et al., Response to c-MET inhibitors in patients with stage IV lung adenocarcinomas harboring c-MET mutations causing exon 14 skipping. Cancer Discov, 2015. 5(8): p. 842-9.; [3] Schuller AG et al. "Regression in Papillary Renal Cell Carcinoma Patient-Derived Xenograft Models". Clin Cancer Res 2015;21:2811-2819.

Savolitinib: targeting c-MET+ lung cancer

1L Exon 14+ NSCLC and PSC development strategy

CHI-MED

China PoC ongoing

- 10-15 patients, open arm
- ORR as primary endpoint
- China PoC to support both China and global registration studies

China registration

- Single arm, 40-60 patients (PoC patients can be included for analysis)
- ORR as primary endpoint (eg. ›40%)
- PFS as a key secondary endpoint (eg. ›6 months)

Global registration

- Single arm, 30-50 patients (Chinese patients can be included for analysis, 70-110 patients)
- Same endpoints as above
- Potential Breakthrough Therapy Designation in the US

Savolitinib in Gastric Cancer
large population, poor survival, clear unmet medical need

- Gastric cancer ranks 5th in incidence, but 2nd in deaths
- c-MET amplification can be detected in 5-10% of gastric cancer and confers poor prognosis

	new cases/year	deaths/year
Global	951,000	723,000
U.S.	28,000	10,950
China	679,100	498,000

Sources: Ferlay J et al. Int J Cancer. 2015; 136:E359-386; Chen W et al. CA Cancer J Clin. 2016; 66:115-132.

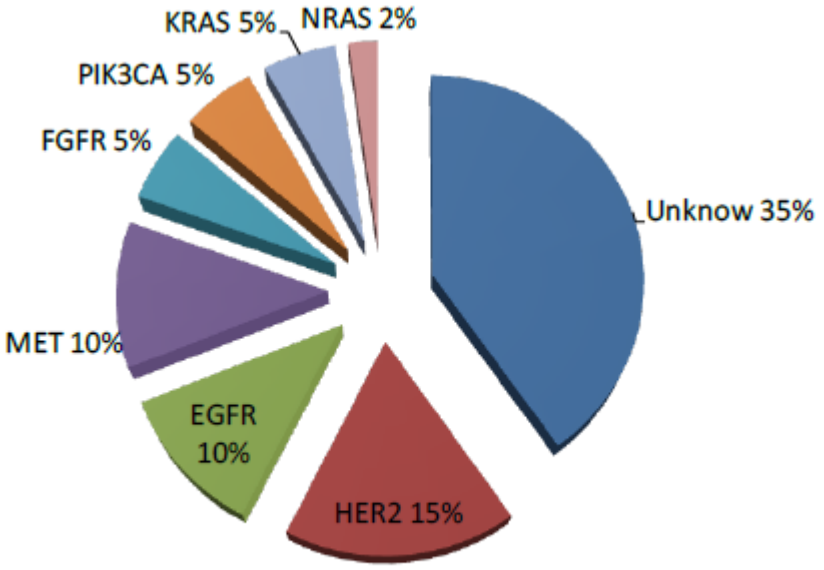
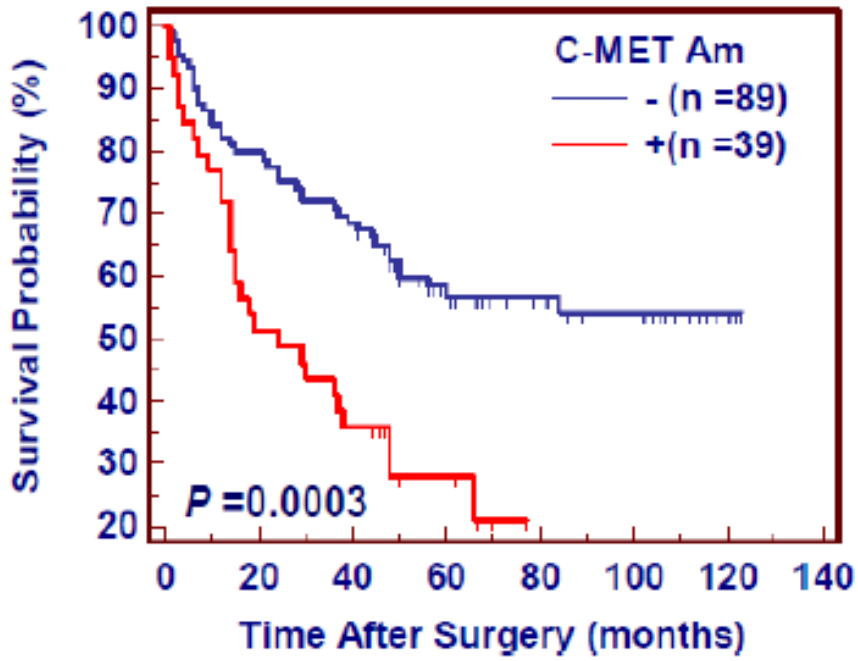


Figure 1 Estimated proportion of possible molecular targets in gastric cancer

Chin. Clin. Oncol., 2013, 2(1), 5



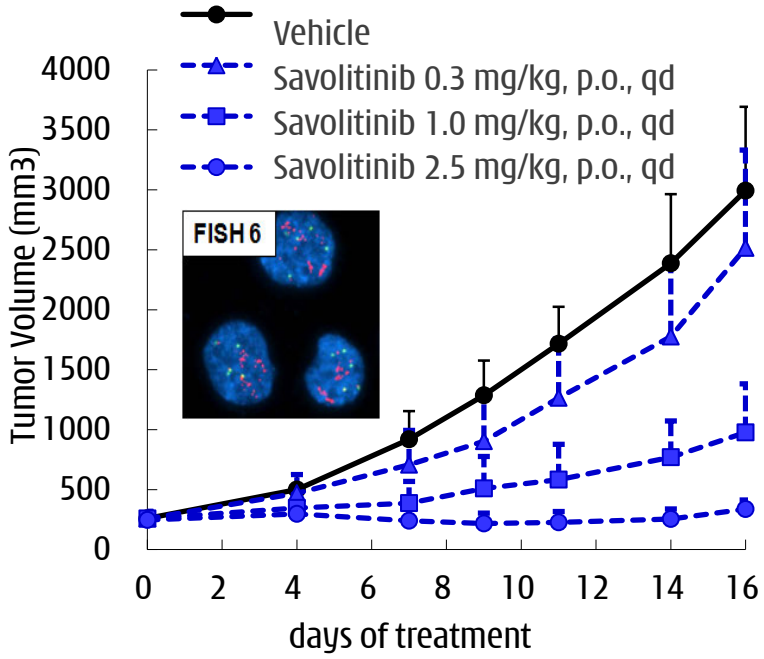
Int. J. Mol. Sci. 2012, 13, 4714-4726

Savolitinib in Gastric Cancer

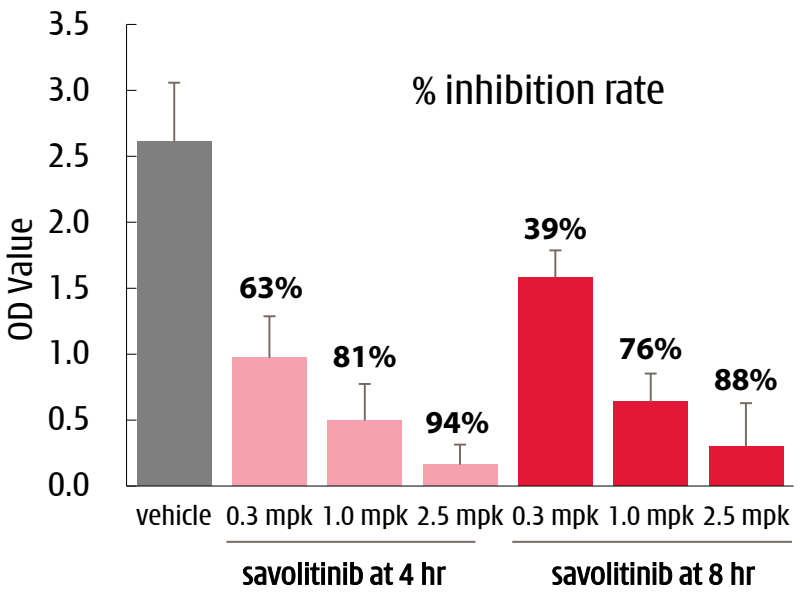
Targeting c-MET amplification in gastric cancer

- Potent activity in the Hs746T model with dose response
- Anti-tumor efficacy correlated well with the target inhibition

Gastric cancer Hs746T xenograft model



P-MET at the End of Efficacy Study



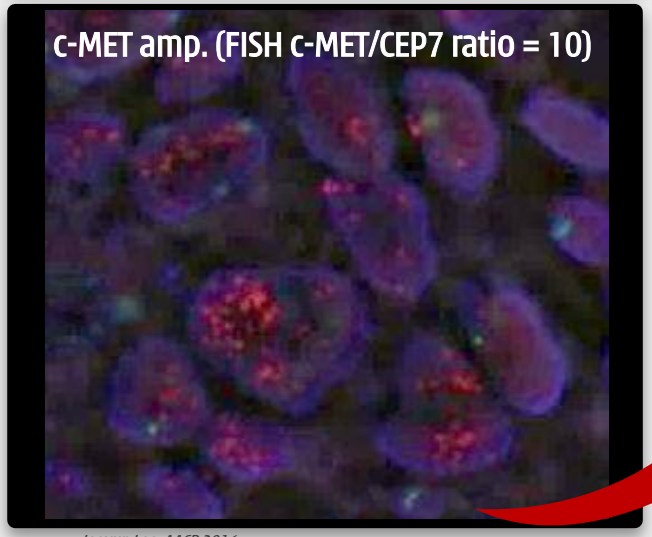
2014 AACR

Savolitinib in Gastric Cancer

Targeting c-MET gene amplification in PoC trials ongoing in China and Korea

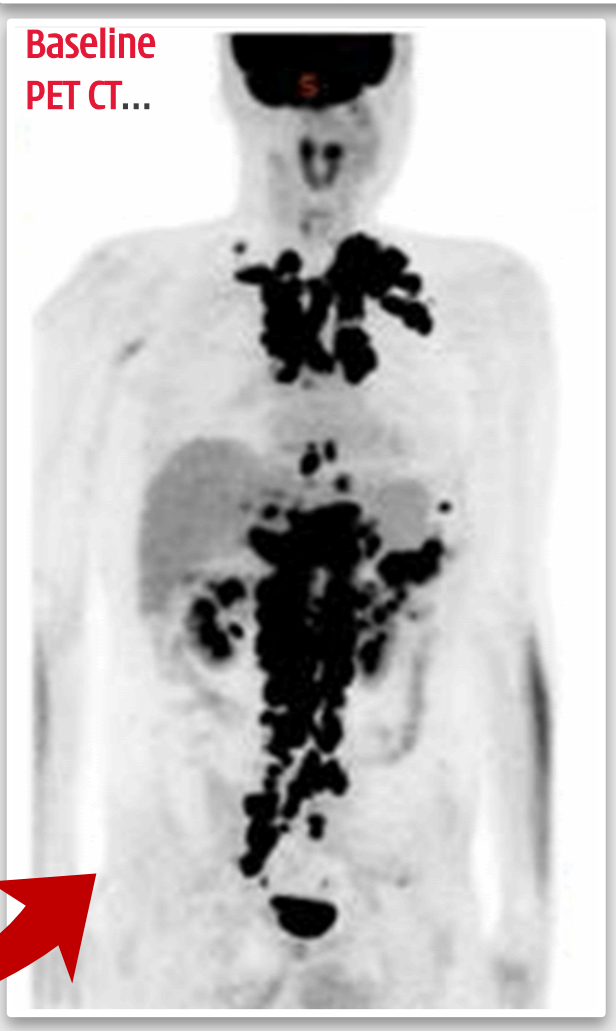
CHI-MED

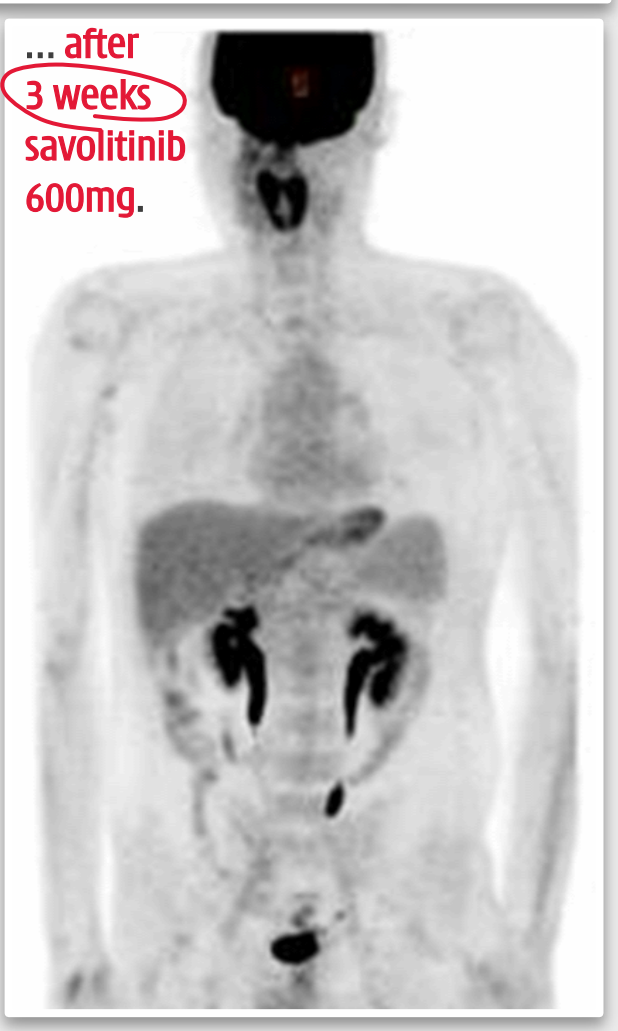
- PoC trials ongoing in parallel in China and Korea
- Encouraging clinical activity seen in both countries in GC patient with c-MET gene amplification
- Durable response observed: one patient in response for >2 years, still on treatment



Jeeyun Lee, AACR 2016.

VIKTORY trial – 34-year old male; surgery ruled-out; failed 4-cycles XELOX





Savolitinib Gastric Cancer development strategy

- Targeting c-MET gene amplification
  - China PoC: 10-15 patients
  - Primary endpoints: ORR (›40%)
  - If positive PoC, expand globally, with China as the main country, for registration under BTT
    - Likely single arm
    - Estimated samples size 100-200
    - ORR›40%

- Targeting c-MET protein overexpression
  - Explore combination therapies, such as chemo, VEGFR inhibitors such as fruquintinib or sulfatinib or IOs

Savolitinib Summary
Current development focus

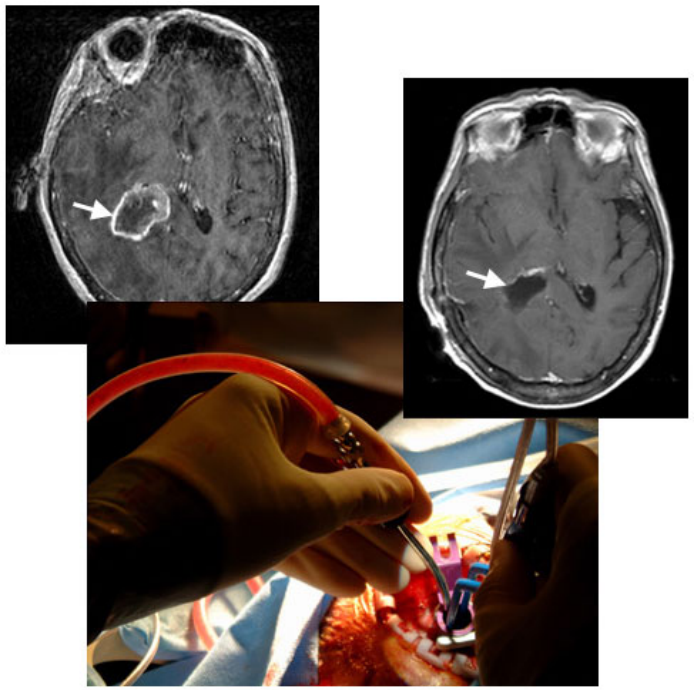
CHI-MED

- Entering registration trials
  - Monotherapy for c-MET+ PRCC, global Phase III start Q2 2017, topline 2019
  - Combo with Tagrisso for EGFR TKI resistant EGFRm+/c-MET+/T790M- NSCLC, global registration trial decision by YE 2017, potential for BTT depending upon the strength of the Phase II data
- Ongoing PoC trials
  - Exon14+ NSCLC
  - Exon 14+ PSC
  - c-MET gene amplified gastric cancer
- Future exploratory opportunities
  - Savolitinib/durvalumab combination therapy for RCC, NSCLC
  - Savolitinib/VEGFR inhibitor combination therapy for RCC, gastric cancer

Epitinib

A brain penetrant EGFR inhibitor

EGFR in the brain



http://neurosurgery.ucla.edu/body.cfm

Primary brain tumor (eg: glioblastoma)

EGFR gene amplification	40%
EGFR overexpression	60%
EGFR mutation (EGFR vIII)	40%

Cancer Res 2000;60:1383; JNCI 2005;97:880; Mol Cancer Res 2009;7:1000.

Tumor origins of brain metastases

Primary Tumor Site	Percentage (%)
Lung	48
Breast	15
Melanoma	9
Lymphoma	1
GI tract	3
Genitourinary tract	11
Osteosarcoma	10
Head and neck	6

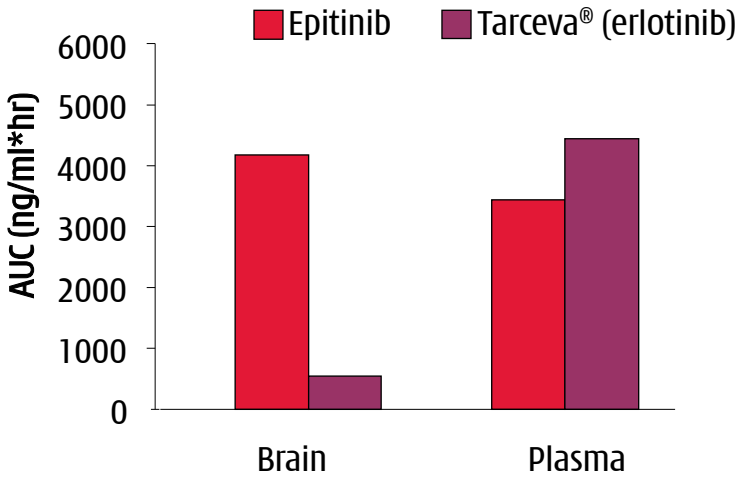
*EGFR signaling plays important role in the tumor types labeled red.

http://emedicine.medscape.com/article/1157902-overview

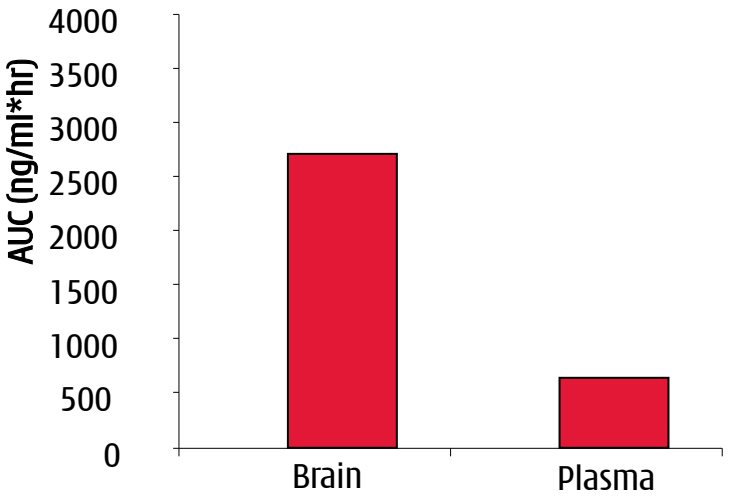
EGFRm+ NSCLC brain metastases and EGFR gene amplified glioblastoma (GBM) are potentially targetable by EGFR TKIs with good brain penetration

Epitinib is designed for brain penetration

Exposures in Rat (5 mpk, po)



Exposures in Dog (2.5 mpk, po)

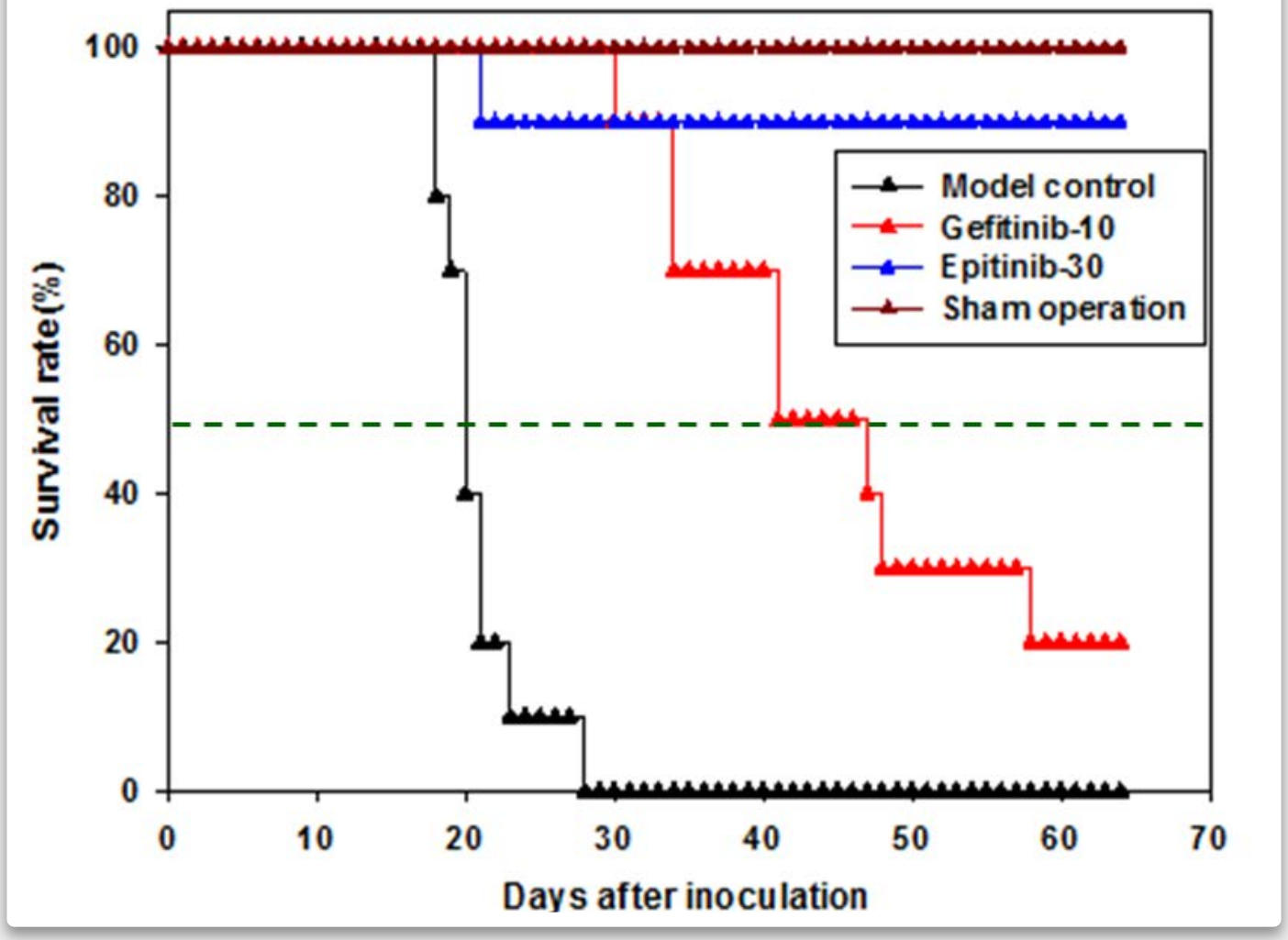


- Following oral administration
  - ↗ In rat: epitinib exposures brain to plasma is 1:1 comparing to erlotinib 1:10
  - ↗ In dog: epitinib brain to plasma is 10:1
  - ↗ High drug exposure has also now been detected in human CSF

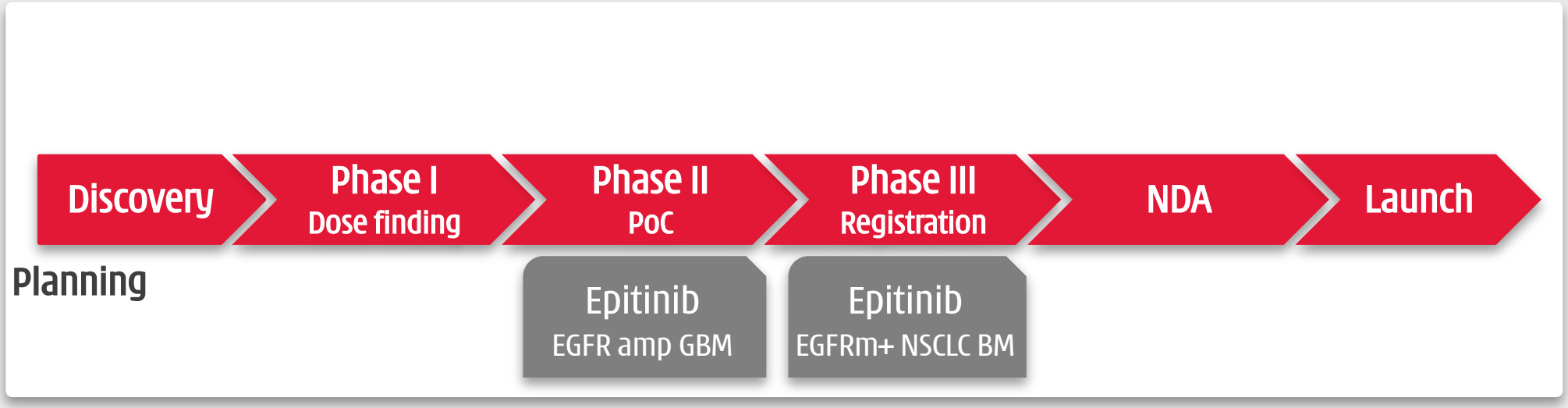
Epitinib demonstrated superior activity in EGFRm+ NSCLC BM model

CHI-MED

Efficacy Study of Epitinib & Iressa (gefitinib) in PC-9 i.c. xenograft Model



Epitinib: ongoing trials



NSCLC with brain metastases (BM)

Lung cancer ranks 1st both in incidence and in deaths globally

	new cases/year	deaths/year
Global	1.82 million	1.59 million
U.S.	222,500	155,870
China	733,300	610,200

About Lung cancer with brain metastases (BM)

- Over the course of the disease, up to 50% of patients develop BM with 10-15% at initial diagnosis
- Poor prognosis with mOS ~6 months
- No effective treatment available. Whole brain radiotherapy (WBRT) leads to poor Quality of Life (QoL)
- Patients with EGFR mutations have a higher chance of BM, while current EGFR TKIs have limited brain exposure

The Conmana (icotinib) BRAIN study

- First Phase III study to compare TKI with chemo+radiation
- More aggressive/difficult to treat patients with leptomeningeal metastases (LM) were excluded
- Positive trial, but level of efficacy for icotinib is sub-optimal:
  - ↗ PFS=6.8 m, ORR=55%, DCR=78.8%

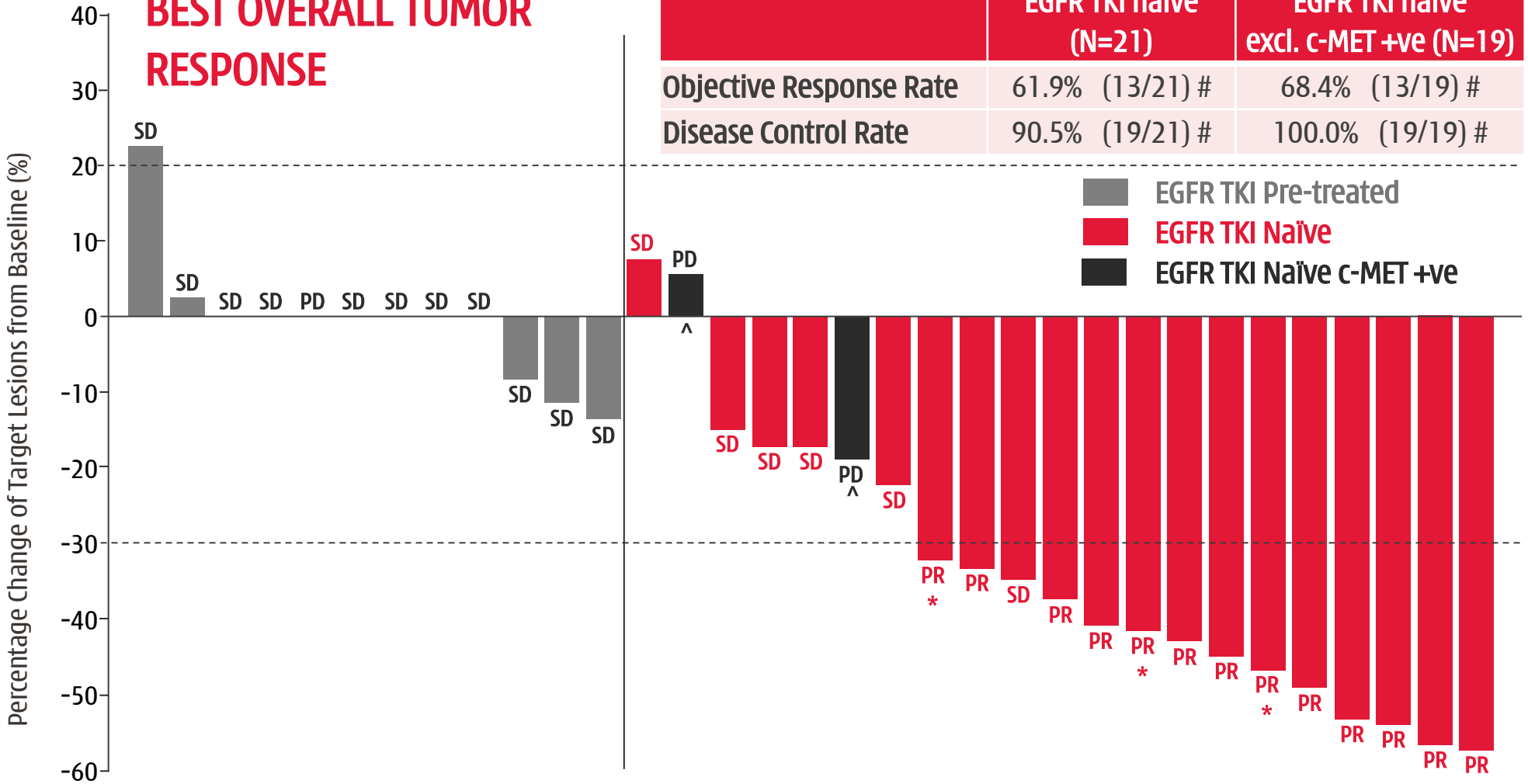
Epitinib

PoC study in patients with EGFRm+ NSCLC with BM

CHI-MED

BEST OVERALL TUMOR RESPONSE

	EGFR TKI naïve (N=21)	EGFR TKI naïve excl. c-MET +ve (N=19)
Objective Response Rate	61.9% (13/21) #	68.4% (13/19) #
Disease Control Rate	90.5% (19/21) #	100.0% (19/19) #

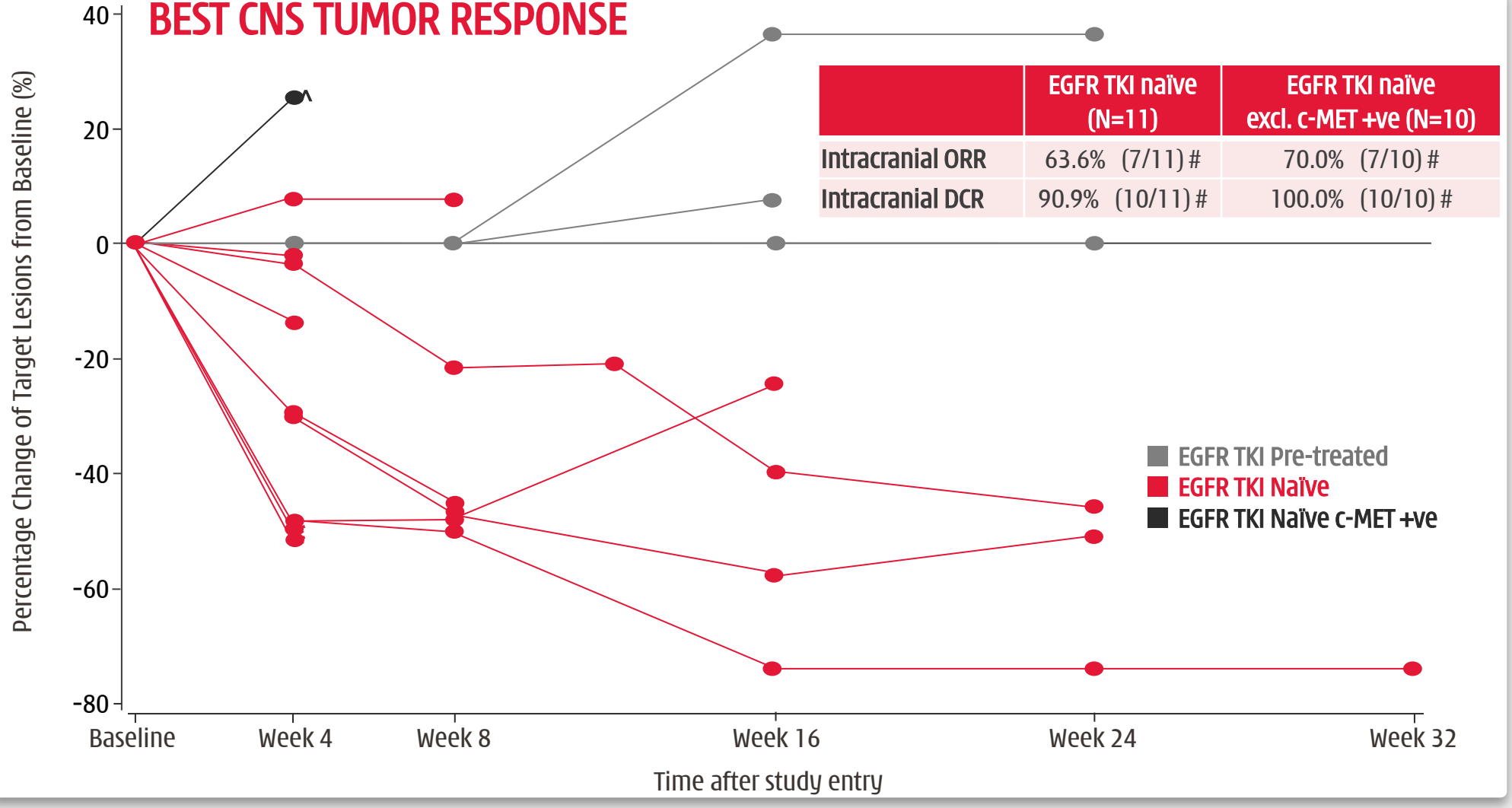


Dose expansion stage - data cut-off 20 Sept, 2016; * Unconfirmed PR, due to no further assessment at cut-off date; # Includes both confirmed and unconfirmed PRs; ^ c-MET amplification/high expression identified. Source: WCLC 2016.

Epitinib:
PoC study in patients with EGFRm+ NSCLC with BM

CHI-MED

BEST CNS TUMOR RESPONSE



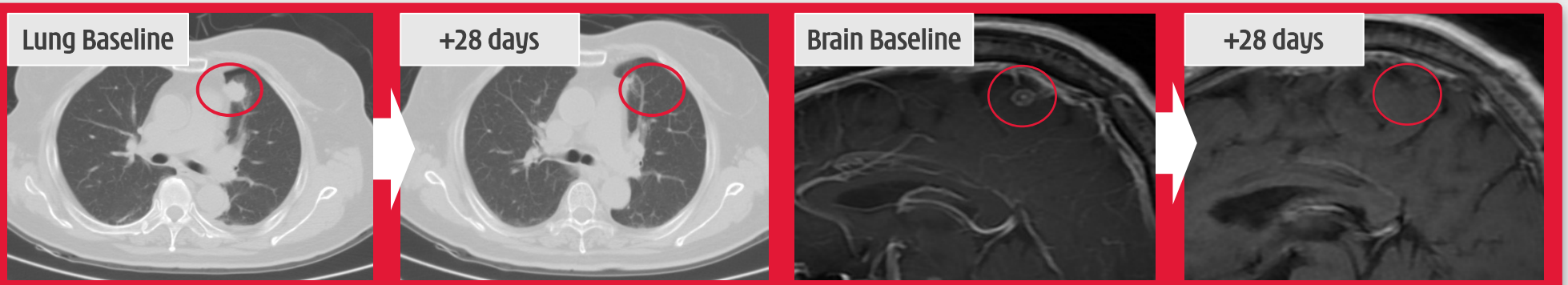
	EGFR TKI naïve (N=11)	EGFR TKI naïve excl. c-MET +ve (N=10)
Intracranial ORR	63.6% (7/11) #	70.0% (7/10) #
Intracranial DCR	90.9% (10/11) #	100.0% (10/10) #

Dose expansion stage - data cut-off 20 Sept, 2016; * Unconfirmed PR, due to no further assessment at cut-off date; # Includes both confirmed and unconfirmed PRs; ^ c-MET amplification/high expression identified

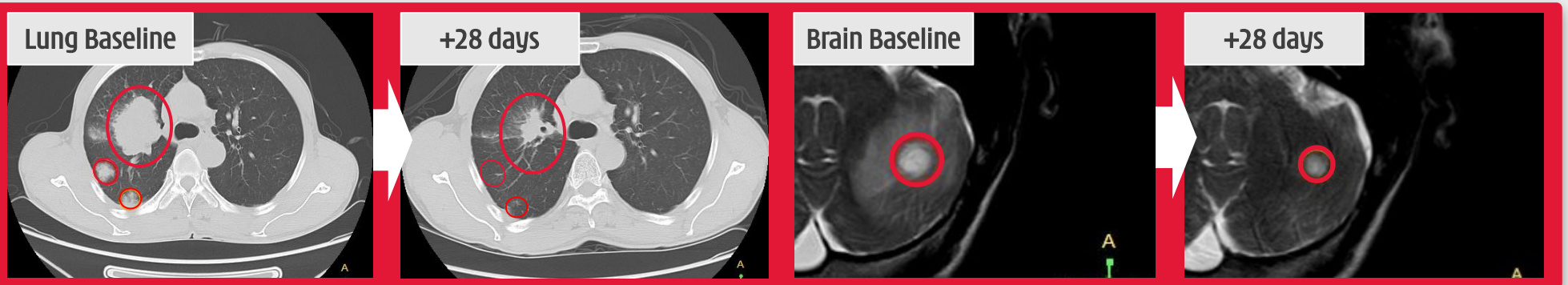
Epitinib Case Reports

CHI-MED

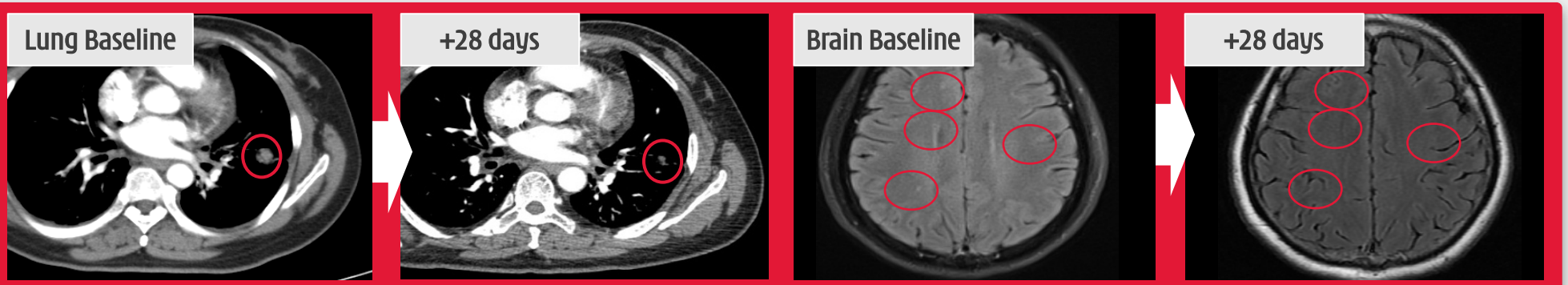
62 year old female



57 year old male



52 year old male

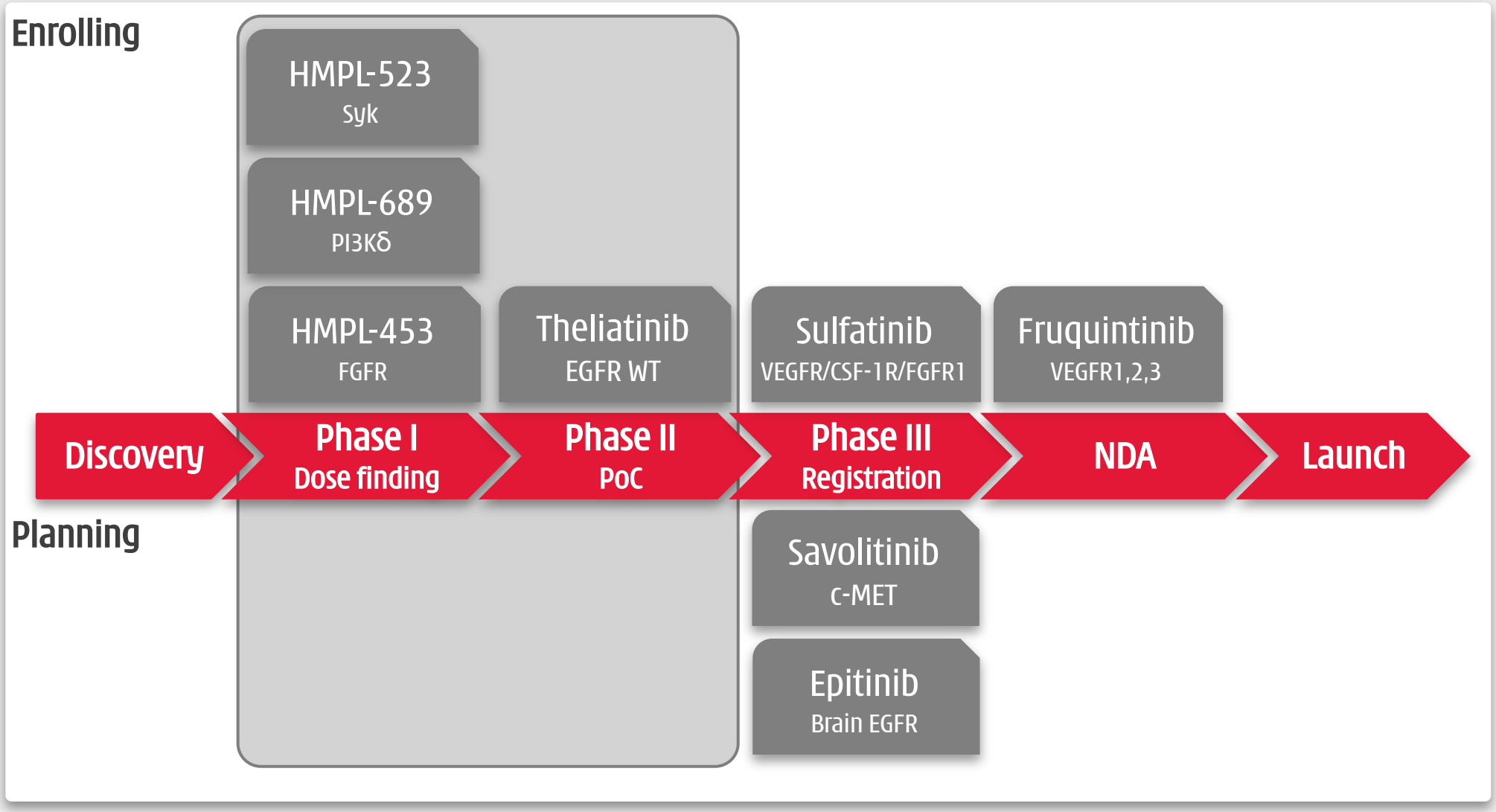


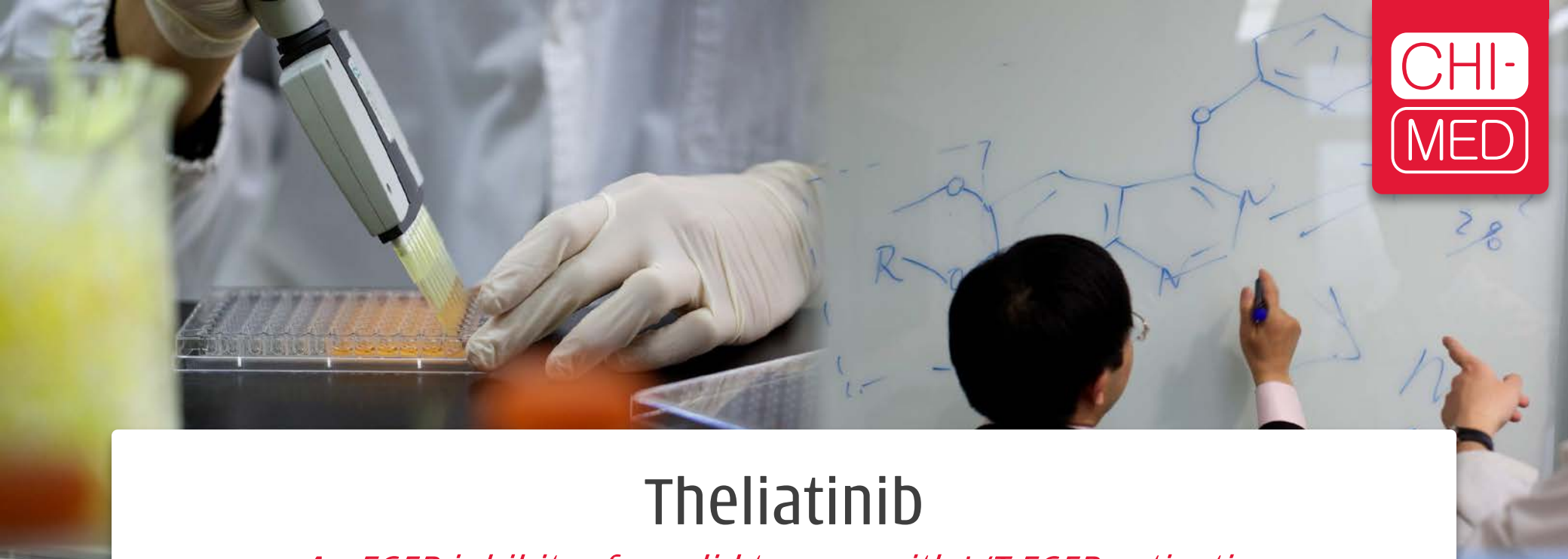
Epitinib in patients with EGFRm+ NSCLC with BM
Summary and development plans

- Promising PoC efficacy data: higher ORR and DCR than icotinib; PFS still maturing
- Partial responses were also seen in patients with leptomeningeal metastases (LM)
- Acceptable safety profile consistent with other EGFR inhibitors
- Target population is EGFR TKI treatment naïve EGFRm+ NSCLC patients
- Randomized, active controlled, Phase III registration initiation expected H2 2017 in China
  - ↗ LM may be a niche untreatable indication for possible fast track registration
- Global: combo with fruquintinib in EGFRm+ NSCLC worth exploring

2nd Wave - Pre-POC Portfolio

8 clinical candidates – current status





Theliatinib

An EGFR inhibitor for solid tumors with WT EGFR activation

Major unmet medical need for tumors with wild type (WT) EGFR activation

CHI-MED

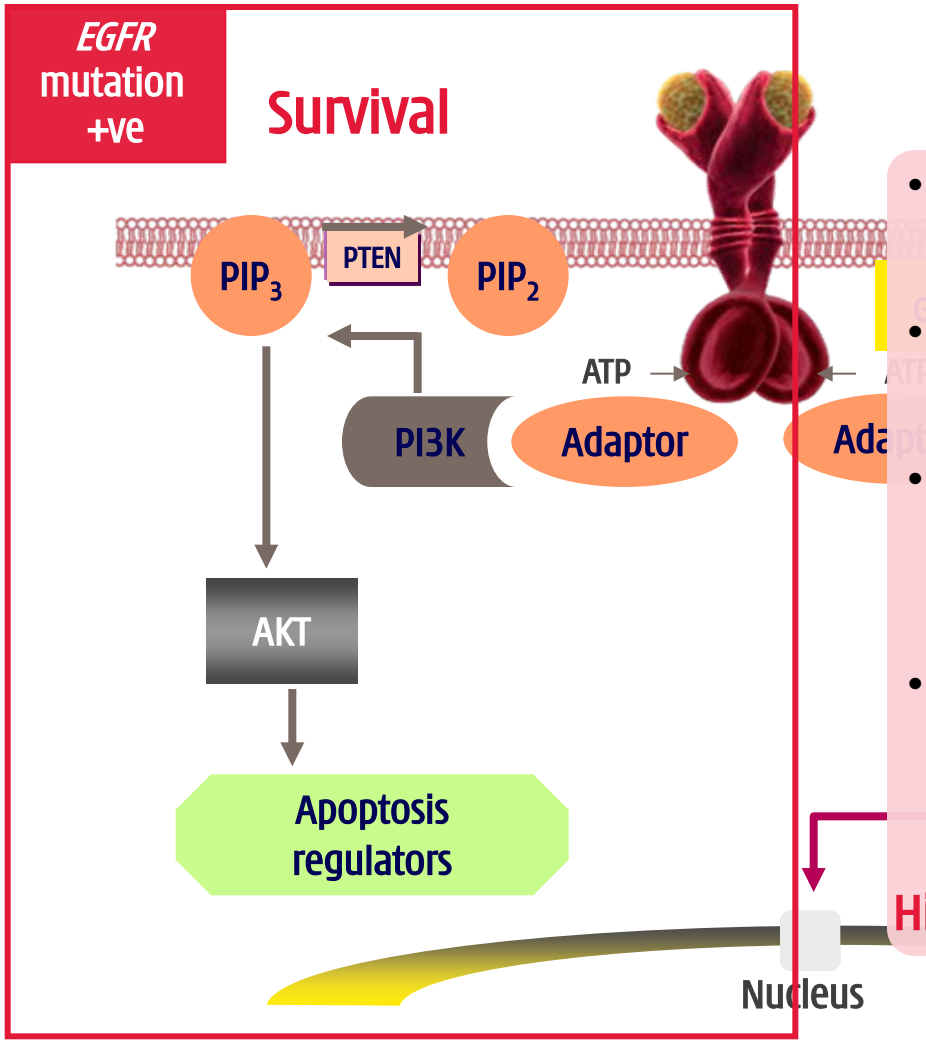
- EGFR activation (gene amplification or protein overexpression) affects multiple tumor types
- Many failures of clinical trials with TKIs or mAbs targeting WT EGFR

Tumor Types	Wild-type: Gene Amplification	Wild-type: Over Expression	Mutations
NSCLC	29%	62%	15-50%
Esophagus	8-30%	30-90%	12% (esophageal adenocarcinoma)
Stomach	29%	44-52%	‹5%
Glioblastoma	36-51%	54-66%	27-54% (EGFR variant III)
Colorectal	4.5%	*53%*	8%
Head and neck	10-30%	*66-84%*	42% (EGFR variant III)

TKIs approved: Iressa®, Tarceva®

MAbs approved Erbitux®, Vectibix®

EGFR activation: two distinct pathways – mutation vs wild type



Proliferation

- Ligand independent, high level of pEGFR: TKIs highly effective, mAbs not
- Preferential signalling through the PI3K-mediated anti-apoptotic pathway – 'oncogene addiction'
- Reduced affinity for ATP means EGFR TKIs have less competition for binding sites; lower concentrations sufficient to inhibit
- Successful inhibition of mutated EGFR produces 'apoptotic shock'

Higher incidence of complete or partial response

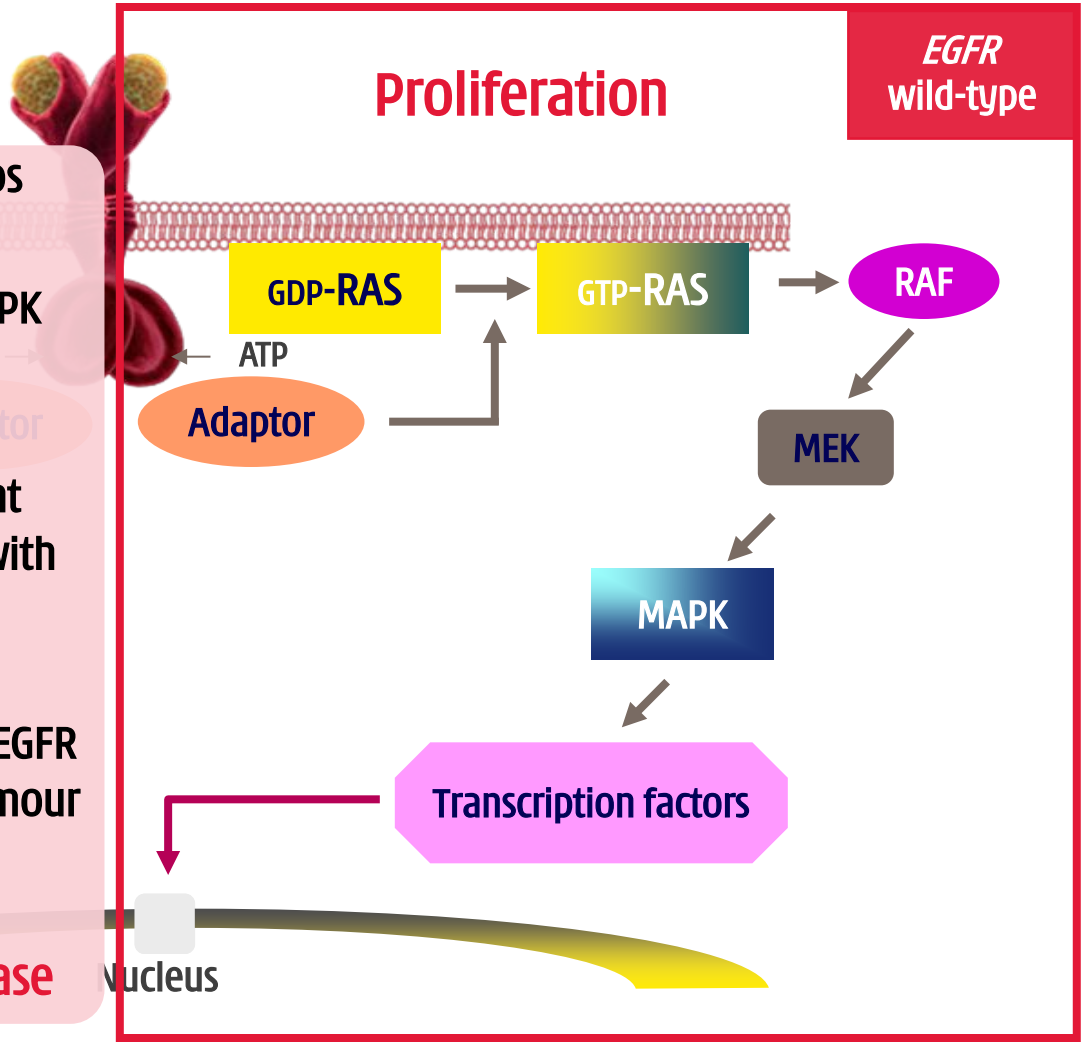
Sordella, et al. Science 2004

EGFR activation: two distinct pathways – mutation vs wild type

Survival

- Ligand dependent activation: mAbs active, TKIs poor (to date)
- Greater signalling through the MAPK pathway producing excessive cell proliferation
- Higher affinity for ATP than mutant receptor, so greater competition with EGFR TKIs for binding sites; higher concentrations needed to inhibit
- Successful inhibition of wild-type EGFR reduces proliferation and halts tumour growth

Higher incidence of stable disease



Sordella, et al. Science 2004

The difference is all in the structures

- EGFR activating mutations lead to confirmation changes that accelerate the ATP mediated signaling
- First generation EGFR TKIs preferentially bind to the mutant EGFR proteins over the wild type

Cancer Cell. 2007 March; 11(3): 217-227.

Structures of lung cancer-derived EGFR mutants and inhibitor complexes: Mechanism of activation and insights into differential inhibitor sensitivity

Summary

Mutations in the EGFR kinase are a cause of non-small cell lung cancer. To understand their mechanism of activation and effects on drug binding, we studied the kinetics of the L858R and G719S mutants and determined their crystal structures with inhibitors including gefitinib, AEE788 and a staurosporine. We find that the mutations activate the kinase by disrupting autoinhibitory interactions, and that they accelerate catalysis as much as 50-fold *in vitro*. Structures of inhibitors in complex with both wild-type and mutant kinases reveal similar binding modes for gefitinib and AEE788, but a marked rotation of the staurosporine in the G719S mutant. Strikingly, direct binding measurements show that gefitinib binds 20-fold more tightly to the L858R mutant than to the wild-type enzyme.

Targeting tumors with wild-type EGFR activation

- Big population and largely unmet
  - Multiple tumor types: lung, particularly lung SCC, CRC, esophagus, head and neck, breast, etc.
  - mAbs less effective for gene amplified population
  - Frequently overlap with other targets and may require combination therapies
- A high bar, but is it impossible? Three things important:
  - High affinity to better compete with ATP
  - High drug exposures at MTD dose to provide sufficient target coverage
  - More defined target patient
    - EGFR amplification/overexpression, cutoff?
    - Negative in Kras, ALK, c-MET, etc

Theliatinib has improved affinity to WT EGFR

- Binding affinity

Binding Affinity to WT EGFR	Ki (nM)
Theliatinib	0.05
Gefitinib	0.35
Erlotinib	0.38

- Phase I first in human study
  - ↗ Dose escalation ongoing, well tolerated, MTD has not been reached
  - ↗ Good pharmacokinetic properties. Drug exposure at 300 mg once daily is well above exposures expected for efficacy
  - ↗ Early encouraging anti-tumor activity observed
  - ↗ Expansion in esophageal cancer initiated

Esophageal cancer (EC): No effective treatment options

CHI-MED

- Major issue in Asia
  - Poor prognosis: 5 year survival 10-20%

	new cases/year	deaths/year
U.S.	16,940	15,690
China	477,900	375,000

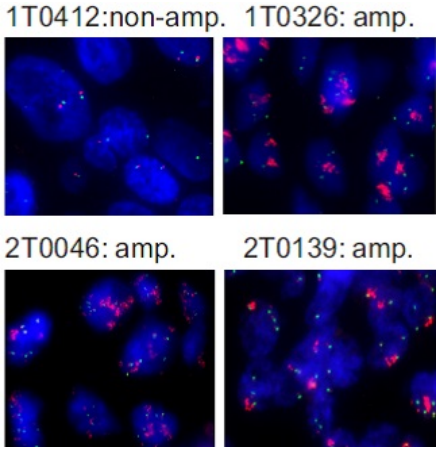
- Major difference in histology and risk factors
  - Caucasian: adenocarcinoma associated with increasing BMI
  - Asian/Africans: squamous cell carcinoma associated with smoking
- Treatment options
  - Largely palliative in intent
  - 1st line chemotherapies, including platinum- and FU-based therapies, taxanes
  - No SOC after 1st line
  - No targeted therapies approved

WT EGFR activation in Chinese esophageal cancer patients: a Chi-Med study

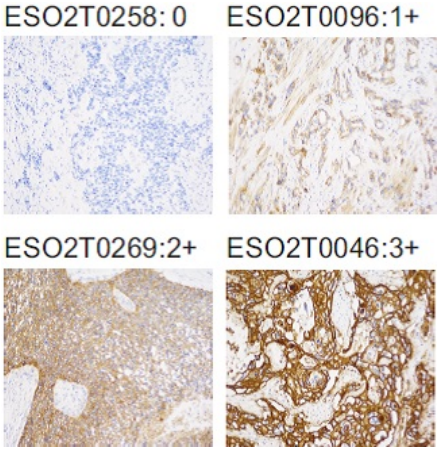
Squamous	EGFR high expression (IHC≥2+)	EGFR amp.	K-ras/B-raf/PIK3CA mutation
39/43 (91%)	30/43 (70%)	3/43 (7%)	0/43 (0%)

- Most cases are squamous cell carcinoma
- EGFR OE (IHC≥2+) 70% (IHC 3+ 42%) and Amp (FISH 6) 7% comparing to literature reports of OE 30~90% and Amp of 6~23.2%
- No mutations found in the 43 samples for K-ras (G12, G13, Q61), B-raf (G464, V600) or PIK3CA (E542, E545 and H1047)
- High level of EGFR (wt) activation in EC and low incidence of Ras/Raf/PIK3CA mutations make EGFR an attractive target to explore

Examples of EGFR FISH

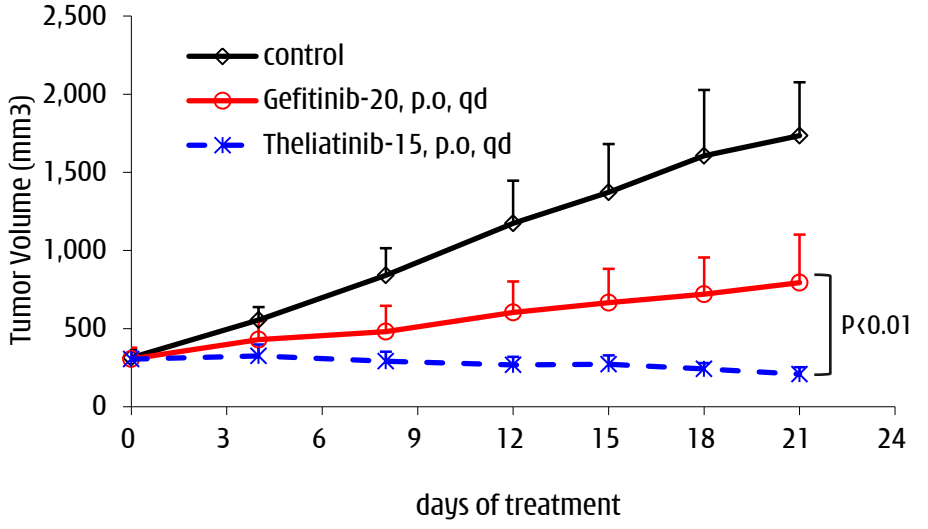


Examples of EGFR IHC Scoring

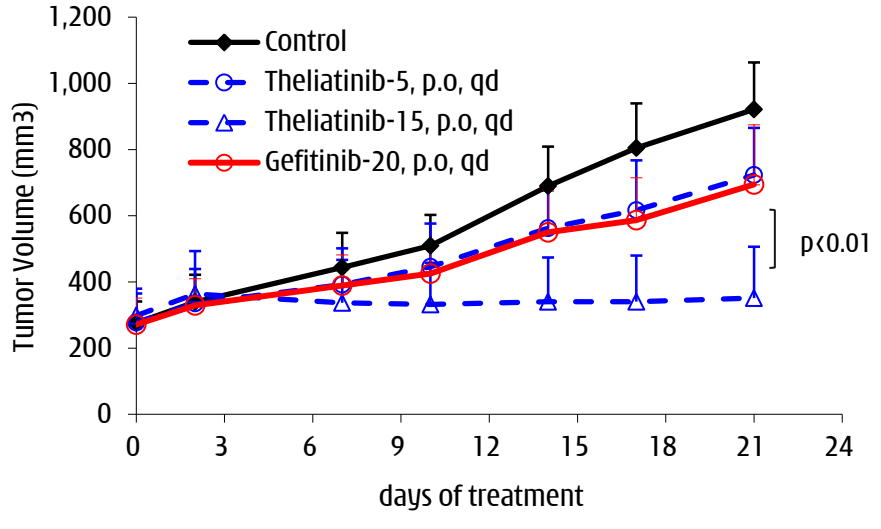


Theliatinib demonstrated superior anti-tumor activity in EC PDX models

PDECX1T0326 (EGFR amplification, H score=290)



PDECX1T1315 (EGFR overexpression, H score=295)



- At clinically relevant doses, theliatinib demonstrated strong anti-tumor activity and appeared to be superior to gefitinib
- In a large panel of PDX, there appeared to be a good correlation between theliatinib efficacy and the level of EGFR protein expression (manuscript accepted for publication, OncoTarget, 2017)

Gefitinib Phase III in esophageal cancer failed to meet OS, but…

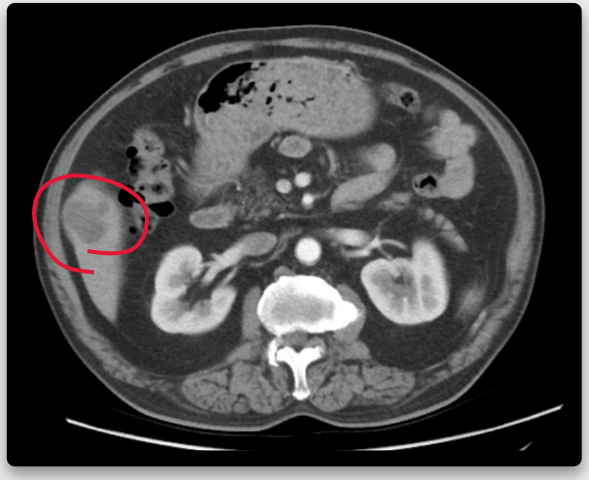
- 450 patients with histologically confirmed EC or GEJ tumors, failed 1-2L chemotherapies, were randomized 1:1 to receive gefitinib (500 mg) or oral placebo once daily: PFS was 1.6 months in the gefitinib arm vs. 1.2 months in the placebo arm (HR = 0.80, p = 0.020); OS in the gefitinib arm vs placebo was 3.7 vs 3.6 months (p›0.05)
- Subgroup analysis in EGFR FISH available 295/450 patients showed good efficacy in patients with EGFR gene amplification. *(2014 ASCO Abstract #4016)*
- Data suggest that with proper patient selection and a superior EGFR TKI, significant OS benefit is possible

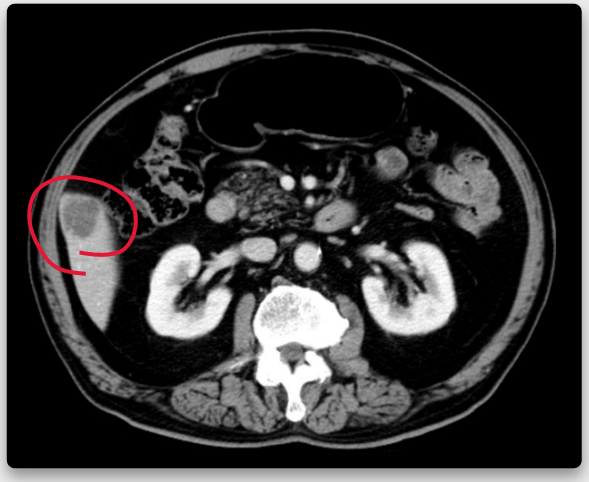
Subgroup	Treatment	OS	PFS	DCR
Gene Amp. (18 pt, 6.0%)	Gefitinib / Placebo	HR=0.19, p=0.007	Not shown	Not shown
Copy no. gain (CNG) (46 pt., 15.6%)	Gefitinib / Placebo	HR=0.53, p=0.042	HR=0.58, p=0.080	42% vs 13%, p=0.035
No CNG	Gefitinib / Placebo	HR=0.89, p=0.395	HR=0.83, p=0.144	24% vs 14 %, p=0.053

Petty RD et al. Epidermal growth factor receptor copy number gain (EGFR CNG) and response to gefitinib in esophageal cancer (EC): Results of a biomarker analysis of a phase III trial of gefitinib versus placebo (TRANS-COG). J Clin Oncol 32:5s, 2014 (suppl; abstr 4016).

Theliatinib PoC Phase I expansion in EC ongoing: an early case

- Man, 62, diagnosed with stage IV **esophageal squamous cell cancer** cT3N0M1 with **liver metastasis** on May 4, 2016.
- **High protein overexpression** - EGFR IHC local test: >75% of tumor cells 3+.
- Previous anti-cancer treatments: May 4, 2016 to Sep 23, 2016 - nimotuzumab/placebo + paclitaxel + cisplatin - **six cycles with best tumor response: disease progression.**
- Oct 11, 2016 began theliatinib 400mg daily treatment.
- Dec 12, 2016 - Cycle 3 Day 1 (C3D1) tumor assessment: **Target lesion (liver metastasis) shrank -33%** (36mm to 23mm diameter) - unconfirmed partial response.
- Withdrew from study on Jan 23, 2017 due to AEs - Grade 1 (diarrhea / pruritus / dental ulcer) Grade 2 (epifolliculitis / dermatitis).





Theliatinib summary and development plans

- WT EGFR activation affects multiple cancers, most without effective treatment
- Theliatinib has greater affinity to WT EGFR protein and has shown strong anti-tumor activity in EC PDX models with good correlation to level of EGFR expression
- Phase I dose escalation ongoing
  - Well tolerated, MTD has not been reached
  - Drug exposures well above expected efficacious exposure
  - Expect to complete dose escalation H2/2017
- Proof of concept study in tumors with WT EGFR activation
  - Expansion in esophageal cancer ongoing, expect to enroll 10-15 patients in stage 1 with pre-defined molecular profile for patient selection
  - Other cancers to consider include NSCLC and head and neck. The patient selection criteria are being worked out

Additional Early Stage Programs

HMPL-523 -Syk inhibitor,

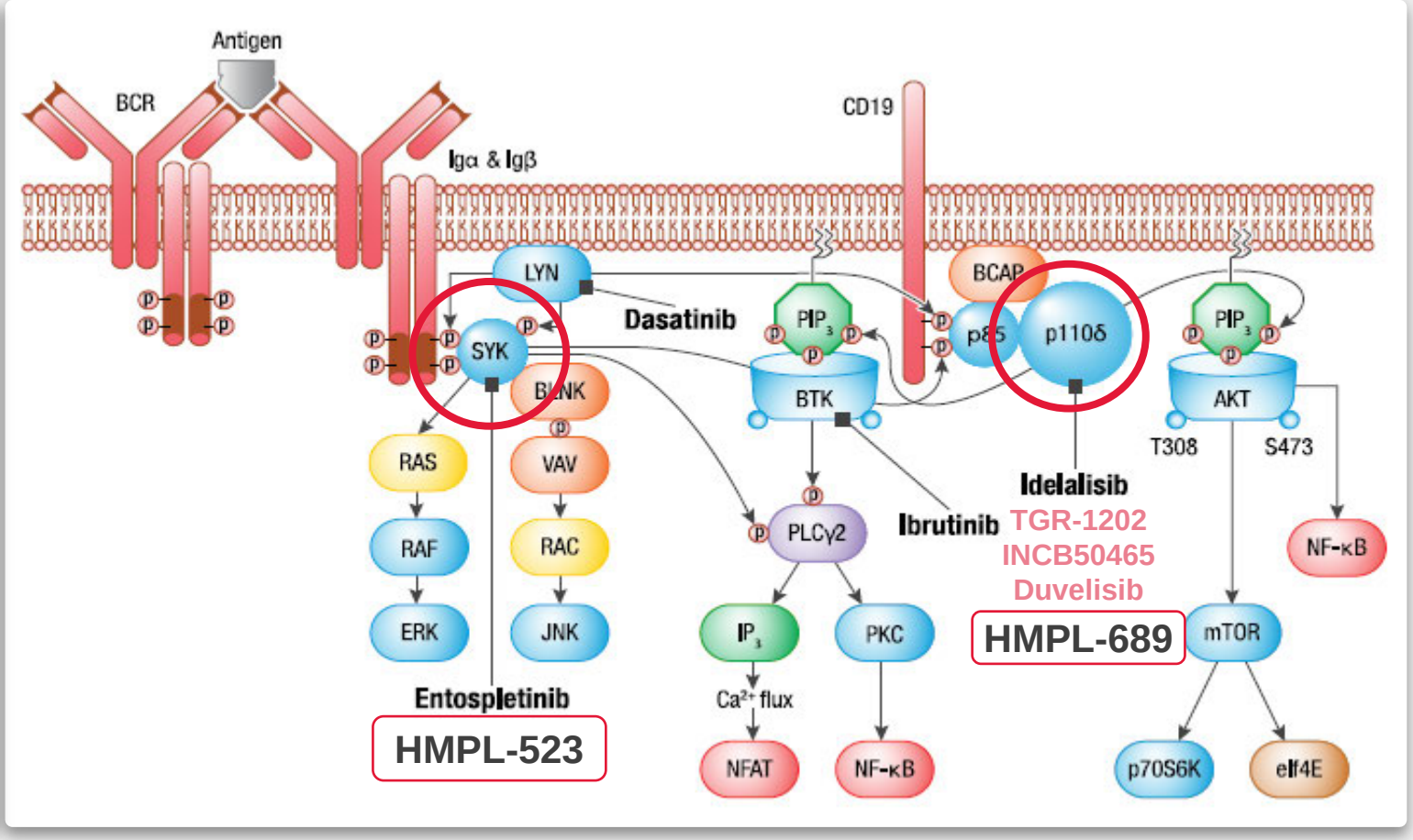
HMPL-689 - PI3Kδ inhibitor,

and HMPL-453 - selective FGFR inhibitor

… all progressing as planned in dose escalation

HMPL-523: potential first-in-class Syk inhibitor

- Syk a key signaling molecule in B cell activation, proliferation, and migration
- Potential for both immunology and oncology indications, particularly hematologic cancers



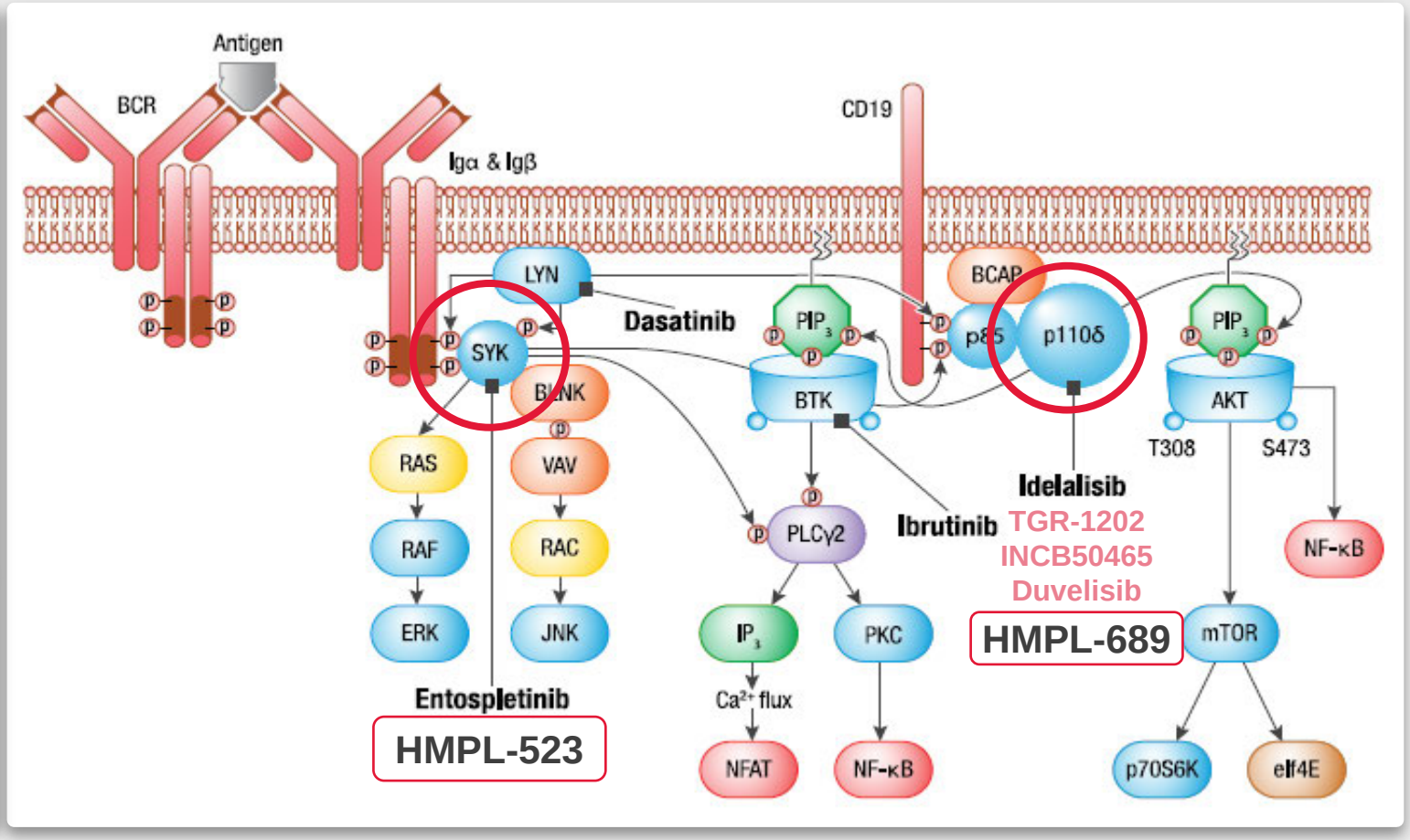
HMPL-523: potential first-in-class Syk inhibitor

- Development status
  - Completed dose escalation and expansion in healthy subjects, data disclosed at 2016 ACR conference
    - US IND on hold, plan to submitting GLP toxicity data for M1 mid-2017
  - Dose escalation in lymphoma patients ongoing both in AU and in China, expect to initiate dose expansion H2/2017
    - Targeting to present preliminary hematological malignancies efficacy data by YE 2017

- Development plans
  - China: focus on hematologic malignancies with high likelihood of success and fast track registration potential
  - AU or US: plan to explore novel combination

HMPL-689: validated target for B cell lymphomas

- Potential for first in China and best-in-class globally
- Potential for novel combinations such as with HMPL-523

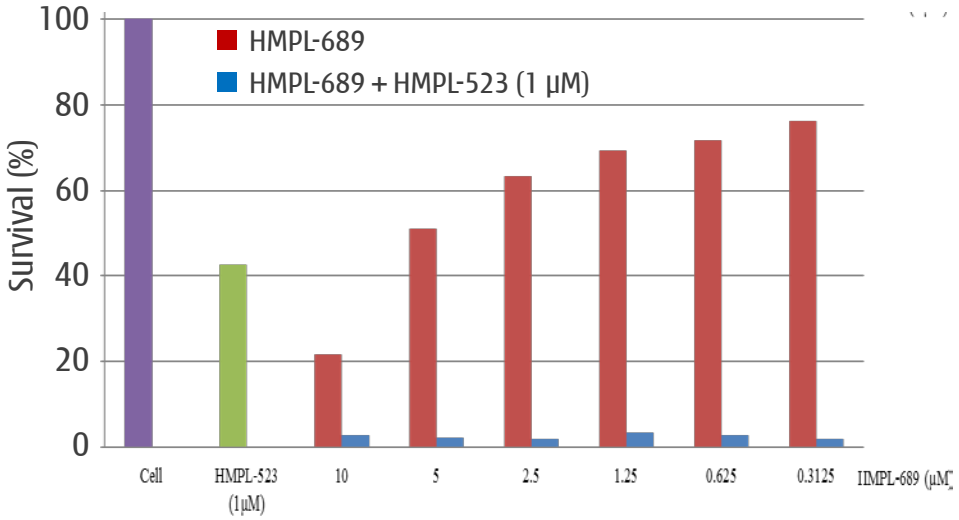


HMPL-689:
A high potent and selective PI3Kδ inhibitor

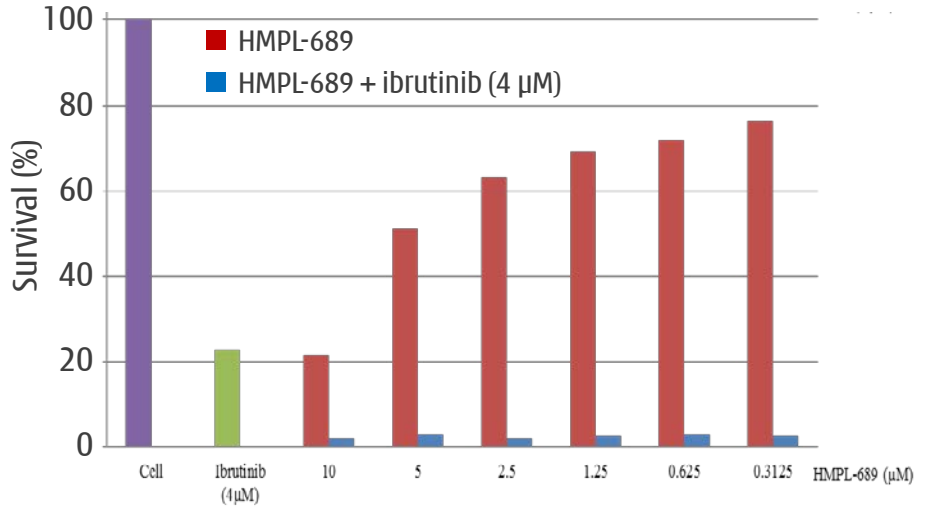
- Development status
  - Completed Phase I dose escalation in AU with favorable PK and safety profile
    - Efficacious dose range defined
- Development plans
  - China
    - IND cleared, dose escalation in hematologic cancer patients to begin in 3Q 2017
    - Focus on mature indications for fast track approval in China
  - AU or US
    - Explore for novel combinations

HMPL-689: Combinations have potential to improve DLBCL treatment

HMPL-689 Combination with HMPL-523 in SU-DHL-5 Cell

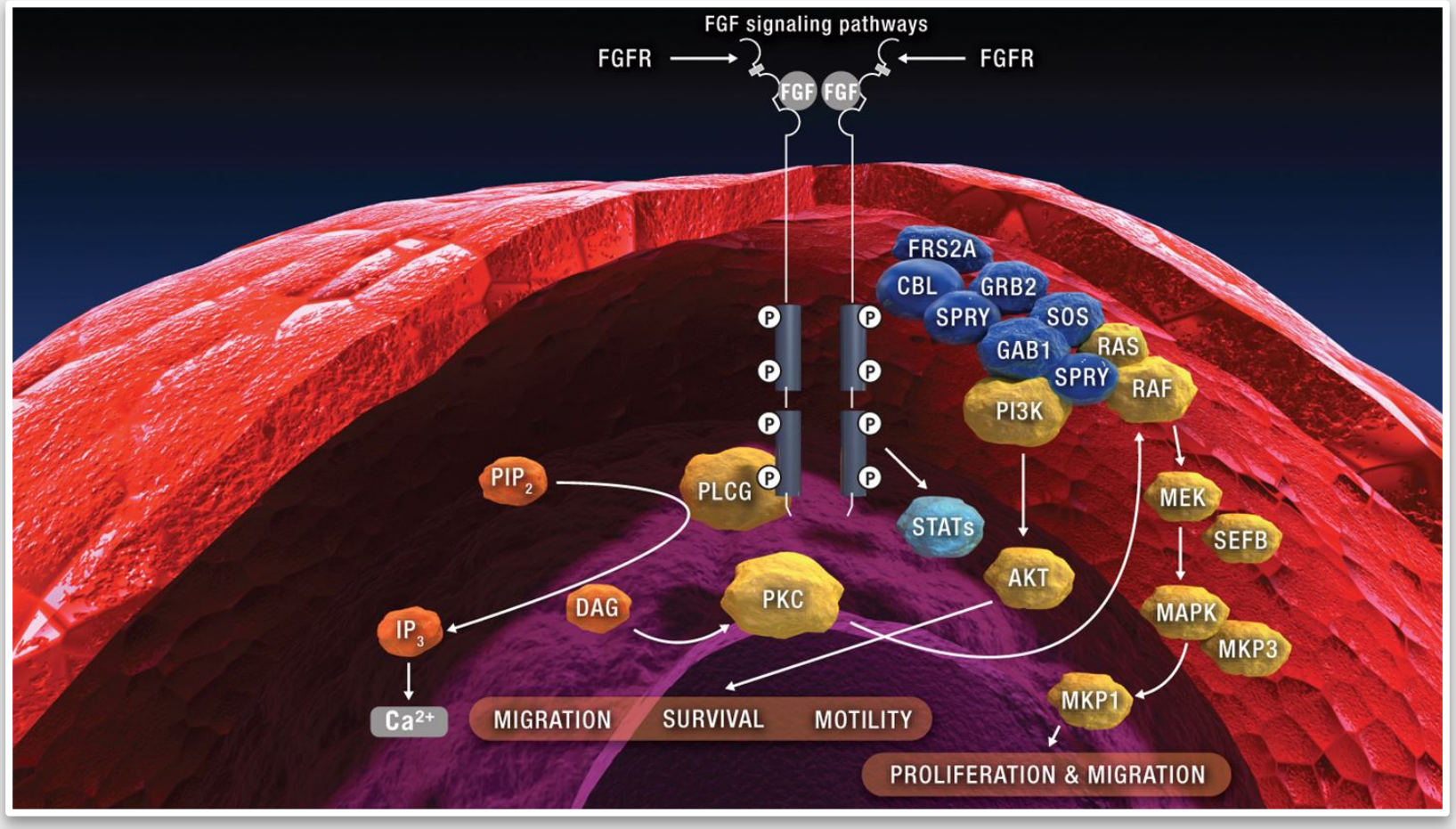


HMPL-689 Combination with ibrutinib in SU-DHL-5 Cell



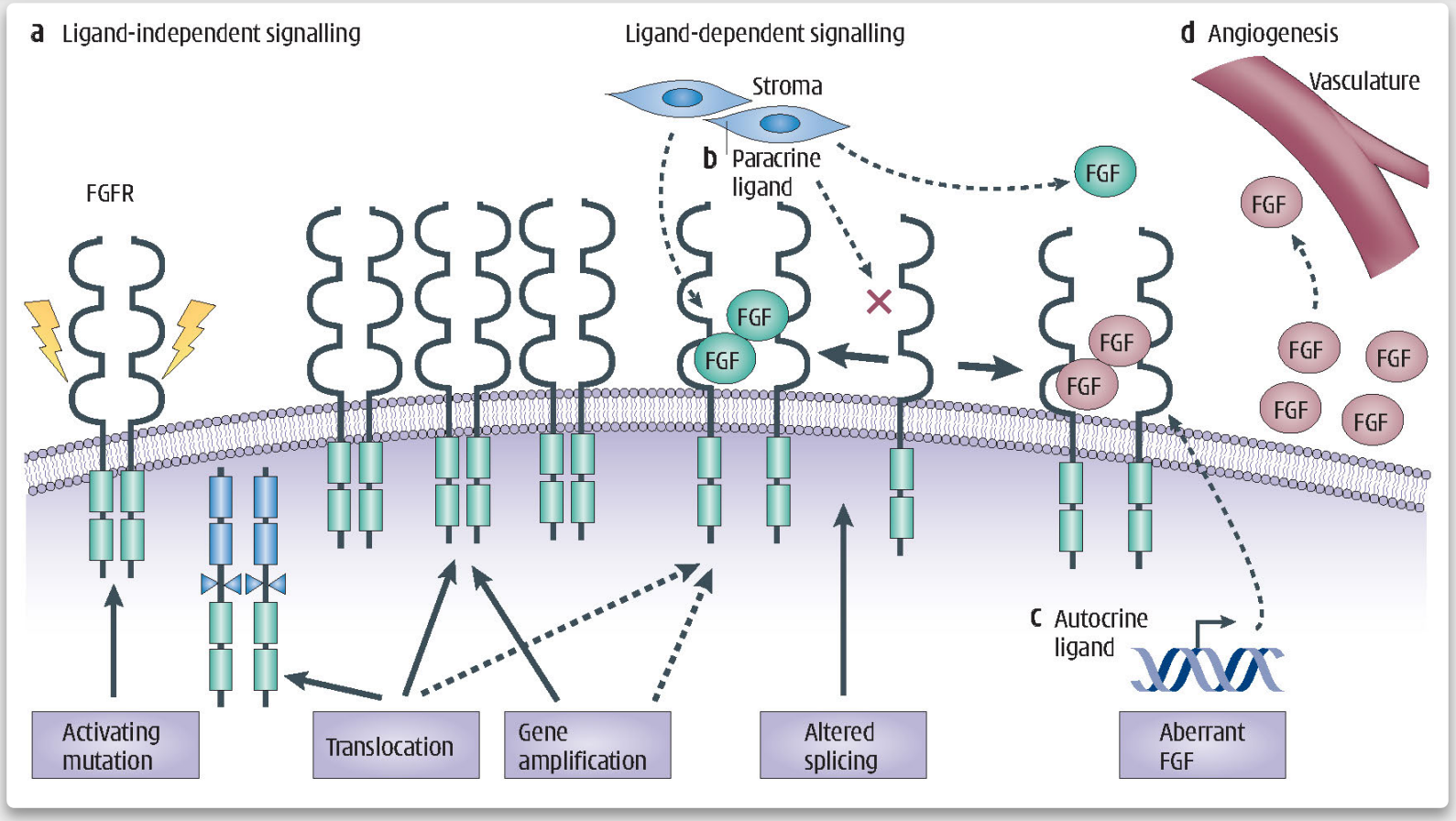
Significant synergy was observed when HMPL-689 was combined with a Syk or BTK inhibitor against difficult to treat DLBCL cell line SU-DHL-5

HMPL-453: a selective FGFR1,2,3 inhibitor



In normal physiology, FGF/FGFR signaling is involved in embryonic development (Organogenesis and Morphogenesis), tissue repair, angiogenesis, neuroendocrine and metabolism homeostasis.

FGFR genetic alterations are oncogenic drivers



There are multiple oncogenic driver genetic alterations in FGFR pathway: gene amplification, mutation, translocation, fusion, splicing, etc.

Turner N *et al.* Nat Rev Cancer 2010;10(2):116-129

HMPL-453: a selective FGFR inhibitor
targeting tumor with driver gene alterations in FGFR1, 2, 3

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	Gene amplification	Gene translocation	Gene mutation
FGFR1	**Lung squamous** (7~15%) **H&N squamous** (10~17%) **Esophageal squamous** (9%) **Breast** (10~15%)	**Lung squamous** (n/a) **Glioblastoma** (n/a) **Myeloproliferative syndrome** (n/a) **Breast** (n/a)	**Gastric** (4%) **Pilocytic astrocytoma** (5~8%)
FGFR2	**Gastric** (5~10%) **Breast** (4%)	**Intra-hepatic cholangiocarcinoma** (14%) **Breast** (n/a)	**Endometrial** (12~14%) **Lung squamous** (5%) .....
FGFR3	**Bladder** (n/a) **Salivary adenoid cystic** (n/a)	**Bladder** (3~6%) **Lung squamous** (3%) **Glioblastoma** (3%) **Myeloma** (15~20%)	**Bladder** (60~80% NMIBC; 15~20 MIBC) **Cervical** (5%)

- Diverse and complicated genetic changes and multiple tumor types with low incidence
- Cholangiocarcinoma (CCA) and bladder cancer are made much progress in clinic to date

BGJ398 Phase II PoC in cholangiocarcinoma (2016 ASCO GI)

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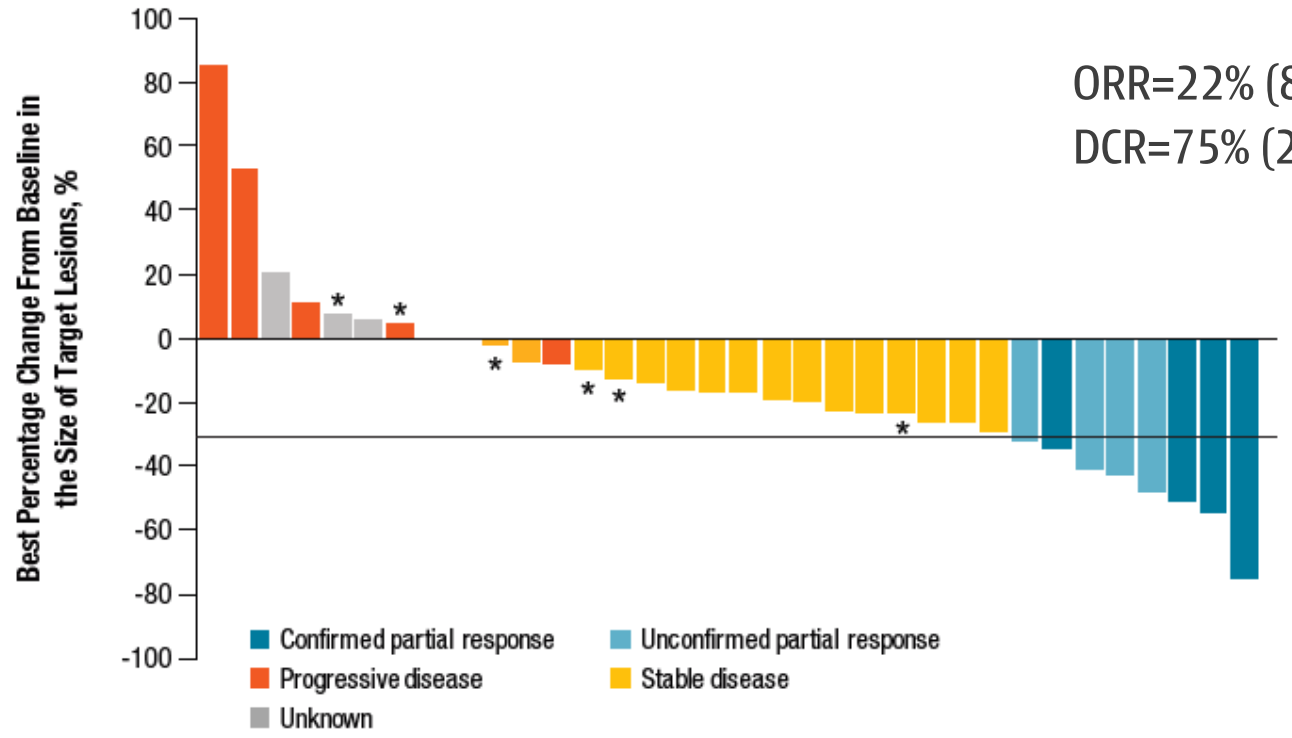
Figure 3. Best Percentage Change From Baseline in the Size of Target Lesions With BGJ398 Treatment (n = 34)[a,b]

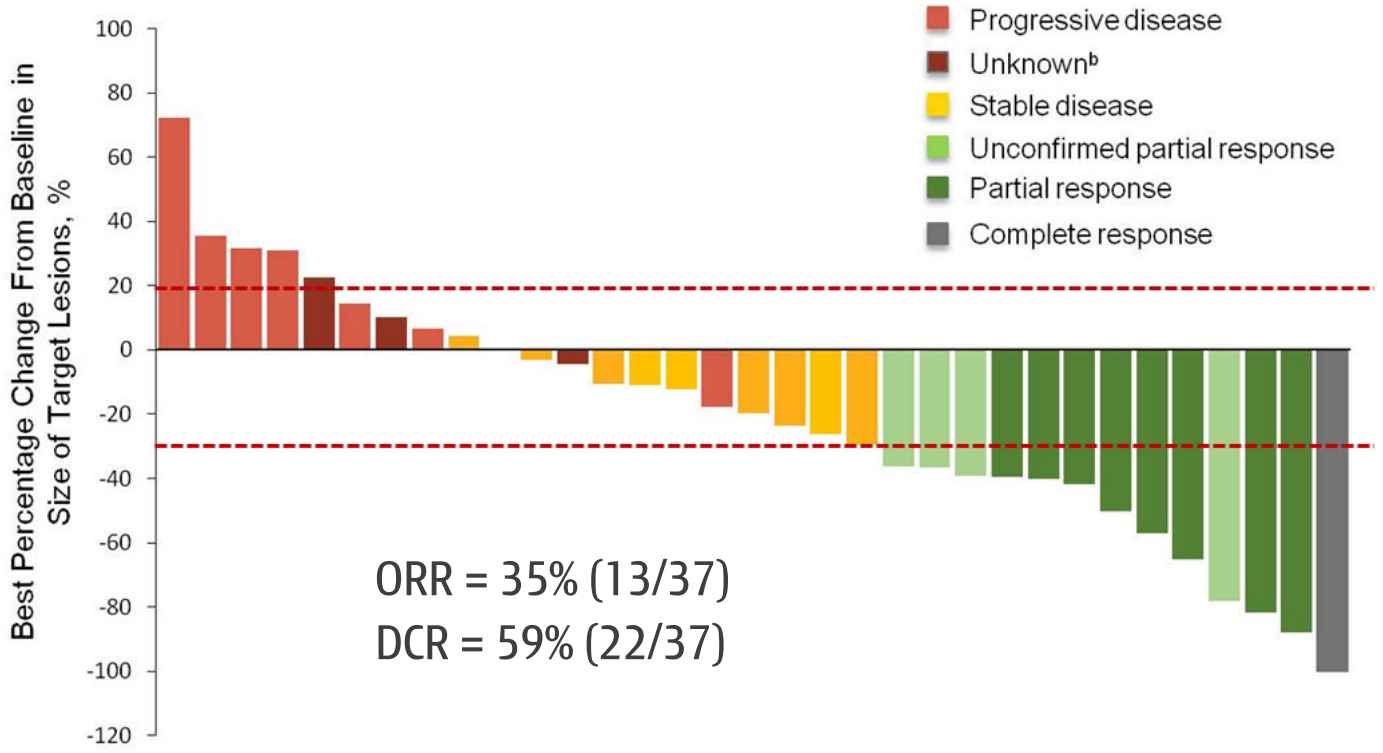


[a] Two patients were not included in the analysis (best percentage change could not be calculated because the scan modality changed [n = 1] and patient had no postbaseline scan due to treatment discontinuation [n = 1]).

[b] Patients marked with an asterisk had *FGFR2* mutations (n = 2) or amplification (n = 3), or *FGFR3* amplification (n = 1). All other patients had *FGFR2* fusions (n = 28).

BGJ398 Phase II PoC in bladder cancer (2016 ASCO)

Percentage Change From Baseline in Target Lesion Size with BGJ398 Treatment (N=33)[a]



[a] Data are from the 33 patients with assessment of measurable lesions at baseline and post-baseline with the same assessment method

[b] Unknown includes post-baseline assessment performed too early to be considered stable disease (n = 2), method change at first post-baseline assessment (patient ongoing at data cutoff, n = 1), and best response unknown due to data error (n = 1).

HMPL-453

- Status and plans
  - ↗ AU dose escalation ongoing
  - ↗ China IND cleared, Phase I dose escalation expected to kick off mid-2017

Rapidly progressing pipeline:
March 2017 Key Programs

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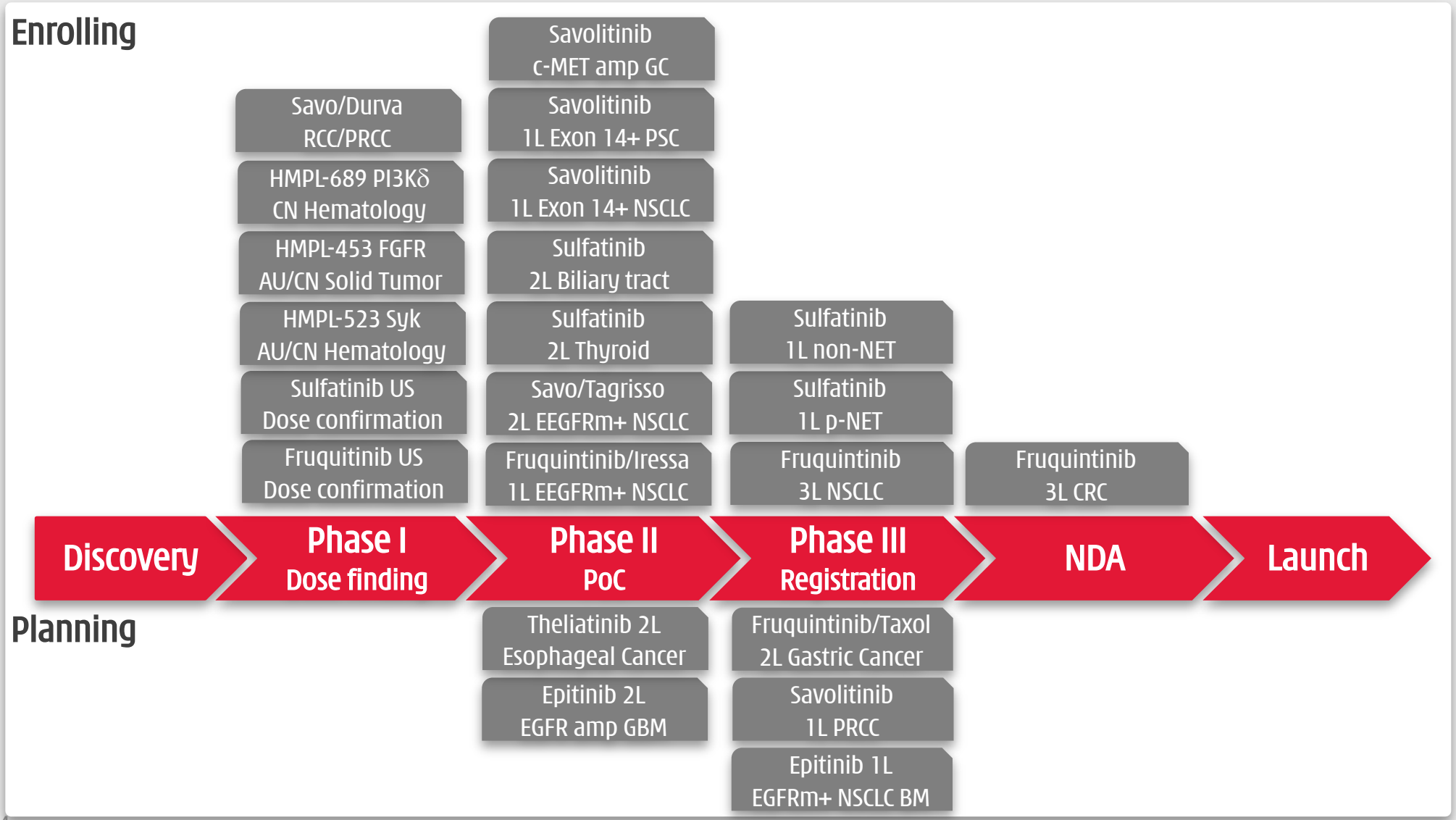
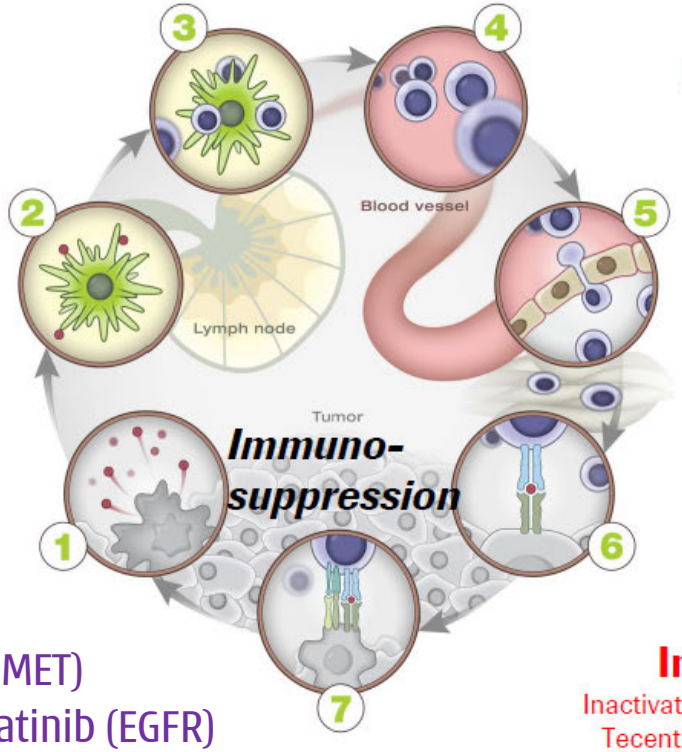


Research Strategy: The 3rd Wave

The next wave new candidates:
IO focused, potential to combine with existing programs a priority

Immune desert
Insufficient T cell response

Priming & activations
- *aOX40*
- *4-1BB*



Excluded infiltrate
Inadequate T cell homing

Anti-angiogenesis
- VEGFR (fruquintinib)
- VEGFR/FGFR (sulfatinib)
- FGFR (HMPL-453)

Trafficking
- CCRs

Antigen release
- Savolitinib (c-MET)
- Epitinib/Theliatinib (EGFR)
- HMPL-453 (FGFR)
- HMPL-523 (Syk)
- HMPL-689 (PI3Kδ)
- ERK, RIP3K, IDH

Inflamed
Inactivated T cell response:
Tecentriq most effective

Negative regulators
- Treg (HMPL-689)
- CSF-1R (sulfatinib)/selective CSF-1R
- IDOi, AhRi
- *TIM3, TCBs*

- Clinical
- Pre-clinical
- *Italics: antibody*

Derived from Chen DS et al. Oncology Meets Immunology: The Cancer-Immunity Cycle. Immunity , Volume 39 , Issue 1 , 1 - 10.

Chi-Med R&D update summary

- Current pipeline: deep and broad
  - 8 clinical candidates, 30 active trials globally
  - Three major partnerships: AstraZeneca, Lilly, and Nestlé Health Science
- Steady flow of late stage results delivery
  - 4 compounds in 8 pivotal registration trials by year end
  - Nearing first product launch in company history
    - Fruquintinib in 3L CRC in China: NDA mid-2017, target launch in 2018
- Next wave of discoveries: IO focus
  - Tumor antigen release by targeting driver genes
  - Immune cell activation
  - Tumor immune evasion

Expected near-term catalysts

During the balance of 2017

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Target to publish data on 4 drug candidates in 5 Phase II-III studies:

- ✓ **Savolitinib:**
  1. Phase II **median overall survival data in PRCC**;
  2. **Phase IIb data in 2nd-line NSCLC** combinations with Tagrisso® & Iressa®;
  3. Phase II dose finding data in ccRCC combination with durvalumab (PD-L1).
- ✓ **Fruquintinib:**
  4. **Phase III FRESCO study full data set** publication in colorectal cancer.
- ✓ **Sulfatinib:**
  5. Preliminary Phase II POC data in medullary and differentiated thyroid cancer.
- ✓ **HMPL-523 (Syk):**
  6. Preliminary Phase Ib proof-of-concept data in hematological cancer.

Target multiple late-stage/global clinical & regulatory milestones by 2017 YE:

- ✓ **Savolitinib:**
  1. Initiate **global Phase III study in PRCC**;
  2. Initiate **global Phase III study in 2nd-line NSCLC** in combination with Tagrisso®;
- ✓ **Fruquintinib:**
  3. **Submit New Drug Application** ("NDA") in China in 3rd-line CRC;
  4. Initiate **China Phase III study in 2nd-line gastric cancer**;
  5. **Complete enrollment of Phase III FALUCA** study in 3rd-line NSCLC;
  6. Initiate **U.S. Phase I bridging study** in Caucasian patients.
- ✓ **Epitinib:**
  7. Initiate **China Phase III in 1st-line EGFR-mutant NSCLC** with brain metastasis;
  8. Initiate China Phase II study in glioblastoma (primary brain cancer).
- ✓ **Sulfatinib:**
  9. Initiate **U.S. Phase II study in NET**.
- ✓ **HMPL-523:**
  10. Initiate **Australian Phase Ib/II expansion study in hematological cancer**.
- ✓ **HMPL-689 (PI3Kδ):**
  11. Initiate Phase I studies in China in hematological cancer.
- ✓ **HMPL-453 (FGFR):**
  12. Initiate Phase I studies in Australia/China in solid tumor.

Transforming into a fully integrated Biopharma in China

Christian Hogg, Chief Executive Officer

Zhenping Wu, Head of Pharmaceutical Sciences

High level - Go-to-market
Building all required competencies

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Manufacturing

Active Pharmaceutical Ingredient ("API") manufacturing

Drug Product - Formulation & Packaging

Manufacturing License Holder

Commercial

Pharmaco-vigilance

Medical Affairs

Compliance

Marketing

Government Affairs Pricing & Policy

Sales Management & Administration

Medical Detailing

- Tier 1 - Major Hospitals
- Tier 2 or below - Primary Hospitals

Commercial / Distribution

- Commercial channel management & sales
- Pharmacy promotion and patient education

Transforming into a fully integrated Biopharma in China: Manufacturing

Zhenping Wu, Head of Pharmaceutical Sciences

Active Pharmaceutical Ingredients (API)

API manufacturing

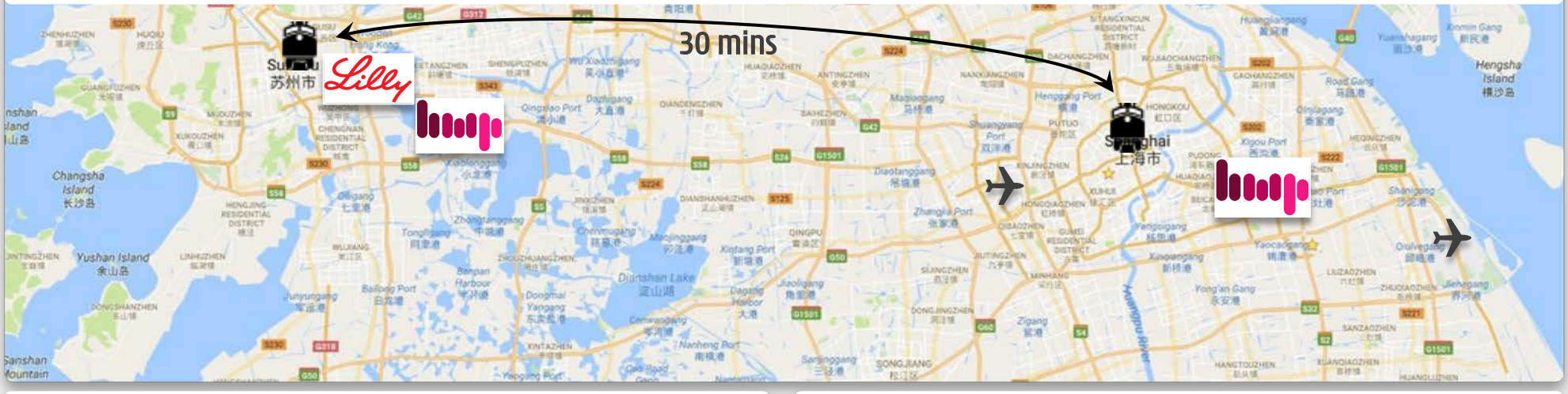
- Leverage the high quality contract manufacture API vendors available in China with track record
- Strong working relationship has been built over many years with selected global quality vendors

ASYMCHEM

STA 合全药业 | WuXi AppTec

Drug Product - Formulation & packaging

HMP Suzhou Drug Product facility built approx. 100km from main Shanghai R&D facility



HMP Suzhou Formulation facility - 4,000 sqm.

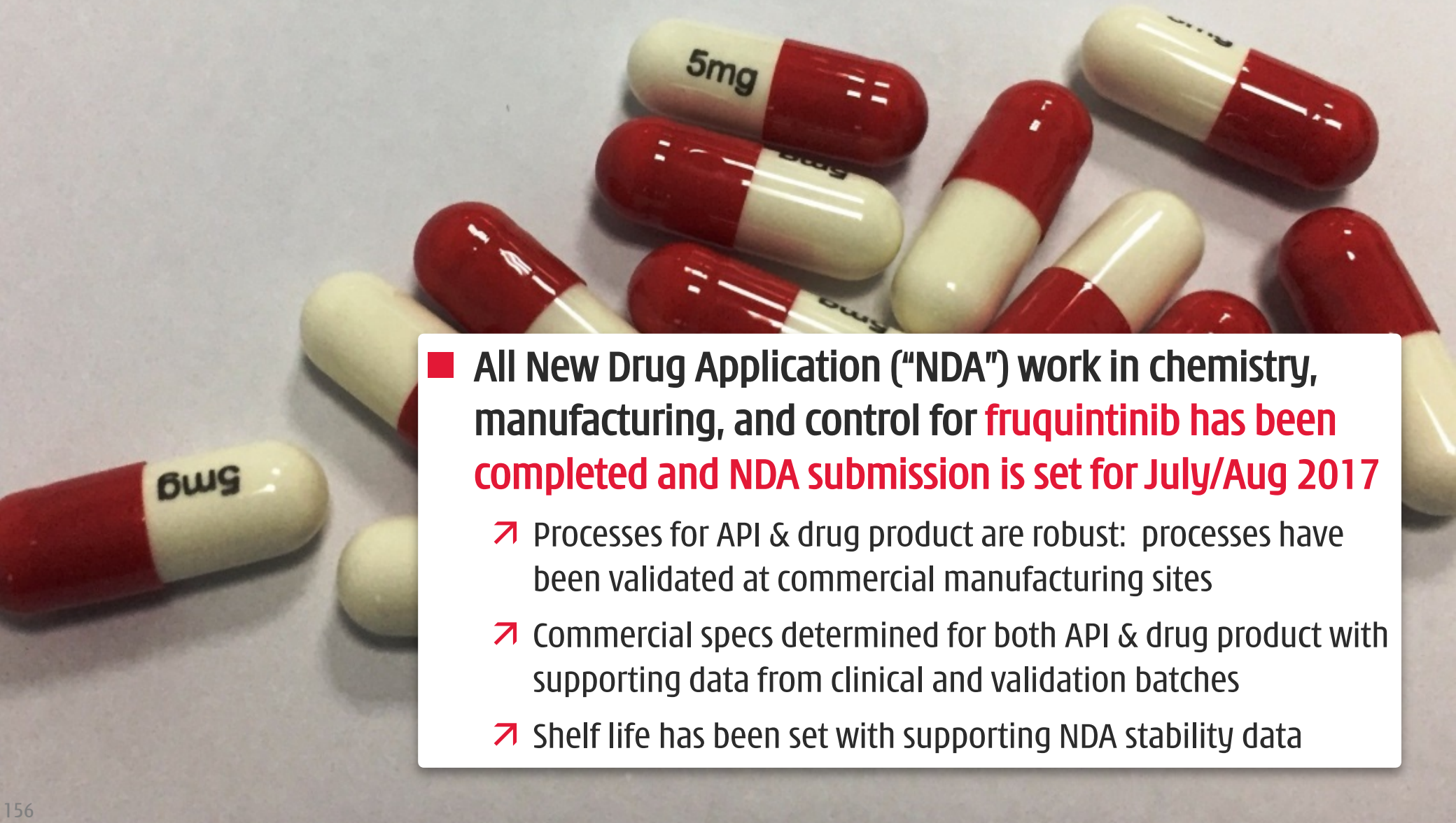
Main HMP Shanghai R&D facility - 5,000 sqm.

HMP Suzhou Drug Product facility: Global GMP standards

- Facility will be the commercial manufacturing site for all Chi-Med new products in China
- In operation since 2014 and designed to meet global Good Manufacturing Practice ("GMP") standards
- 1st phase complete to support all fruquintinib commercial and clinical supply needs
- 2nd phase expansion ongoing to support commercialization of all other products
- Current organization has ~40 employees in production, engineering, supply chain, quality control and quality assurance

HMP Suzhou Drug Product facility: Global GMP standards

Fruquintinib manufacturing of commercial Drug Product – ready to go



- **All New Drug Application ("NDA") work in chemistry, manufacturing, and control for fruquintinib has been completed and NDA submission is set for July/Aug 2017**
  - ↗ Processes for API & drug product are robust: processes have been validated at commercial manufacturing sites
  - ↗ Commercial specs determined for both API & drug product with supporting data from clinical and validation batches
  - ↗ Shelf life has been set with supporting NDA stability data

Fruquintinib manufacturing of commercial Drug Product – ready to go

- **Both the API vendor and the Suzhou plant are ready for the pre-approval & GMP inspections**
  - ↗ Multiple batches have been prepared at the commercial sites successfully demonstrating the sites are capable of producing high quality commercial products
  - ↗ Processes and protocols follow global quality standards

Transforming into a fully integrated Biopharma in China: Commercial

Christian Hogg, Chief Executive Officer

16 years spent building Rx commercial infrastructure

CHI-MED

Non-Consolidated Joint Ventures

Chi-Med Subsidiaries

Prescription Drugs

50%

Shanghai Hutchison Pharma ("SHPL")

Prescription Drugs

Partner: Shanghai Pharma Group

2016 Revenue: $222.4m

2015 Revenue: $181.1m

51%

Hutchison Sinopharm ("HSP")

Rx Drug Commercial Co.

Partner: Sinopharm Group

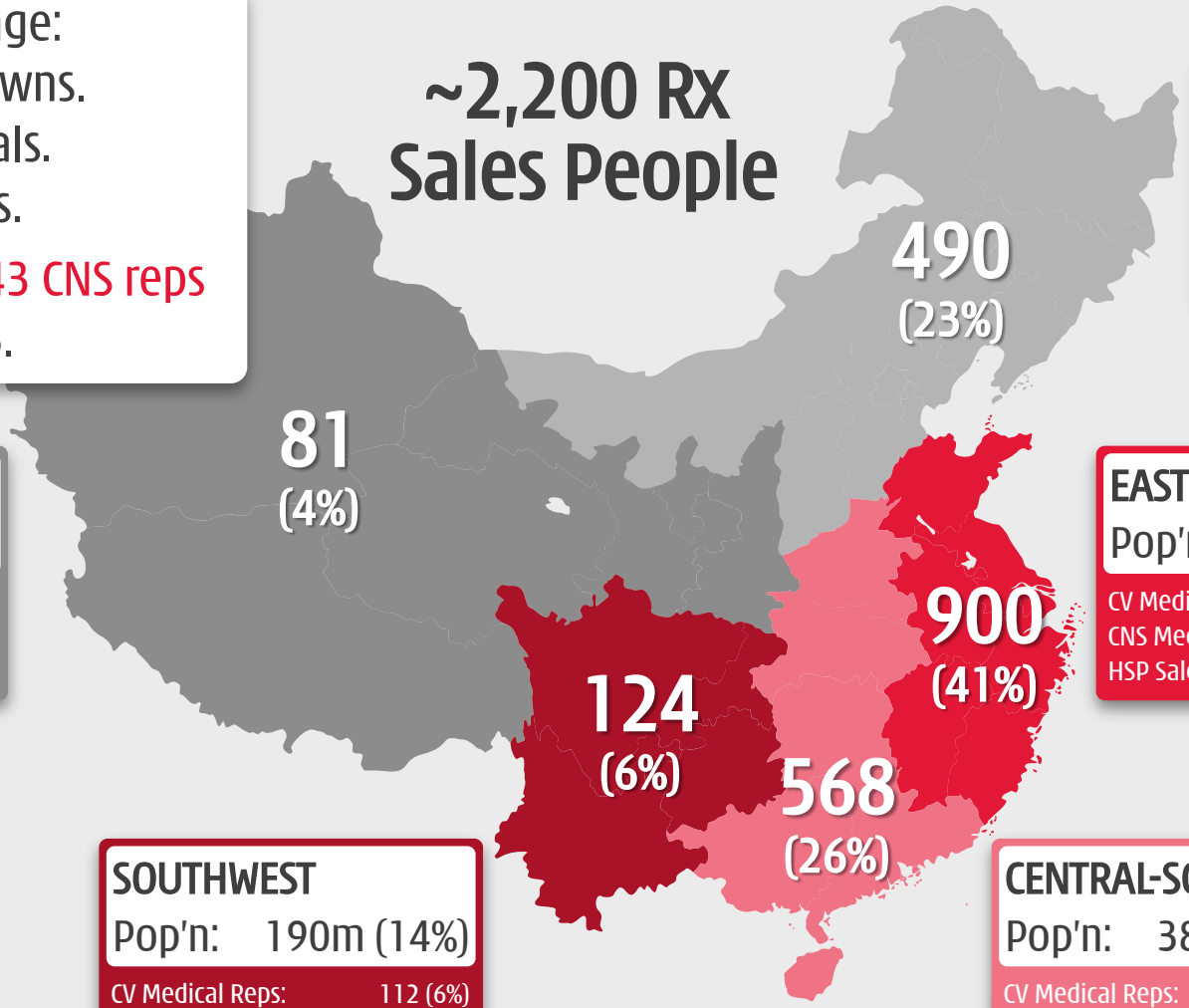
2016 Revenue: $149.9m

2015 Revenue: $105.5m

Capable Commercial Teams – since Chi-Med took-over operation of SHPL revenues are up >20X (<$10m in 2001) & HSP revenues up >3X (<$50m 2014)

A powerful Rx Commercial Platform in China

- National Coverage:
  ~300 cities & towns.
  ~18,700 hospitals.
  ~87,000 doctors.
- New team of 143 CNS reps built since 2015.



NORTH
Pop'n: 320m (23%)

CV Medical Reps:	458 (23%)
CNS Medical Reps:	32 (22%)
HSP Sales staff:	0 (0%)

WEST
Pop'n: 100m (7%)

CV Medical Reps:	76 (4%)
CNS Medical Reps:	5 (3%)
HSP Sales staff:	0 (0%)

EAST
Pop'n: 393m (28%)

CV Medical Reps:	808 (40%)
CNS Medical Reps:	61 (43%)
HSP Sales staff:	31 (100%)

SOUTHWEST
Pop'n: 190m (14%)

CV Medical Reps:	112 (6%)
CNS Medical Reps:	12 (9%)
HSP Sales staff:	0 (0%)

CENTRAL-SOUTH
Pop'n: 383m (28%)

CV Medical Reps:	535 (27%)
CNS Medical Reps:	33 (23%)
HSP Sales staff:	0 (0%)

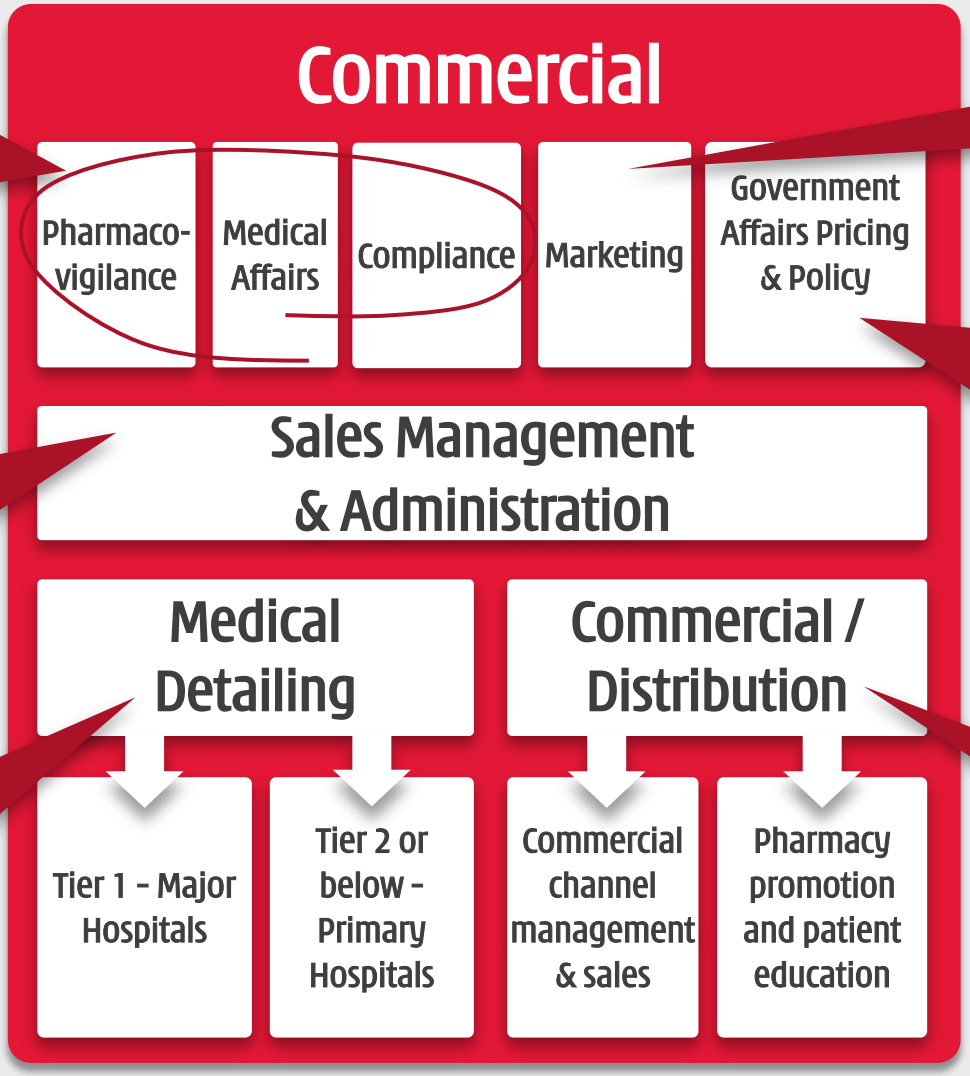
Notes: 2010 Population - China State Census;
CV = Cardiovascular; CNS = Central nervous system.
Chi-Med Rx sales team data = 31 December 2016

Deep competence & infrastructure in most areas

CHI-MED

4 staff covering Pharmacovigilance/MA (mature CV drug)
5 staff on compliance

39 staff:
11 central mkt. team
28 local mkt. team



Central/State level:
7 staff – State policy / management
Local level:
12 staff hospital bidding; medical insurance; pricing

28 sales offices in
11 sales regions
covering all 30 provinces

›2,000 staff covering
›4,700 Tier 1 & ›14,000 Tier 2 or below hospitals

›240 staff managing
›2,400 local comm. partners

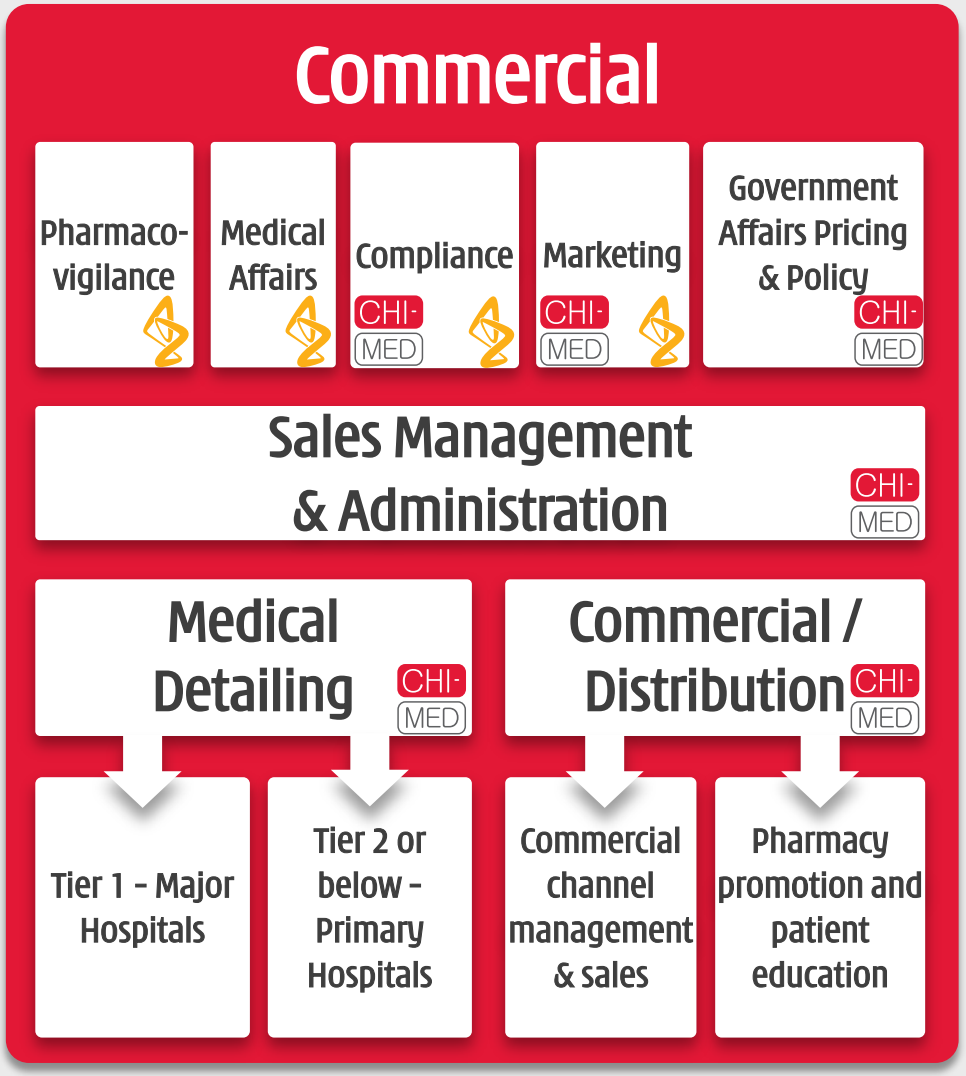
Case Study: Local company TKIs in China

Existing Chi-Med Commercial Platform – Speed to Peak Sales

		ATAN® Apatinib			Conmana® Icotinib		
COMPANY	Manufacturer	**Jiangsu Hengrui**			**Betta Pharma**		
	Listing : Ticker	Shanghai: 600276.SS			Shenzhen: 300558.SZ		
	Market Cap ($US - Mar 29, '17)	$18.3 billion			$4.2 billion		
	Founded	1970			2003		
	Commercial Team (# Reps @ YE2015)	5,491			296		
SALES SINCE LAUNCH	China FDA Approval (competitive status?)	Oct 2014 (only 3L GC drug)			Jun 2011 (multiple EGFR TKIs)		
	Launch Date	July 2015			August 2011		
	Yr 1 (Rev. US$m / Est. Mkt %)	2015	40	20%	2011	9	1%
	Yr 2 (Rev. US$m / Est. Mkt %)	2016	116	30%	2012	48	2%
	Yr 3 (Rev. US$m / Est. Mkt %)				2013	78	3%
	Yr 4 (Rev. US$m / Est. Mkt %)				2014	116	5%
	Yr 5 (Rev. US$m / Est. Mkt %)				2015	145	6%

 Sources: Betta Pharma IPO prospectus; Goldman Sachs.

Using Chi-Med structure to take over Seroquel



Strong outcome: 2016 sales of $34.4m (>20% organic growth in year 1)

Fruquintinib Go-to-market strategy – Roles & Responsibilities

Manufacturing

Active Pharmaceutical Ingredient ("API") manufacturing — CHI-MED

Drug Product – Formulation & Packaging
Manufacturing License Holder — CHI-MED

Commercial

- Pharmaco-vigilance — CHI-MED
- Medical Affairs — CHI-MED
- Compliance — Lilly
- Marketing — Lilly
- Government Affairs Pricing & Policy — Lilly

Sales Management & Administration — Lilly

- **Medical Detailing** — Lilly
  - Tier 1 – Major Hospitals
  - Tier 2 or below – Primary Hospitals
- **Commercial Distribution** — Lilly
  - Commercial channel management & sales
  - Pharmacy promotion and patient education

Ready to launch our products in China

Manufacturing

Active Pharmaceutical Ingredient ("API") manufacturing

Drug Product – Formulation & Packaging

Manufacturing License Holder

Commercial

- Pharmaco-vigilance
- Medical Affairs
- Compliance
- Marketing
- Government Affairs Pricing & Policy

Sales Management & Administration

Medical Detailing

- Tier 1 – Major Hospitals
- Tier 2 or below – Primary Hospitals

Commercial Distribution

- Commercial channel management & sales
- Pharmacy promotion and patient education

Global Commercialization Strategy

- Building China commercialization capability
- Selectively partner outside China after Proof-of-Concept
  - ↗ If accelerates global expansion
  - ↗ To gain global commercial experience
- Ultimately commercialize our products ourselves globally

Q&A


CHI-
MED
HUTCHISON CHINA MEDITECH
Thank you