Verastem Oncology

Addressing RAS Pathway Blockade & Resistance

VS-6766 & Defactinib Combination Data in KRAS Mutant Solid Tumors

Investor Conference Call and Webcast

NASDAQ: VSTM

April 27, 2020

Speakers

Verastem Oncology

Brian Stuglik
CEO

Jon Pachter
CSO

Dan Paterson
COO

Rob Gagnon
CFO

Lead Investigator

Udai Banerji,
MBBS, MD, DNB, PhD, FRCP

Professor Udai Banerji is the deputy head of the Drug Development Unit where he is involved in running the portfolio of more than 40 Phase I trials. He plays a key role bridging pre-clinical and clinical drug discovery by designing and conducting Phase I studies.

In addition to clinical trials, Professor Banerji leads the Clinical Pharmacodynamics Biomarker Group and the Clinical Pharmacology – Adaptive Therapy Groups at The Institute of Cancer Research. His laboratory interests include anticancer drug resistance and pharmacological aspects of cancer evolution.

Professor Banerji holds a PhD from The Institute of Cancer Research and completed his medical oncology training at The Royal Marsden Hospital.

Agenda

Topic	Presenter
• Introduction	• Brian Stuglik
• RAS Pathway: Current Approaches and Unmet Needs • RAS Pathway Blockade: Bypass Mechanisms and Resistance • VS-6766 and Defactinib	• Jon Pachter
• Phase 1 Combination Data	• Udai Banerji
• Next Steps • Concluding Remarks	• Dan Paterson & Brian Stuglik

Safe Harbor Statement

This presentation includes forward-looking statements about, among other things, Verastem Oncology's products and product candidates, including anticipated regulatory submissions, approvals, performance and potential benefits of Verastem Oncology products and product candidates, that are subject to substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements.

Additional information regarding these factors can be found in Verastem Oncology's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in any subsequent filings with the SEC, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors that May Affect Future Results," as well as in our subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission (SEC) and available at www.sec.gov and www.verastem.com.

The forward-looking statements in this presentation speak only as of the original date of this presentation, and we undertake no obligation to update or revise any of these statements.

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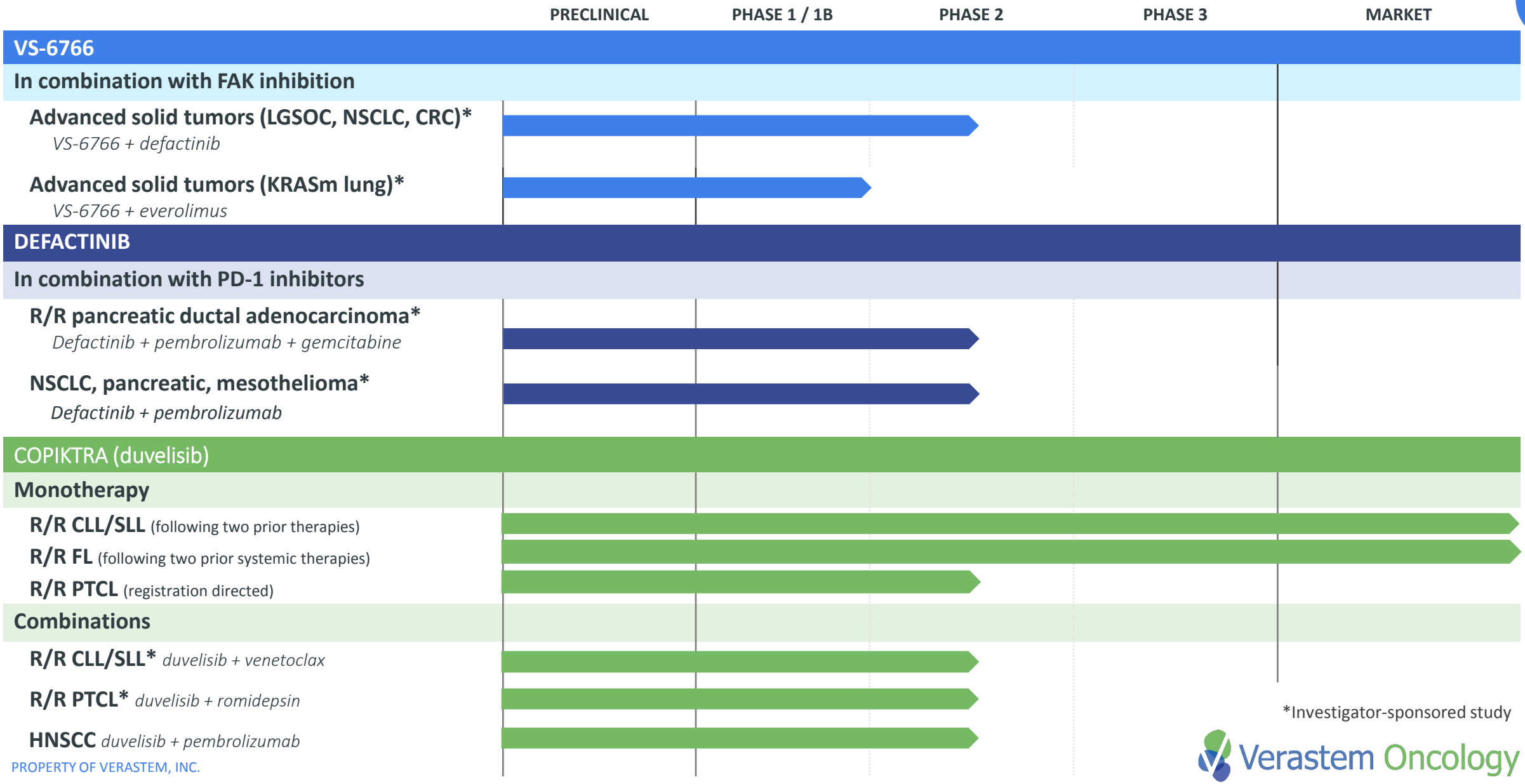
We are a biopharmaceutical company committed to developing and commercializing new medicines for patients battling cancer

New lead clinical program has best-in-class potential	VS-6766 (RAF/MEK) and defactinib (FAK) inhibition clinically active against KRAS mutant variants, especially KRAS G12V & G12D
Rapid development pathway to market	Clinical proof-of-concept achieved in KRAS mutant low-grade serous ovarian cancer (LGSOC); goal to initiate registration-directed trial in 2020
Significant downstream market opportunity and blockbuster potential	30% of all human cancers are driven by mutations in RAS family of genes; VS-6766 combinations poised to fuel the future pipeline
Strong balance sheet and investor syndicate	Cash runway into the fourth quarter of 2021; recent financing funded by several premier life science investors
Revenue-generating commercial asset with multiple planned indication expansion opportunities	COPIKTRA® (duvelisib) generated $12.3M in 2019 and $5.0M in 1Q20 in approved indications; actively working toward label expansions in PTCL and other hematologic malignancies

Key Pipeline Programs Aligned with New Strategic Direction



*Investigator-sponsored study

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RAS Pathway: Current Approaches and Unmet Needs

Jon Pachter, PhD

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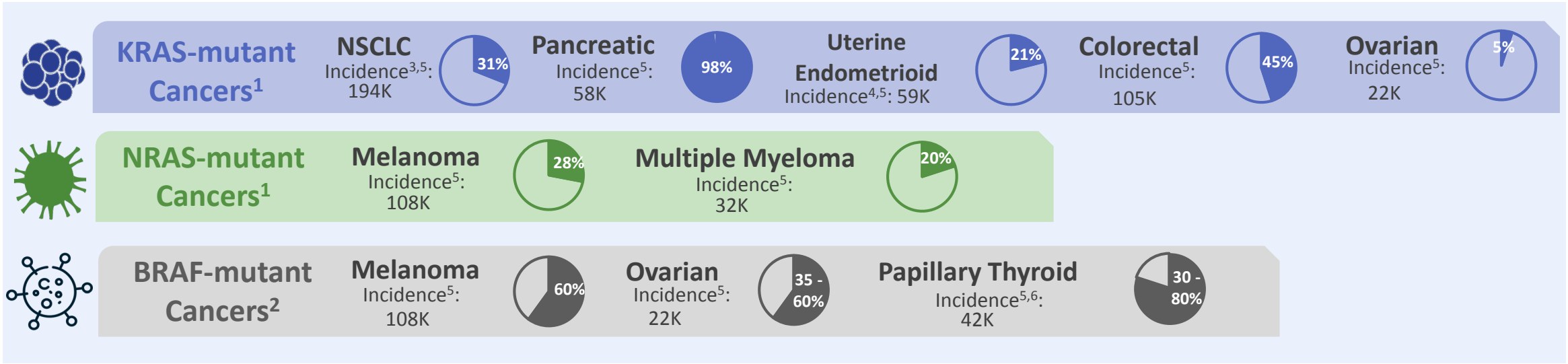
High Unmet Needs in RAS/RAF/MEK/ERK-Driven Cancers



Breadth of potential opportunity

- 30% of all human cancers are driven by mutations of the RAS family of genes

Established prognostic significance

- Patients with mutations of the RAS family have an overall worse prognosis

Challenges with conventional approaches

- Modest progress; limited number of approved therapies
- Single agent therapies (e.g. MEK inhibitors) associated with resistance
- Tolerable combination regimens with MEK inhibitors have been challenging

Incidence Sources:

[1]Reference for RAS mt frequencies – Cox et al. Nature Reviews 13: 828, 2014
[2]Reference for BRAF mt frequencies – Turski et al. Mol Cancer Ther 15: 533, 2016
[3]85% of lung cancer is NSCLC (Lu et. al. Cancer Manag Res. 2019)
[4] 90% of all uterine cancers are of the endometrial type (ACS)
[5] Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30
[6] 8 out of 10 thyroid cancers are of the papillary type (ACS)

References:

McCormick F Clin Cancer Res 15April2015
Adderley H et al. EBioMedicine 01Mar2019
Papke B et al. Science 17Mar2017
Ryan M et al. Nature Reviews Clinical Oncology 01Oct2018
NIH cancer.gov/research/key-initiatives/ras

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RAS Pathway Blockade: Bypass Mechanisms and Resistance

Jon Pachter, PhD

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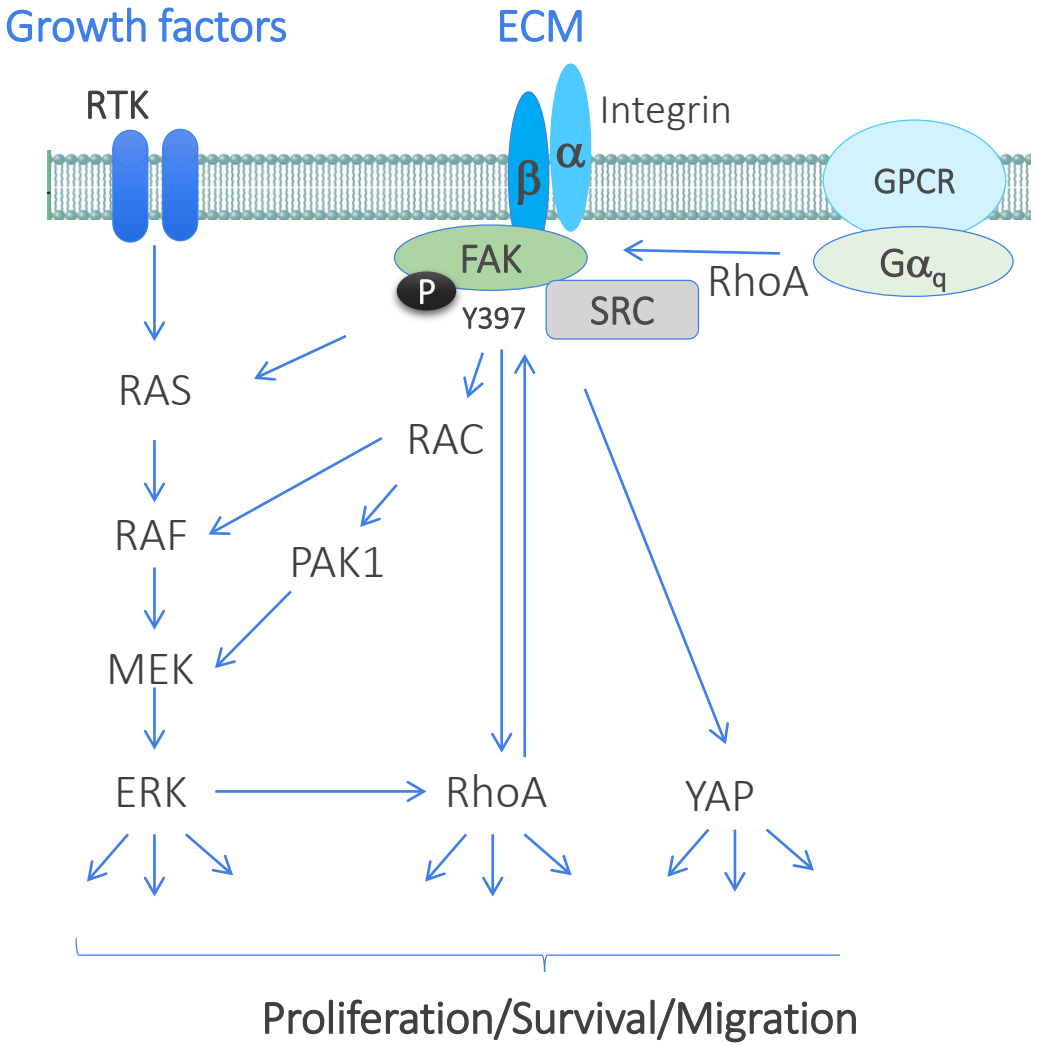
Overcoming Key Resistance Mechanisms to MEK Inhibitors



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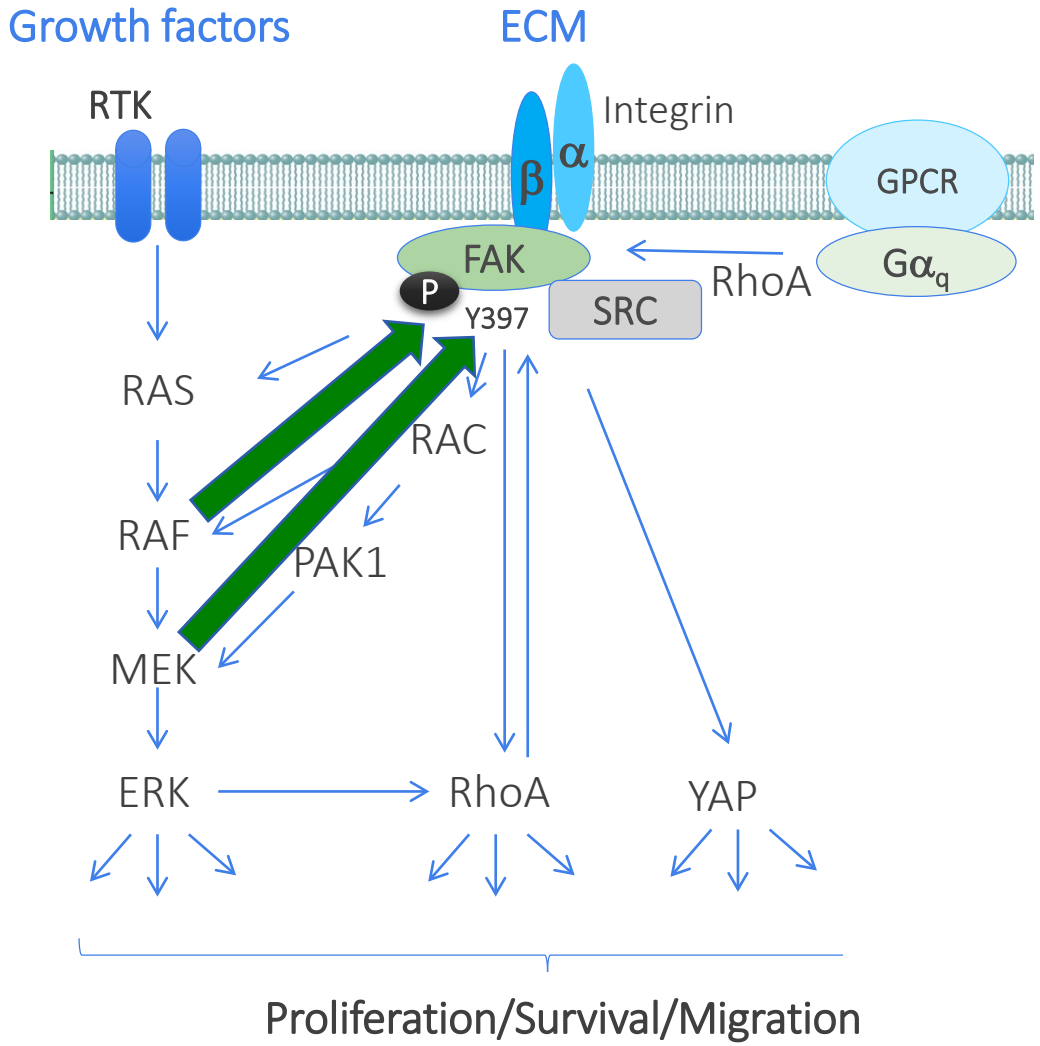
References:
Banerji, BTOG Dublin, Jan 23, 2019
Slack-Davis, JCB 162:281, 2003
Feng, Cancer Cell, 2019
Konstantinou, Cancer Discovery 3:444, 2013
Hirata, Cancer Cell 27:574, 2015

Overcoming Key Resistance Mechanisms to MEK Inhibitors



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➡ = Feedback Reactivation

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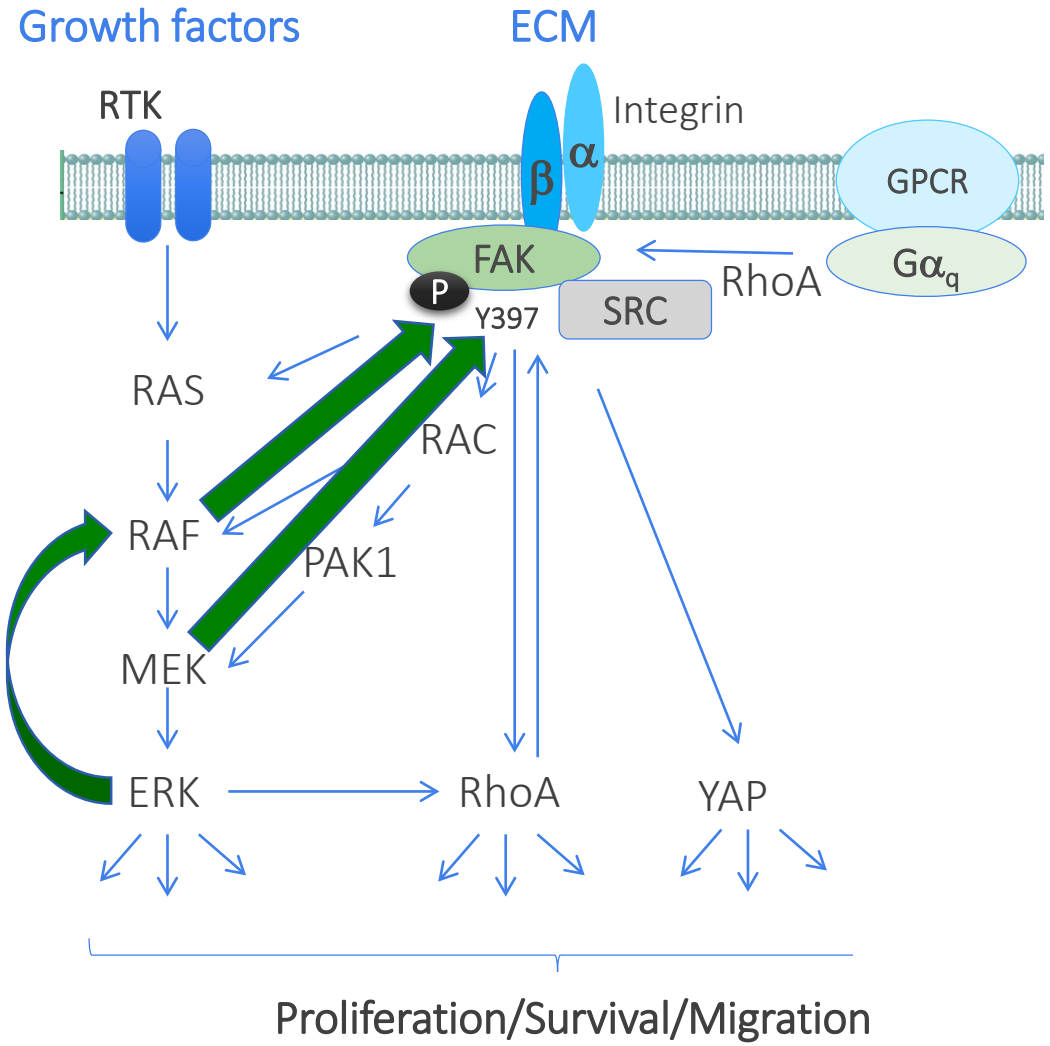
References:
1. Chen, Mol Cancer Res 2018
2. Banerji, BTOG Dublin, Jan 23, 2019

More Complete Shutdown requires Addressing Multiple Resistance Mechanisms



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References:
[1]Chen, Mol Cancer Res 2018
[2]Banerji, BTOG Dublin, Jan 23, 2019
[3]Ishii et al., *Cancer Res*, 2013

VS-6766 and Defactinib

Jon Pachter, PhD

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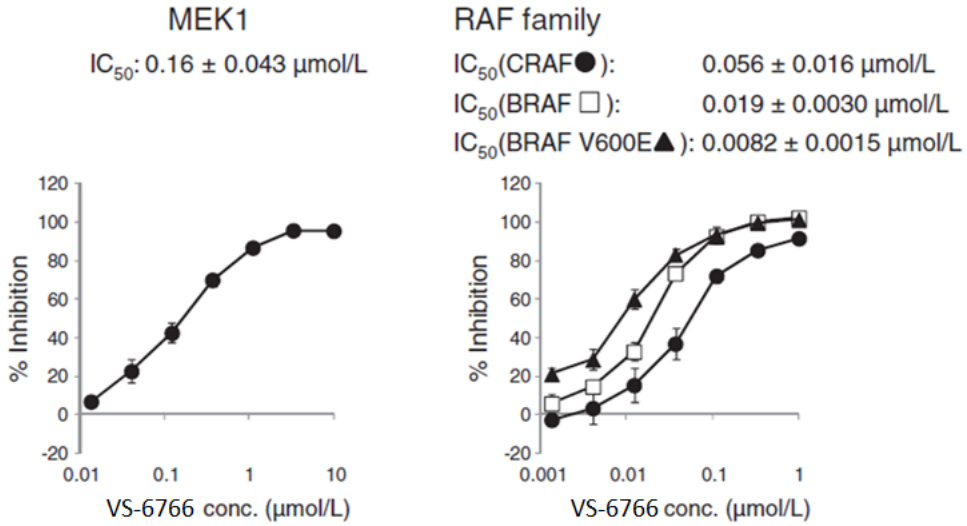
VS-6766 is a Unique Small Molecule RAF/MEK Inhibitor

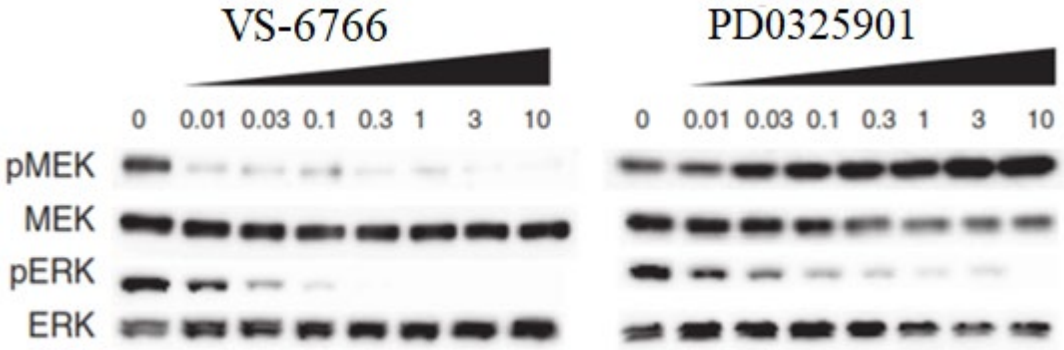
- VS-6766 inhibits both MEK & RAF kinase activities



- Standard MEK inhibitors paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF

RAS → RAF → MEK → ERK → Proliferation & Survival

- By inhibiting RAF phosphorylation of MEK, VS-6766 has advantage of not inducing pMEK
- VS-6766 inhibits ERK signaling more completely; may confer enhanced therapeutic activity



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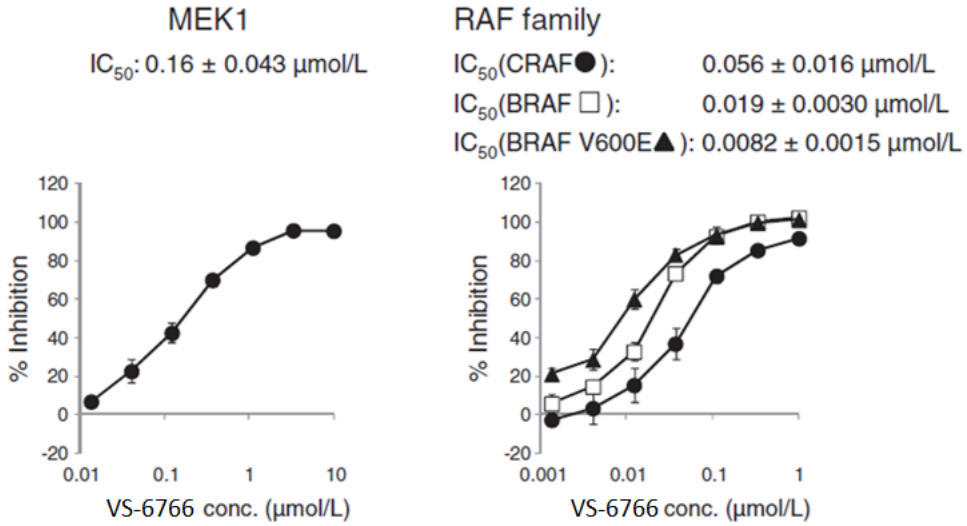

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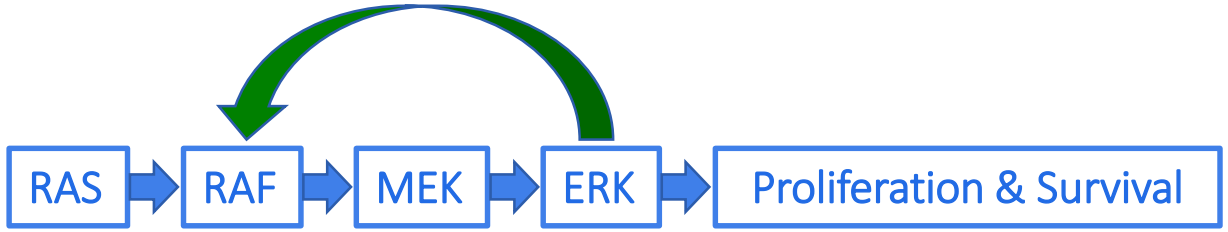

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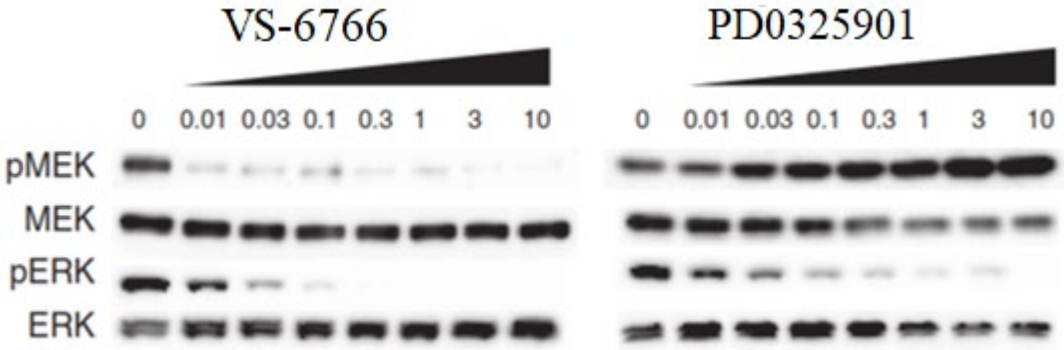

Reference:
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VS-6766 inhibits CRAF

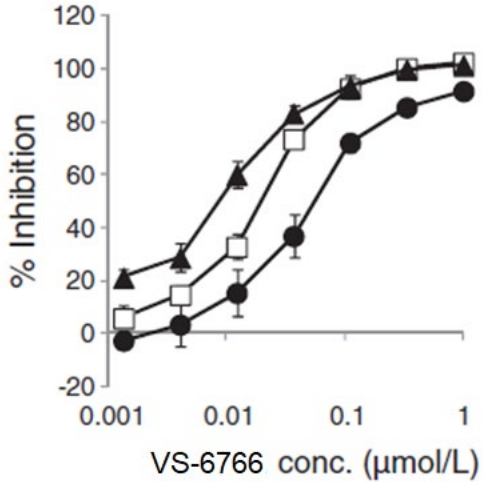
A central mediator of KRAS-G12V driven NSCLC

RAF family

IC_{50}(CRAF●): 0.056 ± 0.016 µmol/L

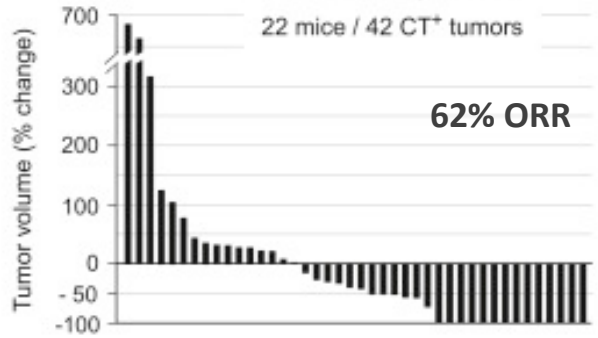
IC_{50}(BRAF □): 0.019 ± 0.0030 µmol/L

IC_{50}(BRAF V600E▲): 0.0082 ± 0.0015 µmol/L

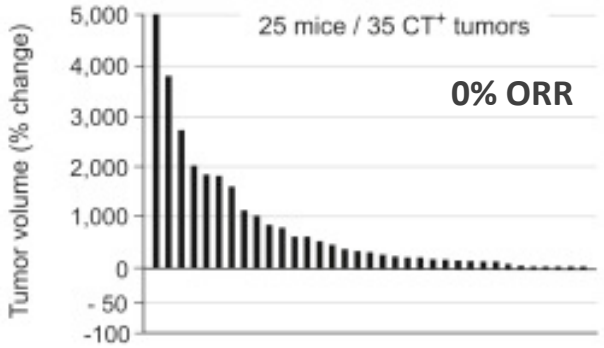


CRAF drives KRAS^{G12V} NSCLC[1,3]

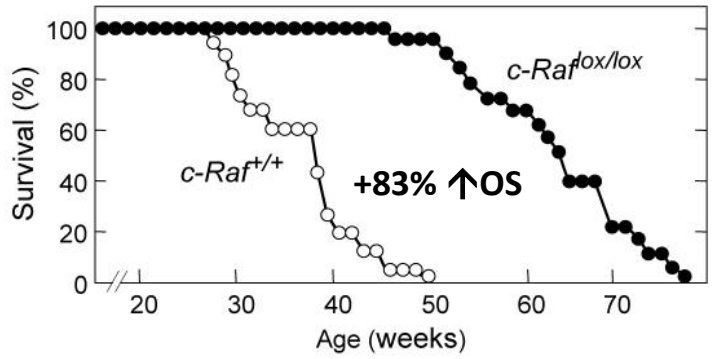
CRAF KO



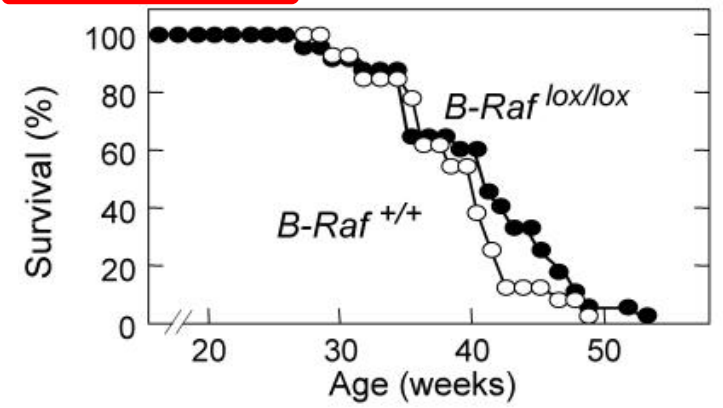
CRAF WT



CRAF KO vs. WT



BRAF KO vs. WT



CRAF, but not BRAF, ablation improves survival of mice with KRAS^{G12} induced lung tumor formation across two different models

Source: Ishii et al. *Cancer Res* (2013), Blasco, R. B. *et al. Cancer Cell* (2011), Lito, P. *et al. Cancer Cell* (2014), Sanclemente, M. *et al. Cancer Cell* (2018)

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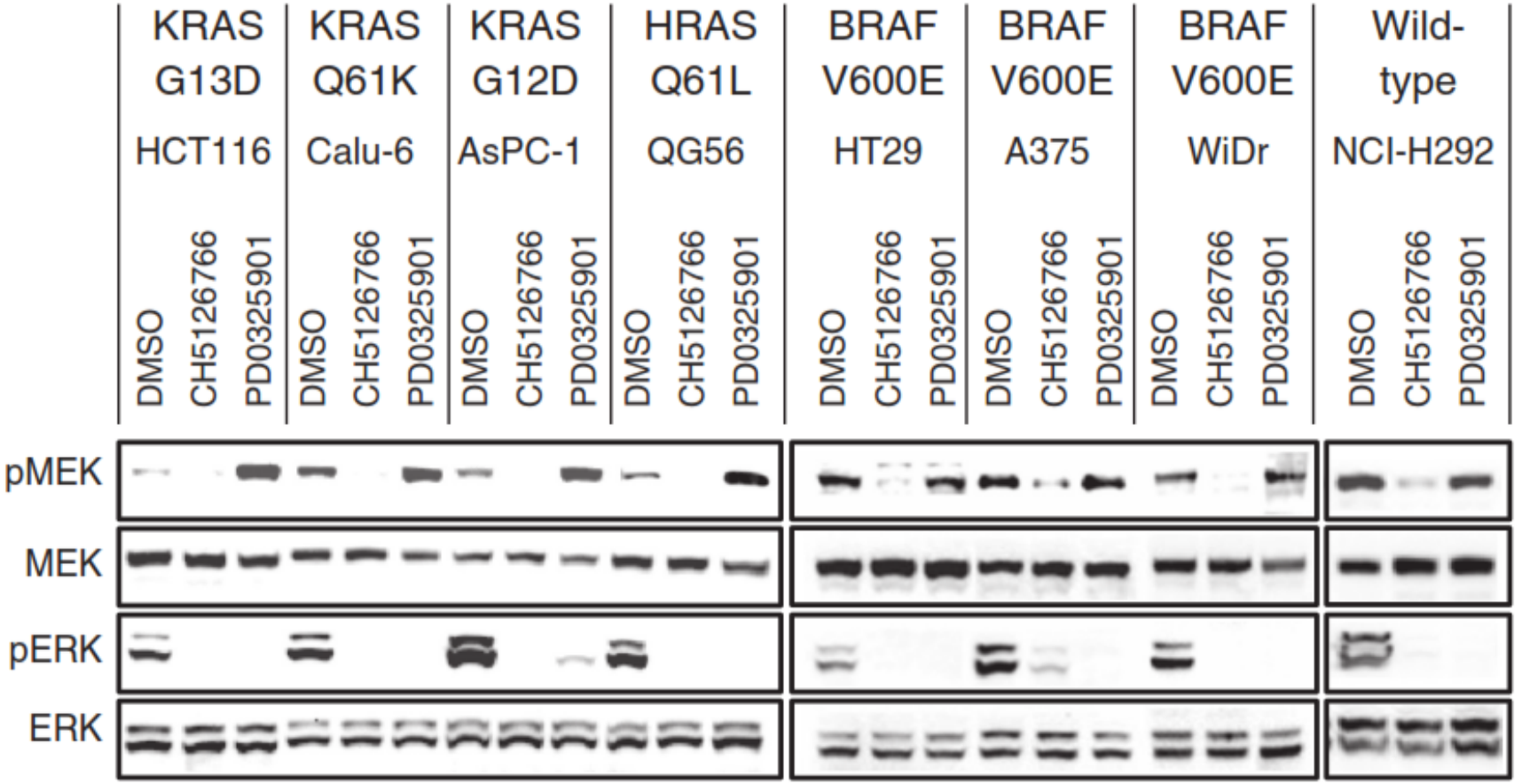
VS-6766 is Effective against Multiple RAS & RAF Mutations*

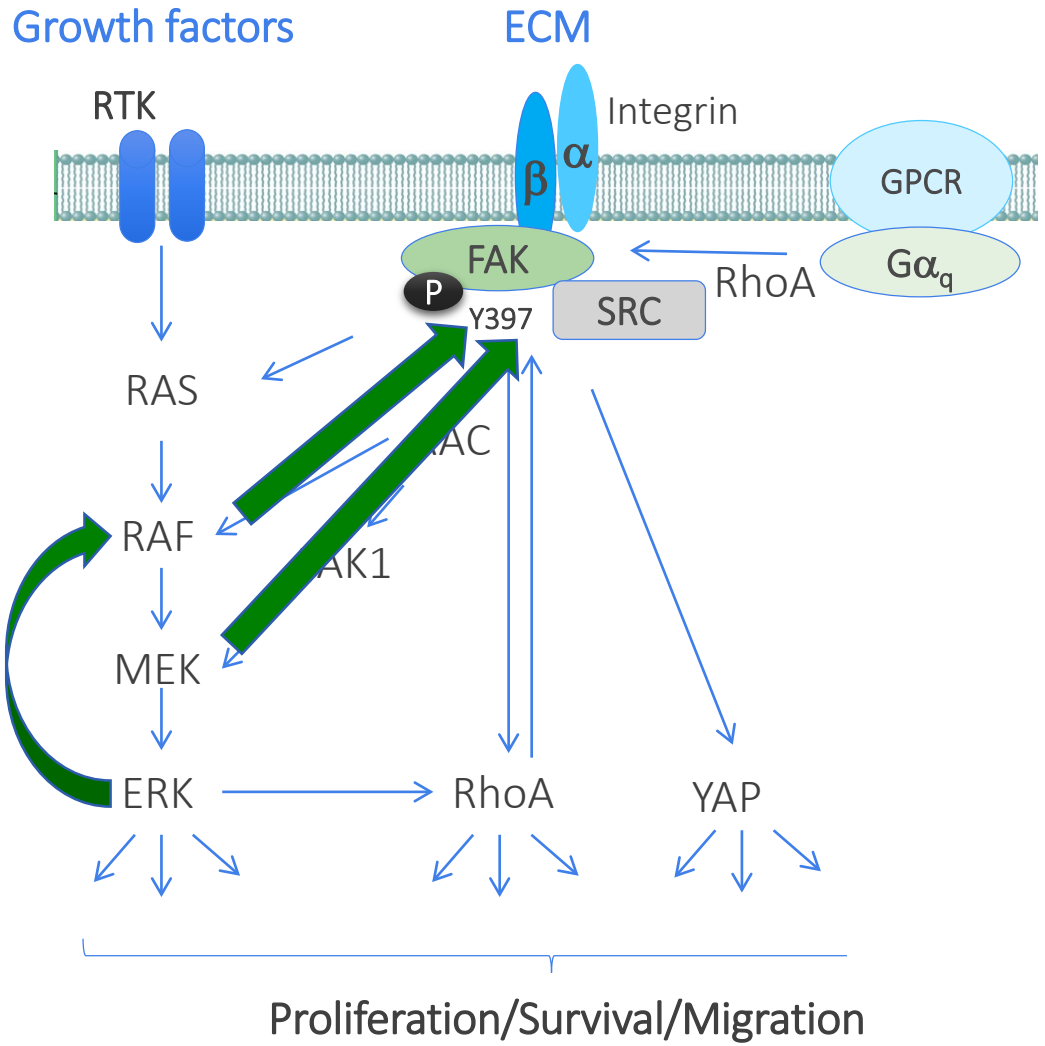
Potential to act more broadly or be combined with agents targeting specific mutations only



*Preclinical Reference:
Ishii et al., Cancer Research, 2013

CH5126766 = VS-6766
PD0325901 (mirdametinib) is a conventional MEK inhibitor

More Complete Shutdown requires Addressing Multiple Resistance Mechanisms



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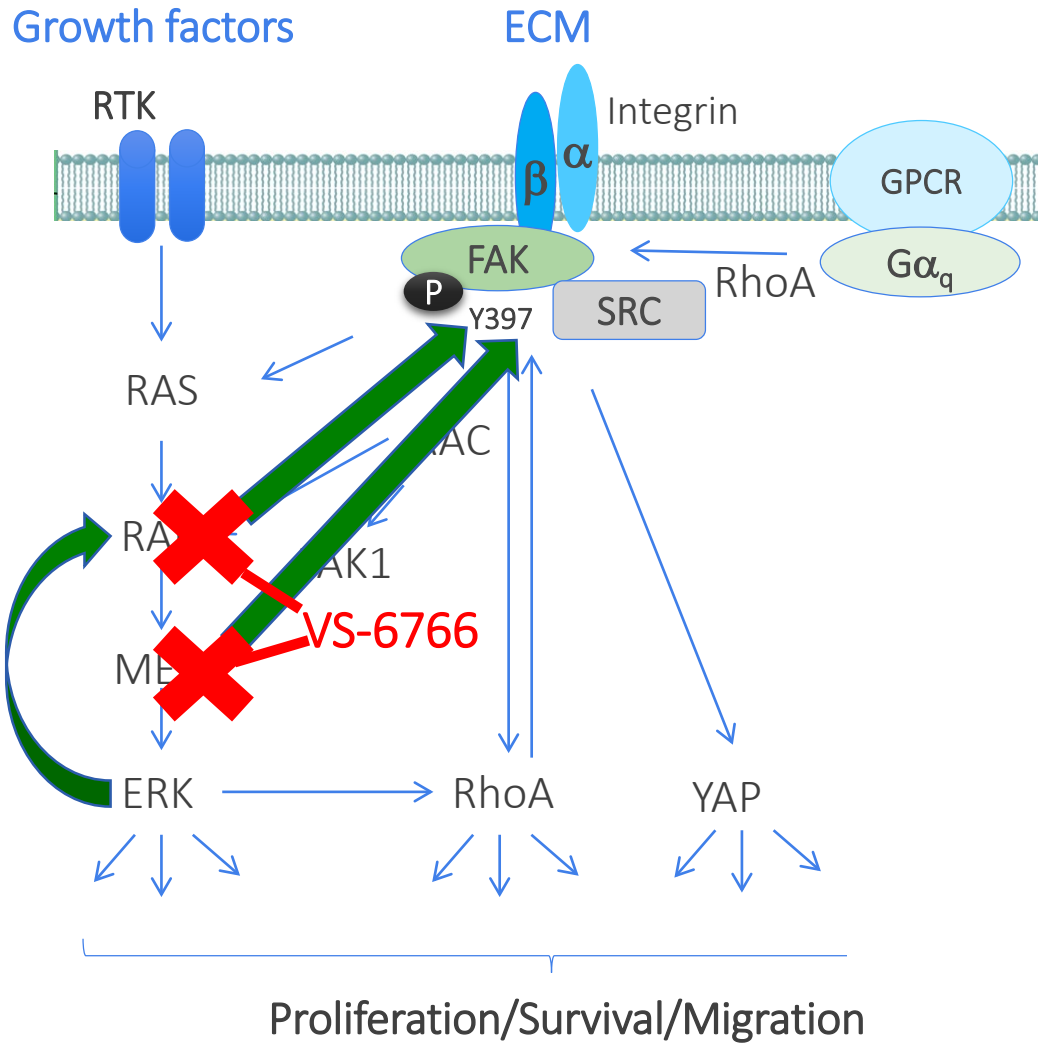

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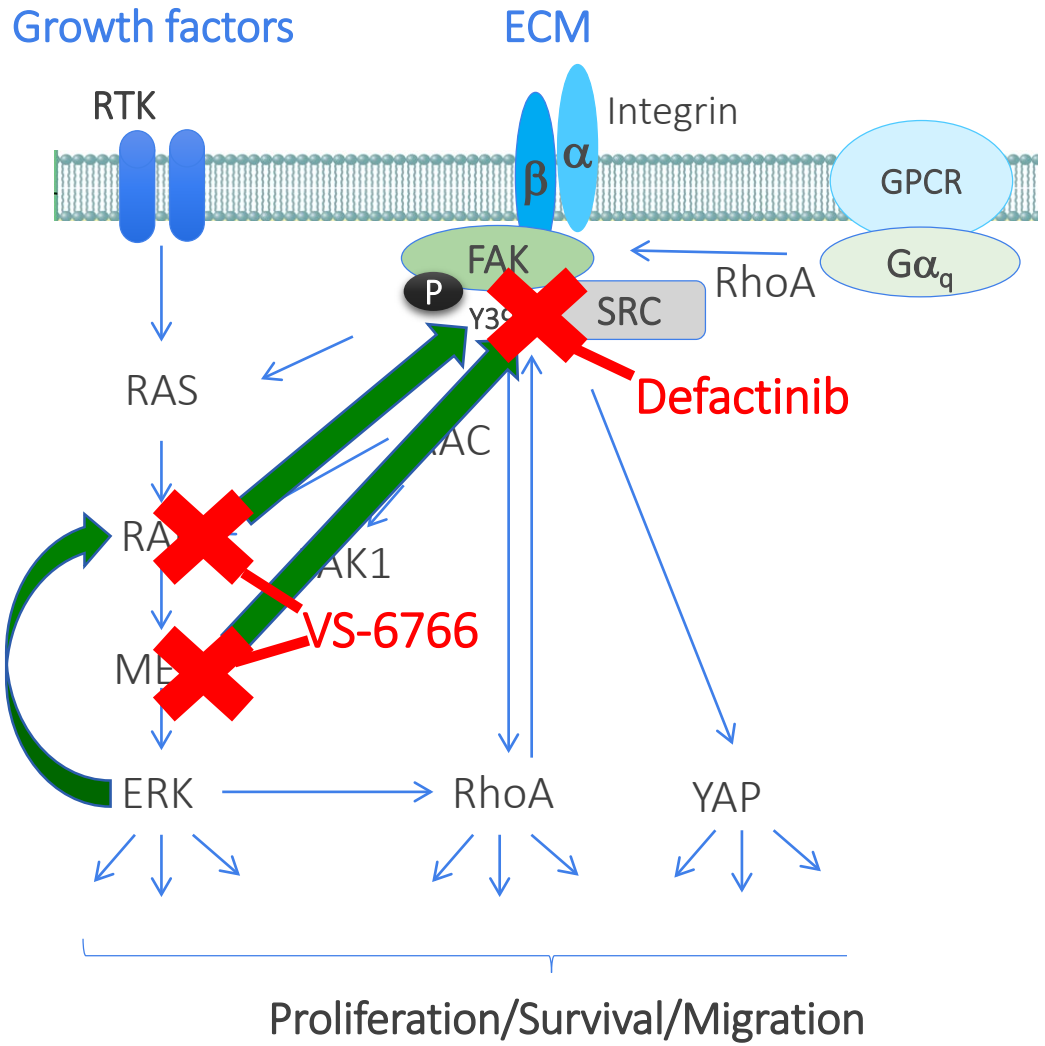

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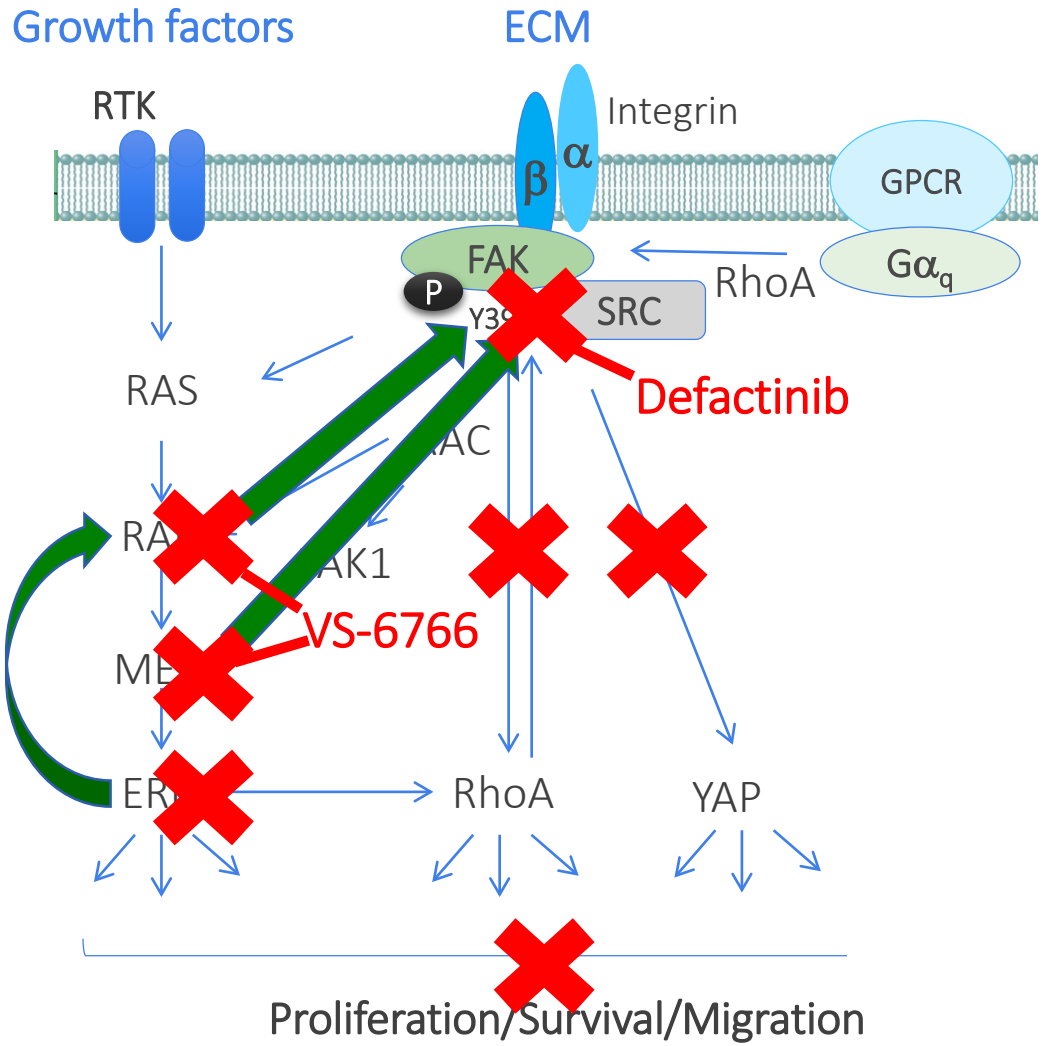

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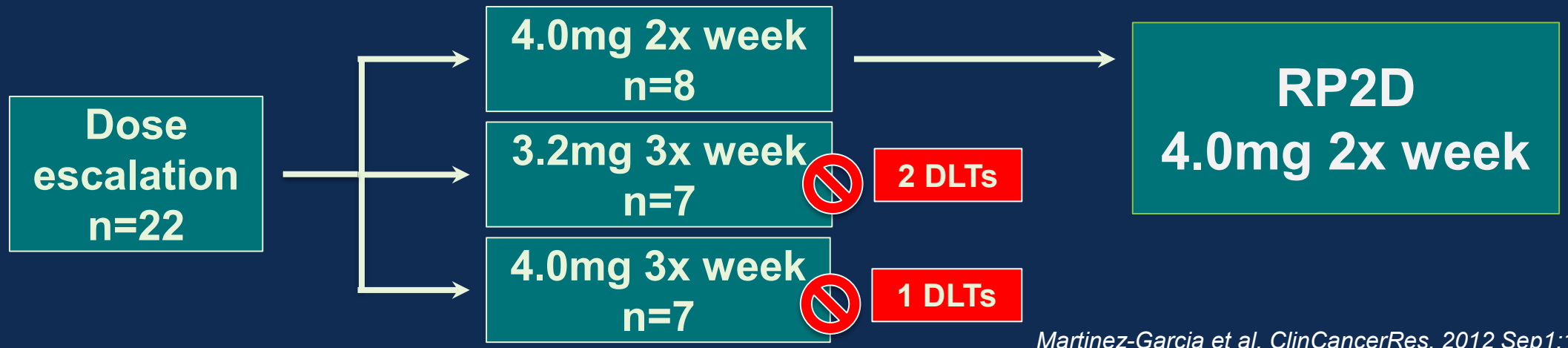
Background

- In view of promising activity, a different trial design was investigated to mitigate toxicity
- Mean terminal $t_{1/2}$ of ≈ 60 hours
  - 2x-weekly and 3x-weekly scheduling, in 4 week cycles
- Led by the Drug Development Unit at RMH/ICR



Martinez-Garcia et al. ClinCancerRes. 2012 Sep1;18(17):4806-19

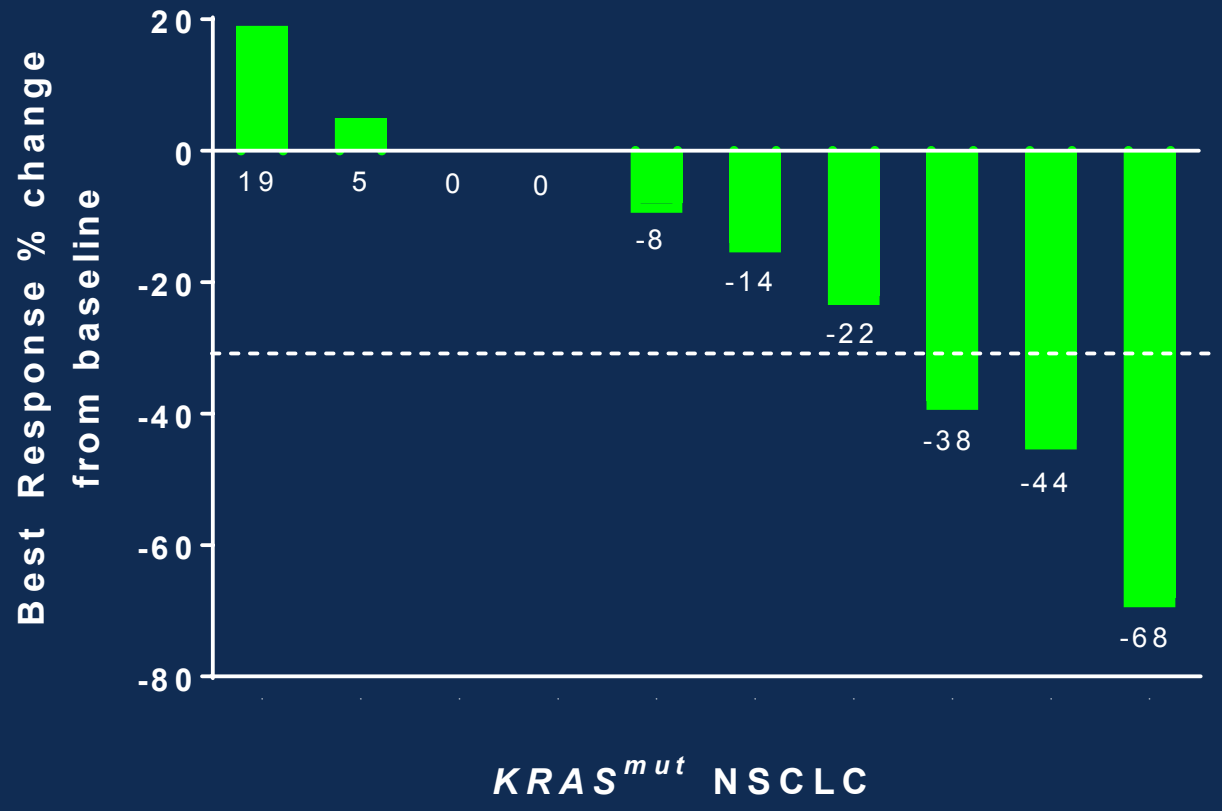
Adverse Events

Adverse event details	Expansion: 4mg 2x weekly n=26		Martinez-Garcia *et al.* CCR 2012 Patient treated at OD MTD n=6
	All grades	≥ Gr. 3	≥ Gr. 3
Rash-related	22 (84.6 %)	5 (**19.2 %**)	3 (**50.0 %**)
CK elevation	15 (57.7 %)	2 (**7.6%**)	1 (**16.7 %**)
Blurred vision	13 (50 %)	0	0
Peripheral oedema	10 (38.5 %)	0	0
Diarrhoea	9 (34.1 %)	1 (3.8 %)	0
Mucositis/Mouth ulcer	8 (30.8 %)	1 (3.8 %)	0
Fatigue	6 (23.1 %)	1 (3.8 %)	0
Nausea	5 (19.2 %)	0	0

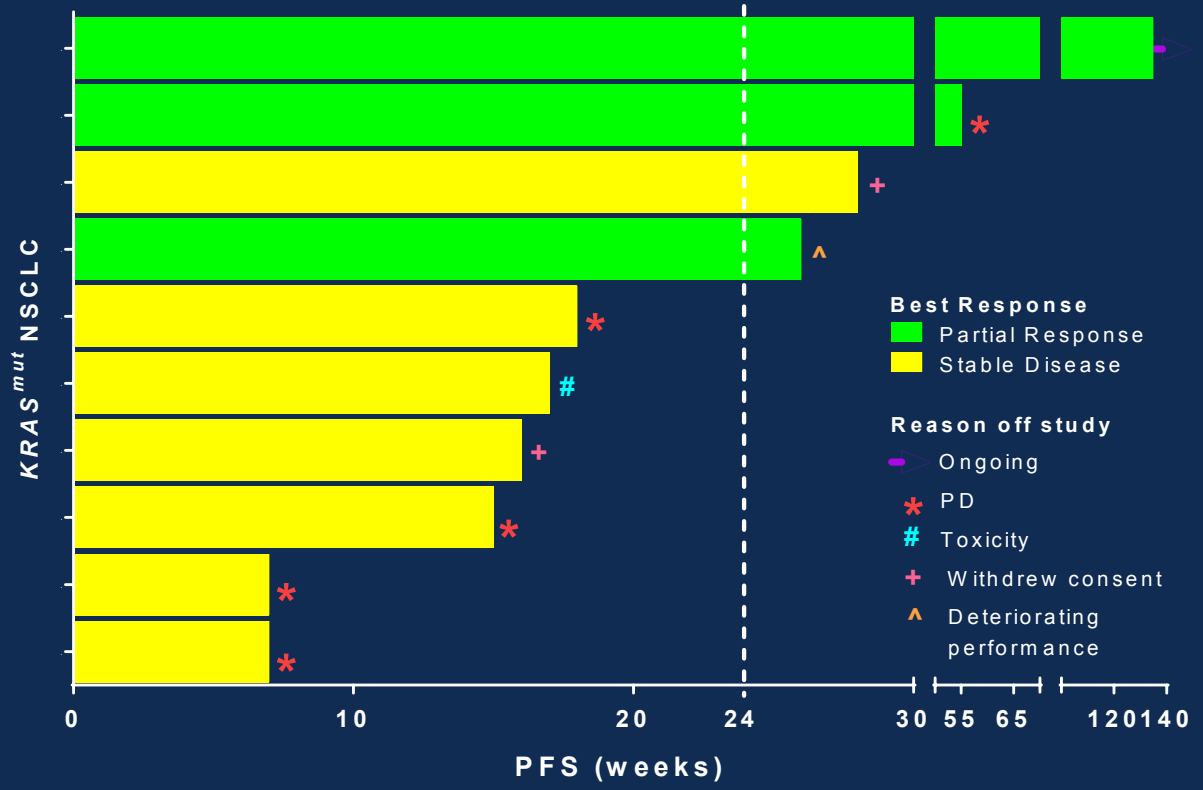
Martinez-Garcia et al. Clin Cancer Res. 2012 Sep 1;18(17):4806-19

Results: *KRAS*^{mut} NSCLC - Adenocarcinoma

Best response by RECIST v1.1

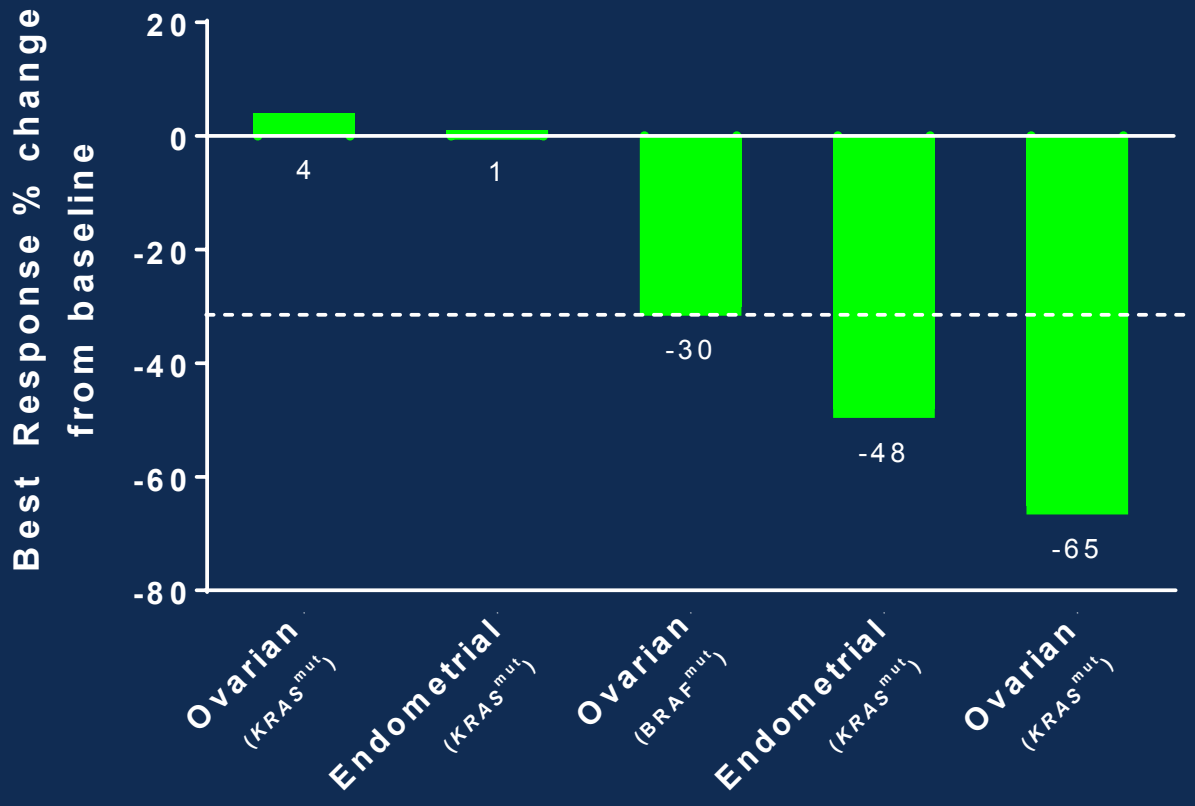


Progression Free Survival



Results: Gynaecological cancers

Best response by RECIST v1.1



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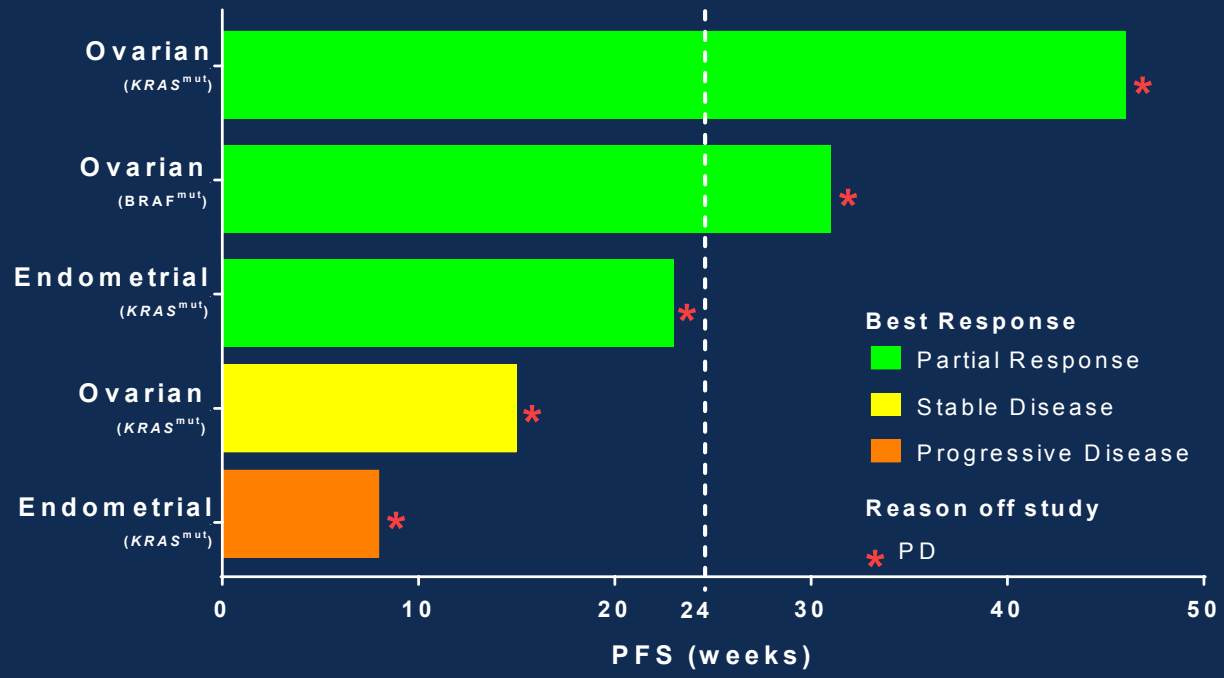
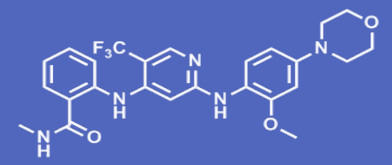


Defactinib: Selective FAK inhibitor

Defactinib 

Focal Adhesion Kinase (FAK)

- Non-receptor tyrosine kinase:
  Mediates signaling downstream of integrins & growth factor receptors
- Key roles in drug resistance
  - RAF & MEK inhibitors
  - Chemotherapy
- Immuno-Oncology/Tumor Microenvironment
  - FAK inhibition reduces stromal density:
    ↑ entry of cytotoxic T cells into tumor
  - FAK inhibition reduces immuno-suppressive Tregs, M2 macrophages & MDSCs

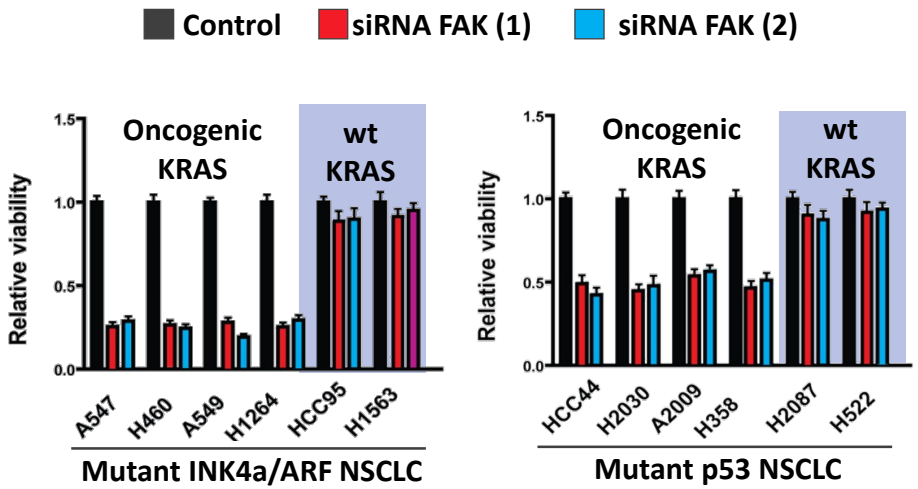
Defactinib (VS-6063)

- Selective inhibitor of FAK & related kinase PYK2
- Good pFAK target inhibition in tumors of patients following oral defactinib administration
- Early signs of clinical efficacy
- Studied in 500+ patients with good safety profile observed to date
  - Only ≥Gr 3 toxicity over 2.5% was hyperbilirubinemia – Not associated liver AEs
- Preliminary results show it is generally well-tolerated in combination
  - MEK/RAF, PD-1, Chemo

Reference:
Jones, Invest New Drugs, 2015; Kang, J Natl Cancer Inst. 2013; Diaz Osterman, Elife 2019; Tong, Respiratory Res 2019, Serrels Cell 2015; Jiang et al Nat Med 2016; Banerji, BTOG Dublin, Jan 23, 2019; Data on file

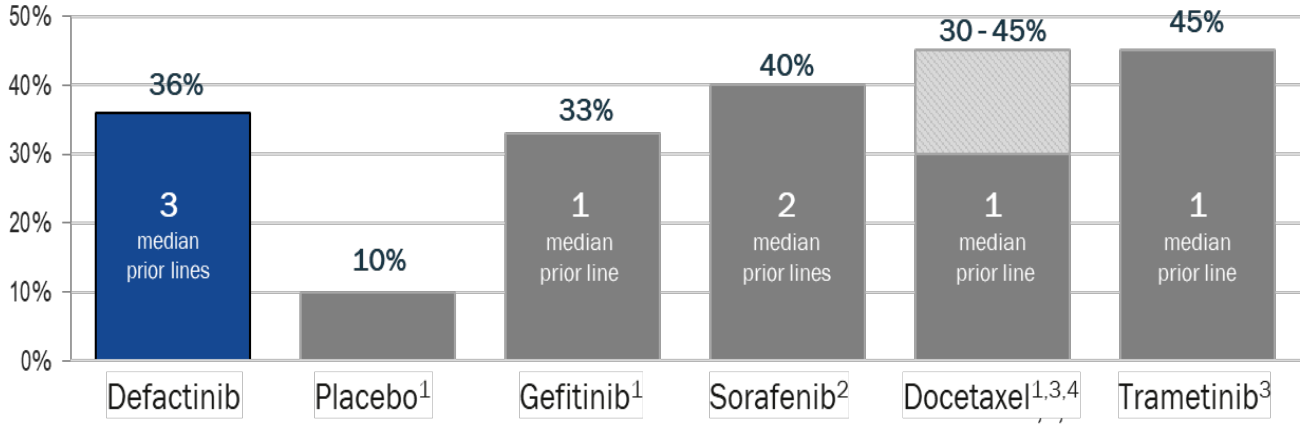
Defactinib Monotherapy Shows Clinical Activity in KRAS Mutant NSCLC

KRAS mt is necessary for sensitivity to FAK inhibition in NSCLC cell lines



Reference:
Konstantinidou G et al. Cancer Discovery 2013;3:444-57

12-week PFS rate of experimental agents for KRAS mt NSCLC



"In this cohort of heavily pretreated patients, there were signs of single-agent activity comparable to other targeted agents and docetaxel. Future directions include possible combination studies with existing standard and emerging therapies, including checkpoint inhibitors."
—Dr. David Gerber, IASLC 2015; Lung Cancer 2020

References:
1. Phase 3 INTEREST, Douillard et al., JCO 2010
2. Phase 3 MISSION, Mok et al., ESMO 2012
3. Phase 2, Blumenschein et al., Ann Oncol 2015
4. Phase 2, Janne et al., Lancet 2013

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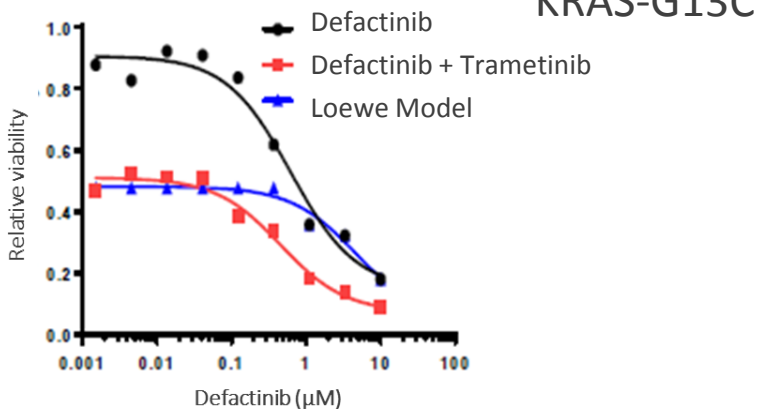
Screen for Synergy with Defactinib Identified MEK Inhibitors (& VS-6766) as Top Hit

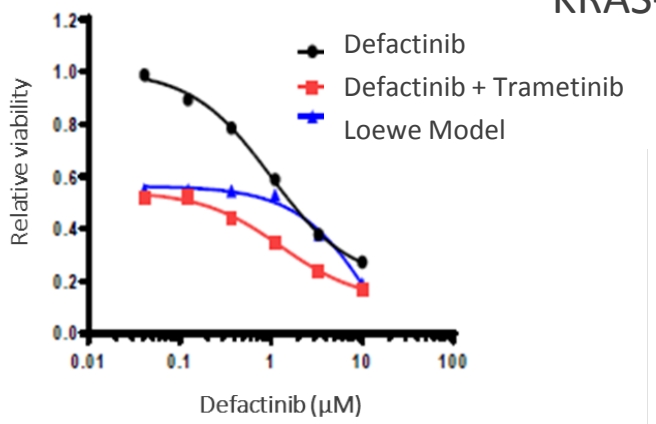
TOV-21G CELLS KRAS-MUTANT OVARIAN CANCER

KRAS-G13C

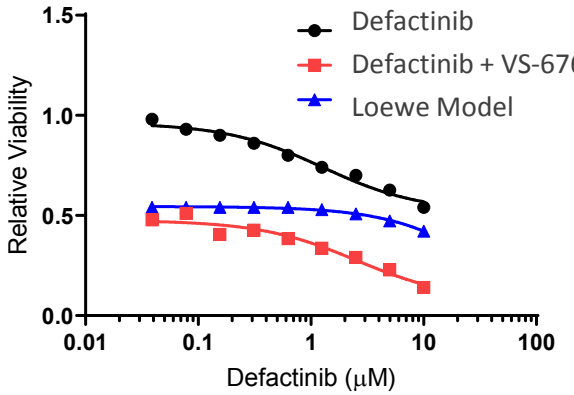


H441 CELLS KRAS-MUTANT NON-SMALL-CELL LUNG CANCER

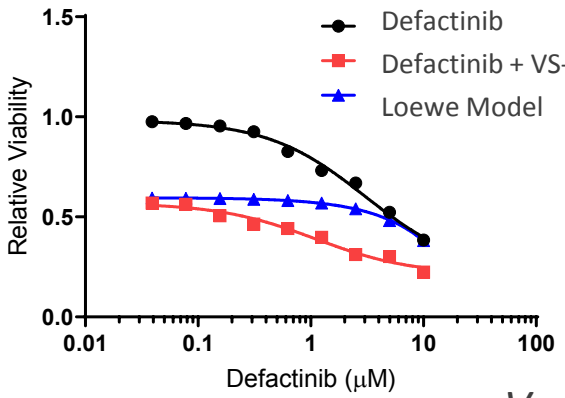
KRAS-G12V



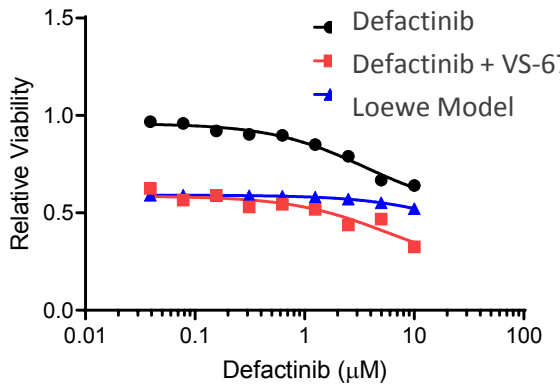
SW982 CELLS SARCOMA BRAF:pV600E



MERO-14 CELLS MESOTHELIOMA



CAL-51 CELLS TRIPLE NEGATIVE BREAST CANCER



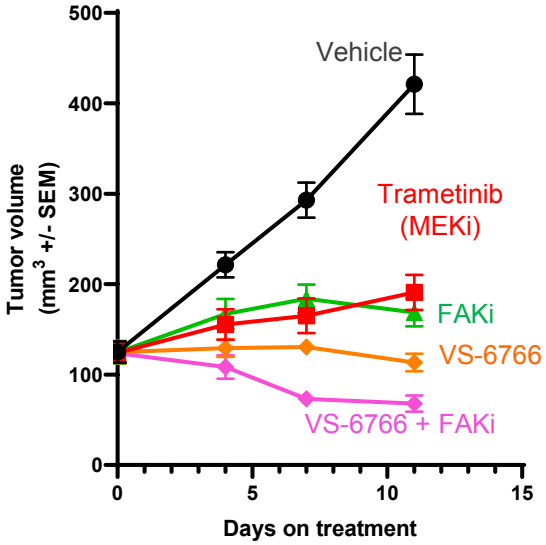
Verastem, data on file

Verastem issued patent on FAK/MEK inhibitor combinations

FAK Inhibition Enhances Efficacy of RAF/MEK Pathway Blockade across Preclinical Tumor Models

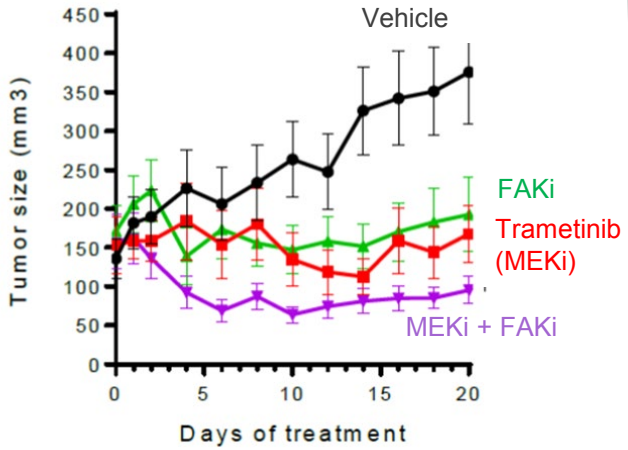
MEKi + FAKi

RAF/MEKi + FAKi in ovarian cancer model (KRAS mutant TOV-21G)



Coma and Pachter, Verastem (unpublished)

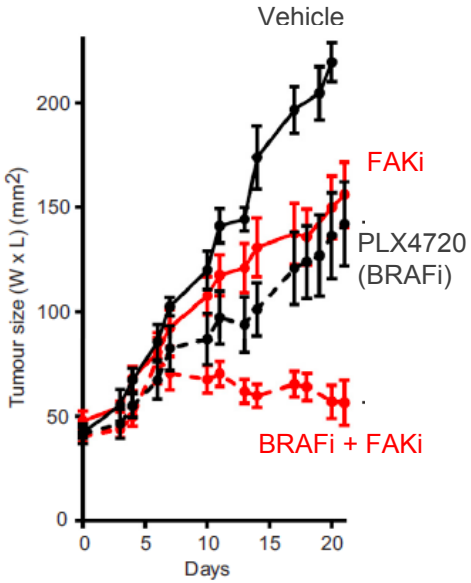
MEKi + FAKi in uveal melanoma model (GNAQ mutant 92.1)



Paradis and Gutkind, UCSD (unpublished)

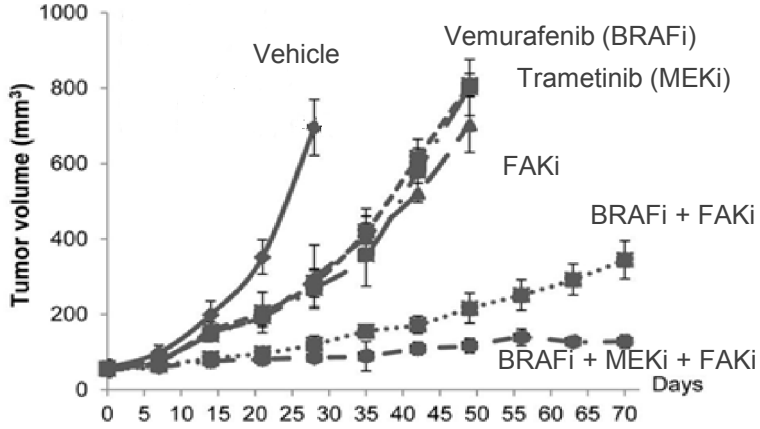
BRAFi + FAKi

BRAFi + FAKi in melanoma model (BRAF-V600E 5555)



Hirata *et al. Cancer Cell* (2015)

BRAFi + FAKi in colorectal cancer model (BRAF-V600E HT-29)



Chen *et al., Mol. Cancer Ther.* (2018))

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Phase 1 VS-6766 and Defactinib Combination Data in KRAS Mutant Solid Tumors – Initial Results

Udai Banerji, MBBS, MD, DNB, PhD, FRCP

Verastem Oncology

Ongoing Investigator-Sponsored Basket Study of VS-6766 + Defactinib in KRAS^{M} Cancers

***Refractory to conventional treatment or for which no conventional treatment exists**

Dr. Udai Banerji
Royal Marsden Hospital

Phase I

Advanced Solid Cancers

- VS-6766 oral twice wkly x 3 wks every 4 wks
- Defactinib oral BID daily x 3 wks q 4 wks
- 3 cohorts with increasing doses explored
  - Cohort 1: VS-6766 3.2 mg & Defactinib 200 mg
  - Cohort 2a: VS-6766 4 mg & Defactinib 200 mg
  - Cohort 2b: VS-6766 3.2 mg & Defactinib 400 mg

Advanced NSCLC KRAS mutant* (N=20)	*14 enrolled by March 2020* *Median prior lines = 2* *Majority prior PD-(L)1 treatment*
LGSOC* (N=20)	*9 enrolled by March 2020* *Median prior lines ≥2* *Prior MEKi allowed*
Advanced CRC RAS mutant* (N=10)	*10 enrolled by March 2020* *Median prior lines = 2-3* *Prior VEGFi allowed*
Advanced Solid Tumors Enriched for RAS* (Biopsy Amenable) (N=6)	*6 enrolled by March, 2020*

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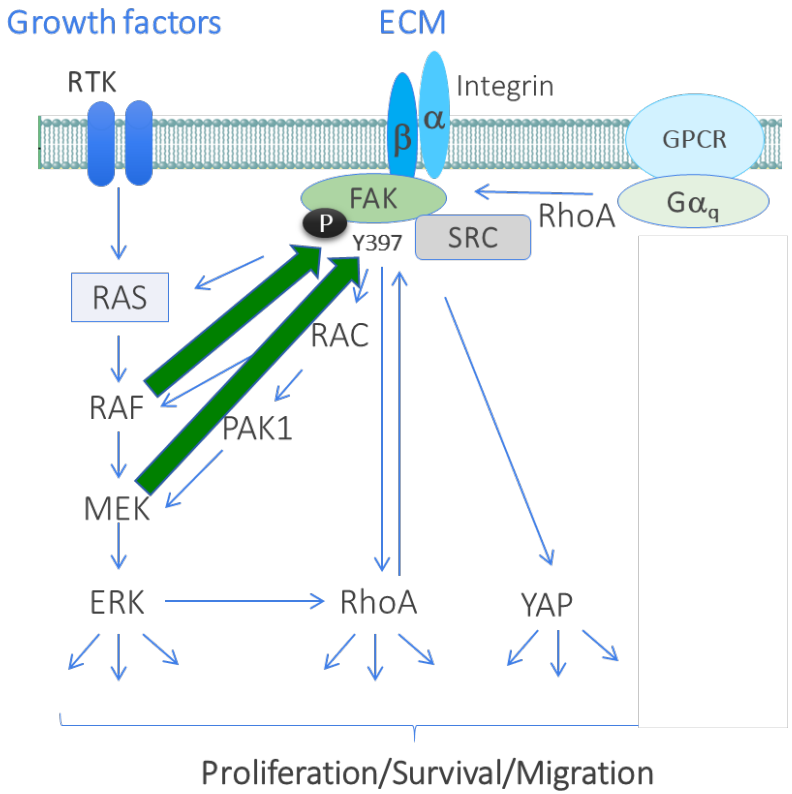
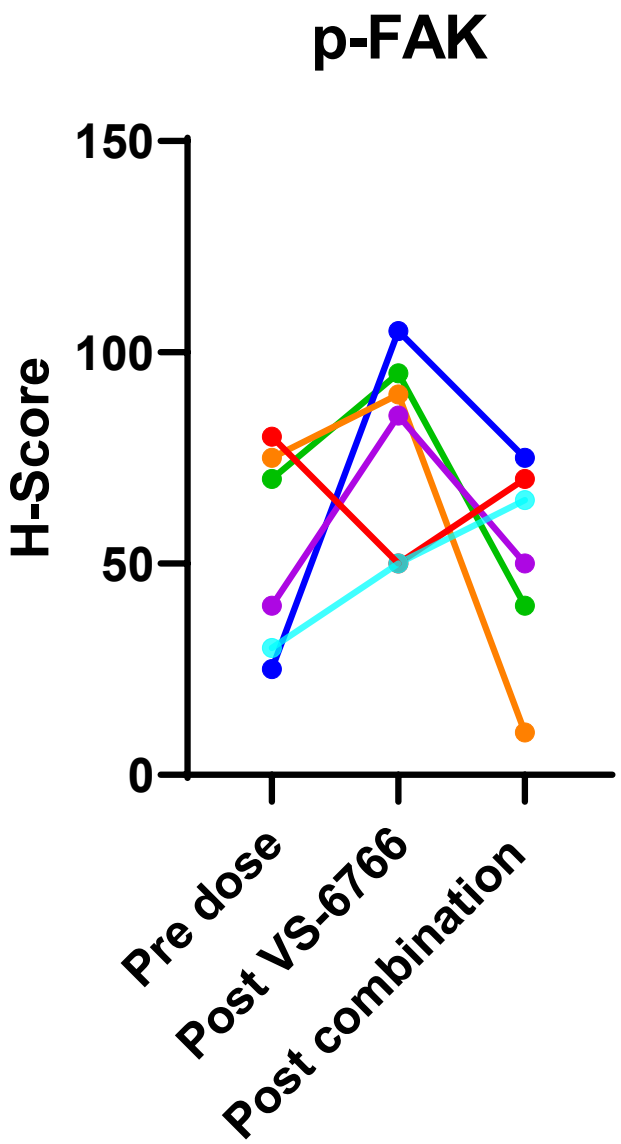
References: Banerji, AACR VM 1, April 27, 2020, CT143; Data on file

Overcoming Key Resistance Mechanisms to MEK Inhibitors



= Feedback Reactivation



- MEK inhibition induces compensatory activation of pFAK preclinically and clinically
  - Trametinib induced ↑ pFAK (Y397) preclinically in KRAS mt NSCLC cell lines
  - Also observed in patients
    - VS-6766 induced ↑ pFAK (Y397) as a potential resistance mechanism in the majority of patients
    - Combination with defactinib reduced this compensatory pFAK signal

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References:
Banerji, BTOG Dublin, Jan 23, 2019
Banerji, AACR VM 1, April 27, 2020, CT143

VS-6766 3.2 mg + Defactinib 200 mg Selected as RP2D

The ROYAL MARSDEN NHS Foundation Trust

Treatment Related Adverse Events Occurring in ≥ 10 Patients (Total) Q4 2019 Update

	Dose Escalation Phase						Dose Expansion Phase				Total N=46
	VS-6766 3.2mg Def 200mg Cohort 1 n=3		VS-6766 4mg Def 200mg Cohort 2a n=6		VS-6766 3.2mg Def 400mg Cohort 2b n=3		**VS-6766 3.2mg Def 200mg Cohort 1 n=17**		VS-6766 4mg Def 200mg Cohort 2a n=17		
Adverse Event Details*	Gr1/2	Gr3/4	Gr1/2	Gr3/4	Gr1/2	Gr3/4	Gr1/2	Gr3/4	Gr1/2	Gr3/4	
Rash	2		6		3		16		12	3	42
CK elevation	2		2	1	1		7	1	8	3	25
AST elevation			1		1		5		10	1	18
Hyperbilirubinemia	1	1	1	1	1		7		6		18
Visual disturbance			1		2		5		8		16
ALT elevation			1		1		3		8		13
Diarrhoea	2		1		1		4		5		13
Fatigue			2				3		8		13
Oral Mucositis^							4		6	2	12
Nausea	1		3		2				6		12
Peripheral Edema							4		6		10

- Most Adverse Events (AE) were Grade 1/2
  - All changes were reversible
- No DLTs in Cohort 1 or 2a
- DLTs Cohort 2b: Gr 2 rash in 2/3 of patients; MTD not reached
- Due to chronic Grade 2 AEs in patients on treatment > 6 months

RP2D

- **VS-6766 3.2 mg** oral twice wkly (3 wks of every 4 wks)
- **Defactinib 200 mg** oral BID (3 wks of every 4 wks)

References: Banerji, AACR VM 1, April 27, 2020, CT143; Data on file

*AEs were graded by NCI CTC v4; highest grade only recorded for each patient; data preliminary and subject to change; ^also includes glossitis/mouth ulcers

Pharmacokinetic Profiles of VS-6766 + Defactinib in Combination Similar to that seen in Single Agent Studies

VS-6766

Cohort	Dose (mg)	N	Subject	$AUC_{0\text{-}24h}$ (h*ng/mL)	C_{max} (ng/mL)
1	3.2 (with 200mg VS)	3	Mean	6179	354
			CV%	32.1	30.4
2a	4 (with 200mg VS)	5	Mean	5353	289
			CV%	15.8	16.0
2b	3.2 (with 400mg VS)	1	FRA101-007	3302	229

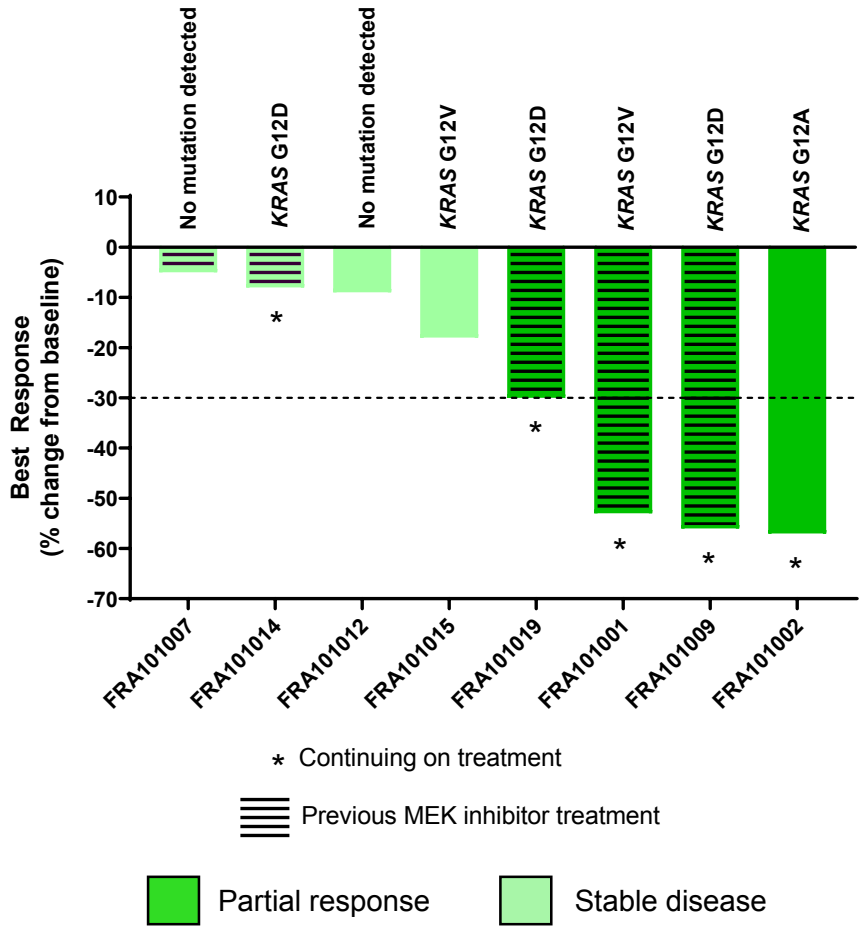
Defactinib

Cohort	Dose (mg)	N	Subject	AUClast (h*ng/mL)	Cmax (ng/mL)
1	200 (with 3.2mg RO)	3	Mean	2071	273
			CV%	103	80
2a	200 (with 4mg RO)	5	Mean	2252	318
			CV%	124	117
2b	400 (with 3.2mg RO)	3	Mean	2807	360
			CV%	31	32

Reference: Banerji, AACR VM 1, April 27, 2020, CT143

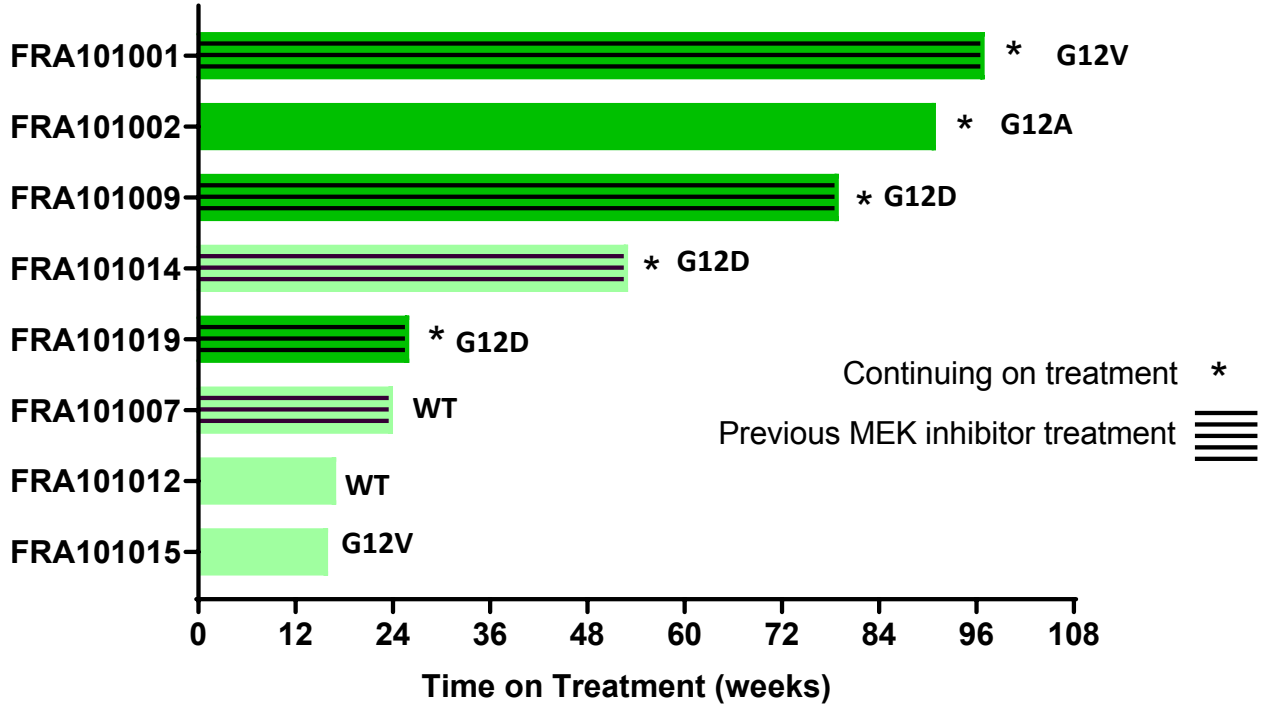
Efficacy – Low Grade Serous Ovarian Cancer

Best response by RECIST



- All PRs confirmed with subsequent scan per RECIST

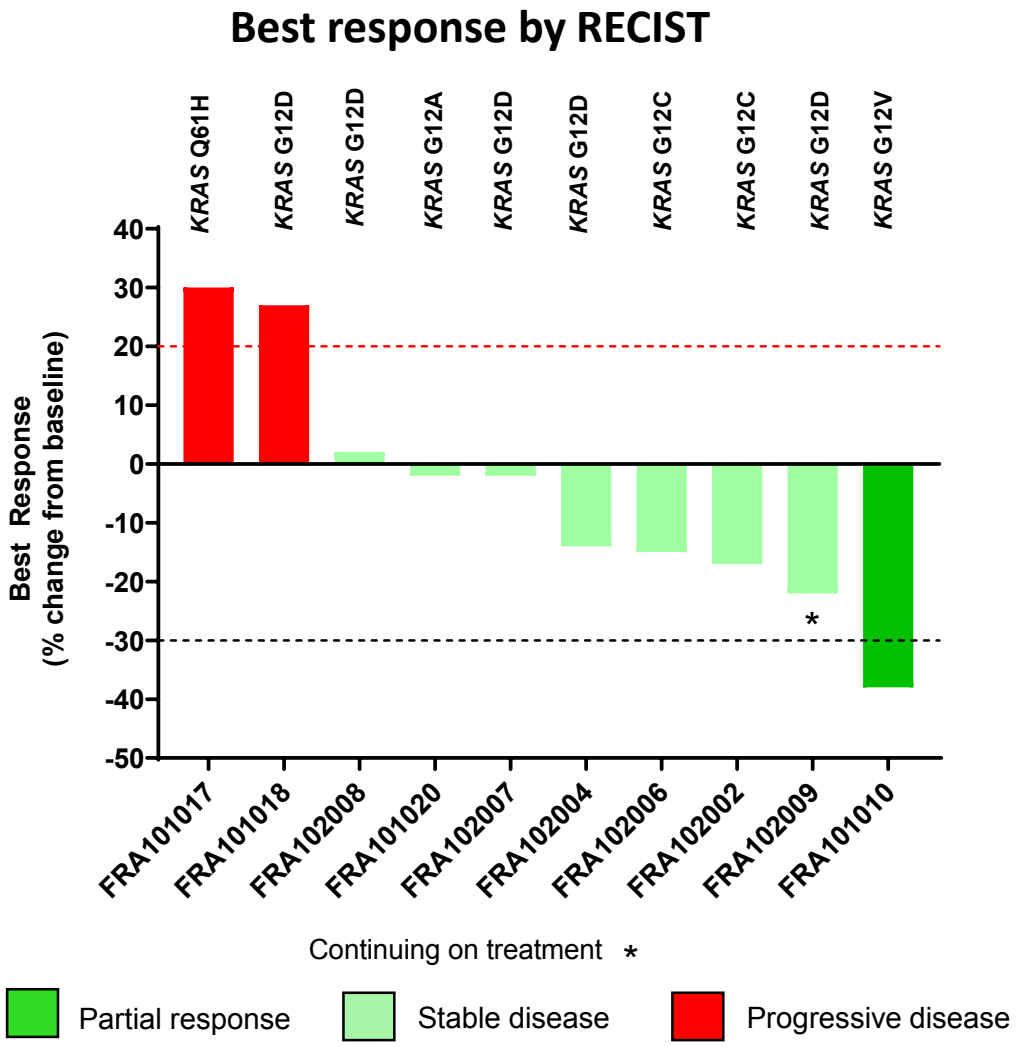
Time on treatment

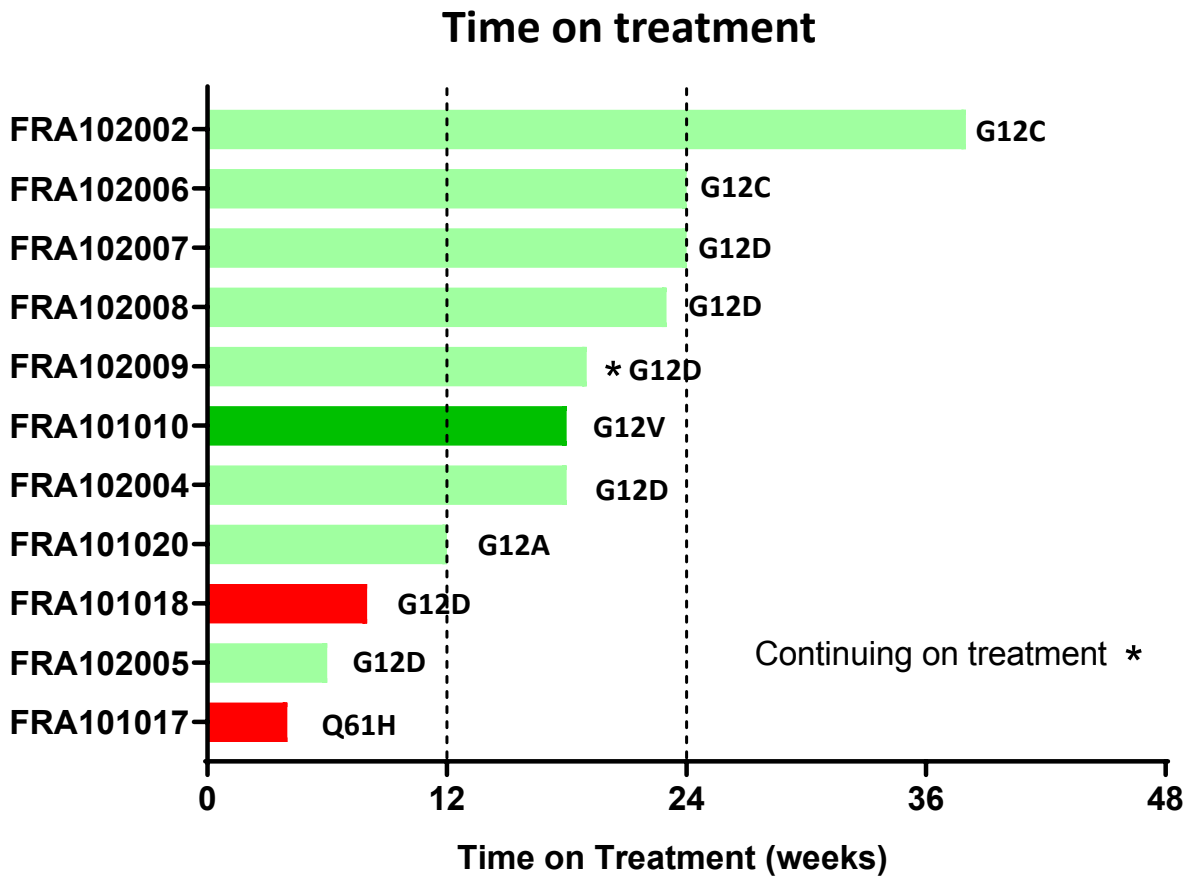


- Response rates: LGSOC KRAS^{M} = 67% (4/6); All LGSOC = 50% (4/8)
  - Also, 1 patient with KRAS mutant mucinous ovarian cancer had PR (> 60% reduction) with > 1 year on therapy
- ORR for LGSOC in the current literature is <10 % chemotherapy, 13% letrozole, 26% for trametinib, 24% for binimetinib, 15% for selumetinib

References: Annals of Oncology, 10/2019, V30, v897-898; Journal of Clinical Oncology 2015 33:15_suppl, TPS5610; Farley, J. *et al. Lancet Oncol.* (2013); Banerji, AACR VM 1, April 27, 2020, CT143

Efficacy – KRAS mutant NSCLC





- 3 patients received treatment for 24 weeks
- Median time on treatment for this cohort was approximately 18 weeks (range 4-38 weeks)

14/20 pts enrolled in KRAS mt NSCLC cohort;
1 additional confirmed PR in KRAS-G12V mutant patient

Reference: Banerji, AACR VM 1, April 27, 2020, CT143

Summary: VS-6766 + Defactinib

Rationale

- VS-6766 & defactinib have shown single agent clinical activity in KRAS mt cancer
- RAS pathway blockage activates FAK as potential resistance mechanism preclinically & clinically
- FAKi and MEKi are synergistic in reducing viability of cancer cell lines *in vitro* & *in vivo* in multiple models

FRAME study shows promising results & continues to enroll

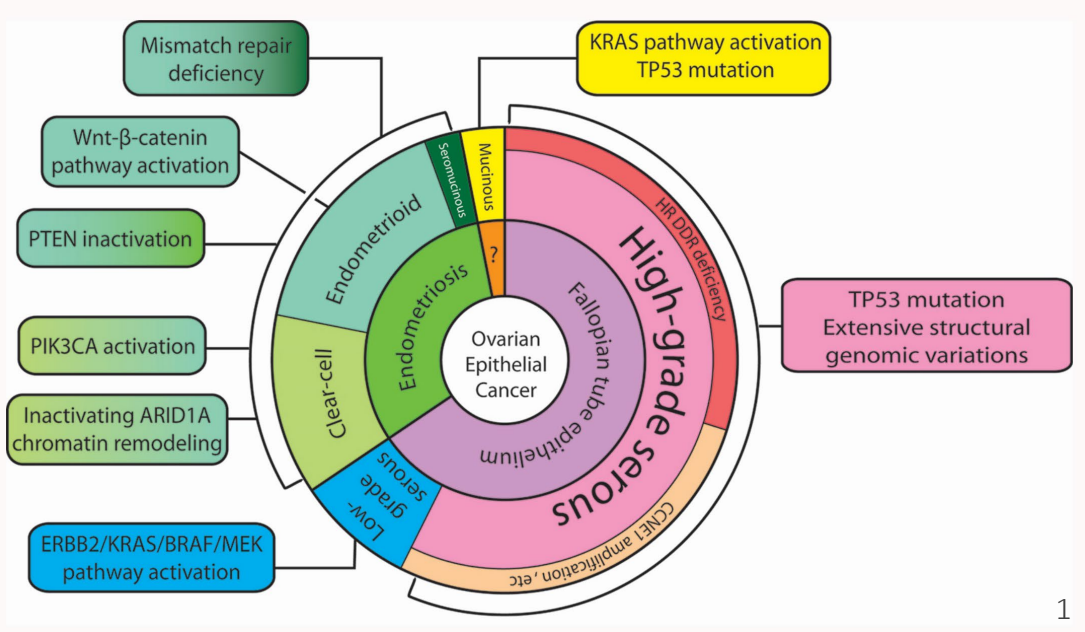
- Most adverse events were grade 1 / 2 with the Intermittent dosing of VS-6766 + defactinib (no PK interaction observed)
- VS-6766 + defactinib combination shows clinical promise in heavily pre-treated refractory patients with KRAS mt disease
  - 67% ORR in KRAS mt LGSOC, including patients progressing on prior MEK inhibitors
  - High rate of disease control and tumor regression in NSCLC with several patients out to 24 weeks
  - The study continues to enroll with additional responses in LGSOC, NSCLC and colorectal since Nov cut off

Next Steps and Closing Remarks

Dan Paterson / Brian Stuglik

Verastem Oncology

LGSOC – Strong Proof of Concept, High Unmet Need



1

Am J Pathol. 2016 Apr;186(4):733-47

	Incidence	10 y Prevalence
Worldwide	~13,000	~80,000
US	~1,000	~6,000

*Based on LGSOC representing 5% of epithelial ovarian cancer

- LGSOC represents ~4-10% of epithelial ovarian cancer[2]
- Long survival results in high prevalence rate
- RAS pathway mt frequency 50%[3]
- No FDA-approved therapy

Combination of VS-6766 + Defactinib offers potential for:

- Long duration of therapy
- High market share
- Speed to market opportunity
- Two product revenue streams

In LGSOC, G12V & G12D are the dominant KRAS mutations, and G12V confers a more aggressive phenotype (Tsang et al., J. Pathol 231: 449, 2013)

1 http://www.gynecologycancer.org/contact
2 SEER data, 2011-2016
3 http://molecularcasestudies.cshlp.org/content/5/6/a004341.full

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Clinical Activity in Discrete KRAS Codon 12 Variants (G12V, G12D)

Summary: VS-6766 + Defactinib in KRAS mt ovarian & lung cancers

Tumor Type		G12V	G12D	G12A	G12C	Q61H	WT
Ovarian	# patients	3	3	1	0	0	2
	PR	2 (67%)	2 (67%)	1 (100%)			0 (0%)
	Disease Control	3 (100%)	3 (100%)	1 (100%)			2 (100%)
	≥6 months time on therapy	2 (67%)	2 (67%)	1(100%)			0 (0%)
Lung	# patients	1	6	1	2	1	0
	PR	1 (100%)	1 (17%)*	0 (0%)	0 (0%)	0 (0%)	
	Disease Control	1 (100%)	4 (67%)	1 (100%)	2 (100%)	0 (0%)	
	≥3 months time on therapy	1 (100%)	4 (67%)	1 (100%)	2 (100%)	0 (0%)	

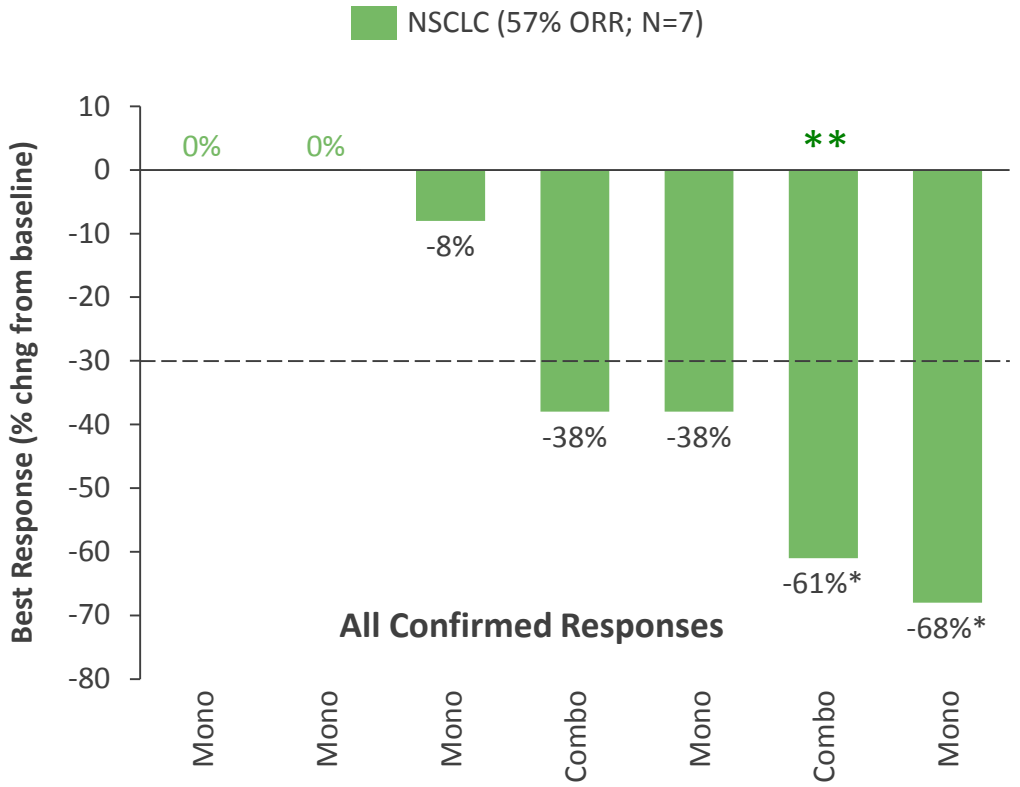
*22% reduction & still on treatment

November 2019 data cut

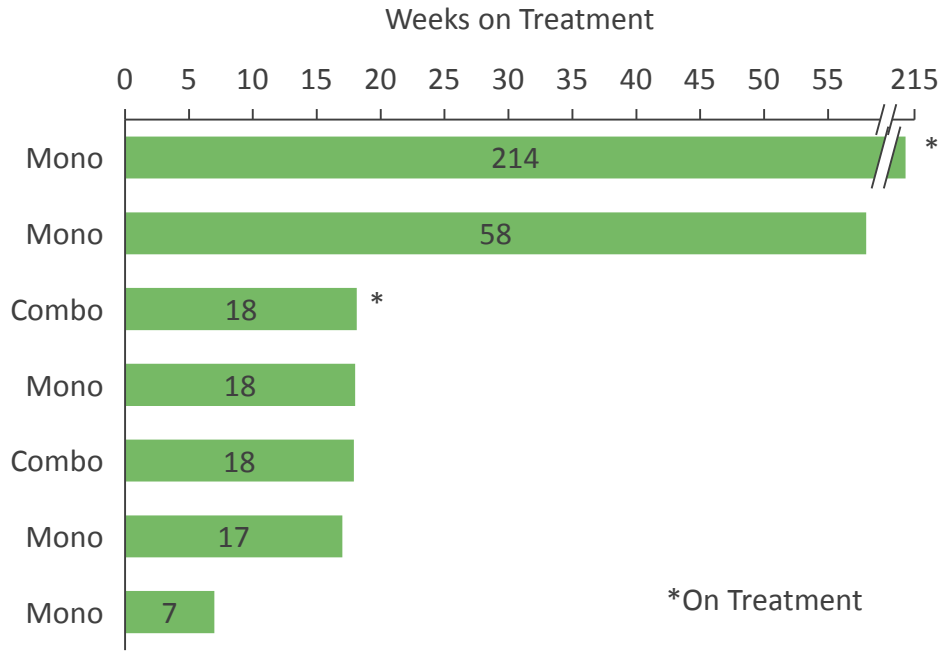
Includes 1 patient with KRAS-G12V mt mucinous ovarian cancer

VS-6766 ± Defactinib has a Confirmed 57% ORR in KRAS^{G12V} NSCLC

Best Response by RECIST in KRAS^{G12V} NSCLC



Time on Treatment for KRAS^{G12V} NSCLC



**March 2020

- All PRs confirmed with subsequent scan per RECIST

Mono = VS-6766 Monotherapy[1]
Combo = VS-6766 + Defactinib

Source: (1) Martinez-Garcia, M. *et al. Clin. Cancer Res.* (2012)

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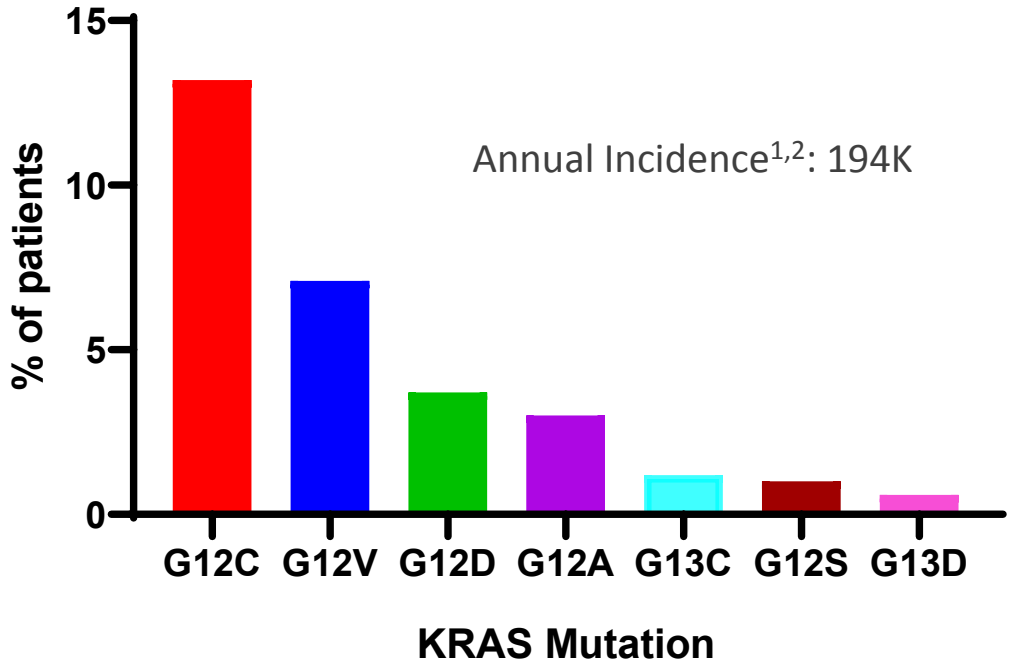
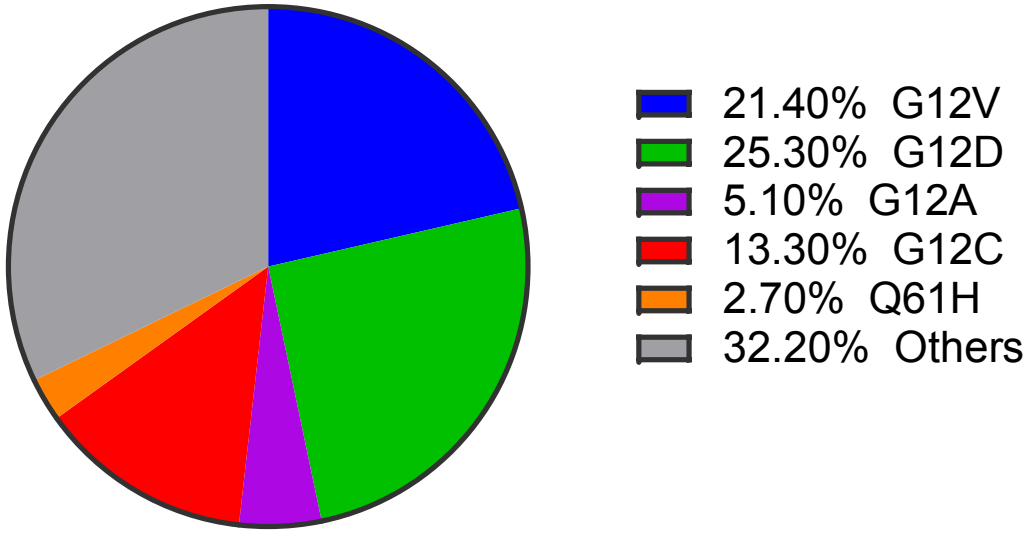
KRAS G12V Represents a Large Opportunity in NSCLC and across Tumors

NSCLC Adenocarcinoma[3]



Annual Incidence[1,2]: 194K

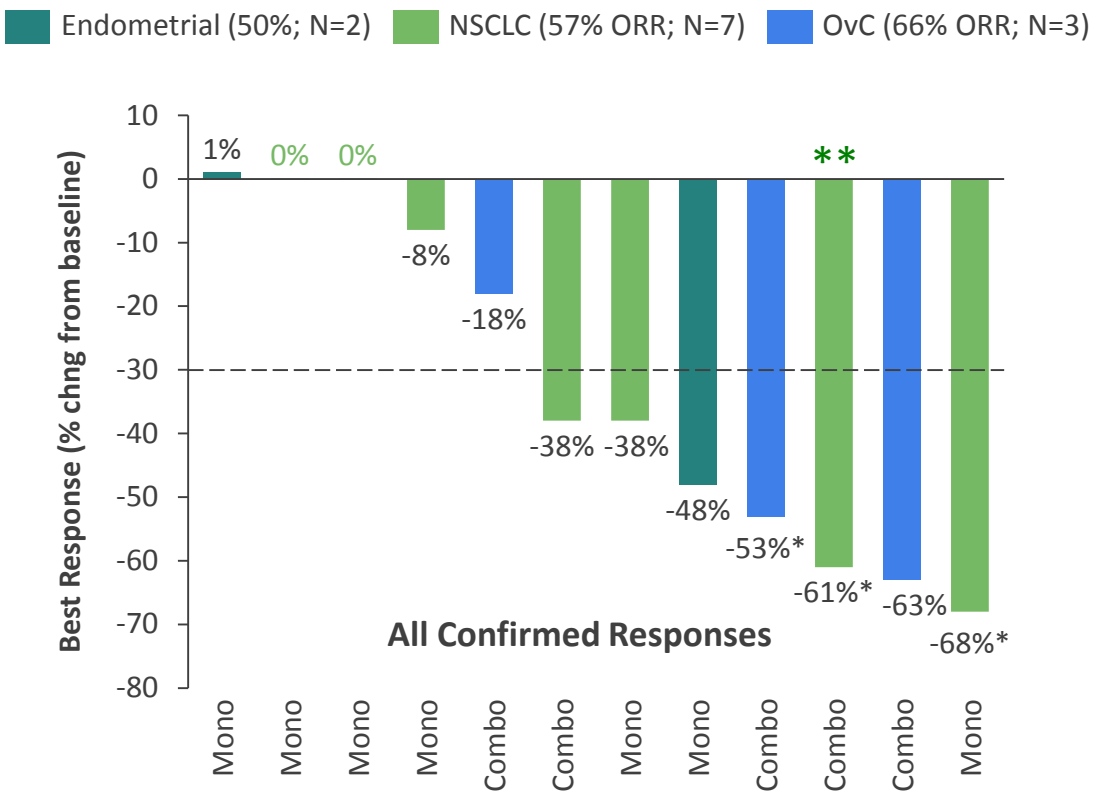
% Frequency in Total of 780 Cancer Patients with KRAS mts[3]



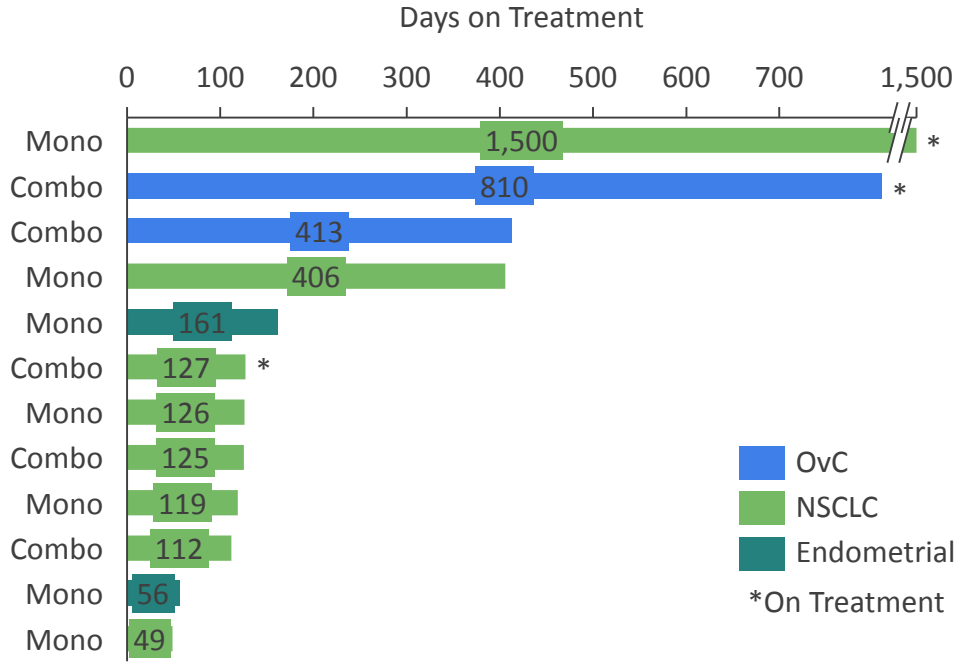
[1] 85% of lung cancer is NSCLC (Lu et. al. Cancer Manag Res. 2019)
[2] Cancer Statistics 2020, Siegel et. al. CA Cancer J Clin 2020;70:7-30
[3] TCGA PanCancer Atlas (cBioPortal analysis)

VS-6766 ± Defactinib has a Confirmed 58% ORR in KRAS^{G12V} Tumors

Best Response by RECIST in KRAS^{G12V} Tumors



Time on Treatment for KRAS^{G12V} Tumors



**March 2020

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Combo = VS-6766 + Defactinib

Source: (1) Martinez-Garcia, M. *et al. Clin. Cancer Res.* (2012)

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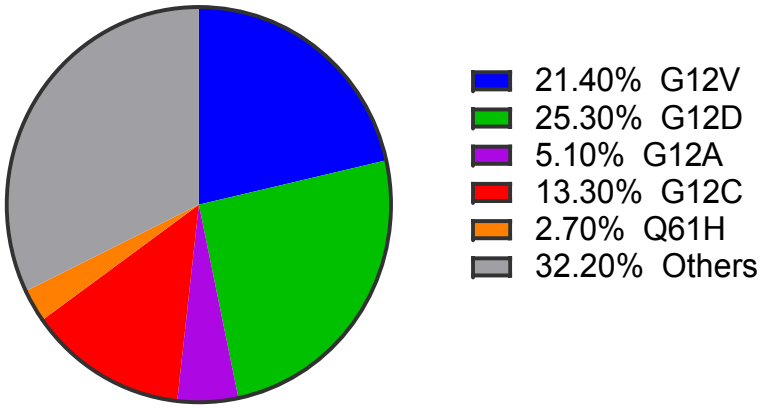
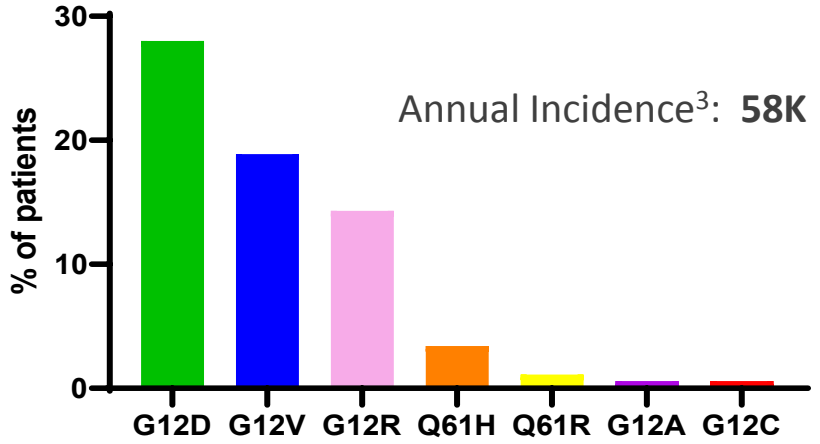
KRAS G12V and G12D Represent ~50% of KRAS Mutations across Human Cancers

% frequency in a total of 780 cancer patients with KRAS mutations[1]

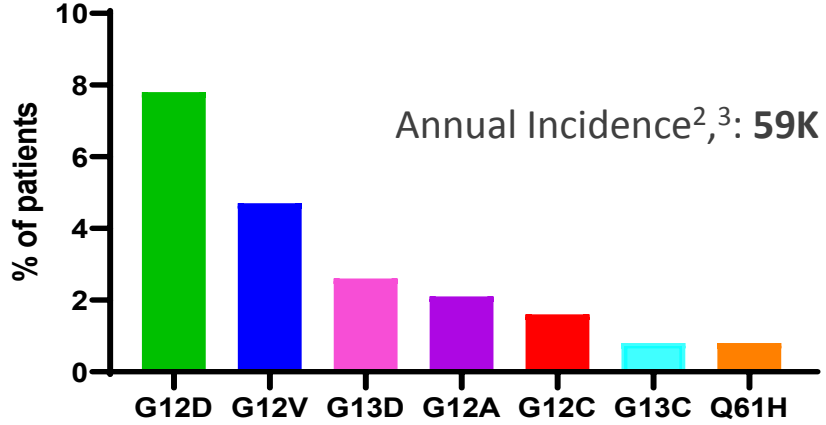


Pancreatic Adenocarcinoma[1]



Annual Incidence[3]: **58K**

Uterine Endometrioid Carcinoma[1]



Annual Incidence[2],[3]: **59K**

[1] TCGA PanCancer Atlas (cBioPortal analysis)
[2] 90% of all uterine cancers are of the endometrial type (ACS)
[3] Cancer Statistics 2020 (Siegel et al. CA Cancer J Clin 2020; 70:7-30)

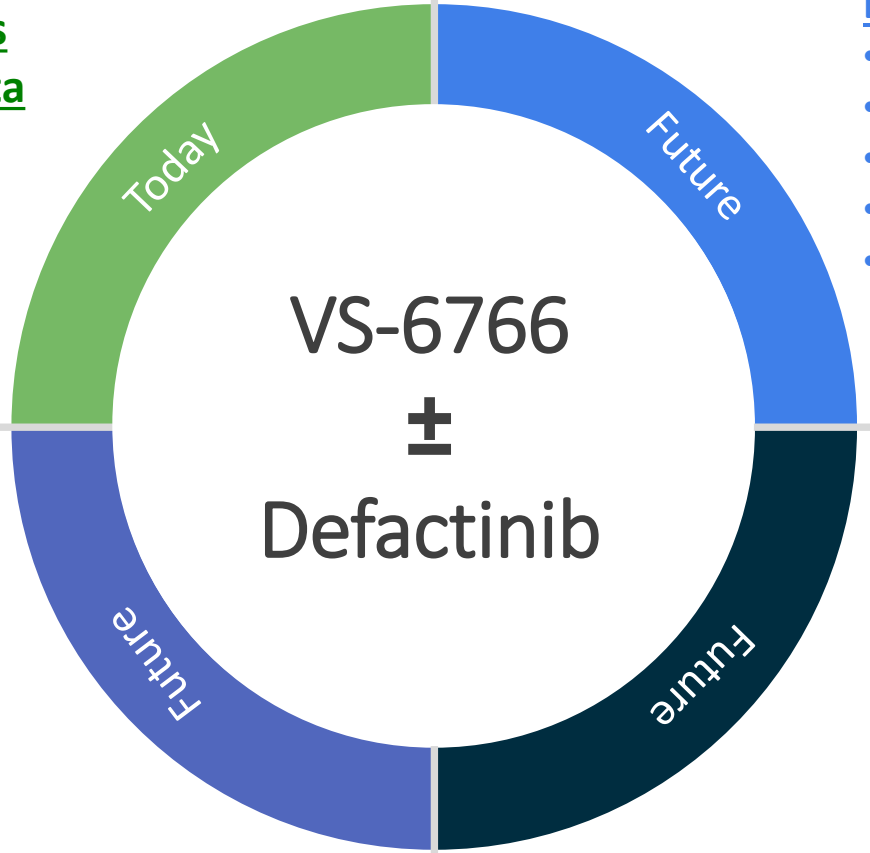
Focusing on High Priority Indications with Significant Opportunities for Growth

High Priority Indications Supported by Initial Data

- LGSOC[1,2]
- KRAS-G12V NSCLC[1,2]
- Pancreatic[1,2]

Expansion Opportunities

- Additional G12V & G12D mt cancers[1]
- Uveal Melanoma[2]
- BRAF mt melanoma[1,2]
- BRAF mt colorectal
- BRAF mt prostate[2]



Other Mutation Opportunities

- GNAQ mutations in uveal melanoma[2]
- NF1 mutations in melanoma
- MAP3K1 mutations in breast cancer

Other Combinations

- KRAS G12C inhibitors
- EGFR inhibitors
- Everolimus[2]
- Anti-PD-1[1,2]

[1] Supported by clinical data
[2] Supported by preclinical data

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Strong Patent Protection for VS-6766 ± Defactinib

- COM for VS-6766 to 2027 & defactinib to 2028, Hatch Waxman should extend to 2032
- VS-6766 intermittent dosing regimen until 2038 if granted
- FAK/MEK combination to 2035
- VS-6766/defactinib combination until 2040 if granted
- Method of manufacture for VS-6766 to 2032
- Other activity related to patent protection is ongoing and will continue into the future

Potential Blockbuster Opportunity with VS-6766 + Defactinib

Key mechanistic attributes

- Potential Best in class RAF/MEK & FAK inhibitors
- More complete RAS pathway shut down addressing key resistance mechanisms
- Uniquely targeting CRAF to shut down KRAS-G12V

Significant commercial potential

- First in class approach to KRAS-G12V & G12D
- No approved therapies in LGSOC
- 30% of all human cancers driven by RAS family mutations

Early clinical experience

- All-oral combination regimen with non-overlapping safety profile
- Initial clinical data with the combination are encouraging including both objective response rate and durability
- KRAS-G12V mutant cancers appear to be particularly responsive to VS-6766 ± defactinib

Next steps

- Goal to initiate LGSOC registration-directed study in 2020
- Complete expansion cohorts in ongoing investigator initiated Phase 1 combination study
- KRAS-G12V & G12D expansion cohorts in NSCLC & pancreatic
- Explore BRAFm-driven indications
- Combinations with KRAS-G12Ci & anti-PD-1

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Q&A