Verastem Oncology

BTIG KOL Event

December 17, 2020

NASDAQ: VSTM

On Today's Call

Prepared Remarks

- Robert (Bert) Hazlett, Managing Director – *Equity Research, BTIG, LLC*
- Kathleen Moore, MD, MS, *Associate Director for Clinical Research and the Director of the Phase 1 Drug Development Unit at the Stephenson Cancer Center at the University of Oklahoma*
- Brian Stuglik, *Chief Executive Officer, Verastem Oncology*
- Jonathan Pachter, PhD, *Chief Scientific Officer, Verastem Oncology*

Joining for Q&A Session

- Rob Gagnon, *Chief Financial Officer, Verastem Oncology*
- Ajay Munshi, *VP Corporate Development, Verastem Oncology*

*On April 23, 2019, we entered into a 4th Amendment to our existing Agreement with Hercules Capital, Inc. whereas we may borrow up to an aggregate amount of $75.0 million, of which $35.0 million was outstanding as of the date of amendment and 6/30/2020.

**The 2018 Notes have an initial conversion rate of 139.5771 shares of Common Stock per $1,000 which translates to an initial conversion price of $7.16 per share of Common Stock.

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. Applicable risks and uncertainties include the risks and uncertainties, among other things, regarding: the satisfaction of closing conditions with respect to the sale of the COPIKTRA assets to Secura Bio; the ability of Secura Bio to achieve the clinical and sales milestones necessary to result in additional consideration payable to Verastem.

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.

Low-Grade Serous Ovarian Cancer

Treatment Landscape and Clinical Perspective

Kathleen Moore, MD, MS, Stephenson Cancer Center at the University of Oklahoma

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- Dr. Moore is currently an Associate Professor in the Division of Gynecologic Oncology at the University of Oklahoma. She is the Associate Director for Clinical Research and the Director of the Phase I Drug Development Unit at the Stephenson Cancer Center at the University of Oklahoma.

- She received her MD from the University of Washington School of Medicine in 2000. She completed her residency in Obstetrics and Gynecology at Magee Women's Hospital, Pittsburgh, PA in 2004 and went on to complete her fellowship in Gynecologic Oncology at the University of Oklahoma in 2007.

- She has been on faculty at the University of Oklahoma since 2007.

- Nationally she serves as the NRG Chair for Ovarian Cancer, Associate Director for GOG-Partners and has participated in many NCI sponsored clinical trial initiatives.

- She has authored over 200 manuscripts and has lead phase I through III trials including those with registration intent.

Treatment Landscape and Clinical Perspective

Kathleen Moore, MD, MS,
Stephenson Cancer Center at the University of Oklahoma

What is Low-Grade Serous Ovarian Cancer (LGSOC)?

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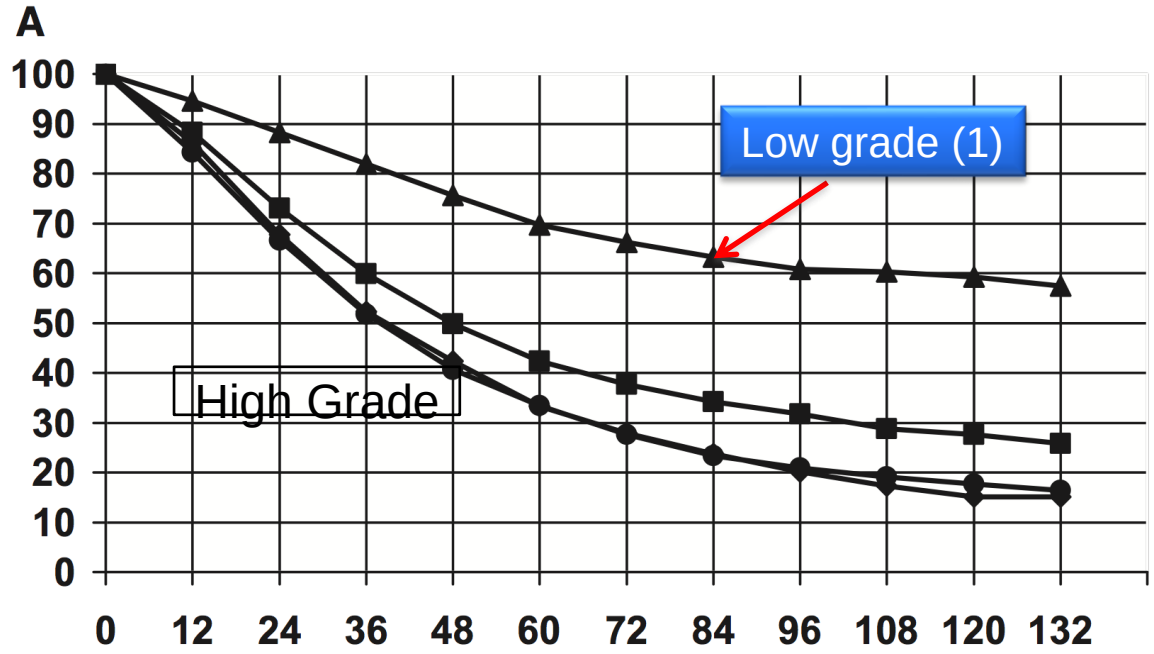
- Epithelial cells line the surface of the ovary and LGSOC is a type of epithelial cell cancer, or “carcinoma”
- A slow growing cancer, that has a median survival of 10 years, so patients remain in treatment for a long time
- ~6,000 patients in the U.S. and ~80,000 worldwide living with the disease
- Approximately half of those diagnosed are in their 20s, 30s, or 40s and 85% of cases will experience recurrence



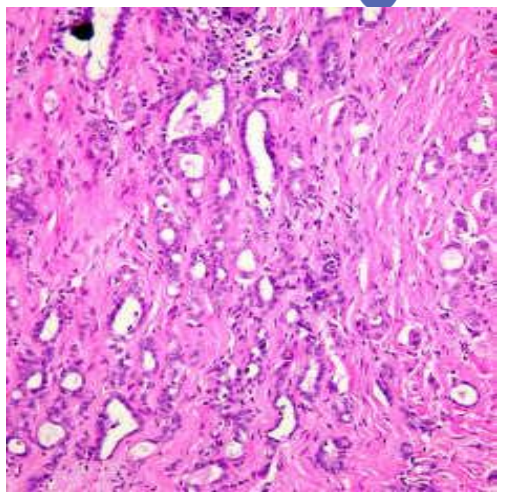
Median survival: SEER data

From Plaxe et al Am J Obstet & Gynecol 2008

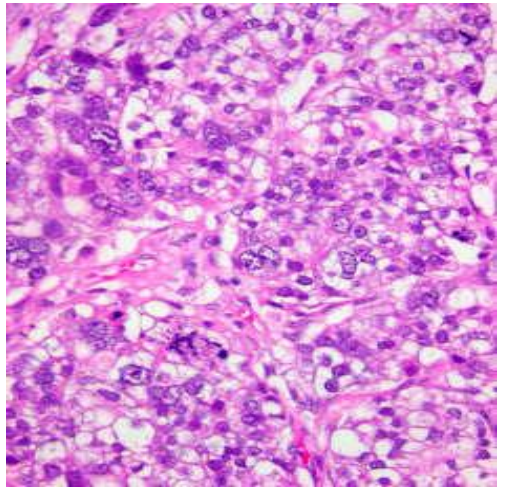
Source: https://cureourovariancancer.org/ca/about/low-grade-serous-ovarian-cancer

LGSOC is a predominantly RAS-driven Subset of Ovarian Cancer

Variable	LGSOC (Grade 1)	HGSOC (Grade 2/3)
Nuclear atypia	Uniform round to oval with little variation	+++ Marked variation
Mitotic Index	<12 mitosis per 10 hpf	>12 mitoses per 10 hpf
Chromatin and variation in size of nucleus	Little	Marked (nuclear size ratio ≥3)
Mutation	KRAS ++ BRAF + ER/PR +++ PAX2 +	P53 +++
Precursor	Serous borderline tumor	Tubal intraepithelial neoplasia



LGSOC



HGSOC

Malpica et al, *Am J Pathol* 2007

LGSOC is Relatively Chemo-Resistant

- **NCDB**
  - **Propensity score-matched, NCDB study of 755 women with advanced LGSOC,**
  - **Median OS for those receiving platinum/taxane-based chemo after primary CRS was 88.2 months compared to 95.9 months among those who were observed and did not receive chemo**

- **OCAC**
  - **Retrospective, multi-site Ovarian Cancer Association Consortium (OCAC) analysis of 714 women with LGSOC demonstrated that stage, residual disease status, and CA-125 were prognostic of survival on multivariable analysis**
  - **Receipt of platinum-based chemotherapy was not associated with survival (HR 0.94; 95% CI 0.69=1.28)**

Glockley, Obstet Gynecol, 2017; May et al, unpublished, 2018

First-line Treatment of Advanced LGSOC: Utilizing Hormonal Therapy

MD Anderson: 1° CRS→C/T +/- HMT (n=203)

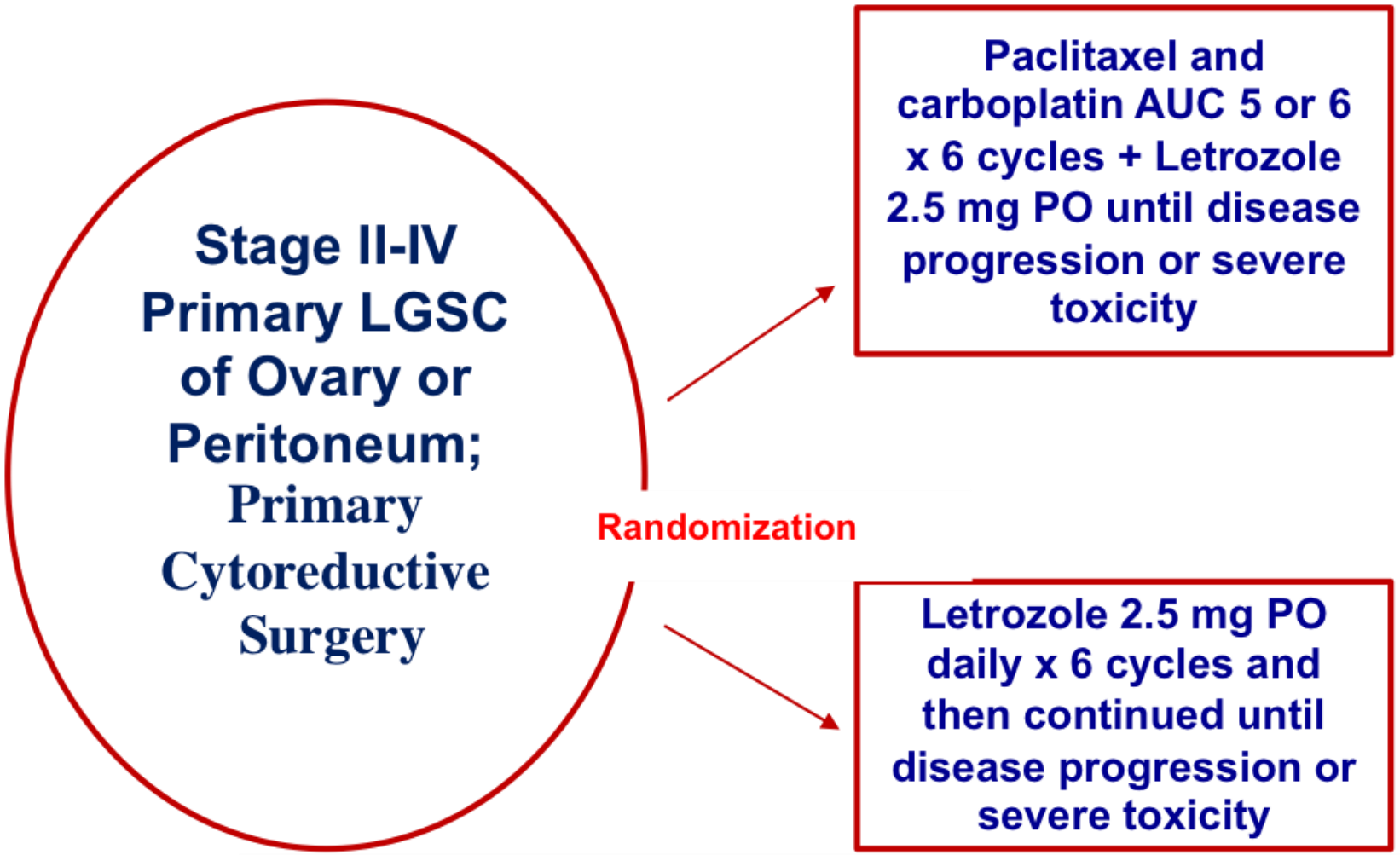
- **70 received Hormonal therapy maintenance (HMT) after C/T**
- **Median PFS carbo/taxol/OBS vs. carbo/taxol/HMT=26.4 vs. 64.9 mos (p<0.001)**
- **Letrozole most common therapy**

JHH/Cleveland Clinic 1° CRS→hormonal monotherapy (n=27)

- **Only 22% recurred after median follow-up of 41 months**
- **Median PFS and OS not reached but 2 year PFS 82.8% and OS 96.3%.**

- **Optimal treatment unknown**

Gershenson et al, J Clin Oncol, 2016;
Fader et al, Gynecol Oncol, 2016



*Patients stratified based on 1) residual disease following primary cytoreductive surgery: a) no gross residual disease vs. b) any gross residual disease and 2) Country/site of trial enrollment: a) US/Canada, b) Asia, and c) Europe.

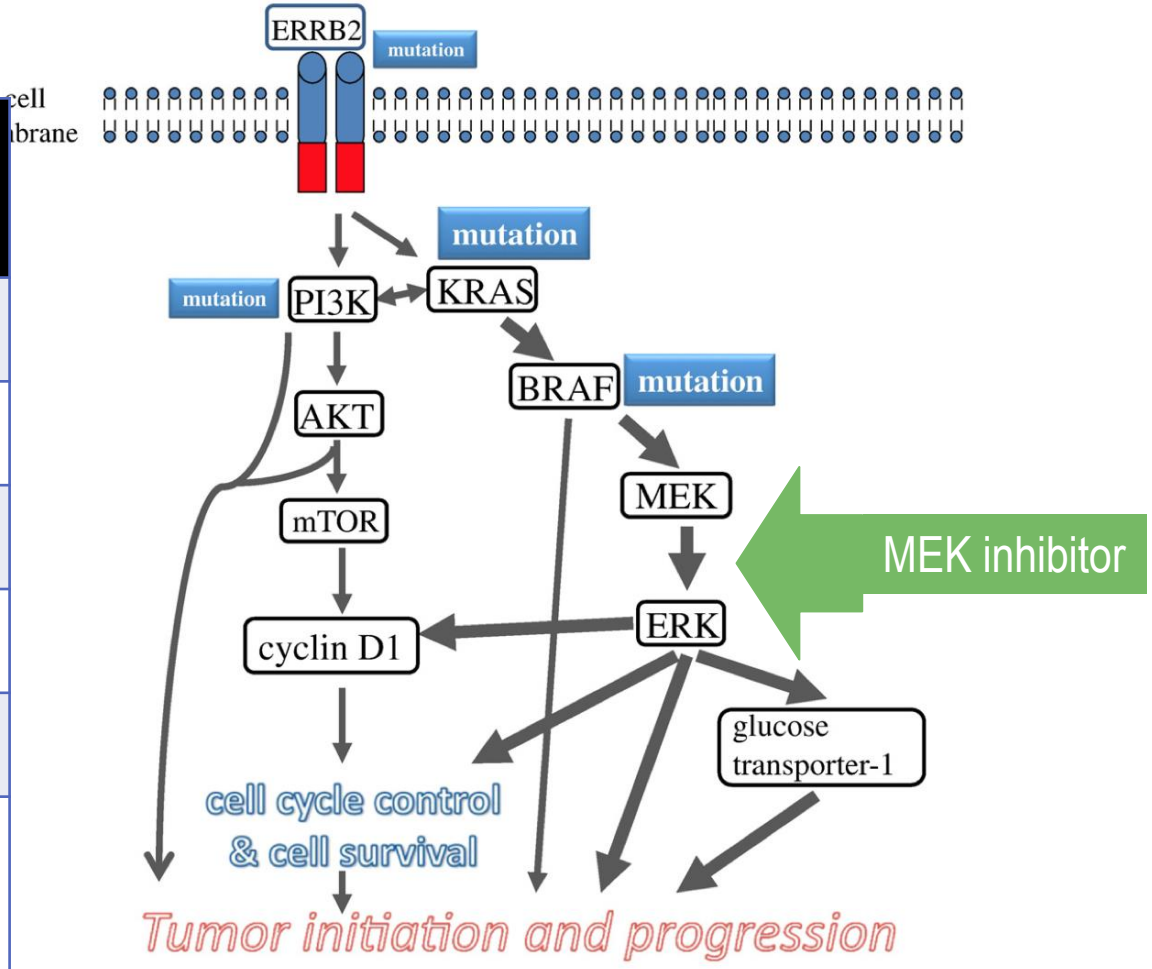
*Randomization will be performed in a 1:1 ratio.

*No central pathology Review

Recurrent LGSOC Responds Poorly to Chemotherapy

	ORR	SD	Number
Carboplatin	3	15	25
PLD	0	11	21
Paclitaxel	1	11	18
Carbo/Paclitaxel	0	7	10
Topotecan	0	5	10
Carbo/ Gemcitabine	0	1	1
Percentage	5%	59%	N=85

Gershenson et al Gyne Oncol 2009



Kurman & Shih 2011

PHASE II TRIAL OF SELUMETINIB- MEK INHIBITOR IN LOW GRADE SEROUS OVARIAN CANCER

	Patients (n=52)
Complete response	1 (2%)
Partial response	7 (13%)
Stable disease	34 (65%)
Progressive disease	8 (15%)
Indeterminate	2 (4%)

Data are number (%).

***Table 3*: Best response to treatment**

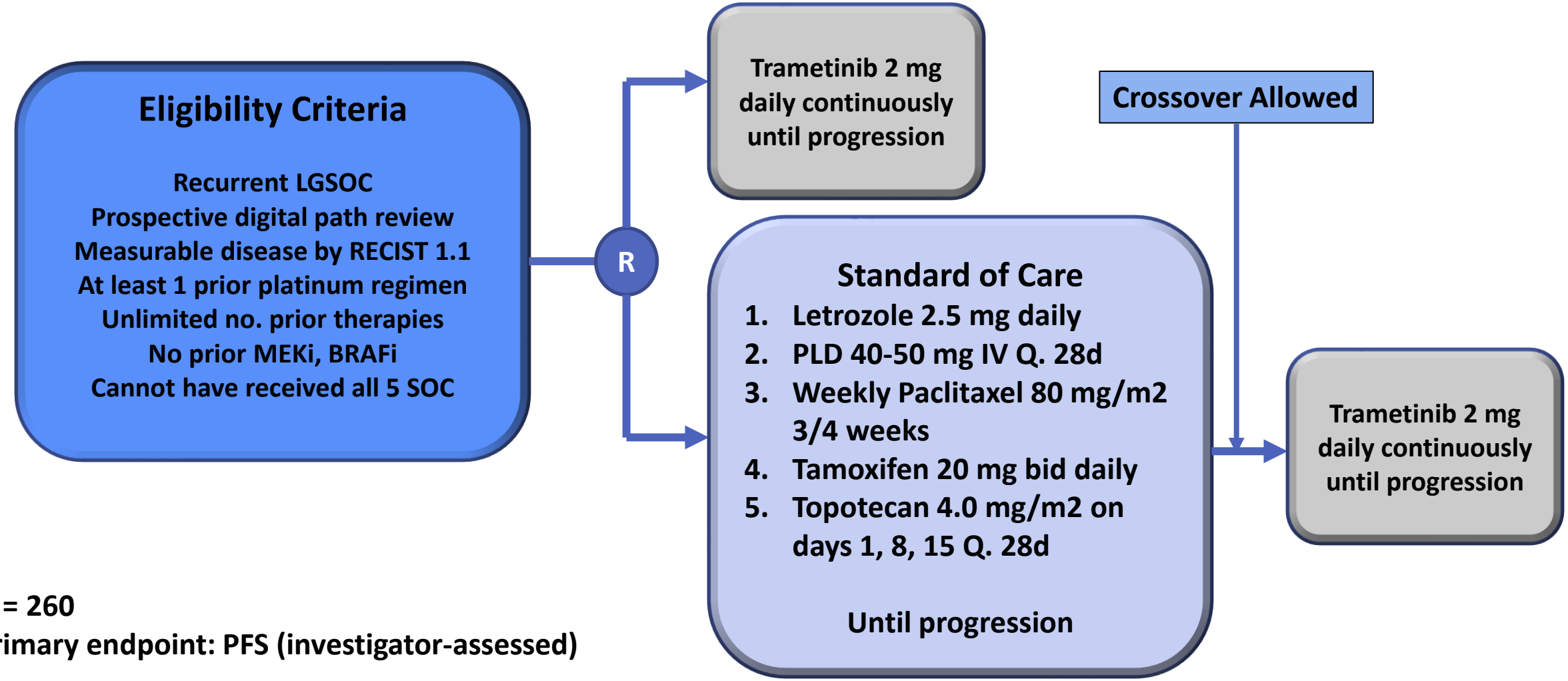
	Number	No tumour response	Tumour response	p value*
Total	34	27 (79%)	7 (21%)	
BRAF mutation				
No	32	25 (78%)	7 (22%)	1·000
Yes	2	2 (100%)	0	
KRAS mutation				
No	20	15 (75%)	5 (25%)	0·672
Yes	14	12 (86%)	2 (14%)	
BRAF or *KRAS* mutation				
No	18	13 (72%)	5 (28%)	0·405
Yes	16	14 (88%)	2 (13%)	

Data are number (%), unless otherwise indicated. *Fisher's exact test.

***Table 8*: Tumour response (complete or partial) by *BRAF* and *KRAS* mutations**

Farley et al Lancet Oncol 2013

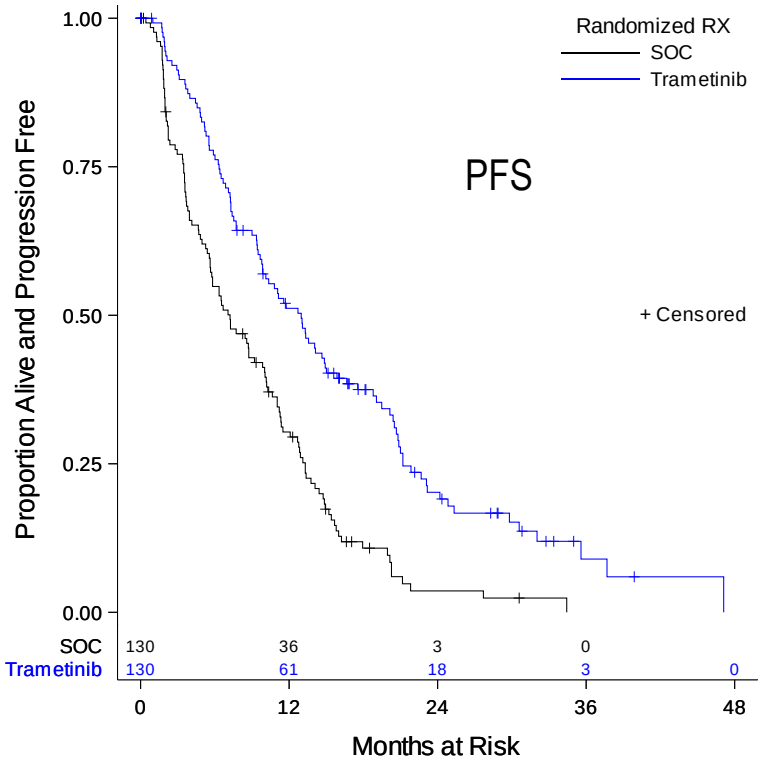
Study Design



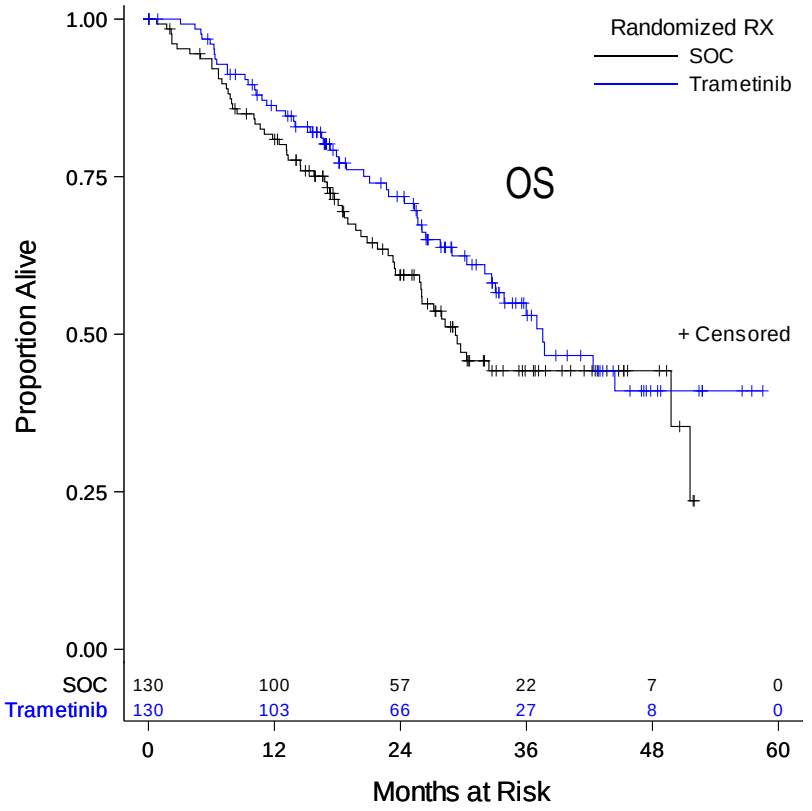
N = 260

Primary endpoint: PFS (investigator-assessed)

TRAMETINIB IN LGSOC



	Trametinib	Control (SOC)
Median (Months) 95% CI	**13.0 (9.9 – 15.0)**	**7.2 (5.6 - 9.9)**
Hazard Ratio 95% CI	**0.48 (0.36 – 0.64)**	
One-sided p-value	**<0.0001**	



	Trametinib	Control (SOC)
Median (Months) 95% CI	**37.0 (30.3 to NE)**	**29.2 (23.5 to 51.6)**
Hazard Ratio 95% CI	**0.75 (0.51 – 0.1.11)**	
One-sided p-value	**0.054**	

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Advancing Research. Improving Lives.™

NCRI National Cancer Research Institute

Response by RECIST 1.1

Arm	No. Pts CR + PR /Treated	Objective Response Rate (95% CI)	Stable Disease Rate	Response Duration Months (95% CI)	Odds Ratio For ORR (95% CI)	P-Value
Trametinib	**34/130**	**26.2% (19.0-34.0)**	**59.2%**	**13.6 (8.1-18.8)**		
					5.4 (2.4-12.2)	**< 0.0001**
Control (SOC)	**8/130**	**6.2% (2.0-10.0)**	**70.8%**	**5.9 (2.8-12.2)**		
Letrozole	6/44	13.6%	70.5%			
Tamoxifen	0/27	0%	66.7%			
Paclitaxel	1/11	9.1%	63.6%			
PLD	1/40	2.5%	80.0%			
Topotecan	0/8	0%	50.0%			

34.8% discontinuation rate for trametinib due to adverse event vs. 12.3% for the control arm

MILO Study Design

Patients with Recurrent/Persistent LGS Carcinoma of the Ovary, Fallopian Tube or Primary Peritoneum
≥1 prior platinum based regimen but ≤ 3 prior lines of chemo
Unlimited prior hormonal therapies (ENGOT Model C)

Stratification:
Platinum-Free Interval (≤ 182 days vs > 182 days)
# of Prior Systemic Chemo Regimens (1 or 2 vs. >2)

Randomization 2:1

- Study initiation: June 2013
- Interim analysis cutoff date: January 2016 (N=303)*
- Updated analysis cutoff date: January 2019 (N=341)

*Study enrollment discontinued after this planned interim PFS analysis crossed the predefined futility boundary (observed hazard ratio of 1.21).

**Crossover allowed following PD on PCC

Binimetinib (N=228)

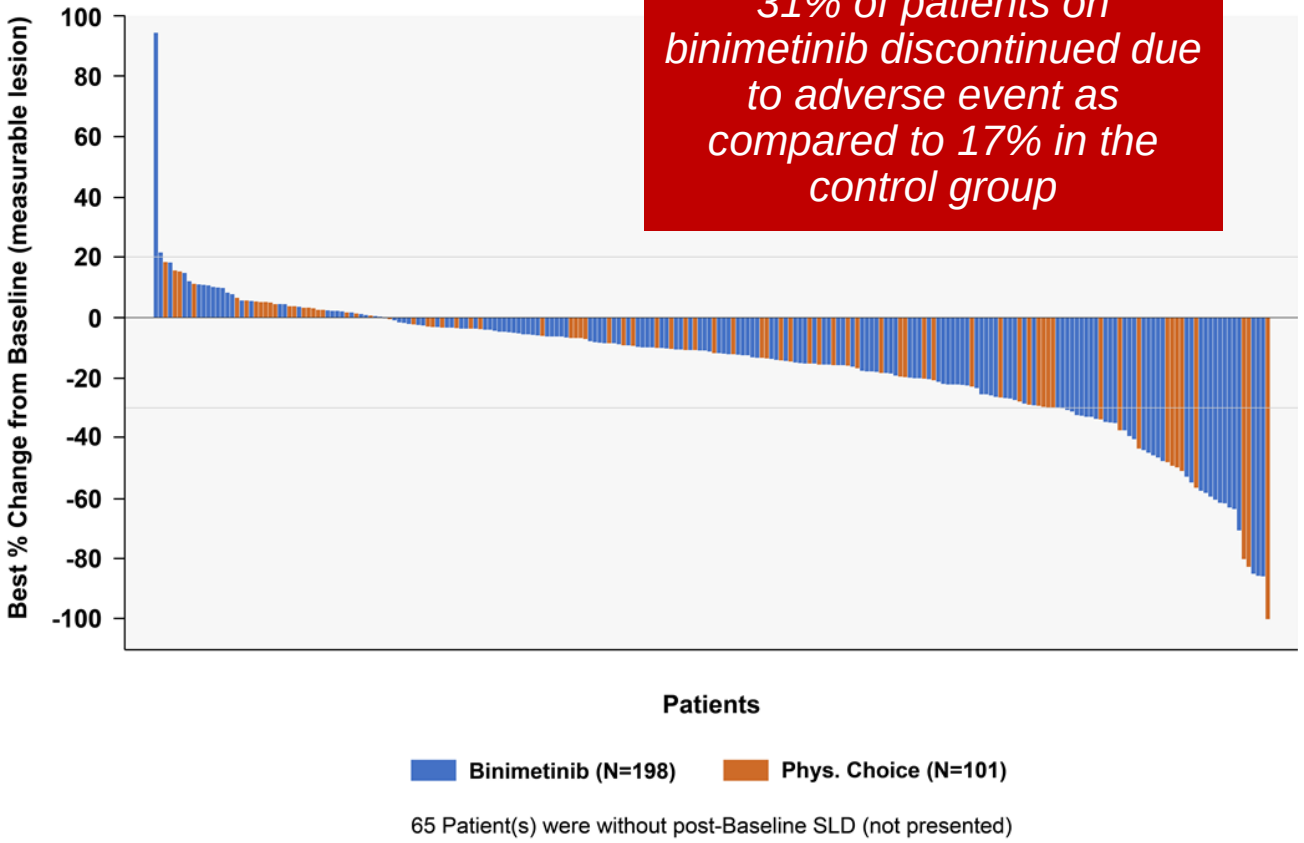
(45mg PO BID)

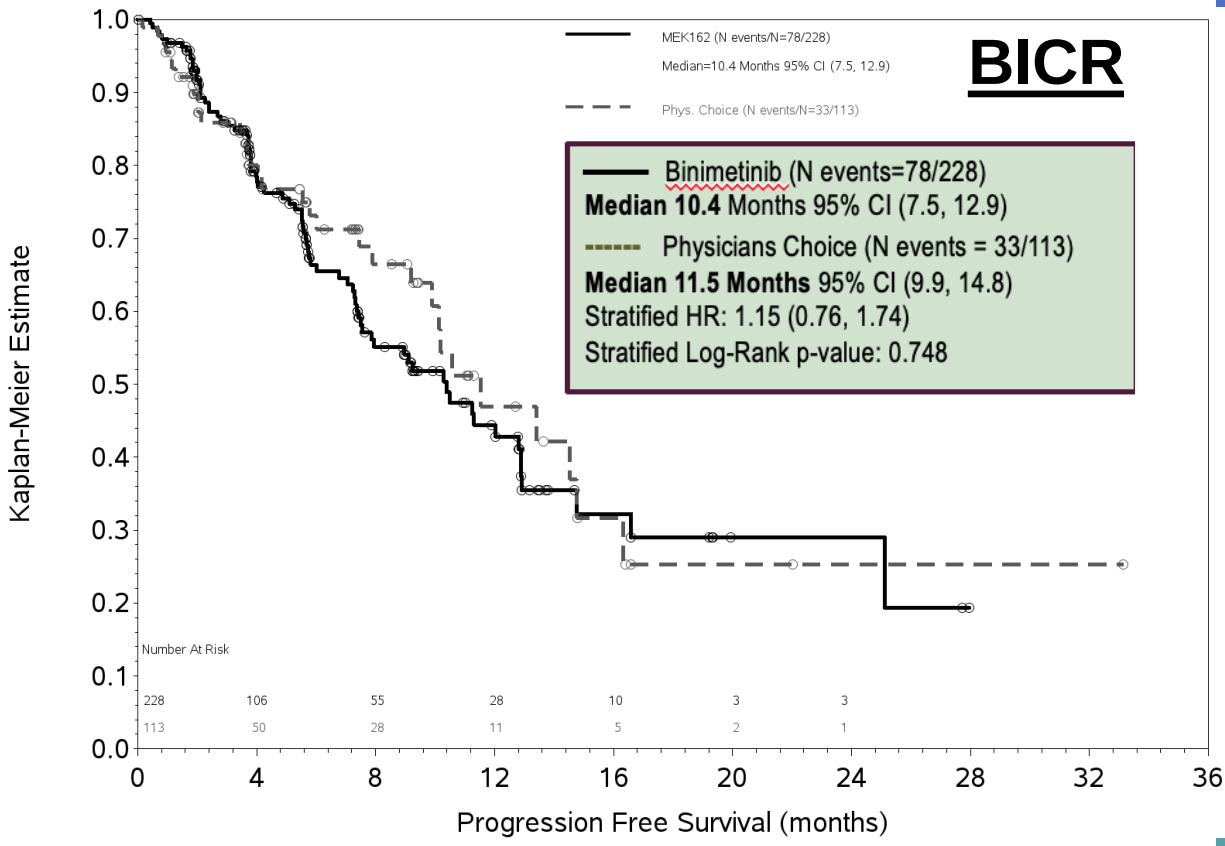
Physicians' Choice of Chemotherapy (N=113)**

Pegylated Liposomal Doxorubicin	Paclitaxel	Topotecan
(40mg/m2 IV, day 1 of 28 day cycle)	(80mg/m2 IV on days 1,8,15 of 28 day cycle)	1.25 mg/m2 IV on Days 1-5 of 21 day cycle)

Binimetinib (MILO Trial) versus Physician Choice

31% of patients on binimetinib discontinued due to adverse event as compared to 17% in the control group





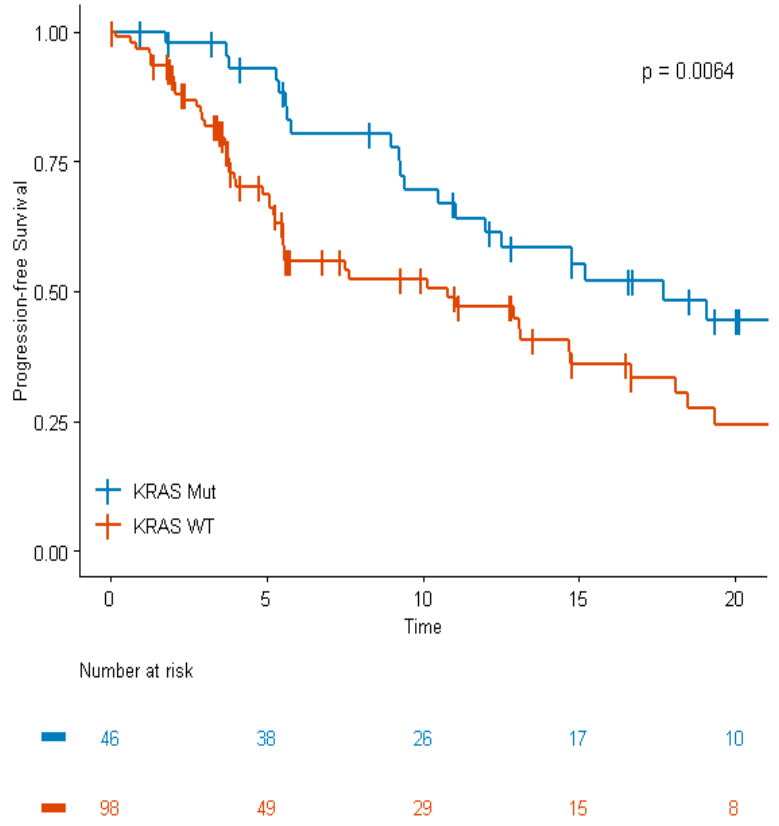
Grisham et al IGCS, Brazil 2019

MILO trial: Standard of care treatment
Median Progression-free survival 11.5 months; Median Overall survival 34 months

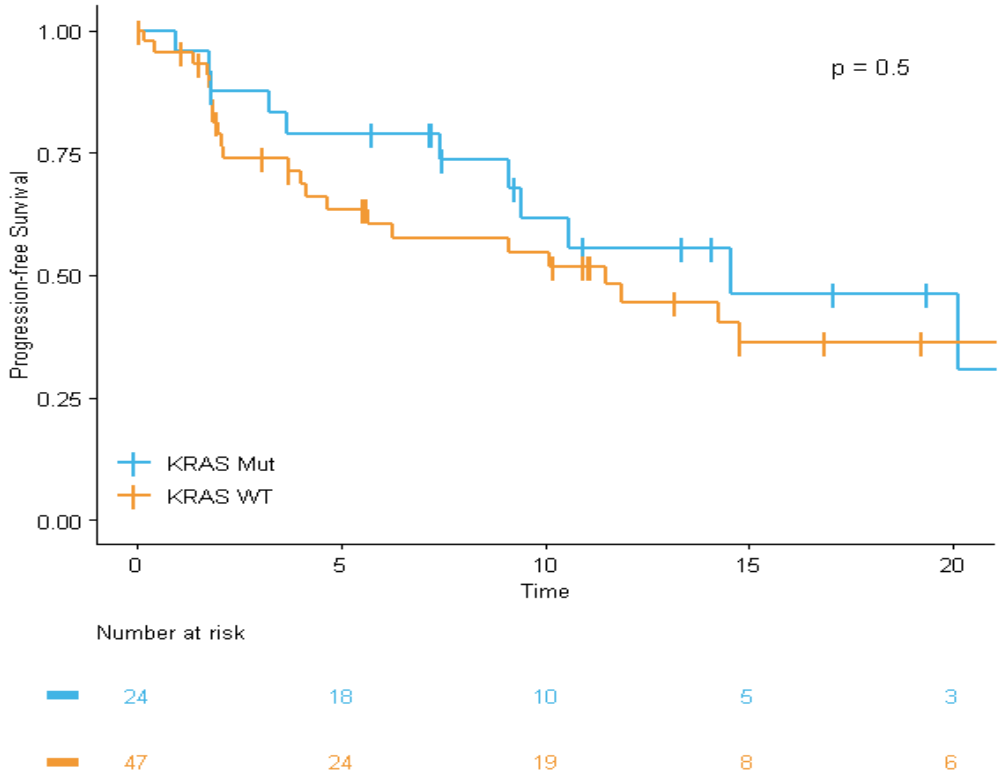
GOG 281 SOC: median PFS 7.2 months; median OS 29.2 months

KRAS MUTATION ASSOCIATED WITH PROLONGED PFS IN PATIENTS TREATED WITH BINIMETINIB

Median PFS for **Binimetinib**
KRAS Mutant: 17.7 months (12, NA)
KRAS WT: 10.8 months (5.5, 16.7) P= 0.006



Median PFS for **Phys Choice**
KRAS Mutant: 14.6 months (9.4, NA)
KRAS WT: 11.5 months (5.7, 26.6) P=0.502



Grisham et al IGCS, Brazil 2019

There is a Continued Need for New Therapeutic Options for LGSOC Patients

- Recurrent low grade serous ovarian cancer responds very poorly to chemotherapy
- Trametinib led to a significant improvement in PFS and is now NCCN listed as an option for recurrent disease
- Similar results were not seen with binimetinib but the study design differed in terms of BICR vs investigator assessment of response
- Other SOC options include anti-estrogen therapies (ORR 9-14%)
- Clinical trials have explored combination MEK and PI3K inhibition without benefit for the combination (NCT01936363), androgen receptor inhibition (38% with PFS6) and CDK4/6 inhibitors + aromatase inhibitors (ongoing studies)
- Although a rare disease, these women live many years while continuously on therapy justifying continued development in this space

Dalton et al Gyne Onc 2017; Grisham et al. Int J Gynecol 2014; Gershenson et al. Gyne Onc 2012; Tang et al. Gyne Onc 2019, Grisham et al. IGCS 2019 Plenary 6

Development History of VS-6766

Jonathan Pachter, PhD, Chief Scientific Officer,
Verastem Oncology

Verastem Oncology

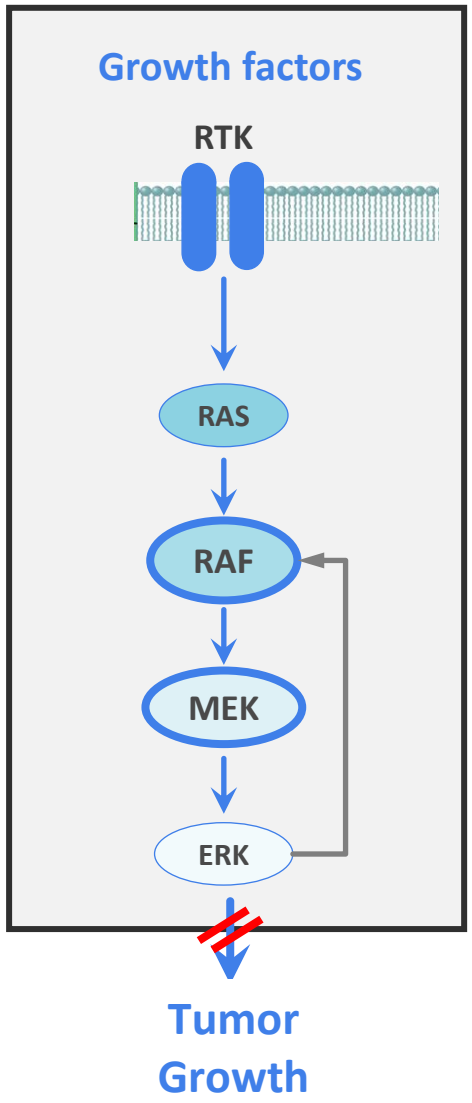
Low-Grade Serous Ovarian Cancer

VS-6766 + Defactinib Current Data

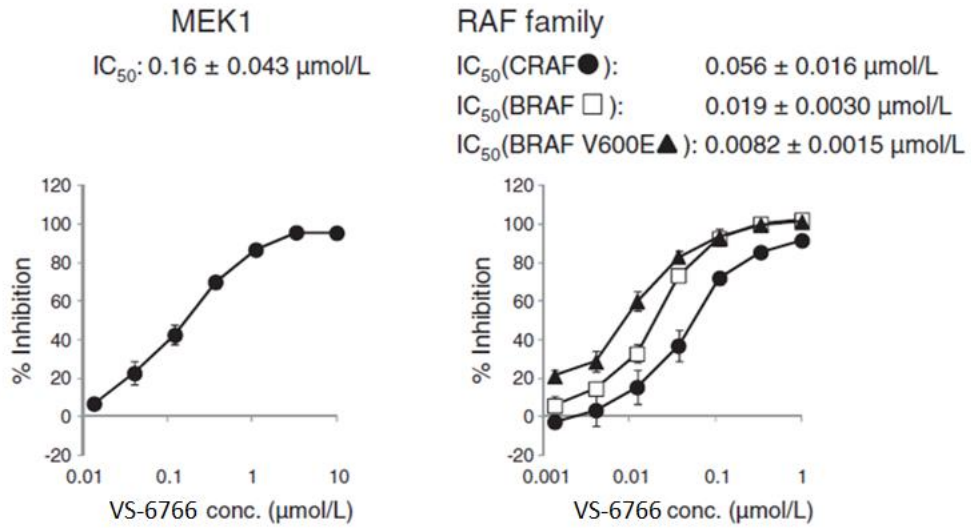
Jonathan Pachter, PhD, Chief Scientific Officer,
Verastem Oncology

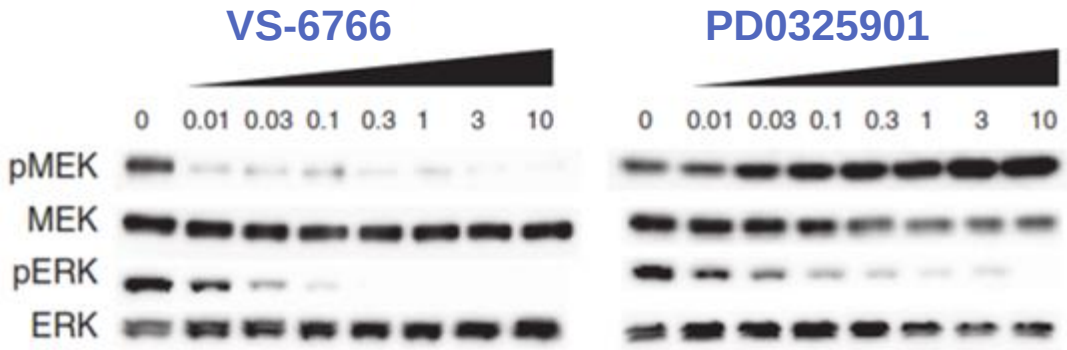
Verastem Oncology

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



- VS-6766 inhibits both MEK & RAF kinase activities
- MEK inhibitors paradoxically induce MEK phosphorylation (pMEK) by relieving ERK-dependent feedback inhibition of RAF
- 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





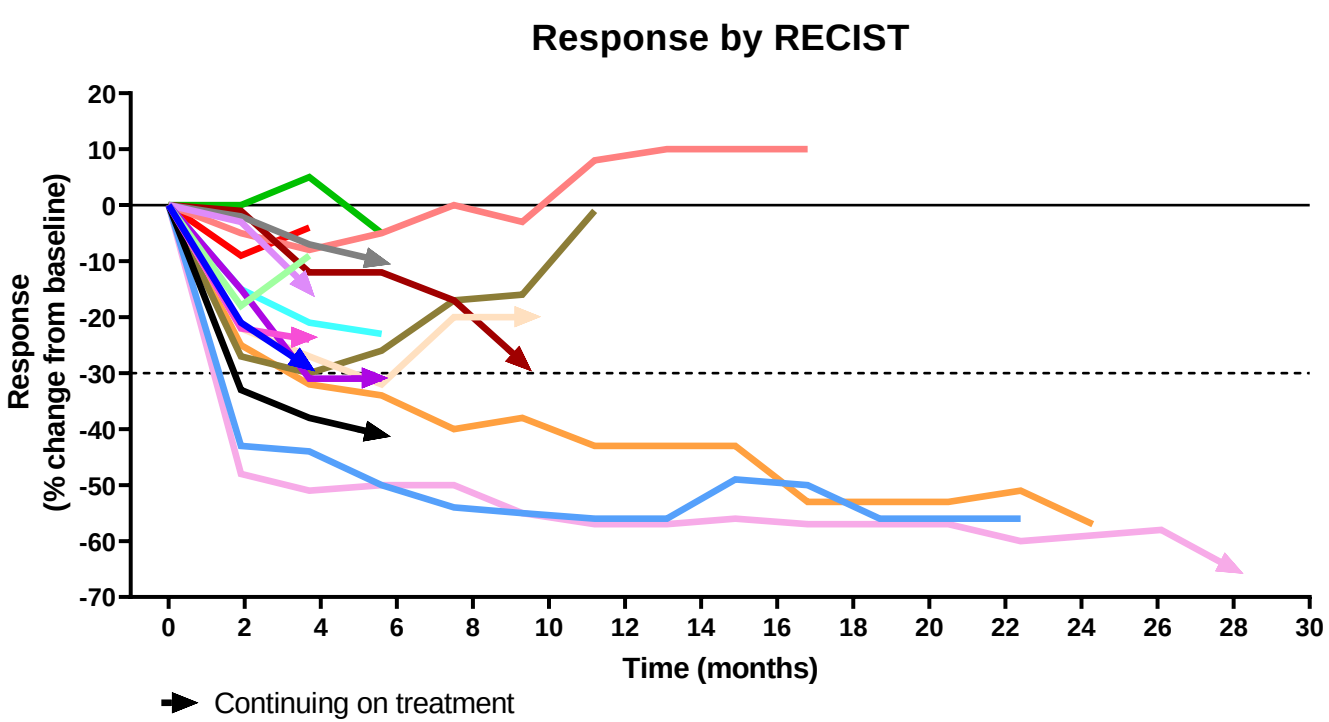
Reference: Ishii et al., *Cancer Res*, 2013; Lito et al., *Cancer Cell*, 2014; Blasco, R. B. et al. *Cancer Cell* (2011); Sanclemente, M. et al. *Cancer Cell* (2018)

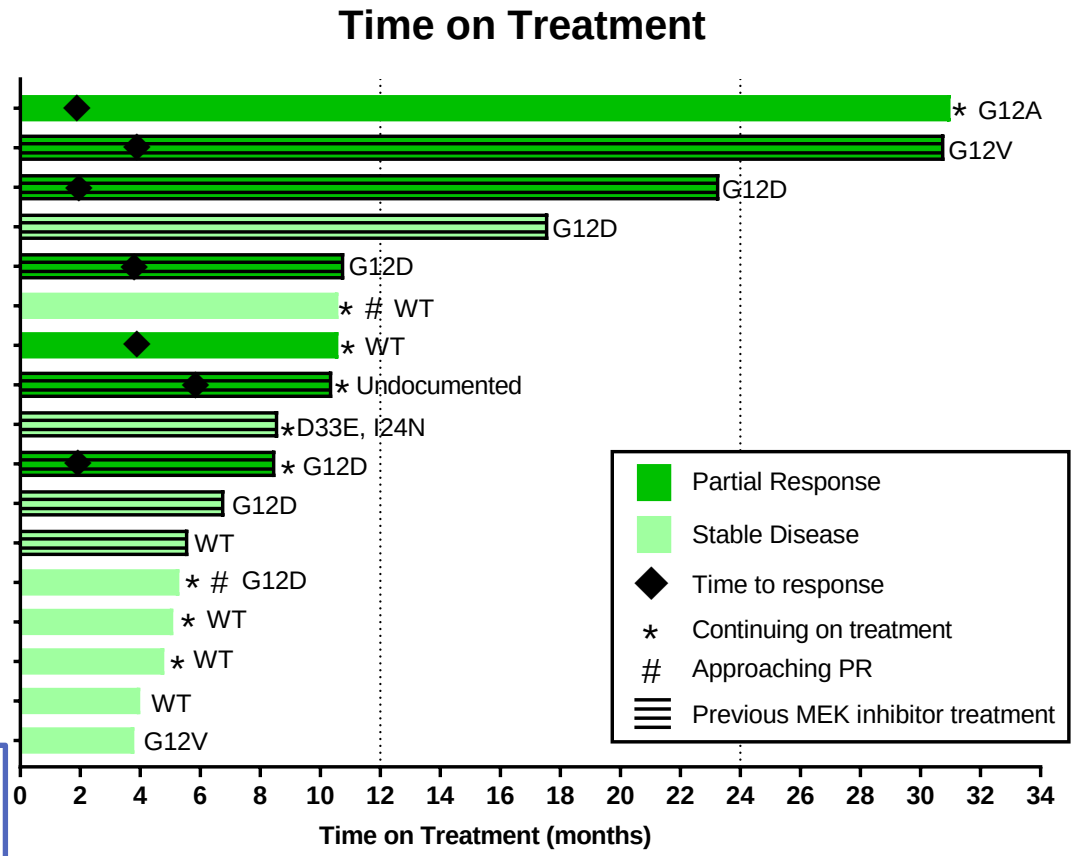
Favorable Tolerability Profile for Novel Intermittent Dosing Regimen of VS-6766 plus Defactinib

	Daily at MTD N=6 28-day cycle	4mg twice weekly N=26 28-day cycle	RP2D (VS-6766 3.2mg twice weekly + defactinib 200mg twice daily) N=26 21 days of 28-day cycle
Adverse Event	**Grade ≥3**	**Grade ≥3**	**Grade ≥3**
Rash related	3 (50%)	5 (19%)	1 (4%)
CK elevation	1 (17%)	2 (8%)	1 (4%)
Blurred vision	-	-	-
Peripheral edema	-	-	-
Diarrhea	-	1 (4%)	-
Mucositis	-	1 (4%)	-
Fatigue	-	1 (4%)	-
Nausea	-	-	-

[1] Chenard-Poirier, *et al*. ASCO 2017.

VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC with Expanded Number of Patients (n=17)





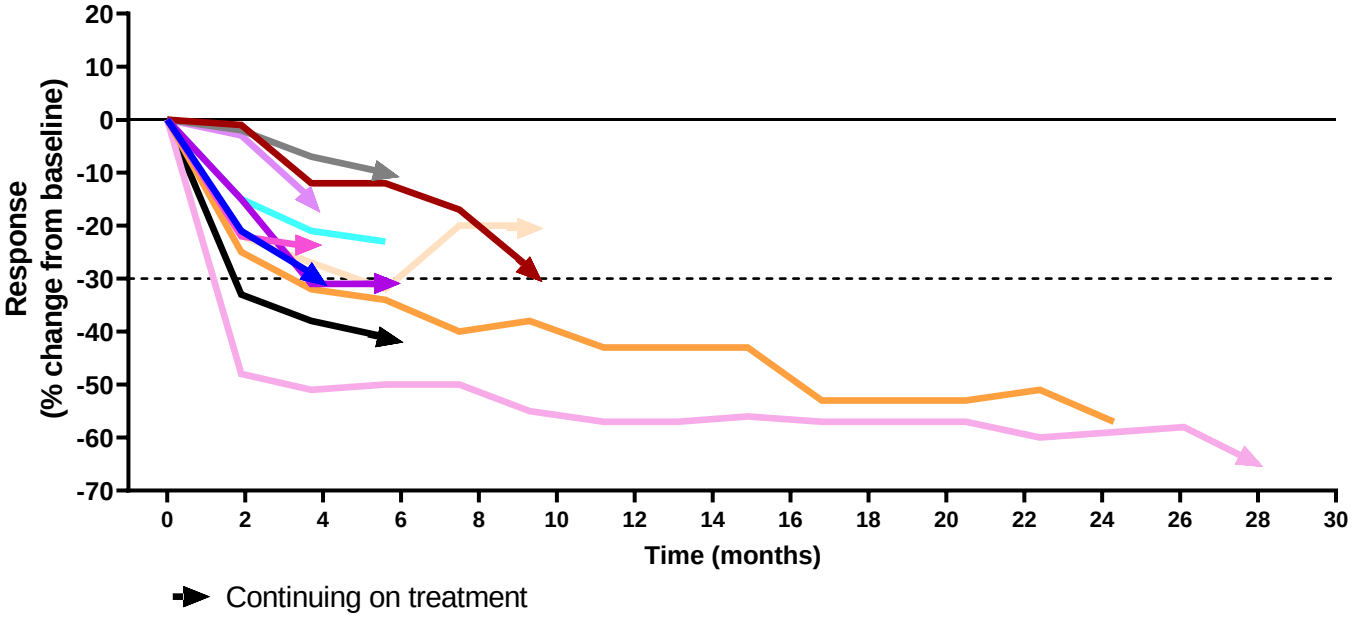
- KRAS-G12 mutations ORR = 56% (5/9); data still maturing
- Current ORR = 41% (7/17); data still maturing
- 5/9 PRs in pts who had previous MEKi[1]
- 9/17 (53%) still on study[2]
- 3 pts on treatment for ~2 yrs or more

[1] Patients came off prior MEKi treatment primarily for progression
[2] Data cutoff date August 17, 2020

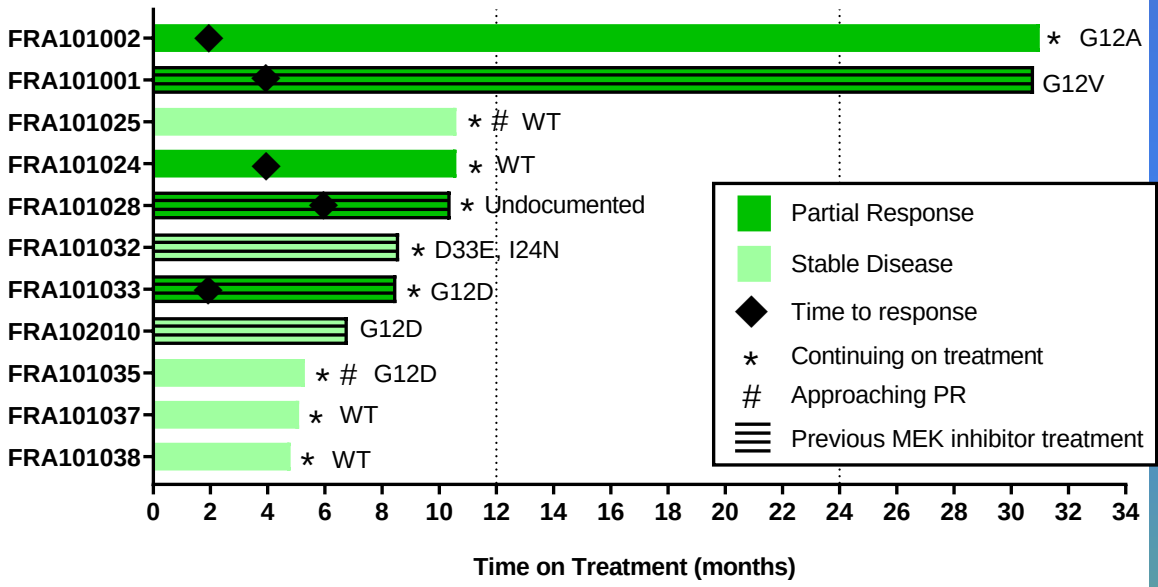
VS-6766 in Combination with Defactinib Shows Robust ORR with Durability in Refractory LGSOC at Phase 2 Dose Level

All patients on RP2D: 3.2 mg VS-6766 (2x/wk) + 200 mg Defactinib (BID) q3/4 wks

Response by RECIST



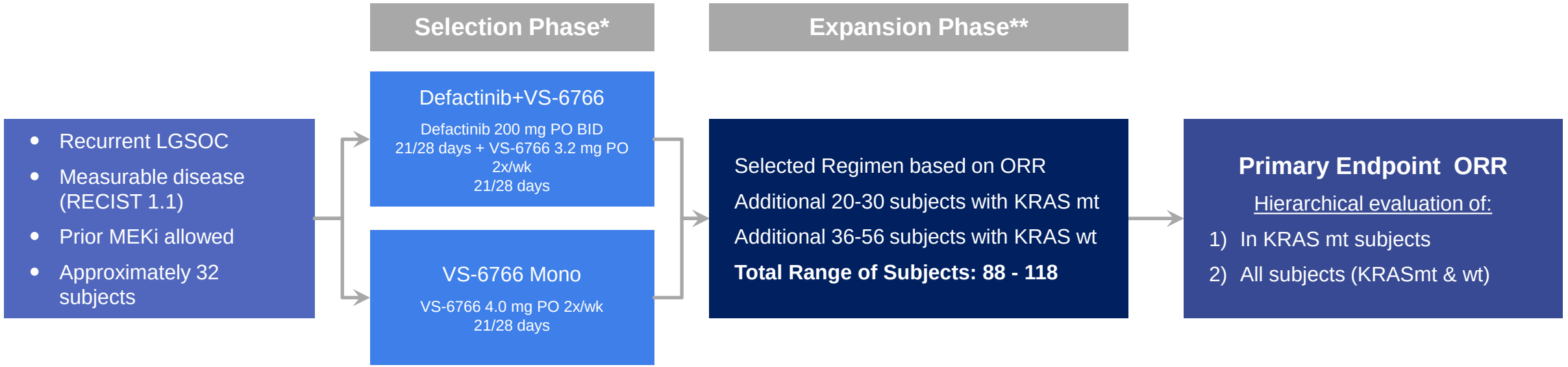
Time on Treatment



- ORR in KRAS mt = 50% (3/6); data still maturing
- Current overall ORR = 45% (5/11); data still maturing
- 9/11 (82%) still on study at RP2D[1]
- 2 pts on treatment for 2.5 yrs

[1] Data cutoff date August 17, 2020

KRAS Mutated (mt) and Wild Type (wt), Phase 2, Recurrent LGSOC Adaptive Design for Potential Accelerated Approval



FDA Was Supportive of Development Strategy and Adaptive Design

This Registration-directed Phase 2 Study Commenced in 4Q20

* Selection Phase – KRAS mt only
** Expansion Phase – final sample size to be adjusted based on adaptive design

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Question & Answer Session
Hosted by Bert Hazlett
Featuring Dr. Kathleen Moore

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Next Steps Beyond LGSOC

Brian Stuglik, Chief Executive Officer,
Verastem Oncology

Jonathan Pachter, PhD, Chief Scientific Officer,
Verastem Oncology

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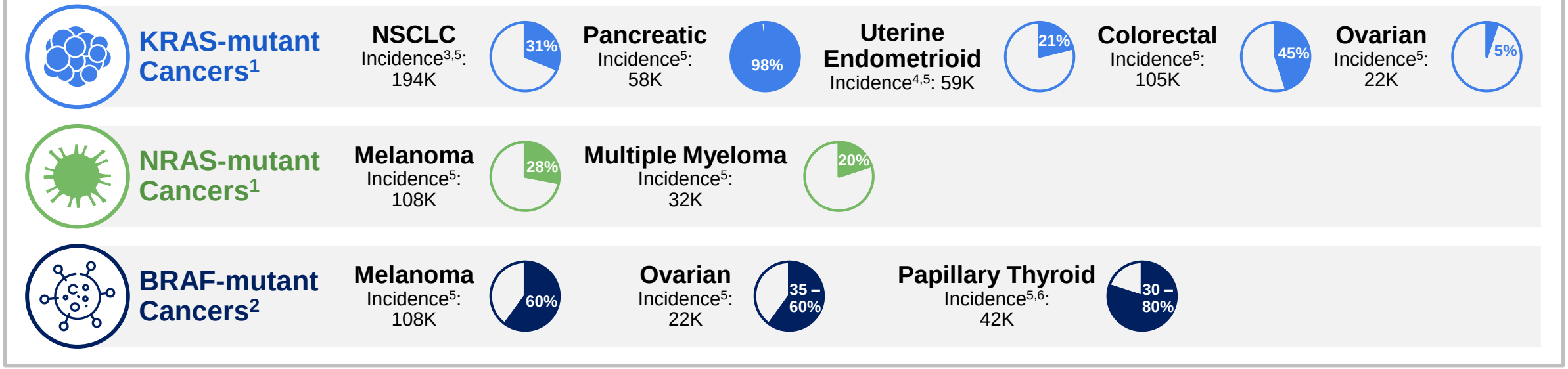
High Unmet Needs in RAS/RAF/MEK/ERK-Driven Cancers



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
- Current RAS inhibitors in development address only a minority of all RAS mutated cancers

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)

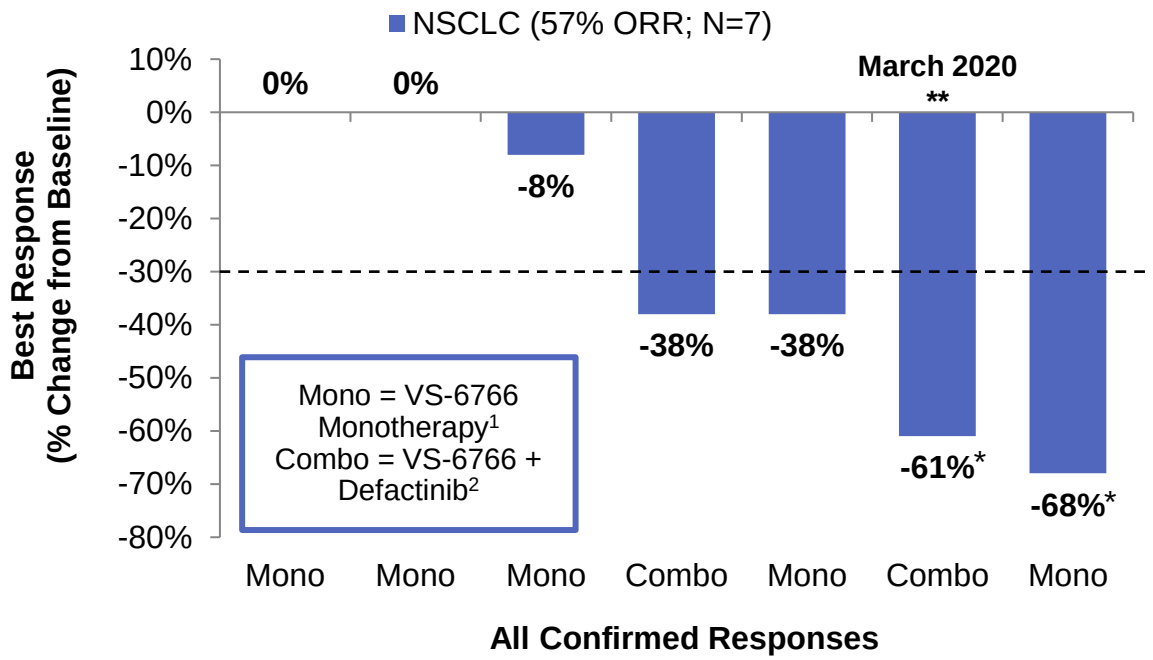
References:

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

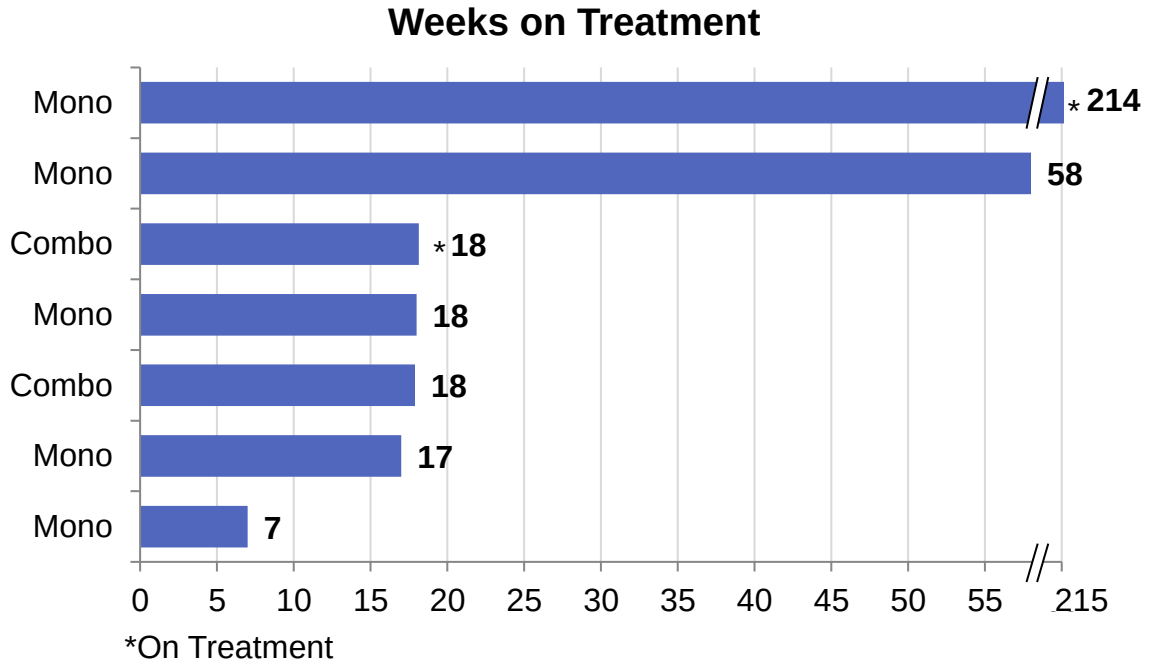
Strong Signal Identified in KRAS^{G12V} to Be Further Validated

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

Best Response by RECIST in KRAS^{G12V} NSCLC



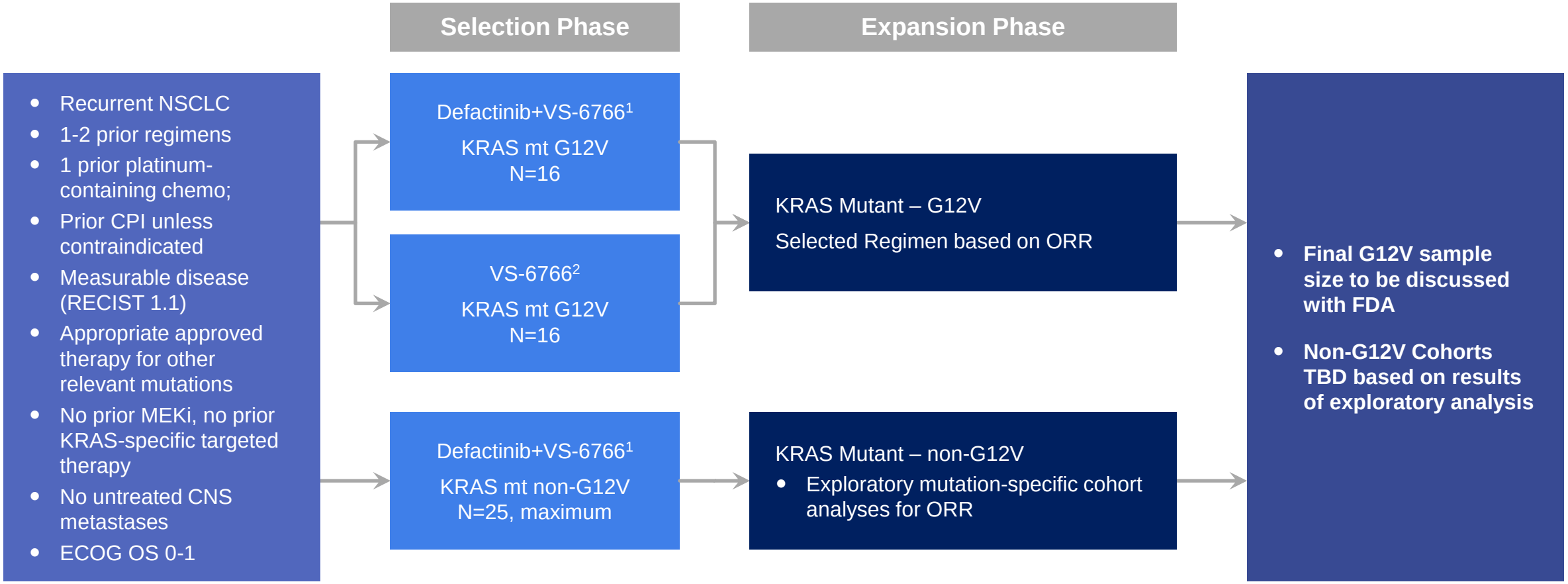
Time on Treatment for KRAS^{G12V} NSCLC



- Preclinical evidence suggests combination with Defactinib may improve efficacy in KRAS^{G12V}
- Activity of VS-6766 as a single agent and in combo with Defactinib in KRAS^{G12V}
- 1 additional confirmed PR in KRAS^{G12V} mutant patient as of Mar-2020

Source: [1] Guo, et al Lancet Oncology 2020 [2] Banerji, AACR VM 1, April 27, 2020, CT143

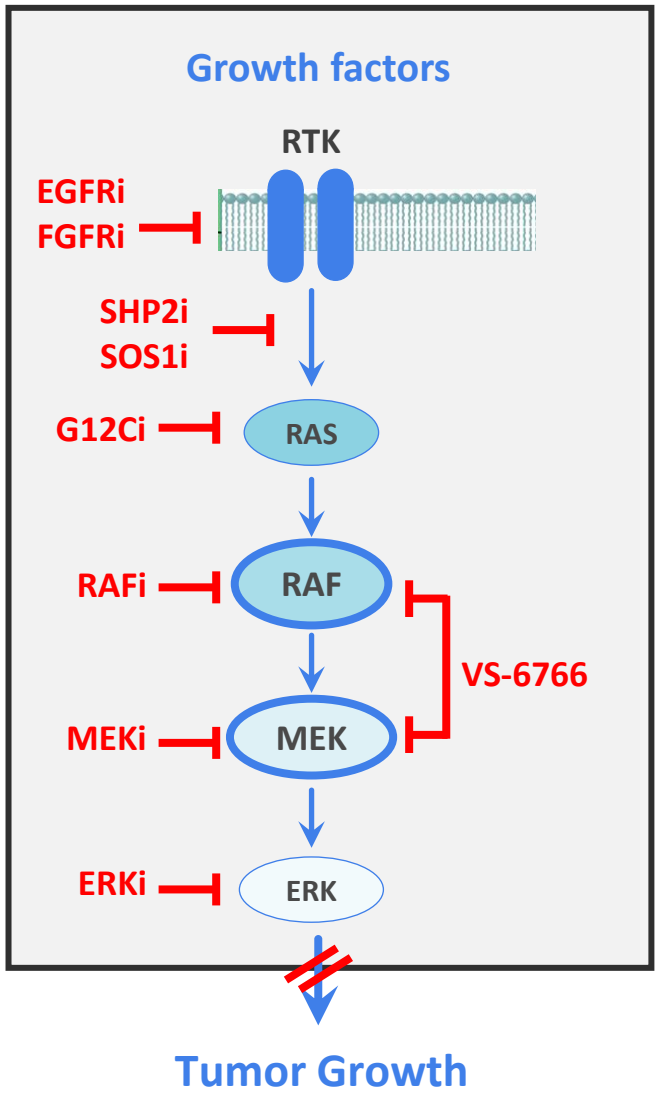
NSCLC Clinical Strategy: KRAS Mutant (mt), Enriched G12V, Phase 2, Recurrent NSCLC for Potential Accelerated Approval



This Registration-directed Phase 2 Study is expected to commence November 2020 with an estimated Primary Completion Date for the Expansion Phase of March 2023 (clinicaltrials.gov)

[1] Defactinib 200 mg PO BID (21/28 days) + VS-6766 3.2 mg PO 2x/wk (21/28 days)
[2] VS-6766 4.0 mg PO 2x/wk (21/28 days)

Vertical Blockade: Establishing VS-6766 as the backbone of therapy for RAS pathway-driven tumors

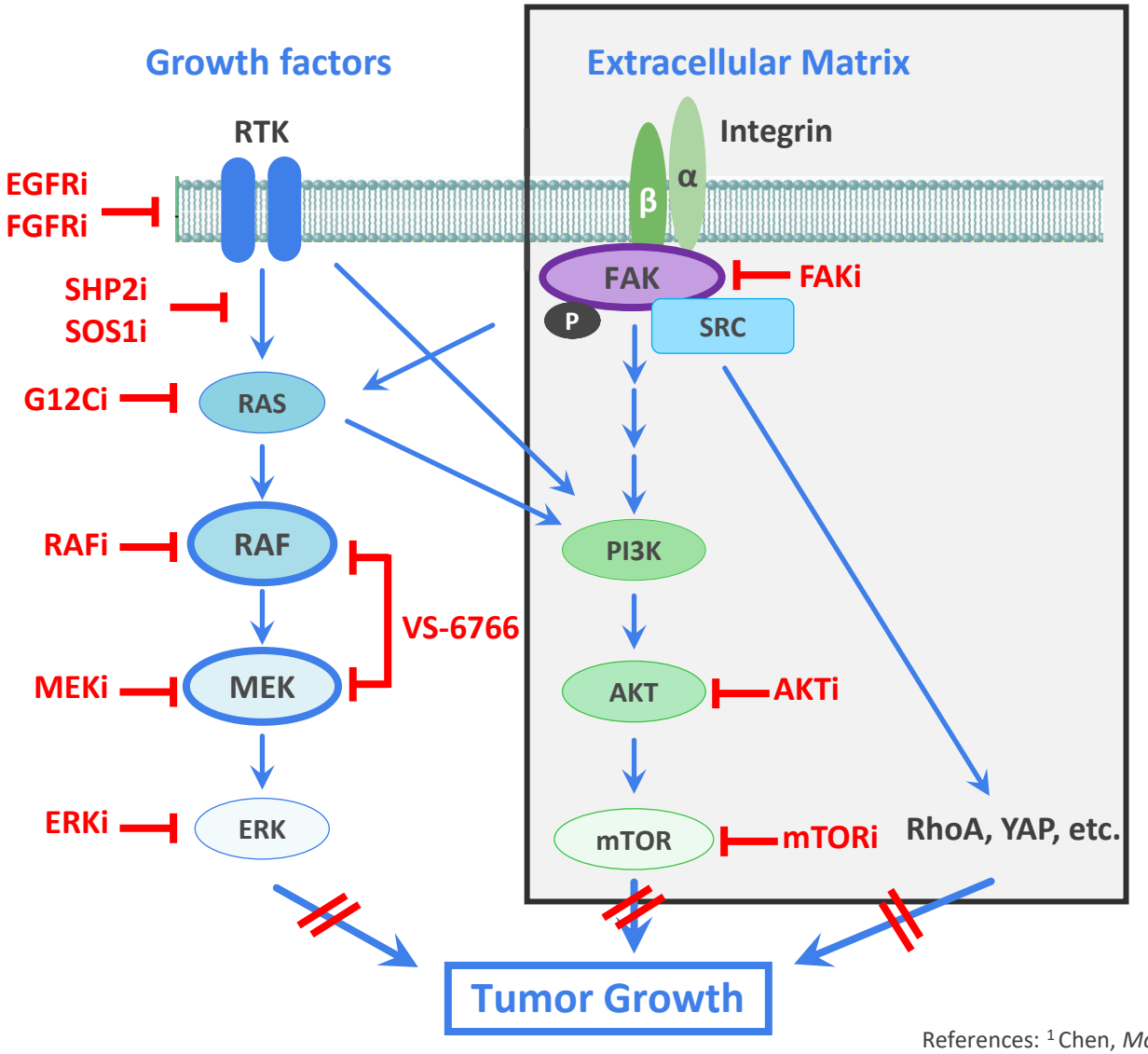


- Current Challenges
  - Blocking any single target in the pathway is insufficient for maximum depth and duration of anti-tumor efficacy
    - e.g. SHP2i, KRAS-G12Ci, RAFi, MEKi, ERKi
  - Vertical inhibition concept is now well established
    - Necessary to block more than 1 target in the pathway
  - Many of these agents (e.g. SHP2i, MEKi) have poor tolerability as monotherapy and in combination

- Solutions offered by VS-6766
  - Vertical inhibition (RAF and MEK blockade) in a single drug
  - Best-in-class tolerability with established twice weekly dosing regimen
    - Should enable tolerable combinations
  - Compelling synergy data (preclinical) emerging for VS-6766 combinations (e.g. with KRAS-G12C inhibitors)

References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

Parallel Pathway Blockade: Establishing VS-6766 as the backbone of therapy for RAS pathway-driven tumors



- Current Challenges
  - Blocking Ras pathway can be circumvented through parallel pathways
    - e.g. PI3K/AKT/mTOR, FAK, RhoA, YAP
  - Combinations of MEKi + AKTi have shown poor tolerability

- Solutions offered with VS-6766
  - Good tolerability with twice weekly VS-6766 opens up intermittent dosing options for combinations
  - Compelling preclinical synergy data with VS-6766 in combination with FAK inhibition and with AKT pathway inhibition (e.g. everolimus)
  - RP2D established for VS-6766 + defactinib and for VS-6766 + mTORi (everolimus) with twice weekly regimen (Udai Banerji, 3Q20)

References: [1] Chen, *Mol Cancer Res* 2018; [2] Banerji, BTOG Dublin, Jan 23, 2019

High Priority Lead Indications with Multiple Growth Opportunities

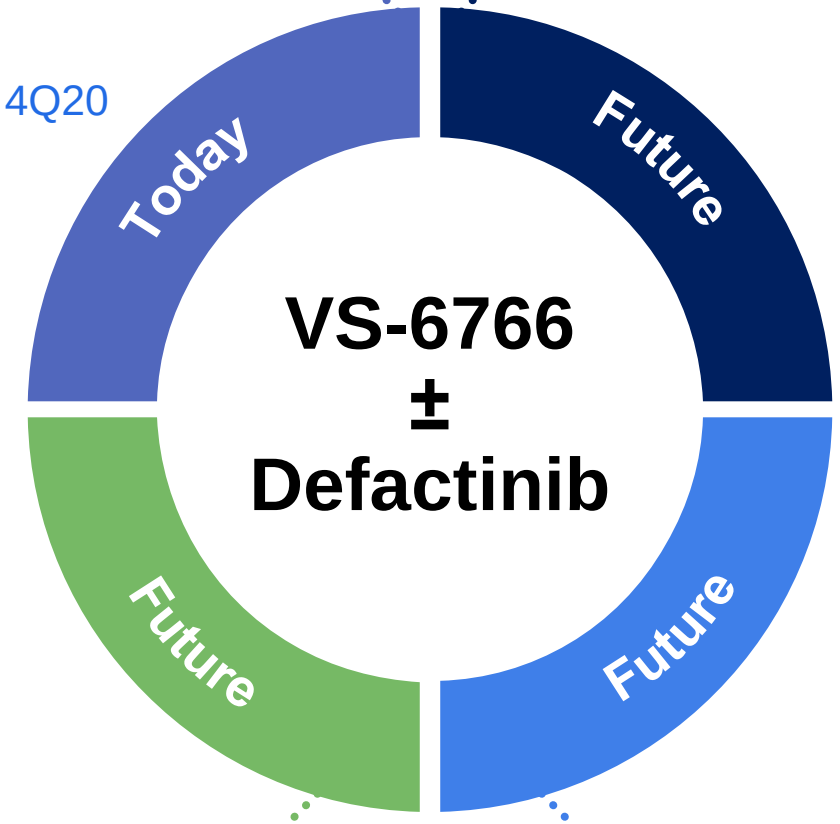
High Priority Indications Supported by Initial Data

Registration-Directed Trials Initiating in 4Q20

- LGSOC[1,2]
- $KRAS^{G12V}$ NSCLC[1,2]

Other Mutation Opportunities

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



Expansion Opportunities

- Pancreatic[1,2] (10 pt cohort initiated)
- KRAS mt endometrial[1] (10 pts initiated)
- Uveal Melanoma[2] (IST initiating)
- BRAF mt melanoma[1,2]
- NRAS mt melanoma
- BRAF mt prostate[2]

Other Combinations

- Anti-PD-1[1,2]
- $KRAS^{G12C}$ inhibitors[2]
- Everolimus[1,2]
- SHP2 inhibitors

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

Question & Answer Session
Hosted by Bert Hazlett
Featuring Verastem Management