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INITIAL RESULTS OF PHASE 1 STUDY OF DCC-2618, A BROAD-SPECTRUM KIT AND PDGFRα INHIBITOR, IN PATIENTS (PTS) WITH GASTROINTESTINAL STROMAL TUMOR (GIST) BY NUMBER OF PRIOR REGIMENS.

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DISCLOSURE SLIDE

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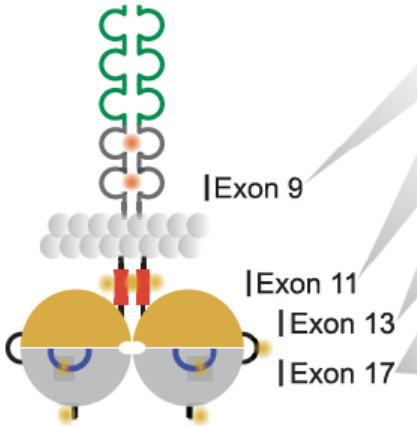
GIST BACKGROUND

- KIT mutations drive ~80% of GISTs
- Majority of patients with KIT primary mutations respond to 1st line imatinib but resistance develops most commonly due to secondary mutations in KIT
- Approved 2nd and 3rd line agents (sunitinib and regorafenib) confer modest clinical benefit compared with imatinib likely due to multiple drug-resistant mutations arising in individual tumors
- Unmet medical need for agents that can address breadth of primary/secondary KIT mutations across lines of therapy



Domain	Gene	1° Mutation Frequency	2° Mutation Frequency
D5	*KIT*	10%	
JM	*KIT*	67	
	PDGFRA	1	
TK1	*KIT*	1	56
	PDGFRA	1	
A-Loop	*KIT*	1	41
	PDGFRA D842V	5	
	PDGFRA	1	3

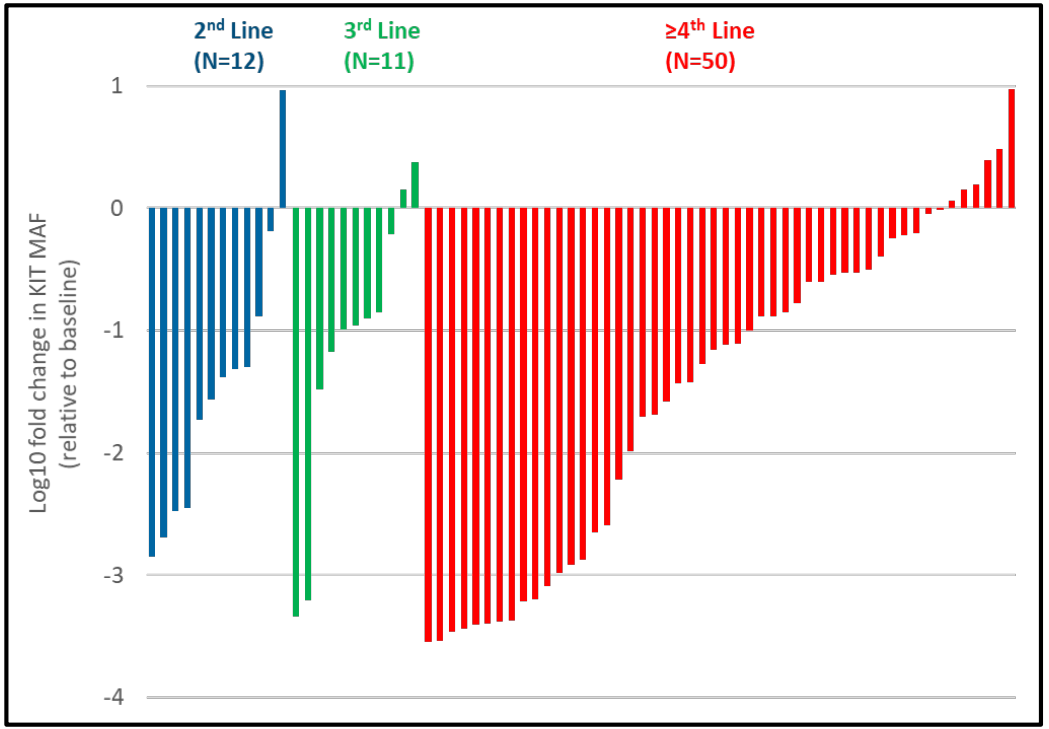
Source: Hemming M et al. Translational insights into gastrointestinal stromal tumors and current clinical advances. Annals of Oncology; 0:1-9, 2018.

DCC-2618 BACKGROUND

- DCC-2618 is a Type II switch control kinase inhibitor of KIT and PDGFRα that has shown inhibition of a broad range of KIT primary and secondary mutations in GIST, preclinically[(1)] and clinically[(2)]
- Data at ASCO 2018[(2)] demonstrated initial clinical benefit of DCC-2618 with encouraging ORR and DCR in 2nd,3rd,≥ 4th line GIST patients
- ctDNA data at ASCO 2018[(2)] demonstrated reductions in mutant allele frequency (MAF) in KIT mutations in 2nd,3rd,≥ 4th line GIST patients
- Enrollment of pivotal, randomized Phase 3 trial INVICTUS[(3)] in ≥4th line GIST patients ongoing

Cumulative Reductions in Circulating MAF of KIT Exons 9, 11, 13, 14, 17 and 18 by Lines of Therapy (n=73)[(1)]

(Note log scale: -1 = 10-fold reduction, -2 = 100-fold reduction)



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Sources: (1) Smith B. et al, AACR 2018, #3925; (2) George S. et al, ASCO 2018 #11511; (3) NCT03353753.

DCC-2618 – Phase 1 Study Design and Methods

Part 1: Dose Escalation

- Key Objectives: MTD, recommended Phase 2 dose (RP2D), safety, tolerability, pharmacokinetics and anti-tumor activity (NCT# 02571036)
- Design: 3+3 design for Patients with advanced refractory cancers (KIT/PDGFRα mutated) with a focus on GIST
- Dose Levels tested: 20, 30, 50, 100, 150, and 200 mg BID; and 100, 150 and 250 mg QD - IPDE(1) to 150mg BID permitted
- CT scans every 2 cycles
- ECOG 0-2; adequate end organ function
- MTD: not determined

Part 2: Dose Expansion @ 150 mg QD (RP2D)

- Various cohorts incl. 3 GIST by line of therapy (2^{nd}-3^{rd}, 4^{th}, > 4^{th} line)
- IPDE to 150mg BID permitted at RECIST progression

2018 ESMO Data Presentation

- GIST patients from Part 1 and Part 2
- Includes full enrollment of GIST expansion cohorts
- Includes patients dosed at ≥ 100 mg daily
- Focused on breakout by line of therapy (2^{nd}, 3^{rd}, and ≥4^{th} line)
- Data cut off of August 31, 2018
- All efficacy data presented is based on local assessment of CT scans

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Note: (1) IPDE=Intra-patient dose escalation.

Demography and Baseline Characteristics
GIST Patients at ≥100 mg/d DCC-2618 (n=178)

	2nd Line (n=38)	3rd Line (n=29)	≥ 4th Line (n=111)[4]	Total (n=178)
Age Median (min, max)	60 (32, 80)	64 (48, 82)	60 (27, 87)	61 (27, 87)
ECOG PS 0-1	38 (100%)	29 (100%)	108 (97%)	175 (98%)
ECOG PS 2	0 (0%)	0 (0%)	3 (3%)	3 (2%)
Primary Mutation[1] n (%)				
KIT Exon 9	4 (11%)	8 (28%)	22 (20%)	34 (19%)
KIT Exon 11	31 (82%)	20 (69%)	71 (64%)	122 (69%)
Other KIT[2]	0 (0%)	1 (3%)	12 (11%)[3]	13 (7%)[3]
PDGFRα	3 (8%)	0 (%)	6 (5%)	9 (5%)
Pts at RP2D (150 mg QD)	32 (84%)	27 (93%)	83 (75%)	142 (80%)

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Notes: (1) Primary mutation per local assessment; (2) KIT exon 13 (4), KIT exon 17 (5), not done (3); (3) Includes one SDH deficient patient; (4) Mean # is 4.63 (range 4- 7).

DCC-2618 Results Provided Encouraging Efficacy across all Lines of Treatment ≥100 mg/d (n=178)

Line of Therapy	Objective Response Rate[1]	Disease Control Rate @ 3 Months	Median Progression Free Survival (mPFS)	Censored Patients for mPFS	Median Treatment Duration[4]
2nd Line (n=38)	18%[2] (7/38)	79%	42 weeks (24, NE)	58%	48 weeks (31, NE)
3rd Line (n=29)	24% (7/29)	83%	40 weeks (24, NE)	52%	NR (36, NE)
≥4th Line (n=111)	9% (10/106)[3]	66%	24 weeks (16, 30)	35%	28 weeks (22, 47)
2nd & 3rd Line (n=67)	21%[2] (14/67)	81%	40 weeks (24, NE)	55%	52 weeks (36, NE)

Notes: (1) Includes 9 unconfirmed responses in 2nd line (n=1), 3rd line (n=3) and ≥4th line (n=5); (2) Does not reflect 1 PR reported after cut off date; (3) Excludes 5 patients due to due to missing data at the time of data cut off (n=2), lack of first tumor assessment (n=1), withdrawal of consent prior to first assessment (n=1) and unrelated death at C1D4 prior to first assessment (n=1); (4) Includes 46 patients who elected for intra-patient dose escalation.

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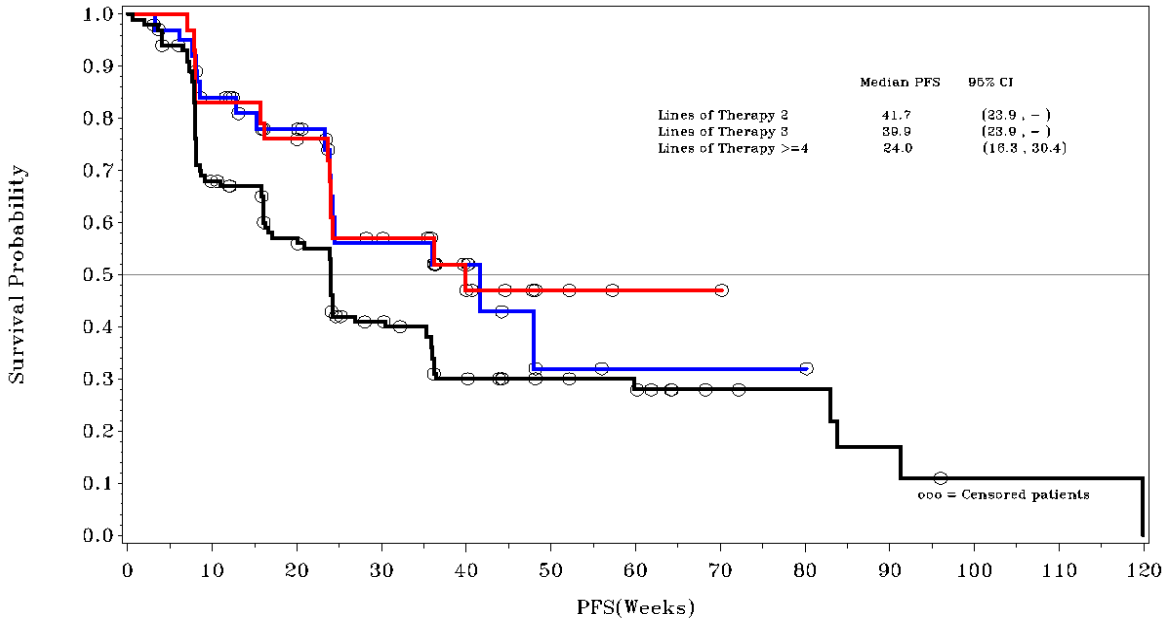
mPFS by Line of Therapy - Patients at ≥100 mg/d DCC-2618 (n=178)

Lines	N	mPFS	Number Censored	Active Patients
2	38	42 weeks	22 (58%)	61%
3	29	40 weeks	15 (52%)	59%
4+	111	24 weeks	40 (36%)	44%

- DCC-2618 demonstrated prolonged progression free survival in a meaningful subset of patients across all lines of treatment
- Following IPDE, 63% (n=29) and 28% (n=13) of patients stayed on study for >8 and >16 weeks, respectively



2nd Line	38	30	21	13	8	2	1	1	1	0	0	0	0
3rd Line	29	24	21	14	8	4	1	1	0	0	0	0	0
≥4th Line	111	71	53	32	20	14	12	6	5	3	1	1	0

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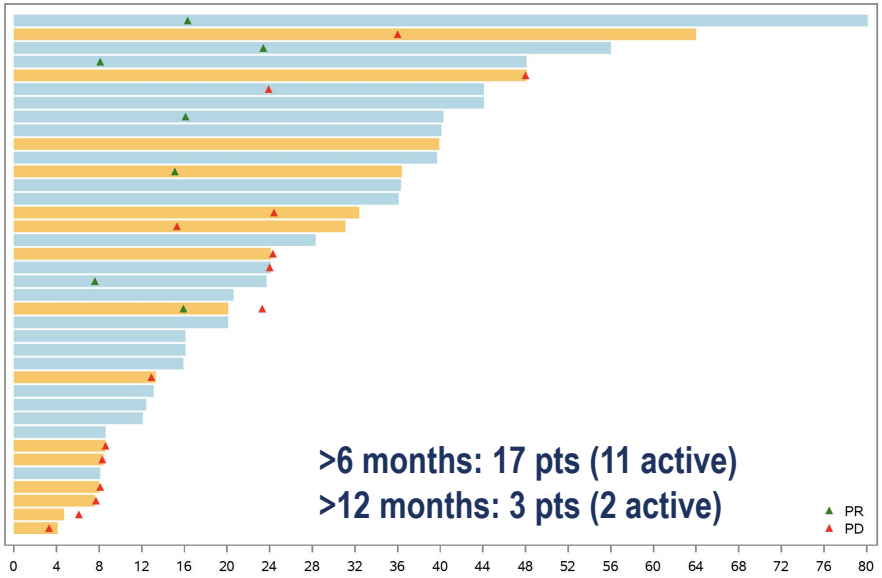
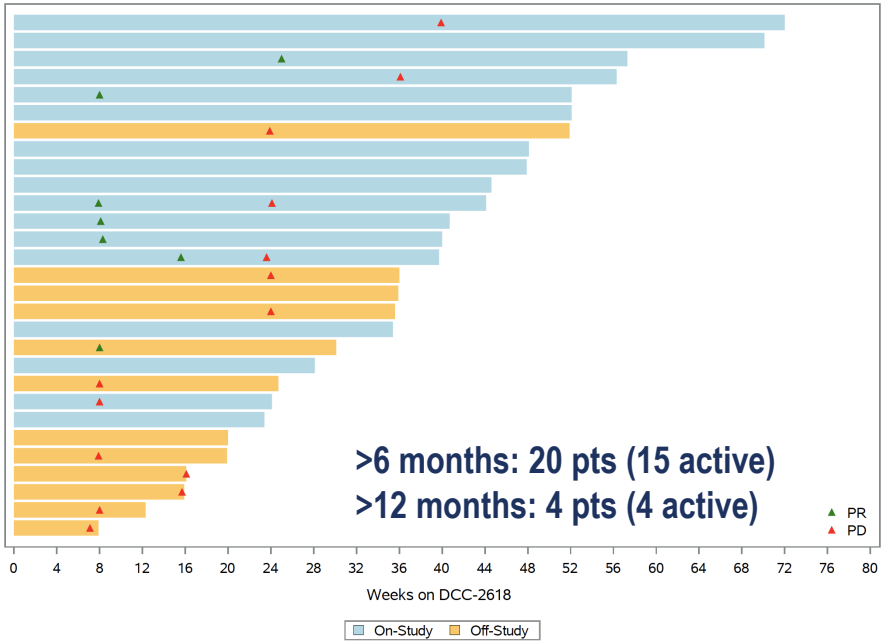
Good Tolerability Allowed for Prolonged Treatment Duration in 2nd & 3rd Line GIST Patients at ≥100 mg/d DCC-2618 (n=67)

2nd Line Patients (n=38)



3rd Line Patients (n=29)



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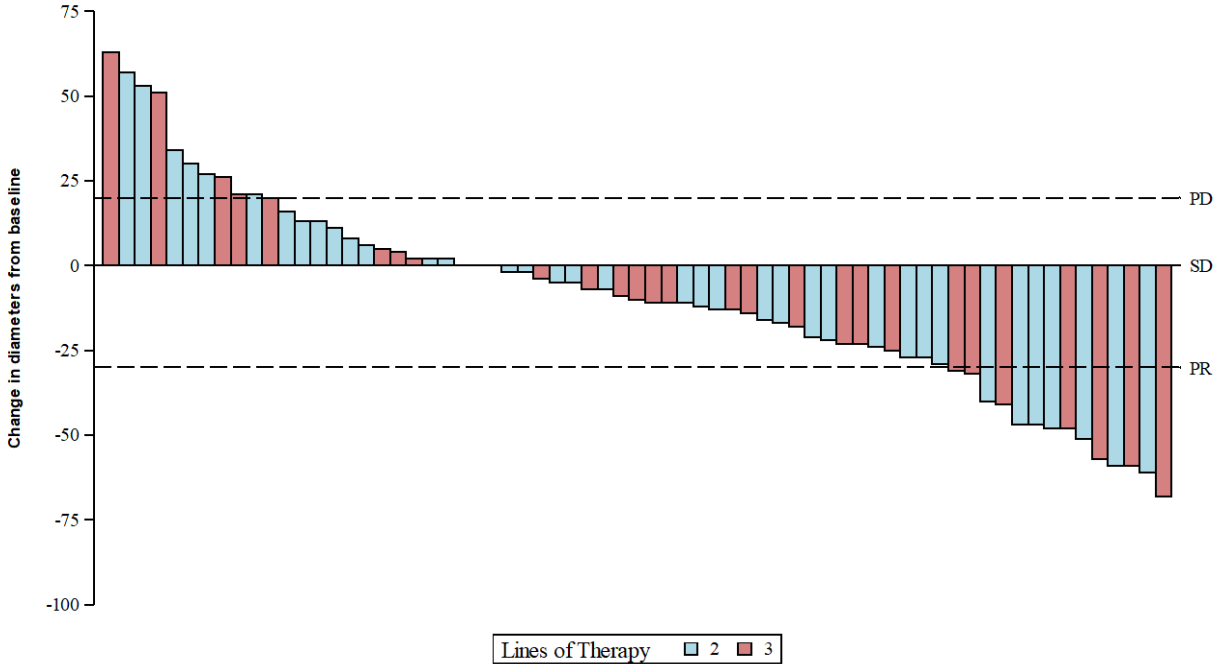
Notes: (1) Includes 4 unconfirmed responses in 2nd line (n=1) and 3rd line (n=3); (2) Does not reflect 1 PR after cut off date; (3) Includes 14 patients who elected for intra-patient dose escalation.

Best Response by RECIST in 2nd & 3rd Line GIST Patients at ≥100 mg/d DCC-2618 (n=67)



PD=Progressive Disease. SD=Stable Disease. PR=Partial Response.

2nd Line (n=38)

- 7/38 PRs(1) (18%) as of data cut off

3rd line (n=29)

- 7/29 PRs(1) (24%) as of data cut off

2nd & 3rd line (n=67)

- 14/67 PRs (1) (21%) as of data cut off

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Notes: (1) Includes unconfirmed responses in 2nd line (n=1) and 3rd line (n=3).

DCC-2618 – TEAE[1] in >10 % of GIST Patients at ≥100 mg/d (n=178)

Out of 178 patients treated with DCC-2618 at ≥100 mg/d

- 24 (14%) experienced dose reductions due to TEAE
- 19 (11%) experienced treatment discontinuations due to TEAE
- Clinically asymptomatic lipase elevations most frequent G3 TEAE

Preferred Term	Grade 1-2 (n=178)	Grade 3-4 (n=178)	Grade 1-4 Total (n=178)
Alopecia	89 (50%)	0 (0%)	89 (50%)
Myalgia	79 (44%)	0 (0%)	79 (44%)
Fatigue	74 (42%)	2 (1%)	76 (43%)
Constipation	60 (34%)	0 (0%)	60 (34%)
Hand-Foot Skin Reaction[2]	56 (32%)	1 (1%)	57 (32%)
Nausea	53 (30%)	0 (0%)	53 (30%)
Decreased appetite	47 (26%)	2 (1%)	49 (28%)
Weight decreased	43 (24%)	0 (0%)	43 (24%)
Abdominal pain	33 (19%)	8 (5%)	41 (23%)
Diarrhea	38 (21%)	3 (2%)	41 (23%)
Lipase increased	21 (12%)	20 (11%)	41 (23%)
Vomiting	32 (18%)	1 (1%)	33 (19%)
Arthralgia	32 (18%)	0 (0%)	32 (18%)
Hypertension	22 (12%)	10 (6%)	32 (18%)
Dry skin	31 (17%)	0 (0%)	31 (17%)
Rash	31 (17%)	0 (0%)	31 (17%)
Muscle spasms	30 (17%)	0 (0%)	30 (17%)
Anemia	14 (8%)	13 (7%)	27 (15%)
Dyspnea	25 (14%)	2 (1%)	27 (15%)
Cough	26 (15%)	0 (0%)	26 (15%)
Headache	25 (14%)	0 (0%)	25 (14%)
Dizziness	23 (13%)	0 (0%)	23 (13%)
Back pain	20 (11%)	2 (1%)	22 (12%)
Blood bilirubin increased	15 (8%)	6 (3%)	21 (12%)
Pain in extremity	21 (12%)	0 (0%)	21 (12%)
Dysgeusia	18 (10%)	0 (0%)	18 (10%)
Hypomagnesaemia	18 (10%)	0 (0%)	18 (10%)
Pruritus	18 (10%)	0 (0%)	18 (10%)

Notes: (1) Treatment Emergent Adverse Events; (2) Palmar-plantar erythrodysaesthesia syndrome was reported in 19 patients.

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Conclusions

- In these initial results, DCC-2618 demonstrated encouraging clinical benefit as measured by mPFS and DCR in 2nd, 3rd, and ≥4th line GIST patients together with favorable tolerability profile at doses ≥100 mg/d including the RP2D of 150 mg QD.
- Initial results across patients in 2nd and 3rd line cohorts are encouraging.
- Although preliminary, the ORR with DCC-2618 in 2nd and 3rd line cohorts (21%) exceeded the values reported for sunitinib in 2nd line patients (7%) and regorafenib in 3rd line patients (5%) in their registration trials (central review).
- Data previously reported for DCC-2618 has demonstrated a broad profile of inhibition across primary and secondary KIT mutations when considering published results from approved TKIs used for treatment of GIST.
  - This profile may explain the encouraging clinical benefit observed across patients in all lines of GIST, including heavily pre-treated ≥4th line patients, and the more favorable results observed in patients with less heavily pretreated disease, however specific analysis of response by mutation status remains ongoing
- The Phase 1 data support further testing of DCC-2618 in both the ongoing pivotal phase 3 trial, INVICTUS (NCT03353753), for ≥4th line GIST patients and the randomized phase 3 trial, INTRIGUE (NCT03673501), for 2nd line GIST patients compared to sunitinib planned for 4Q 2018.

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