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Ripretinib Intra-patient Dose Escalation (IPDE) Following Disease Progression Provides Clinically Meaningful Progression-Free Survival (PFS) in Gastrointestinal Stromal Tumor (GIST) in Phase 1 Study

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Disclosure Information

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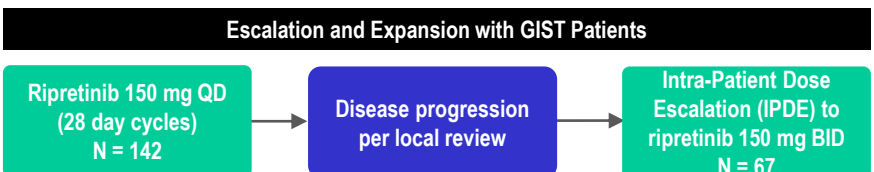
Ripretinib Phase 1 Intra-Patient Dose Escalation Study Design

Patients may dose escalate to ripretinib 150 mg BID after disease progression



Efficacy Endpoint

PFS (per RECIST v1.1 based on **local review**)*

- **PFS 1**: Progression-free survival on ripretinib 150 mg QD defined as Cycle 1, Day 1 to progression
- **PFS 2**: Progression-free survival on ripretinib 150 mg BID defined as the date of IPDE to progression or death

- All patients with radiologic progression had the option to dose escalate
- In this presentation, we review GIST patients who started at ripretinib 150 mg QD and escalated to 150 mg BID
- Data from the escalation and expansion phases were pooled for this presentation

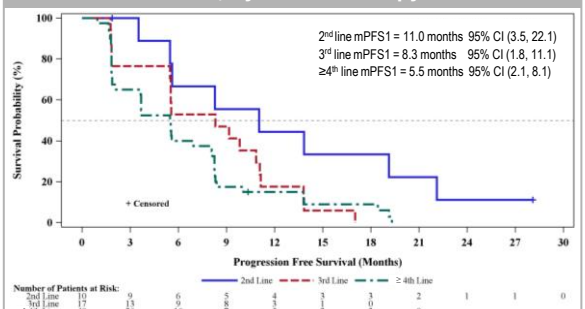
Data cutoff
8 May 2020

*Three patients were dose escalated without progression per RECIST (clinical progression per investigator, n = 2; debulking surgery for non-responding lesions prior to progression n = 1).
BID, twice daily; GIST, gastrointestinal stromal tumor; PFS, progression-free survival; QD, once daily; RECIST, response evaluation criteria in solid tumors.

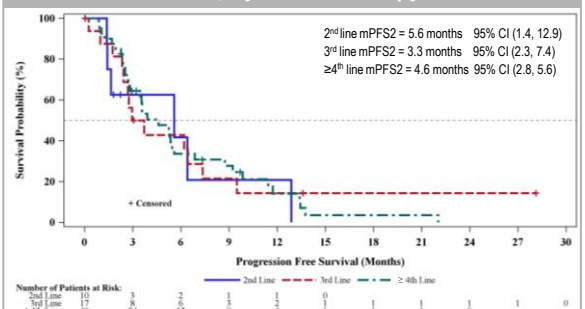
Kaplan-Meier Plots of Progression-Free Survival for GIST IPDE Patients

Patients with GIST who received ripretinib 150 mg QD and escalated to 150 mg BID

Ripretinib 150 mg QD
PFS1, By Line of Therapy



Ripretinib 150 mg BID
PFS2, By Line of Therapy

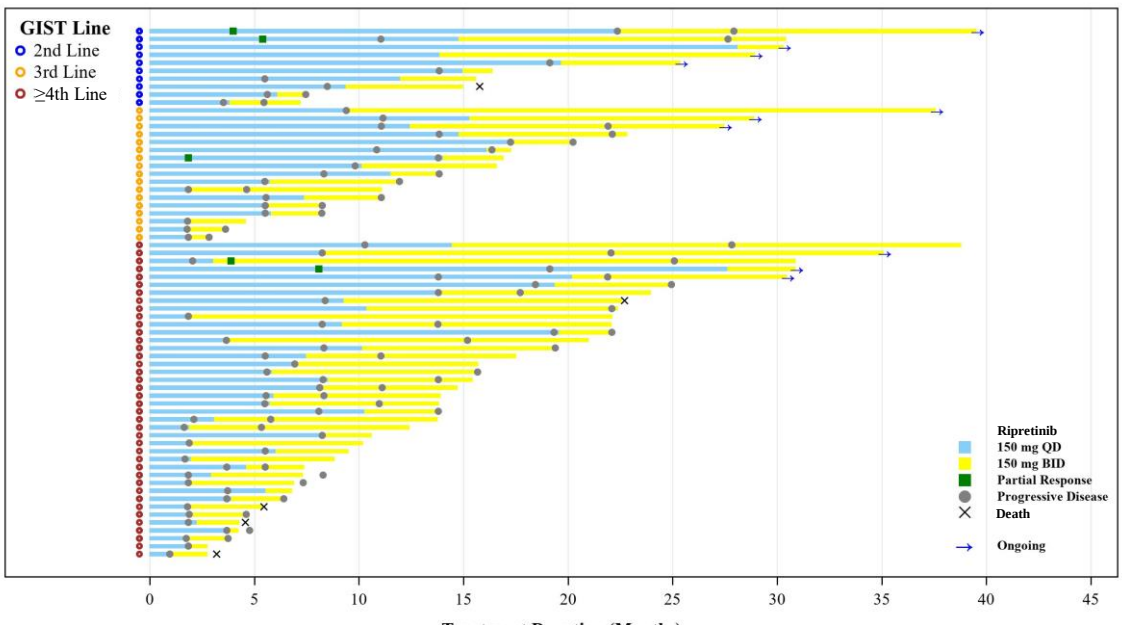


Ripretinib 150 mg BID (n = 67)			
Line of Therapy	2nd line (n = 10)	3rd line (n = 17)	≥4th line (n = 40)
mPFS, months	mPFS1, 11.0 mPFS2, 5.6	mPFS1, 8.3 mPFS2, 3.3	mPFS1, 5.5 mPFS2, 4.6
mPFS2/mPFS1	51%	40%	84%

BID, twice daily; GIST, gastrointestinal stromal tumor; IPDE, intra-patient dose escalation; m, median; PFS, progression-free survival; QD, once daily.

Objective Responses and PFS Events

Patients with GIST who received ripretinib 150 mg QD and escalated to 150 mg BID



BID, twice daily; GIST, gastrointestinal stromal tumor; PFS, progression-free survival; QD, once daily.

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Key Safety Findings

Patients with GIST who received ripretinib 150 mg QD and escalated to 150 mg BID

TEAEs Occurring in >20% of Patients in the Total Dosing Period

Parameters, n (%)	Ripretinib 150 mg QD Period (N=67)		Ripretinib 150 mg QD + 150 mg BID Period (N=67)	
	All Grades	Grade 3/4	All Grades	Grade 3/4
Alopecia	41 (61)	0	49 (73)	0
Fatigue	23 (34)	0	35 (52)	2 (3.0)
Myalgia	33 (49)	0	35 (52)	0
Nausea	24 (36)	0	35 (52)	0
Palmar-plantar erythrodysaesthesia syndrome	24 (36)	0	33 (49)	0
Diarrhoea	13 (20)	1 (1.5)	28 (42)	2 (3.0)
Abdominal pain	15 (22)	0	27 (40)	7 (10)
Muscle spasms	19 (28)	0	27 (40)	0
Lipase increased	22 (33)	14 (21)	25 (37)	16 (24)
Weight decreased	19 (28)	0	24 (36)	0
Constipation	18 (27)	0	23 (34)	0
Decreased appetite	11 (16)	0	22 (33)	1 (1.5)
Hypertension	14 (21)	2 (3.0)	18 (27)	3 (4.5)
Anaemia	3 (4.5)	0	17 (25)	4 (6.0)
Dry skin	11 (16)	0	17 (25)	0
Vomiting	9 (13)	0	16 (24)	0
Back pain	10 (15)	0	15 (22)	0
Cough	12 (18)	0	15 (22)	0
Actinic keratosis	14 (21)	0	14 (21)	0
Dyspnoea	5 (7.5)	0	14 (21)	2 (3.0)
Headache	8 (12)	0	14 (21)	1 (1.5)
Hypokalaemia	8 (12)	1 (1.5)	14 (21)	2 (3.0)

Dose Modifications

Parameters, n (%)	Ripretinib 150 mg QD Period (N=67)	Ripretinib 150 mg QD Period + 150 mg BID Period (N=67)
Any TEAE leading to treatment discontinuation	N/A	10 (15)
Any dose reduction	4 (6.0)	9 (13)
Any dose interruption	24 (36)	40 (60)

BID, twice daily; GIST, gastrointestinal stromal tumor; NA, not applicable; QD, once daily; TEAE, treatment-emergent adverse event.

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Ripretinib Phase 1 IPDE: Conclusions

- In this Phase 1 study, escalation to ripretinib 150 mg BID after progression on ripretinib 150 mg QD provided additional clinically meaningful benefit for patients with advanced GIST
    - This benefit was demonstrated for patients with GIST receiving 2nd, 3rd, or 4th-line therapy
- Comparison of TEAEs reported in the ripretinib 150 mg QD and 150 mg BID periods demonstrated that ripretinib was similarly well-tolerated
- Ripretinib 150 mg QD is currently approved for 4th-line GIST in the United States (FDA), Canada (Health Canada), and Australia (TGA)

Enrollment is ongoing in INTRIGUE, a phase 3, interventional, randomized, multicenter, open-label study of ripretinib vs sunitinib in patients with advanced GIST after treatment with imatinib (NCT03673501)

BID, twice daily; FDA, Food and Drug Administration; GIST, gastrointestinal stromal tumor; IPDE, intra-patient dose escalation; QD, once daily; TEAE, treatment-emergent adverse event; TGA, Therapeutic Goods Administration.