Efficacy and Safety of Ripretinib vs Sunitinib in Patients with Advanced Gastrointestinal Stromal Tumor Previously Treated with Imatinib: A Phase 2 Multicenter, Randomized, Open-Label Study in China

Abstract No. 803

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OBJECTIVE

- To assess the efficacy and safety of ripretinib versus sunitinib as second-line treatment in Chinese GIST patients
- To bridge to the global INTRIGUE study

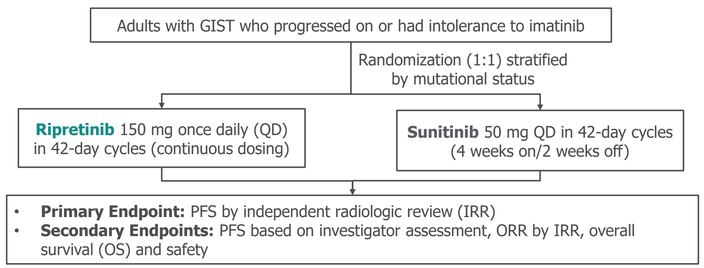
BACKGROUND

- Ripretinib: a switch-control tyrosine kinase inhibitor, an approved ≥4th line GIST therapy
- In INTRIGUE phase 3 study[1], a randomized, phase 3 study in patients with advanced GIST previously treated with imatinib, compared to **sunitinib**, **ripretinib** showed:
  - A comparable progression-free survival (PFS), demonstrating ripretinib's activity as second-line therapy for GIST
  - A higher objective response rate (ORR) and a numerically longer PFS in the *KIT* exon 11-mutated patient population
  - A more favorable safety profile and better responses on patient-reported outcome measures

METHODS

- This study was a randomized, active-controlled, open-label, multicenter, phase 2 study (NCT04633122)

Figure 1. Study design



- Efficacy analyses were performed in:
  - All-patients intention-to-treat (AP ITT) population: all randomized patients
  - *KIT* exon 11 mutation intention-to-treat (Ex11 ITT) population: all patients with *KIT* exon 11 mutations at randomization
- No statistical testing was pre-specified; Nominal *p*-values were presented for descriptive purpose

RESULTS (data cut-off: 20 July 2022)

Baseline characteristics

- Between 6 December 2020 and 15 September 2021, 108 patients were randomized:

Ripretinib: AP ITT n= 54; Ex11 ITT n=35 | **Sunitinib**: AP ITT n= 54; Ex11 ITT n=35

- Demographic and baseline characteristics were generally well balanced between arms (**Table 1**)

Efficacy

- Key efficacy endpoints are presented in **Table 2**
- Subgroup analyses of PFS by IRR based on mutation type revealed a favorable trend with **ripretinib** over **sunitinib** in patients with primary *KIT* exon 11 mutations (**Figure 3**)

Table 1: Patient demographics and baseline characteristics (AP ITT population)

Patient characteristics	Ripretinib (n = 54)	Sunitinib (n = 54)	Total (N = 108)
Age at signing of ICF, median (min, max), years	59.0 (25, 82)	58.5 (28, 81)	59.0 (25, 82)
Sex, male, n (%)	36 (67)	33 (61)	69 (64)
ECOG performance status ≥1, n (%)	31 (57)	31 (57)	62 (57)
Tumor mutation, n (%)			
KIT exon 9	10 (19)	10 (19)	20 (19)
KIT exon 11	35 (65)	35 (65)	70 (65)
Others[a]	9 (17)	9 (17)	18 (17)
Sum of the longest diameters of target lesions by IRR[b], median (min, max), mm	102.8 (17.7, 292.9)	94.4 (12.8, 464.1)	95.1 (12.8, 464.1)
Duration of imatinib treatment, median (min, max), months	41.3 (3.5, 164.1)	37.5 (1.4, 134.9)	37.6 (1.4, 164.1)

[a]*KIT/PDGFRA* wild-type, *PDGFRA* mutations, or *KIT* mutations other than those in exons 9 and 11; [b]The data are only available for 52 patients for each of the arm, as two patients from each of the arm did not undergo baseline tumor evaluation; ECOG: Eastern Cooperative Oncology Group; ICF: informed consent form; IRR: independent radiological review

Table 2: Summary of efficacy endpoints

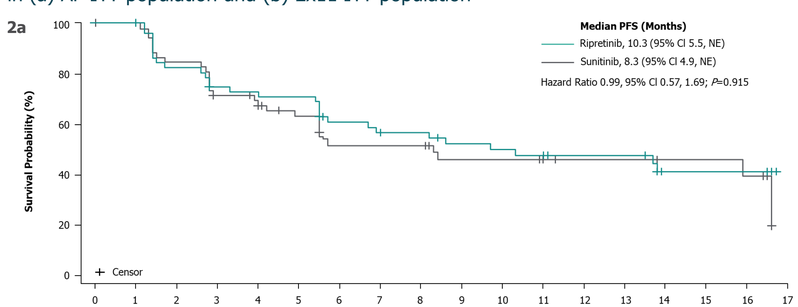
Efficacy endpoints	AP ITT population		Ex11 ITT population	
	Ripretinib (n = 54)	Sunitinib (n = 54)	Ripretinib (n = 35)	Sunitinib (n = 35)
mPFS by IRR (Figure 2), months	10.3	8.3	Not reached	4.9
HR (95% CI)	0.99 (0.57, 1.69)		0.46 (0.23, 0.92)	
mPFS by investigator, months	8.6	8.3	13.8	7.0
HR (95% CI)	0.97 (0.57, 1.64)		0.55 (0.29, 1.07)	
ORR by IRR, n (%)	16 (29.6)	11 (20.4)	13 (37.1)	8 (22.9)

AP ITT: all-patients intention-to-treat; Ex11 ITT: *KIT* exon 11 mutation intention-to-treat; HR: hazard ratio; IRR: independent radiological review; mPFS: median progression-free survival; ORR: objective response rate

Safety

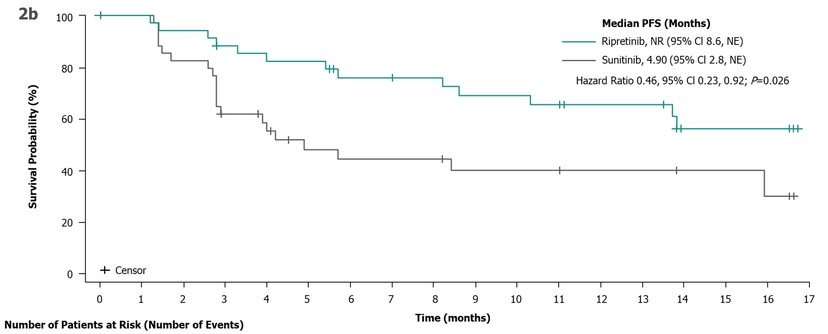
- Fewer grade 3/4 TEAEs and TEAEs leading to dose modification were reported with ripretinib (**Table 3**)
- Fewer grade 3/4 treatment-related TEAEs (TRAEs) were reported with ripretinib (17%) than with sunitinib (56%)
- In ripretinib arm, grade 3/4 TRAEs reported in ≥2% of patients were anaemia (4%) and diarrhoea (4%). Those in sunitinib arm were neutrophil count decreased (26%), platelet count decreased (19%), hypertension (13%), white blood cell count decreased (11%), anaemia (9%), palmar-plantar erythrodysaesthesia syndrome (4%), and lymphocyte count decreased (4%)

Figure 2. Kaplan-Meier plot of progression-free survival based on independent radiologic review in (a) AP ITT population and (b) Ex11 ITT population



Number of Patients at Risk (Number of Events)

Ripretinib	54 (0)	53 (0)	43 (9)	38 (4)	37 (1)	36 (1)	29 (5)	27 (2)	26 (0)	23 (2)	22 (1)	21 (1)	16 (0)	16 (0)	6 (2)	6 (0)	6 (0)	0 (0)
Sunitinib	54 (0)	53 (0)	45 (8)	37 (7)	35 (1)	29 (3)	21 (5)	21 (0)	21 (0)	16 (2)	16 (0)	15 (0)	12 (0)	12 (0)	7 (0)	7 (0)	6 (1)	0 (1)



Number of Patients at Risk (Number of Events)

Ripretinib	35 (0)	34 (0)	32 (2)	29 (2)	28 (1)	27 (1)	23 (2)	23 (0)	22 (0)	20 (2)	20 (0)	19 (1)	15 (0)	15 (0)	5 (2)	5 (0)	5 (0)	0 (0)
Sunitinib	35 (0)	34 (0)	28 (6)	20 (7)	18 (1)	13 (3)	12 (1)	12 (0)	12 (0)	9 (1)	9 (0)	9 (0)	7 (0)	7 (0)	4 (0)	4 (0)	3 (1)	0 (0)

CI: confidence interval; NE: not evaluable; NR: not reached; PFS: progression-free survival

Figure 3. Forest plot of PFS by IRR based on mutation type

CI: confidence interval; mPFS: median progression-free survival; NR: not reached

Table 3: Summary of treatment-emergent adverse events (TEAEs)

TEAEs, n (%)	Ripretinib (n=54)	Sunitinib (n=54)
Any TEAEs	54 (100)	54 (100)
Grade 3/4 TEAEs	19 (35)	35 (65)
Treatment-emergent SAE	9 (17)	12 (22)
TEAEs leading to dose interruption	10 (19)	28 (52)
TEAEs leading to dose reduction	12 (22)	17 (32)
TEAEs leading to treatment discontinuation	5 (9)	8 (15)
TEAEs leading to death	0	2 (4)

SAE: serious adverse event

CONCLUSIONS

- Compared to sunitinib, ripretinib demonstrated comparable efficacy and a more favorable safety profile as second-line therapy in Chinese patients with advanced GIST
- Ripretinib provided greater clinical benefit in those patients with *KIT* exon 11 mutations

References: 1. Bauer S et al. J Clin Oncol. 2022; 40(34):3918–3928.

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