OVERALL SURVIVAL AND LONG-TERM SAFETY WITH RIPRETINIB VS SUNITINIB IN PATIENTS WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR PREVIOUSLY TREATED WITH IMATINIB: FINAL ANALYSES FROM INTRIGUE

John R. Zalcberg[1], Robin L. Jones[2], Jean-Yves Blay[3], Suzanne George[4], Hans Gelderblom[5], Patrick Schöffski[6], Margaret von Mehren[7], Yoon-Koo Kang[8], Albiruni Abdul Razak[9], Jonathan Trent[10], Steven Attia[11], Axel Le Cesne[12], Erika Davis[13], Haroun Achour[13], Matthew L. Sherman[13], Rodrigo Ruiz-Soto[13], Sebastian Bauer[14,15], Michael C. Heinrich[16,17] on behalf of the INTRIGUE study investigators

[1]Monash University School of Public Health and Preventive Medicine and Department of Medical Oncology, Alfred Health, Melbourne, Victoria, Australia; [2]Sarcoma Unit, The Royal Marsden NHS Foundation Trust and Institute of Cancer Research, London, UK; [3]Centre Léon Bérard, Lyon, France; [4]Dana-Farber Cancer Institute, Boston, MA, USA; [5]Leiden University Medical Center, Leiden, Netherlands; [6]University Hospitals Leuven, Department of General Medical Oncology, Leuven Cancer Institute, KU Leuven, Leuven, Belgium; [7]Fox Chase Cancer Center, Philadelphia, PA, USA; [8]Asan Medical Center, University of Ulsan, Seoul, Korea; [9]Toronto Sarcoma Program, Princess Margaret Cancer Center, Toronto, ON, Canada; [10]Sylvester Comprehensive Cancer Center, University of Miami Health System, Miami, FL, USA; [11]Mayo Clinic, Jacksonville, FL, USA; [12]Gustave Roussy, Villejuif, France; [13]Deciphera Pharmaceuticals, LLC, Waltham, MA, USA; [14]Department of Medical Oncology and Sarcoma Center/West German Cancer Center, University Hospital Essen, University Duisburg-Essen, Essen, Germany; [15]German Cancer Consortium (DKTK), Partner Site University Hospital Essen, Essen, Germany; [16]Portland VA Health Care System, Portland, OR, USA; [17]OHSU Knight Cancer Institute, Portland, OR, USA

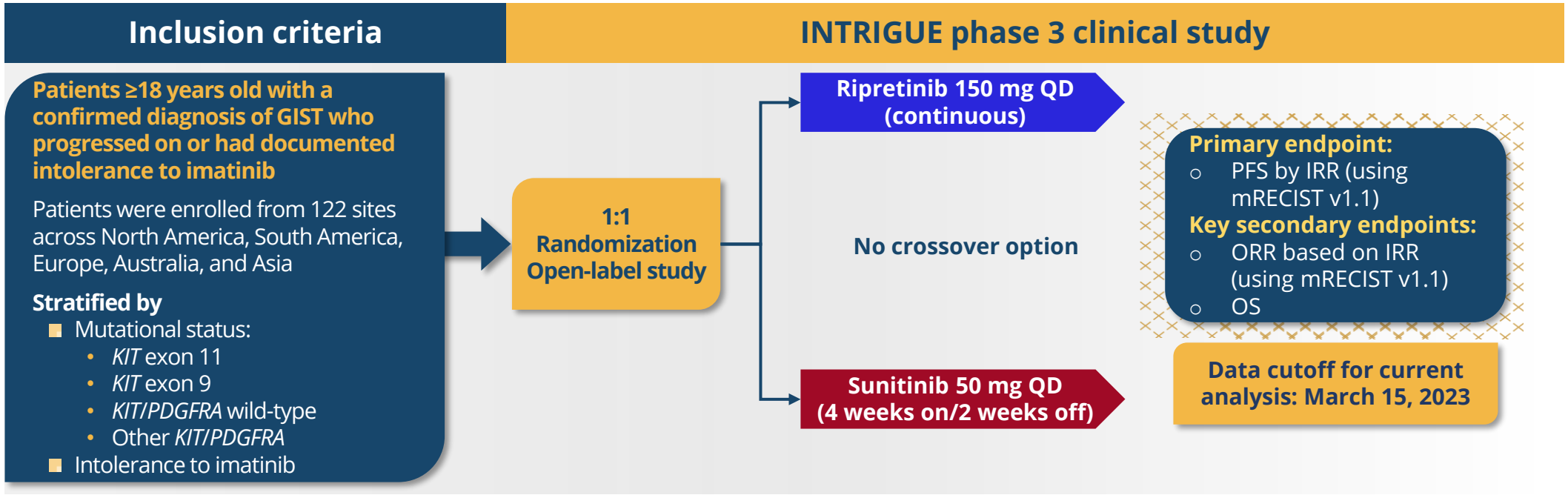
Presented at the 2024 ASCO Gastrointestinal Cancers Symposium, January 18–20, 2024; San Francisco, CA, USA

Introduction: the INTRIGUE trial

- INTRIGUE (NCT03673501) is a randomized, open-label, global, multicenter phase 3 study comparing ripretinib vs sunitinib in patients with advanced GIST who had disease progression on or were intolerant to first-line treatment with imatinib[1]
- Ripretinib is a switch-control *KIT*/*PDGFRA* tyrosine kinase inhibitor approved for patients with GIST who received prior treatment with 3 or more kinase inhibitors, including imatinib[2,3]
- Sunitinib is the approved second-line therapy for patients with advanced GIST following progression on or intolerance to imatinib[4]
- In the INTRIGUE trial, the primary endpoint of superior PFS with ripretinib over sunitinib was not met:
  - In the *KIT* exon 11 ITT population (n = 327), ripretinib demonstrated a median PFS of 8.3 months compared with 7.0 months for sunitinib (HR, 0.88; *P* = 0.36)
  - In the AP ITT population (N = 453), the median PFS with ripretinib was 8.0 months compared with 8.3 months for sunitinib (HR, 1.05; nominal *P* = 0.72)
- At the time of primary analysis of PFS in the INTRIGUE trial, the first IA for OS was conducted:
  - The OS event rates for both the AP ITT and *KIT* exon 11 ITT populations were immature (22.3% and 21.1%, respectively), and the median OS was not reached in either arm for either population[1]
- In the second IA of OS, the event rate was 41% in both ITT populations, with no significant differences in OS between treatment arms[5]
- Ripretinib had a more favorable safety profile with fewer grade 3/4 TEAEs than sunitinib[1]
- Here, we present the final OS analysis and updated safety profile as well as exploratory PFS on next line of therapy from the INTRIGUE trial

1) Bauer S, et al. *J Clin Oncol.* 2022;40:3918-28. 2) Blay JY, et al. *Lancet Oncol*. 2020;21:923-34. 3) QINLOCK. Prescribing information. Deciphera Pharmaceuticals, LLC; 2023. 4) SUTENT. Prescribing information. Pfizer Laboratories; 2021. 5) Jones RL, et al. *J Clin Oncol*. 2023;41(suppl 16):11524.
AP, all patient; GIST, gastrointestinal stromal tumor; HR, hazard ratio; IA, interim analysis; ITT, intention-to-treat; OS, overall survival; PDGFRA, platelet-derived growth factor receptor α; PFS, progression-free survival; TEAE, treatment-emergent adverse event.

Study design and patient disposition



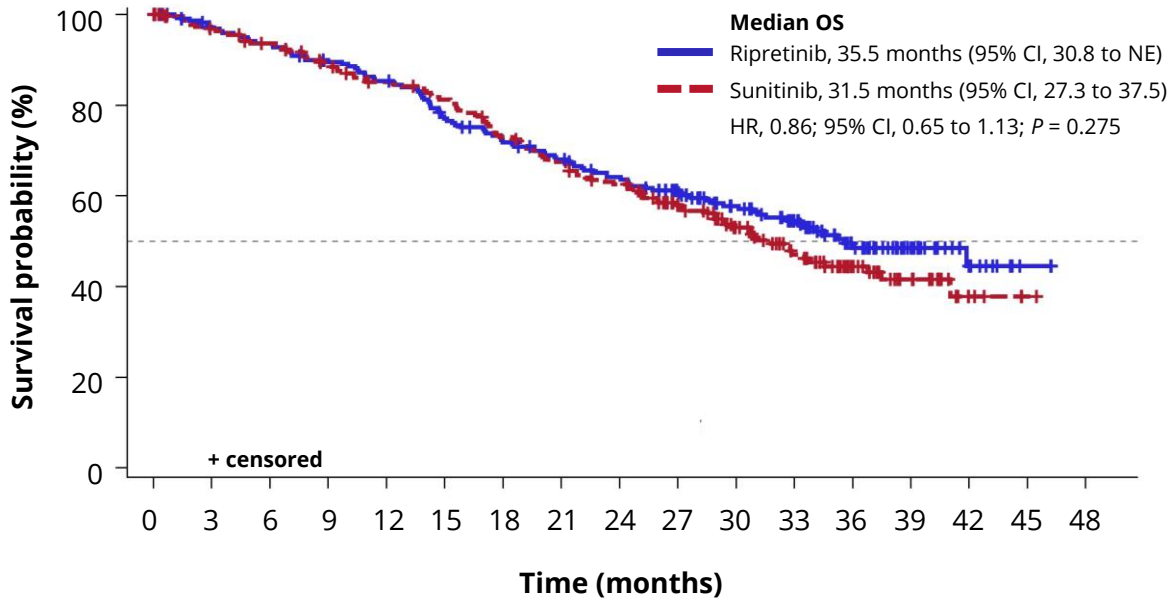
- Of the 453 patients who were randomized, 444 received treatment
- Overall, 40 of 444 treated patients (9.0%; AP ITT population) remained on treatment at the time of data cutoff: 28/223 (12.6%) on ripretinib and 12/221 (5.4%) on sunitinib
- The most common reasons for treatment discontinuation in the AP ITT population were PD as determined by IRR (56.1%), PD assessed by investigator (10.8%), clinical PD (6.1%), withdrawal of consent (5.6%), and AEs (4.7%)
  - Fewer patients discontinued treatment due to an AE for ripretinib vs sunitinib (3.1% vs 6.3%)

Mutational status used for randomization was based on local pathology reports at the time of randomization.
AE, adverse event; AP, all patient; GIST, gastrointestinal stromal tumor; IA, interim analysis; IRR, independent radiological review; ITT, intention-to-treat; mRECIST v1.1, modified Response Evaluation Criteria in Solid Tumors version 1.1; ORR, objective response rate; OS, overall survival; PD, progressive disease; PDGFRA, platelet-derived growth factor receptor α; PFS, progression-free survival; QD, once daily; TEAE, treatment-emergent AE.

Final OS

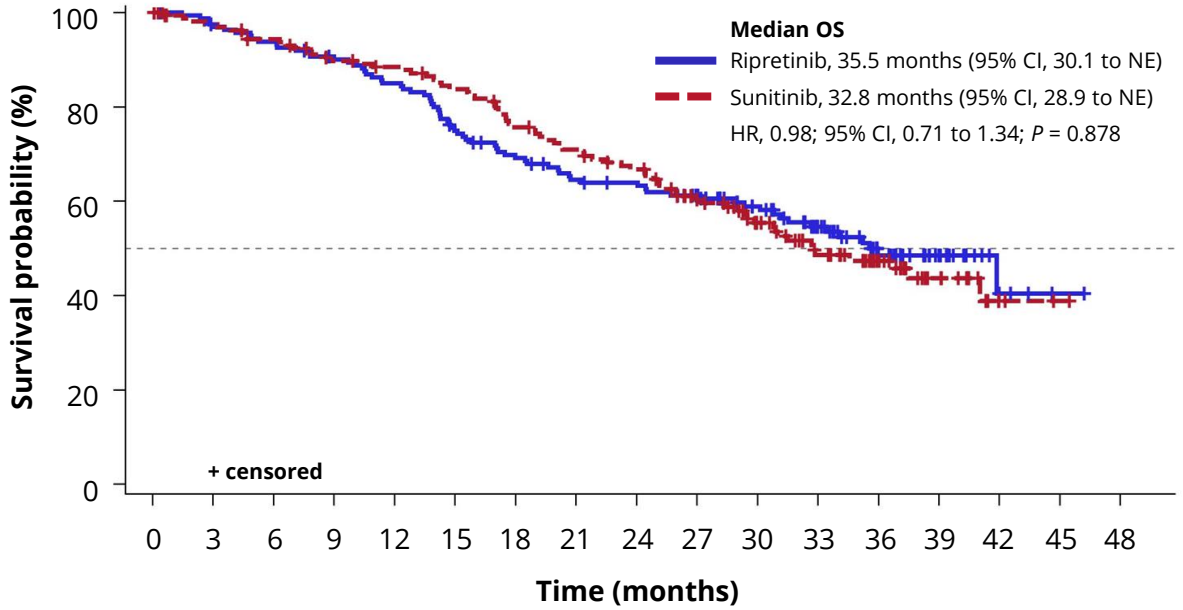
- There were 211 OS events (46.6%) in the AP ITT population; median duration of follow-up in the ripretinib and sunitinib arms were 35.1 (95% CI, 33.3 to 36.5) and 34.1 months (95% CI, 32.1 to 35.6), respectively
- OS was similar with ripretinib vs sunitinib in the AP ITT and *KIT* exon 11 ITT populations

AP ITT



Number at risk																	
Ripretinib	226	212	205	195	185	165	152	142	131	115	92	75	48	28	10	2	0
Sunitinib	227	212	202	187	176	167	149	137	125	102	78	58	38	23	5	1	0

KIT exon 11 ITT



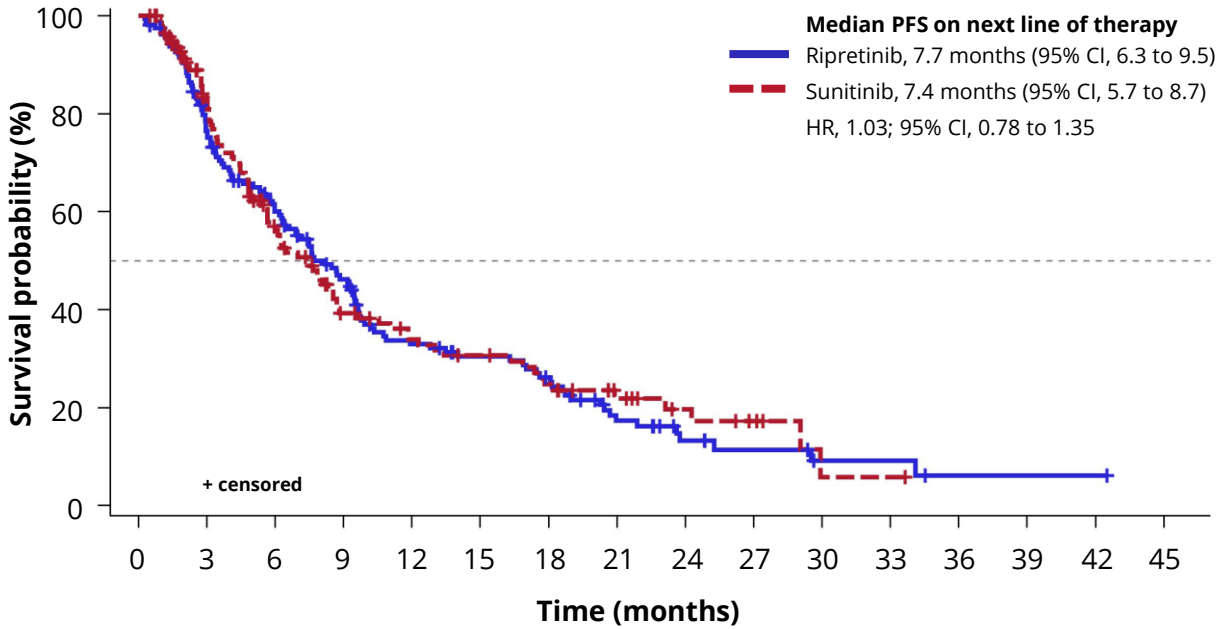
Number at risk																	
Ripretinib	163	156	151	144	135	118	107	98	95	87	71	54	34	18	4	1	0
Sunitinib	164	154	147	137	133	125	112	104	96	79	62	46	32	17	3	1	0

AP, all patient; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; NE, not estimable; OS, overall survival.

PFS on next line of therapy

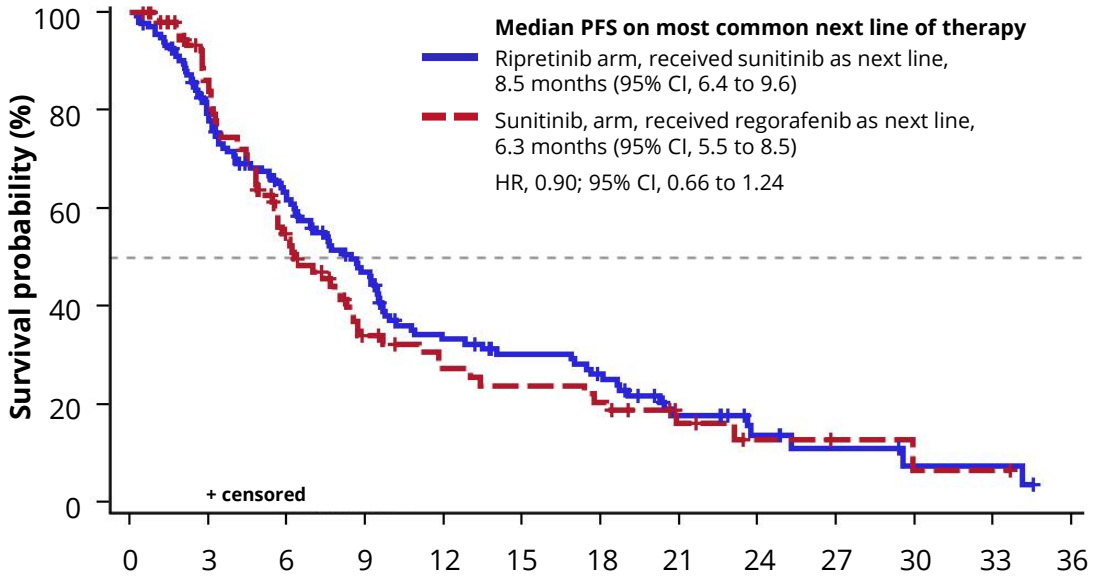
- PFS on next line of therapy by randomized treatment assignment was similar for ripretinib vs sunitinib in the AP ITT population
- Patients in the ripretinib arm who received third-line sunitinib (59.7%) had a median PFS on next line of therapy of 8.5 months compared with 6.3 months for patients in the sunitinib arm who received third-line regorafenib (42.7%)

AP ITT: PFS on next line of therapy



Number at risk																
Ripretinib	158	115	85	62	41	35	29	16	9	6	3	3	1	1	1	0
Sunitinib	142	102	64	39	31	27	21	13	8	5	1	1	0			

AP ITT: PFS on most common next line of therapy



Number at risk													
Ripretinib to sunitinib	135	102	74	53	35	29	24	13	7	4	2	2	0
Sunitinib to regorafenib	97	73	42	22	16	14	12	6	3	2	1	1	0

PFS on next line of therapy is defined as the time interval between the date of first nonprotocol drug therapy, and disease progression on this drug therapy is based on the local assessment or death due to any cause, whichever comes first.
AP, all patient; CI, confidence interval; HR, hazard ratio; ITT, intention-to-treat; PFS, progression-free survival.

Safety

- The long-term safety profile was consistent with the primary analysis; fewer patients had grade 3/4 TEAEs with ripretinib vs sunitinib, and dose interruptions and reductions as well as treatment discontinuations due to TEAEs were lower with ripretinib vs sunitinib
- The median (range) treatment duration was 7.9 (0.2–43.3) months for ripretinib and 6.5 (0.2–44.7) months for sunitinib

Patients with	Ripretinib n = 223	Sunitinib n = 221	Total N = 444
Any TEAE[a]	221 (99.1)	219 (99.1)	440 (99.1)
Any grade 3/4 TEAE	96 (43.0)	149 (67.4)	245 (55.2)
Any drug-related TEAE[b]	211 (94.6)	214 (96.8)	425 (95.7)
Any grade 3/4 drug-related TEAE	61 (27.4)	128 (57.9)	189 (42.6)
Any treatment-emergent SAE	64 (28.7)	61 (27.6)	125 (28.2)
Any drug-related treatment-emergent SAE	19 (8.5)	22 (10.0)	41 (9.2)
Any TEAE leading to dose reduction	45 (20.2)	107 (48.4)	152 (34.2)
Any TEAE leading to dose interruption	70 (31.4)	95 (43.0)	165 (37.2)
Any TEAE leading to study treatment discontinuation	11 (4.9)	20 (9.0)	31 (7.0)
Any TEAE leading to death	6 (2.7)	8 (3.6)	14 (3.2)
Any drug-related TEAE leading to death	0	1 (0.5)	1 (0.2)

Data are shown as n (%).
[a]TEAEs are defined as any AE that occurs after administration of the first dose of study drug and through 30 days after the last dose of study drug or the day before the start of subsequent new anticancer drug therapy, whichever occurs first. Drug-related AEs reported ≥30 days after the last dose of study drug are also considered TEAEs.
[b]Drug-related TEAEs are defined as those related or possibly related to study drug as assessed by the investigator. Any AE with missing relationship to study drug will be counted as related to study drug.
AE, adverse event; SAE, serious AE; TEAE, treatment-emergent AE.

Conclusions

- With 18 months of additional follow-up from the primary analysis, OS was similar between treatment arms in both the AP ITT and *KIT* exon 11 ITT populations
- PFS on next line of therapy was comparable between treatment arms, suggesting that third-line treatment efficacy was not adversely affected by receiving ripretinib in the second-line setting
- Safety remained consistent with the primary analysis; ripretinib demonstrated a favorable safety profile compared with sunitinib for patients with advanced GIST previously treated with imatinib

AP, all patient; GIST, gastrointestinal stromal tumor; ITT, intention-to-treat; OS, overall survival; PFS, progression-free survival.