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Results From the Phase 3 Peak Study of Bezuclastinib + Sunitinib in Advanced GIST: Focus on Exon 9 and Crossover Subgroups

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Heterogeneous Secondary *KIT* Mutations Contribute to GIST Treatment Resistance

- GIST is commonly driven by activating *KIT* mutations, typically in exons 9 and 11[1-4]

- Resistance to monotherapy due to heterogeneity of secondary mutations[5,7]
- Combination of KIT inhibitors has been limited by overlapping toxicities[8]



- Activity against primary mutations, particularly exon 11[2,4]
- ~60% of patients develop resistance within 2 years[4-7]

Sunitinib: mPFS of ~6-8 months[9]

Regorafenib: mPFS of 4.5 months[10]

1L, first line; 2L, second line; 3L, third line; GIST, gastrointestinal stromal tumor; mPFS, median progression-free survival.

1. Nemunaitis J, et al. *Future Oncol*. 2020;16(1):4251-4264. **2.** Kawabata K, et al. *Gastric Cancer*. 2025;28(5):899-910. **3.** Debiec-Rychter M, et al. *Eur J Cancer*. 2006;42(8):1093-1103. **4.** Gramza AW, et al. *Clin Cancer Res*. 2009;15(24):7510-7518. **5.** Szucs Z, et al. *Future Oncol*. 2017;13(1):93-107. **6.** Nishida T, et al. *Cancers (Basel)*. 2021;13(13):3158. **7.** Serrano C, et al. *Ther Adv Med Oncol*. 2023;15:17588359231192388. **8.** Demetri G, et al. *Lancet*. 2006;368(9544):1329-1338. **9.** Bauer S, et al. *J Clin Oncol*. 2022;40(34):3918-3928. **10.** Demetri GD, et al. *Lancet*. 2013;381(9863):295-302.

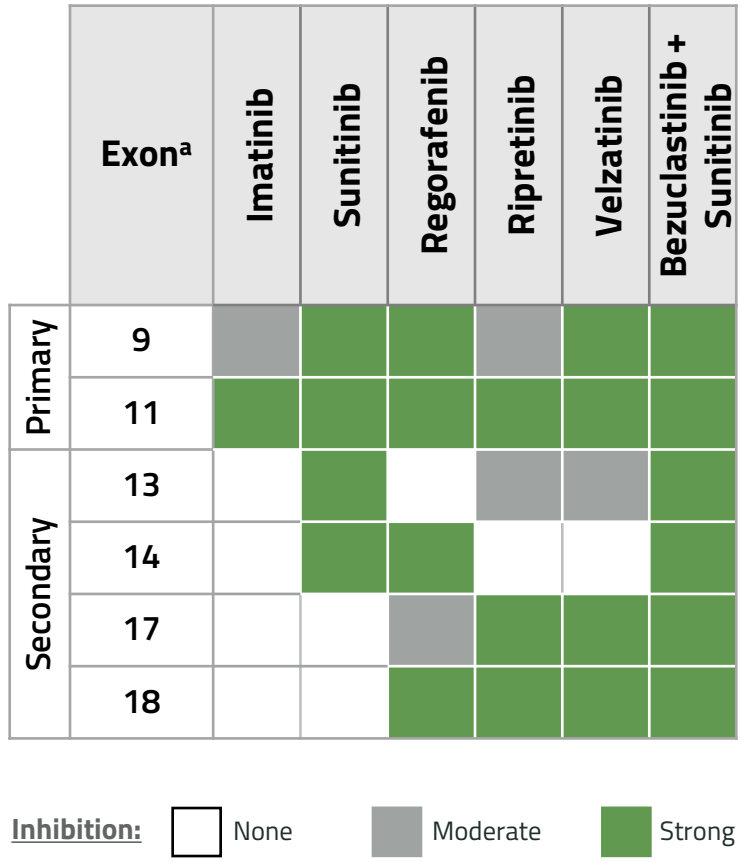
Combination of Bezuclastinib + Sunitinib Inhibits the Broad Spectrum of Primary and Secondary *KIT* Mutations

Bezuclastinib: Next-generation oral KIT inhibitor[1-4]

- In combination with sunitinib, covers the broad spectrum of *KIT* mutations[1-4]
- High selectivity and lack of off-target effects allow for combination[2,3]

Potential efficacy of bezuclastinib + sunitinib combination was demonstrated in a phase 1 study[2,4]:

- Median PFS of 10.2 mos in heavily pretreated patients
- Median PFS of 19.4 mos in a second-line treatment subgroup



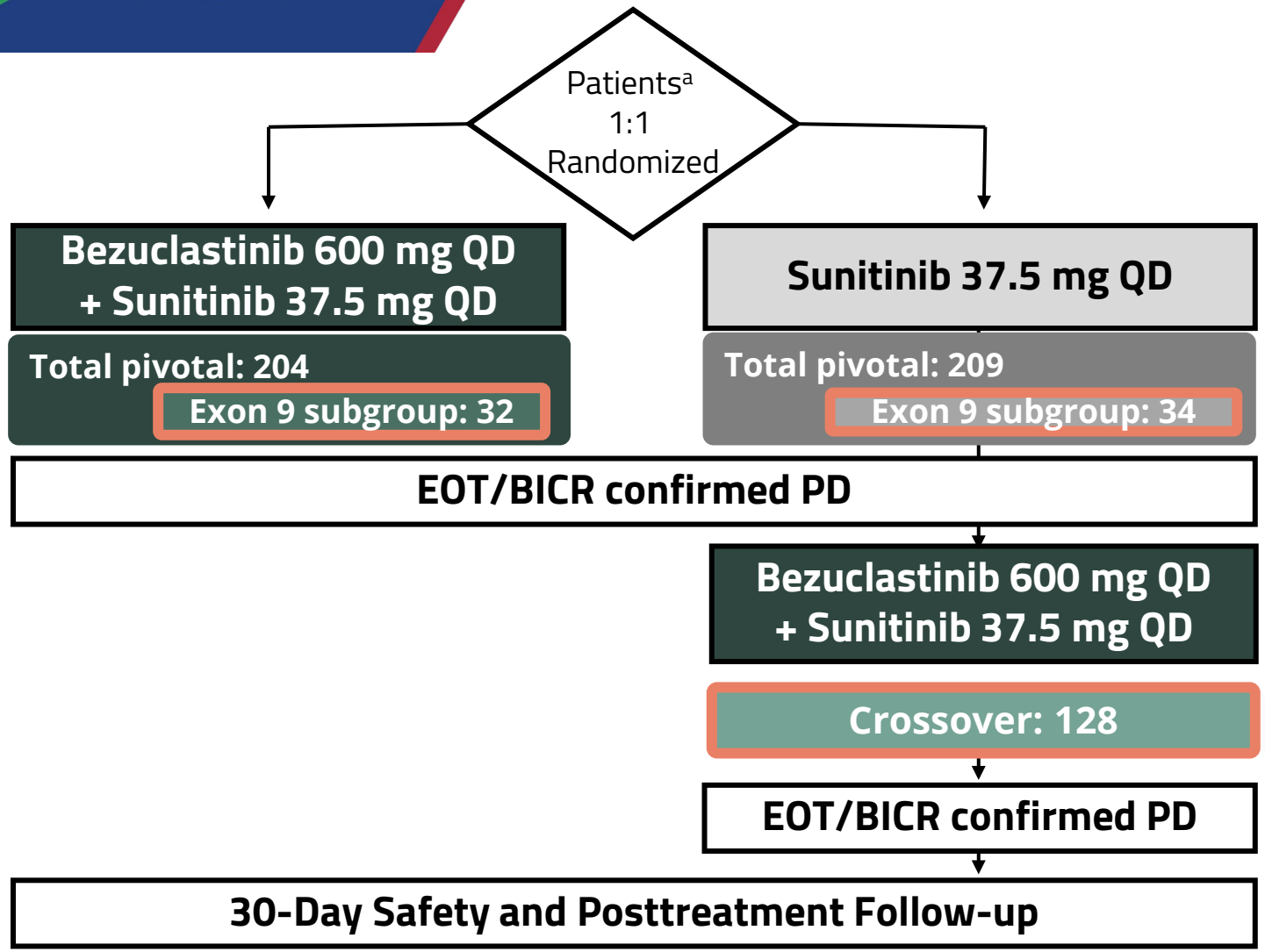
[a]This table of inhibitors is based on preclinical data.

GIST, gastrointestinal stromal tumor; mos, months; PFS, progression-free survival.

1. Wagner AJ, et al. Presented at: CTOS Annual Meeting; November 16-19, 2022; Vancouver, Canada. **2.** Wagner AJ, et al. *JAMA Oncol*. 2021;7(9):1343-1350. **3.** Guarnieri A, et al. Presented at: AACR Annual Meeting; April 8-13, 2022; New Orleans, LA. **4.** Wagner A, et al. ASCO Annual Meeting; May 29-June 2, 2026; Chicago, IL.

Peak Is a Global, Randomized, Open-Label, Phase 3 Study

Evaluating the efficacy and safety of bezuclastinib + sunitinib vs sunitinib as 2L treatment (NCT05208047)



We present results in 3 key populations from part 2 of the Peak clinical study evaluating the efficacy and safety of bezuclastinib + sunitinib in patients with advanced GIST

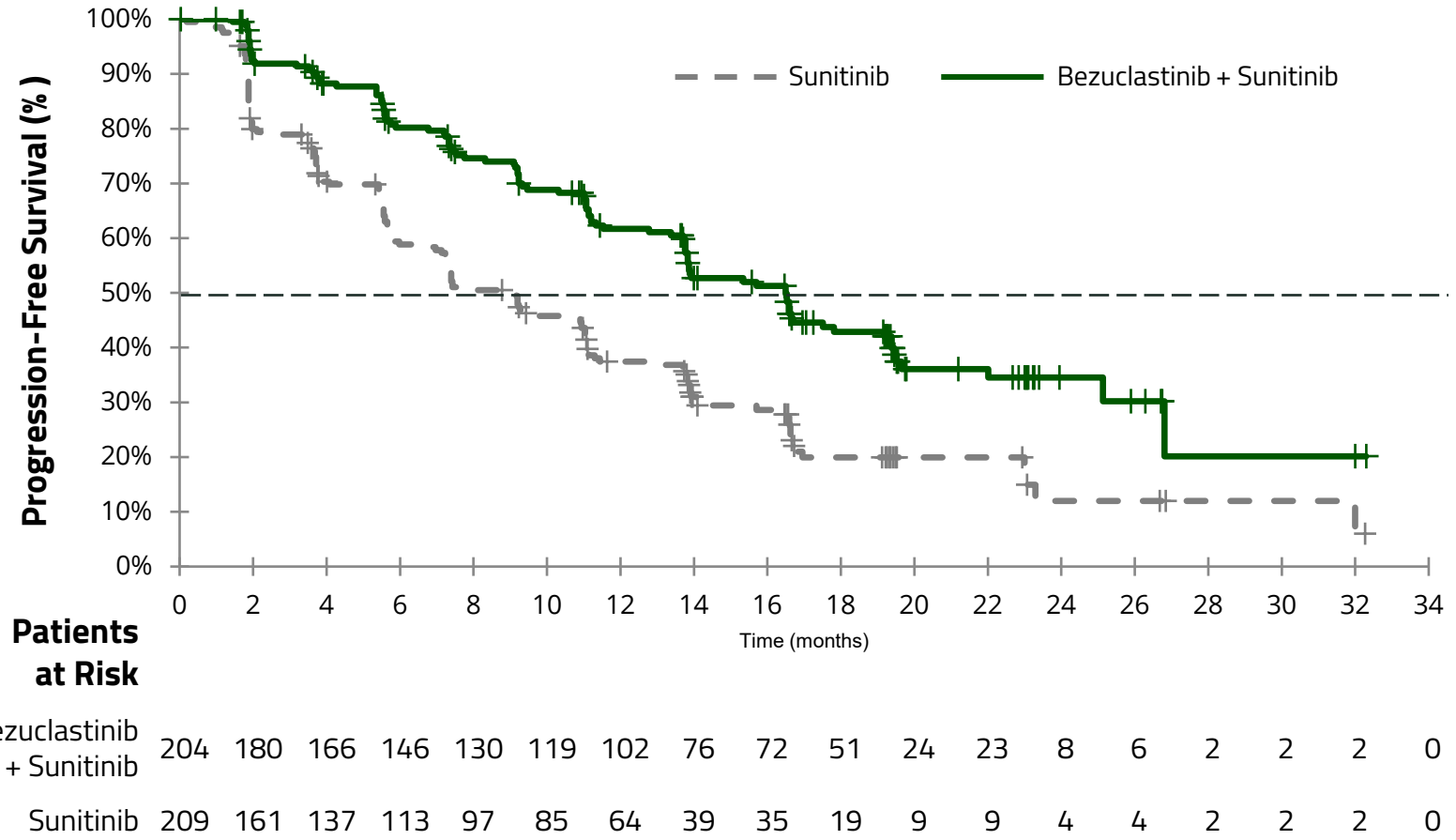
Pivotal Efficacy and Safety	Key End Points • PFS per BICR • ORR per BICR • Overall survival
Exon 9 Subgroup	The *KIT* exon 9-mutant population is of particular interest given the relatively lower sensitivity of exon 9 mutations to imatinib and the demonstrated activity of sunitinib in this molecular subgroup.
Crossover Sunitinib to Combination	End Points • PFS per BICR • ORR per BICR • Safety

[a]Patient stratification: presence/absence of *KIT* exon 9 mutation and intolerance to imatinib.
Statistical assumptions: median PFS of 8 months for sunitinib and 12 months for bezuclastinib + sunitinib.
2L, second line; BICR, blinded independent central review; EOT, end of treatment; GIST, gastrointestinal stromal tumor; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; QD, once daily.

Mutational Heterogeneity of Resistant GIST Is More Effectively Treated With the Combination of 2 TKIs, Bezuclastinib + Sunitinib

Median PFS	
Bezuclastinib + Sunitinib	Sunitinib
16.5 months *95% CI (13.8 to 19.2)*	**9.2 months** *95% CI (7.2 to 11.0)*
Hazard Ratio=0.50 95% CI (0.39 to 0.65); P<0.0001	

Objective Response[a]	
Bezuclastinib + Sunitinib	Sunitinib
45.6% *95% CI (38.6 to 52.7)*	**25.8%** *95% CI (20.0 to 32.3)*
P[b]<0.0001	

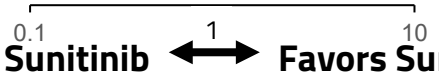


[a]Response defined as complete response or partial response. [b]Two-sided. Based on Cochran-Mantel-Haenszel test stratified by the IRT stratification factors intolerance to imatinib (yes vs no) and *KIT* exon 9 mutation status (present vs absent).
CI, confidence interval; GIST, gastrointestinal stromal tumor; PFS, progression-free survival; TKI, tyrosine kinase inhibitor.

Data cutoff: Sep 30, 2025.
Data in this slide were presented at ASCO 2026.

Bezuclastinib + Sunitinib Demonstrated PFS Benefit vs Sunitinib Monotherapy Across Subgroups, Including Patients With Exon 9

	Subgroup	Bezuclastinib + Sunitinib	Sunitinib	Hazard Ratio (95% CI)	Median, mos	
		Patients with primary outcomes, n/N (%)		Bezu + Sun vs Sun	Bezu + Sun	Sun
Total	**All Patients**	103/192 (53.6)	143/198 (72.2)	0.51 (0.40-0.66)	16.5	9.2
Age	**<65**	69/113 (61.1)	82/114 (71.9)	0.62 (0.45-0.85)	13.8	9.1
	≥65	37/91 (40.7)	66/95 (69.5)	0.36 (0.24-0.55)	19.4	9.2
Sex	**Male**	63/131 (48.1)	99/133 (74.4)	0.46 (0.33-0.63)	16.5	7.4
	Female	43/73 (58.9)	49/76 (64.5)	0.56 (0.37-0.86)	16.5	11.1
Race	**White**	45/80 (56.3)	58/85 (68.2)	0.52 (0.35-0.77)	13.9	9.2
	Not reported	49/96 (51.0)	68/95 (71.6)	0.57 (0.39-0.82)	13.9	9.1
	Other	12/28 (42.9)	22/29 (75.9)	0.24 (0.12-0.51)	19.5	7.6
	Any Exon 9	14/32 (43.8)	18/34 (52.9)	0.60 (0.29-1.23)	25.1	15.7
***KIT* Mutations[a]**	**Any Exon 11**	84/153 (54.9)	119/163 (73.0)	0.51 (0.39-0.68)	15.3	7.4
	Any Exon 11 + 13/14	19/32 (59.4)	27/32 (84.4)	0.44 (0.24-0.80)	16.5	10.9
	Any Exon 11 + 17/18	15/27 (55.6)	22/27 (81.5)	0.39 (0.20-0.75)	13.8	2.0
	Any Exon 13/14	33/51 (64.7)	39/45 (86.7)	0.44 (0.27-0.71)	13.8	5.8
	Any Exon 17/18	32/51 (62.7)	34/43 (79.1)	0.40 (0.24-0.66)	13.8	3.5



Favors Bezuclastinib + Sunitinib ⟷ **Favors Sunitinib**

- Baseline characteristics in exon 9 patients are similar to those in the overall Peak population
- Among patients with exon 9 mutations:
  - 86% (57/66) had no secondary *KIT* comutations, suggesting that many patients are progressing on imatinib because exon 9 is inadequately inhibited
  - 14% (9/66) had secondary *KIT* comutations, supporting the potential benefit of broad combination coverage

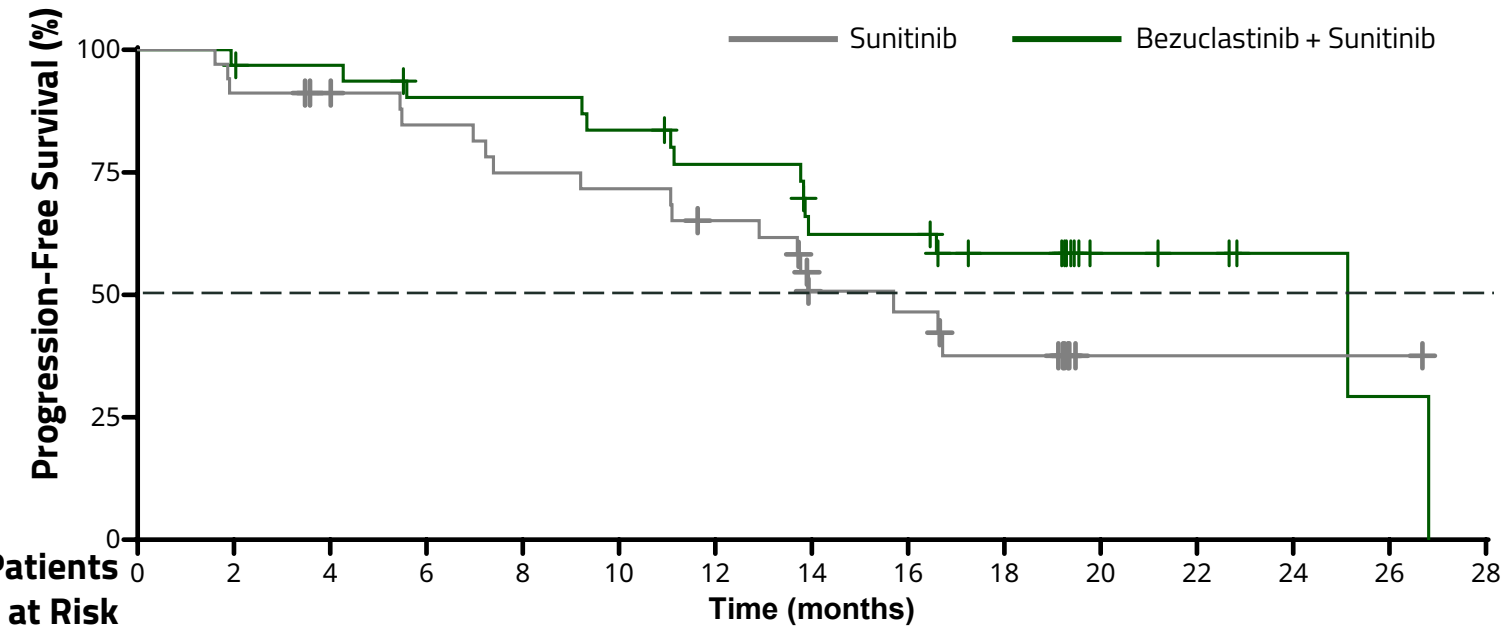
[a]*KIT* mutation determination is based on pooled data from ctDNA samples collected at baseline and tumor-tissue sequencing collected at any time prior to study treatment.
Bezu, bezuclastinib; CI, confidence interval; ctDNA, circulating tumor DNA; mos, months; PFS, progression-free survival; Sun, sunitinib.

Data cutoff: Sep 30, 2025.
Data in the figure were presented at ASCO 2026.

Favorable mPFS and ORR With Bezuclastinib + Sunitinib in Patients With Any Exon 9 Mutation

Median PFS	
Bezuclastinib + Sunitinib	**Sunitinib**
25.1 months *95% CI (13.8 to NE)*	**15.7 months** *95% CI (11.1 to NE)*
Hazard Ratio=0.60 95% CI (0.29 to 1.23); P=0.1591	

Objective Response[a]		
	Bezuclastinib + Sunitinib	**Sunitinib**
	56.3% *95% CI (37.7-73.6)*	**35.3%** *95% CI (19.7-53.5)*
P[b]=0.0875		
Best Overall Response, n (%)		
CR	**3** (9.4)	**1** (2.9)
PR	**15** (46.9)	**11** (32.4)
SD	**13** (40.6)	**19** (55.9)
PD	**1** (3.1)	**3** (8.8)



Patients at Risk															
Bezuclastinib + Sunitinib	32	31	30	27	27	25	22	17	17	13	5	4	2	1	0
Sunitinib	34	31	29	26	23	22	19	12	11	8	1	1	1	1	0

- While sunitinib is expected to drive activity against exon 9, improved disease control with combination treatment in this subgroup may be due to broad coverage targeting outgrowth of resistant clones across the spectrum of *KIT* resistance mutations

[a]Response defined as complete or partial response. [b]Two-sided. Based on Cochran-Mantel-Haenszel test stratified by the IRT stratification factors intolerance to imatinib (yes vs no) and *KIT* exon 9 mutation status (present vs absent).
CI, confidence interval; CR, complete response; NE, not estimable; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; PR, partial response; SD, stable disease.

Data cutoff: Sep 30, 2025.

Patients Who Crossed Over to Combination Therapy Had Improved Disease Control and Response Rate Compared With Sunitinib Monotherapy

Median PFS in Crossover Patients (n=128)	
2L Sunitinib Prior to crossover	3L Crossover Combination
5.7 months *95% CI (3.8 to 7.3)*	**7.4 months** *95% CI (5.6 to 11.0)*

Objective Response in Crossover Patients (n=128)	
2L Sunitinib Prior to crossover	3L Crossover Combination
20.3% *95% CI (13.7 to 28.3)*	**29.7%** *95% CI (21.9 to 38.4)*

- 71% (148/209) of patients had progressed on 2L sunitinib as of data cutoff; 128 patients crossed over from 2L sunitinib to combination (3L)
- 80% (102/128) of patients entering the crossover had not achieved an objective response on sunitinib monotherapy (had a best response of SD or PD)
- In patients with best response of disease progression on sunitinib, ORR was 56% with combination
  - Two patients with PD on monotherapy achieved a CR with combination

2L, second line; 3L, third line; CI, confidence interval; CR, complete response; ORR, objective response rate; PD, progressive disease; PFS, progression-free survival; SD, stable disease.

Data cutoff: Sep 30, 2025.

Bezuclastinib + Sunitinib Is Generally Well-Tolerated With a Favorable Safety Profile During Pivotal and Crossover

	Bezuclastinib + Sunitinib (n=204)	Sunitinib (n=208)[a]	Sunitinib -> Combination Crossover (n=128)
Median treatment duration, weeks (range)	61.4 (1.4 to 150.0)	42.4 (2.0 to 152.0)	23.9 (1.0 to 114.7)
TEAEs, n (%)	204 (100)	207 (99.5)	125 (97.7)
TRAEs, n (%)	202 (99.0)	204 (98.1)	121 (94.5)
Gr3+ TRAEs, n (%)	146 (71.6)	109 (52.4)	50 (39.1)
Bezuclastinib related Gr3+	126 (61.8)	N/A	46 (35.9)
Sunitinib related Gr3+	141 (69.1)	109 (52.4)	45 (35.2)
SARs, n (%)	34 (16.7)	24 (11.5)	15 (11.7)
Bezuclastinib related SAEs	25 (12.3)	N/A	10 (7.8)
Sunitinib related SAEs	31 (15.2)	24 (11.5)	14 (10.9)
TRAEs leading to death, n (%)	0	1 (0.5)	0
Reductions of either drug due to TRAEs, n (%)	114 (55.9)	92 (44.2)	33 (25.8)
DC of study treatment due to TRAEs, n (%)	15 (7.4)	8 (3.8)	3 (2.3)

- The incidence of TEAEs and TRAEs was similar between treatment arms and combination crossover
- No TRAEs leading to death in patients on bezuclastinib + sunitinib combination or combination crossover
- Only TRAEs leading to discontinuation in >1 patient on the combination arm were neutropenia (2.9%), increased ALT/AST (1.5%), and diarrhea (1.0%); and in the combination crossover arm was diarrhea (1.6%)

[a]One patient randomized to sunitinib but never dosed.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DC, discontinuation; Gr, grade; N/A, not applicable; SAE, serious adverse event; SAR, serious adverse reaction; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Data cutoff: Sep 30, 2025.

Bezuclastinib + Sunitinib Is Generally Well-Tolerated With a Favorable Safety Profile During Pivotal and Crossover

All grade TEAEs ≥20% in either treatment arm	Bezuclastinib + Sunitinib (n=204)		Sunitinib (n=208)[a]		Sunitinib -> Combination Crossover (n=128)	
Preferred term, n (%)	**All Grade**	**Grade 3+**	**All Grade**	**Grade 3+**	**All Grade**	**Grade 3+**
Diarrhea	159 (77.9)	16 (7.8)	138 (66.3)	15 (7.2)	65 (50.8)	7 (5.5)
ALT/AST increased[b]	115 (56.4)	22 (10.8)	35 (16.8)	3 (1.4)	60 (46.9)	9 (7.0)
Hypertension	106 (52.0)	60 (29.4)	108 (51.9)	57 (27.4)	22 (17.2)	6 (4.7)
Taste disorder[b]	97 (47.5)	0	52 (25.0)	0	27 (21.1)	0
Nausea	81 (39.7)	1 (0.5)	56 (26.9)	2 (1.0)	36 (28.1)	2 (1.6)
Hair color changes	79 (38.7)	0	37 (17.8)	0	18 (14.1)	0
Fatigue	72 (35.3)	9 (4.4)	70 (33.7)	5 (2.4)	35 (27.3)	10 (7.8)
Neutropenia[b]	71 (34.8)	31 (15.2)	70 (33.7)	32 (15.4)	33 (25.8)	10 (7.8)
PPES	59 (28.9)	6 (2.9)	95 (45.7)	5 (2.4)	19 (14.8)	2 (1.6)
Vomiting	56 (27.5)	2 (1.0)	45 (21.6)	4 (1.9)	27 (21.1)	2 (1.6)
Decreased appetite	55 (27.0)	6 (2.9)	46 (22.1)	0	19 (14.8)	1 (0.8)
Anemia	54 (26.5)	19 (9.3)	42 (20.2)	10 (4.8)	35 (27.3)	13 (10.2)
Abdominal pain	51 (25.0)	6 (2.9)	52 (25.0)	4 (1.9)	22 (17.2)	4 (3.1)
Stomatitis	46 (22.5)	6 (2.9)	68 (32.7)	10 (4.8)	7 (5.5)	0
GERD	45 (22.1)	0	30 (14.4)	0	19 (14.8)	0
Dyspepsia	43 (21.1)	5 (2.5)	29 (13.9)	0	13 (10.2)	0
Thrombocytopenia[b]	39 (19.1)	2 (1.0)	55 (26.4)	9 (4.3)	8 (6.3)	0

- TEAEs reported at a higher frequency (>15%) in combination arm: ALT/AST increased, taste disorder, and hair color changes. The most frequently reported TEAEs with the combination crossover were diarrhea and ALT/AST increased
- Majority of grade 3+ TEAEs were reported at a similar rate between treatment arms; ALT/AST increased and anemia reported at higher incidence in combination. The most frequently reported grade 3+ TEAEs with combination crossover were anemia, fatigue, neutropenia and ALT/AST increased
- The safety profile of the combination is generally consistent with sunitinib monotherapy, and no new safety risks were identified

[a]One patient randomized to sunitinib but never dosed; [b]Pooled terms.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GERD gastroesophageal reflux disease; PPES, palmar-plantar erythrodysesthesia; TEAE, treatment-emergent adverse event.

Data cutoff: Sep 30, 2025.

All Grade TEAEs ≥20% Demonstrate Balance Between Arms in Patient Subgroup With Any Exon 9 Mutation

All grade TEAEs ≥20% in either treatment arm	Bezuclastinib + Sunitinib (n=32)		Sunitinib (n=34)	
Preferred term, n (%)	**All Grade**	**Grade 3+**	**All Grade**	**Grade 3+**
Diarrhea	27 (84.4)	4 (12.5)	28 (82.4)	4 (11.8)
ALT/AST increased[a]	20 (62.5)	4 (12.5)	7 (20.6)	1 (2.9)
Neutropenia[a]	18 (56.3)	8 (25.0)	18 (52.9)	7 (20.6)
Hypertension	17 (53.1)	10 (31.3)	20 (58.8)	12 (35.3)
PPES	13 (40.6)	1 (3.1)	16 (47.1)	1 (2.9)
Taste disorder[a]	13 (40.6)	0	9 (26.5)	0
Anemia	11 (34.4)	5 (15.6)	8 (23.5)	2 (5.9)
Nausea	11 (34.4)	0	9 (26.5)	0
Stomatitis	9 (28.1)	3 (9.4)	17 (50.0)	1 (2.9)
Vomiting	9 (28.1)	0	14 (41.2)	1 (2.9)
Fatigue	8 (25.0)	1 (3.1)	16 (47.1)	0
Pyrexia	8 (25.0)	0	4 (11.8)	1 (2.9)
Abdominal pain	7 (21.9)	1 (3.1)	9 (26.5)	1 (2.9)
White blood cell count decreased	7 (21.9)	1 (3.1)	6 (17.6)	1 (2.9)
Asthenia	6 (18.8)	2 (6.3)	9 (26.5)	0
GERD	6 (18.8)	0	9 (26.5)	0
Headache	6 (18.8)	0	8 (23.5)	0
Thrombocytopenia[a]	6 (18.8)	1 (3.1)	9 (26.5)	1 (2.9)
Arthralgia	5 (15.6)	0	8 (23.5)	0
Dyspepsia	5 (15.6)	1 (3.1)	7 (20.6)	0
Decreased appetite	4 (12.5)	0	7 (20.6)	0
Constipation	3 (9.4)	1 (3.1)	8 (23.5)	0

- TEAEs reported at a higher frequency (>15%) in combination arm: ALT/AST increased
- TEAEs reported less frequently in combination arm: stomatitis and fatigue
- The safety profile in patients with any exon 9 mutation is generally consistent with the pivotal study, and no new safety risks were identified

[a]Pooled terms;
ALT, alanine aminotransferase; AST, aspartate aminotransferase; GERD, gastroesophageal reflux disease; PPES, palmar-plantar erythrodysesthesia; TEAE, treatment-emergent adverse event.

Data cutoff: Sep 30, 2025.

Mutational Heterogeneity of Resistant GIST Is More Effectively Treated With the Combination of 2 Kinase Inhibitors, Bezuclastinib + Sunitinib

- 2L treatment with combination demonstrates significant efficacy benefit vs sunitinib
- A majority of patients with exon 9 mutations have no secondary *KIT* comutations, suggesting that patients with GIST may be progressing on imatinib because exon 9 is inadequately inhibited
- Improved disease control with combination treatment in the exon 9 subgroup supports that broad coverage prevents outgrowth of resistance clones
- Results in crossover subgroup indicate that the majority of patients with GIST treated in the 2L would achieve improved disease control with broader coverage than achieved with sunitinib alone
- Manageable safety profile with combination across pivotal, crossover, and exon 9 subgroup, with no new safety risks identified

2L, second line; GIST, gastrointestinal stromal tumor.

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