VIRTUAL 2020 ESMO congress

Clinical Benefit with Ripretinib as ≥4th Line Treatment in Patients with Advanced Gastrointestinal Stromal Tumors (GIST): Update from the Phase 3 INVICTUS Study

John Zalcberg, Michael Heinrich, Suzanne George, Sebastian Bauer, Hans Gelderblom, Patrick Schöffski, Cesar Serrano, Robin L. Jones, Steven Attia, Gina D'Amato, Ping Chi, Peter Reichardt, Julie Meade, Vienna Reichert, Kelvin Shi, Rodrigo Ruiz-Soto, Margaret von Mehren, Jean-Yves Blay

VIRTUAL 2020 ESMO congress

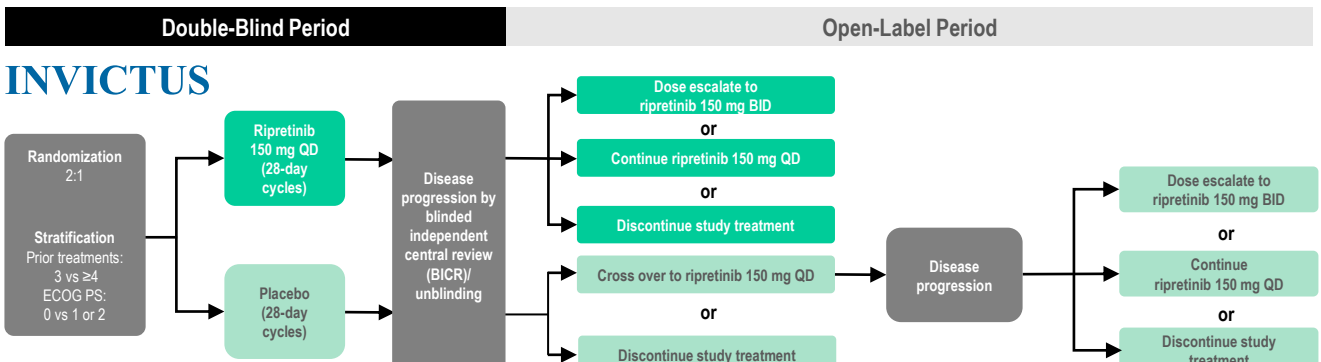
DISCLOSURE INFORMATION

- Dr. Zalcberg received honoraria from Pfizer, Merck Serono, Specialized Therapeutics, Targovax, Halozyme, Gilead Sciences, Deciphera, and Bayer
- Dr. Zalcberg acts in an advisory/consultancy role for Pfizer, Merck Serono, Targovax, MSD, Sirtex Medical, Halozyme, Lipotek, CEND, and Novella
- Dr. Zalcberg has received travel accommodations and paid expenses from Merck Serono, AstraZeneca, MSD, Deciphera, and Sirtex
- Dr. Zalcberg holds stocks for GW Pharmaceuticals, Ophthea, Madrigal Pharmaceuticals, Aimmune, Vertex, Bluebird Bio, Alnylam, Biomarin, Sage Therapeutics, Dova Pharmaceuticals, Therapeutics MD, Juno Therapeutics, Kite Pharma, Kiadis Pharma, CSL limited, Cochlear, Amarin, Frequency Therapeutics, Global Blood Therapeutics, Gilead, Uniqure, Sangamo, Acceleron, Concert Pharmaceuticals, MyoVant, Orphazyme, Moderna, and Zogenix
- Dr. Zalcberg acts as the chair for the Australian Clinical Trials Alliance, co-chair for the National Oncology Alliance, and co-chair for All.Can Australia

VIRTUAL 2020 ESMO congress

INVICTUS: Randomized Phase 3 Study Design

Ripretinib as ≥4th line therapy in patients with advanced GIST



Primary Endpoint

PFS
(per modified RECIST based on **B**linded **I**ndependent **C**entral **R**eview [BICR])

Select Secondary Endpoints

- **Objective response rate (ORR)** assessed by BICR (key endpoint)
- **Overall survival (OS)**

Post-primary follow-up analysis*

Data cutoff

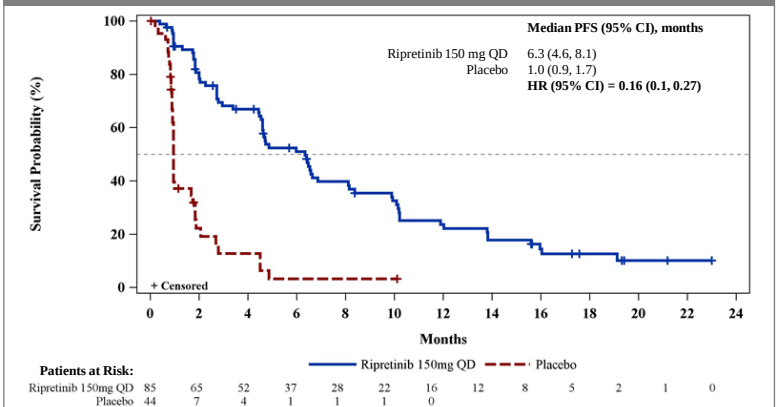
9 March 2020

*Data from this study (including the primary endpoint) were initially evaluated at the 31 May 2019 data cutoff.
BID, twice daily; ECOG PS, Eastern Cooperative Oncology Group performance score; PFS, progression-free survival; QD, once daily.

Progression Free Survival and Objective Response Rate*

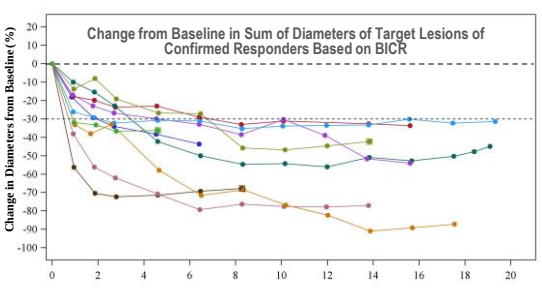
ITT population

Kaplan-Meier Estimate of PFS



The only patient remaining on placebo at the May 31, 2019 data cutoff crossed over to the ripretinib 150 mg QD treatment without BICR PD upon the study unblinding in Aug 2019. The PFS was censored on the last day before crossover.

	Ripretinib (n = 85)	Placebo (n = 44)
Events, n (%)	66 (77.6%)	37 (84.1%)
Censored, n (%)	19 (22.4%)	7 (15.9%)
PFS 6 months, % (95% CI)	51.0% (39.4, 61.4)	3.2% (0.2, 13.8)
PFS 12 months, % (95% CI)	23.6% (14.6, 34.0)	NE (NE, NE)
PFS 18 months, % (95% CI)	12.6% (6.0, 21.9)	NE (NE, NE)
ORR, n (%) 95% CI	10 (11.8%) 5.8, 20.6	0 0.0, 8.0
DOR, months, median, (95% CI)	14.5 (3.7, NE)	NE (NE, NE)

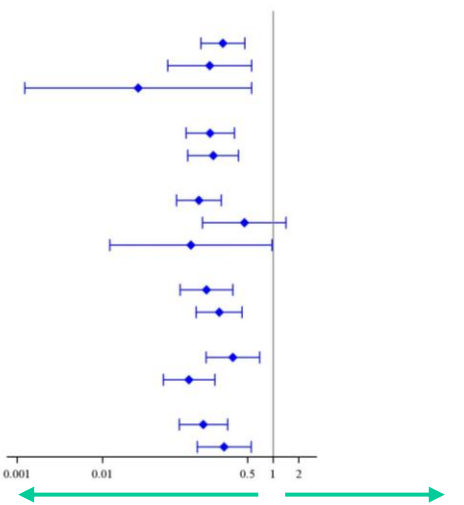


*Data from this study (including the primary endpoint) were initially evaluated at the 31 May 2019 data cutoff.

BICR, blinded independent central review; CI, confidence interval, DOR, duration of response; HR, hazard ratio; ITT, intent-to-treat (all randomized patients); NE, not estimable; ORR, objective response rate; PD, disease progression; PFS, progression-free survival; QD, once daily.

Ripretinib Showed PFS Benefit in All Assessed Patient Subgroups

Subgroup	Ripretinib 150 mg QD (N)	Placebo (N)	Hazard Ratio (95% CI)
Age Group			
18 - 64 Years	57	22	0.26 (0.14, 0.46)
≥ 65 - 74 Years	20	12	0.18 (0.06, 0.56)
75 Years or Older	8	10	0.03 (0.00, 0.56)
Gender			
Male	47	26	0.18 (0.10, 0.35)
Female	38	18	0.20 (0.10, 0.39)
Race			
White	64	33	0.14 (0.07, 0.25)
Non-White	13	7	0.46 (0.15, 1.42)
Not Reported	8	4	0.11 (0.01, 0.97)
Country			
US	40	20	0.17 (0.08, 0.34)
Non-US	45	24	0.23 (0.12, 0.43)
Screening ECOG			
0	38	19	0.34 (0.16, 0.69)
1 or 2	47	25	0.10 (0.05, 0.21)
Number of Prior Systemic Anti-cancer Treatments			
3	54	27	0.15 (0.08, 0.29)
≥ 4	31	17	0.27 (0.13, 0.55)

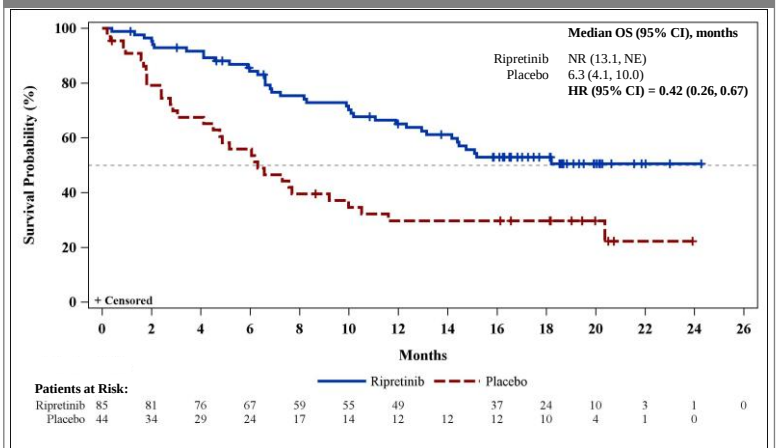


CI, confidence interval; ECOG, European Cooperative Oncology Group; PFS, progression-free survival; QD, once daily.

Overall Survival*

ITT population

Kaplan-Meier Estimate of OS



Overall survival data includes all time periods, including dose escalation to 150 mg BID. Placebo curve includes patients who crossed over to ripretinib treatment.

	Ripretinib (n = 85)	Placebo (n = 44)
Events, n (%)	38 (44.7%)	31 (70.5%)
Censored, n (%)	47 (55.3%)	13 (29.5%)
OS 6 months, % (95% CI)	84.3% (74.5, 90.6)	55.9% (39.9, 69.2)
OS 12 months, % (95% CI)	65.1% (53.6, 74.5)	29.7% (16.8, 43.7)
OS 18 months, % (95% CI)	53.0% (41.3, 63.3)	29.7% (16.8, 43.7)
OS 24 months, % (95% CI)	50.6% (38.5, 61.4)	NE (NE, NE)

- With 9 months of additional follow-up after the primary analysis, the median OS for patients randomized to ripretinib has extended from 15.1 months to “not reached”

*Data from this study (including the primary endpoint) were initially evaluated at the 31 May 2019 data cutoff.

BID, twice daily; CI, confidence interval; HR, hazard ratio; ITT, intent-to-treat (all randomized patients); NE, not estimable; NR, not reached; ORR, objective response rate; OS, overall survival; QD, once daily.

VIRTUAL 2020 ESMO congress

Safety Summary

Safety findings were consistent with the previous primary analysis results

TEAEs in >15% of Patients & Grade 3/4 TEAEs

Preferred Term, n (%)	Ripretinib any grade (n = 85)	Ripretinib grade 3/4 (n = 85)†	Placebo any grade (n = 43)*	Placebo grade 3/4 (n = 43)*†
Alopecia	44 (52)	0	2 (4.7)	0
Fatigue	40 (47)	3 (3.5)	10 (23)	1 (2.3)
Nausea	35 (41)	3 (3.5)	5 (12)	0
Abdominal pain	34 (40)	6 (7.1)	13 (30)	2 (4.7)
Constipation	31 (37)	1 (1.2)	9 (21)	0
Myalgia	30 (35)	2 (2.4)	5 (12)	0
Decreased appetite	26 (31)	1 (1.2)	9 (21)	2 (4.7)
Diarrhea	26 (31)	1 (1.2)	6 (14)	1 (2.3)
Palmar-plantar erythrodysesthesia syndrome	19 (22)	0	0	0
Vomiting	19 (22)	3 (3.5)	3 (7.0)	0
Headache	17 (20)	0	2 (4.7)	0
Weight decreased	17 (20)	0	5 (12)	0
Arthralgia	16 (19)	0	2 (4.7)	0
Muscle spasms	16 (19)	0	2 (4.7)	0
Edema peripheral	16 (19)	1 (1.2)	3 (7.0)	0
Blood bilirubin increased	15 (18)	1 (1.2)	2 (4.7)	0
Anemia	14 (17)	9 (11)	8 (19)	6 (14)
Dry skin	14 (17)	0	5 (12)	0
Hypertension	13 (15)	6 (7.1)	2 (4.7)	0

*44 patients were randomized to placebo, but 1 did not receive treatment.
†Corresponding grade 3/4 TEAEs to TEAEs in >15% of patients receiving ripretinib.

QD, once daily; TEAE, treatment-emergent adverse event.

TEAEs Leading to Dose Modification

	Ripretinib (n = 85)	Placebo (n = 43)*
Any TEAE leading to dose reduction, n (%)	7 (8.2)	1 (2.3)
Any TEAE leading to dose interruption, n (%)	22 (26)	9 (21)
Any TEAE leading to treatment discontinuation, n (%)	7 (8.2)	5 (12)
Any TEAE leading to death, n (%)**	6 (7.1)	10 (23)

*44 patients were randomized to placebo, but 1 did not receive treatment. **One death in each arm considered possibly related to blinded study drug.

- After 9 months of additional follow-up, the increase in TEAEs and the number of new TEAEs leading to dose modification or death in patients was minimal

VIRTUAL 2020 ESMO congress

INVICTUS: Conclusions

- With an additional 9 months of follow-up from the primary results of the phase 3 randomized INVICTUS trial, ripretinib continues to provide clinically meaningful benefit with a well-tolerated safety profile in patients with advanced GIST who have received at least 3 prior TKIs
    - Median PFS was 6.3 months with ripretinib vs 1.0 month with placebo
    - Median OS was not reached with ripretinib vs 6.3 months with placebo
    - ORR was 11.8% with ripretinib vs 0% with placebo
    - Safety findings were consistent with the previous primary analysis results
- 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)

FDA, Food and Drug Administration; GIST, gastrointestinal stromal tumor; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; QD, once daily; TGA, Therapeutic Goods Administration; TKI, tyrosine kinase inhibitor.

ACKNOWLEDGEMENTS

- We would like to thank the patients, their families, and caregivers, the investigators, and the investigational site staff of the INVICTUS study
- The INVICTUS study was sponsored by Deciphera Pharmaceuticals, LLC, Waltham, MA, USA
- Writing and editorial support was provided by AlphaBioCom, LLC, King of Prussia, PA, USA and was funded by Deciphera Pharmaceuticals, LLC