CHOOSE STIVARGA® (regorafenib) FOR YOUR 3L GIST PATIENTS

The only approved 3L treatment following imatinib and sunitinib in patients with gastrointestinal stromal tumor (GIST)[1]

ENTER

Indication

STIVARGA is indicated for the treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.

Important Safety Information

WARNING: HEPATOTOXICITY

- **Severe and sometimes fatal hepatotoxicity has occurred in clinical trials.**
- **Monitor hepatic function prior to and during treatment.**
- **Interrupt and then reduce or discontinue STIVARGA for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence.**

Please see additional Important Safety Information throughout this brochure and click for full Prescribing Information for STIVARGA, including the Boxed Warning.

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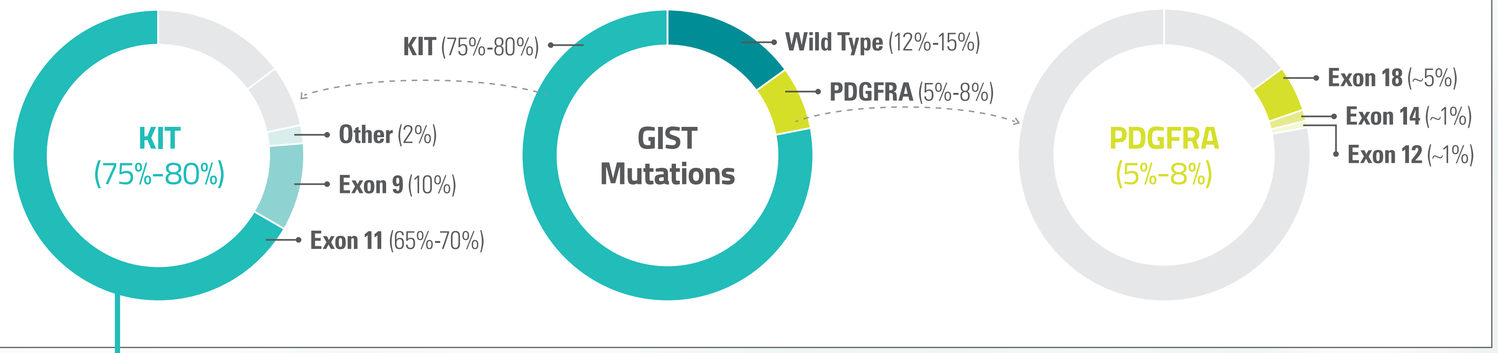
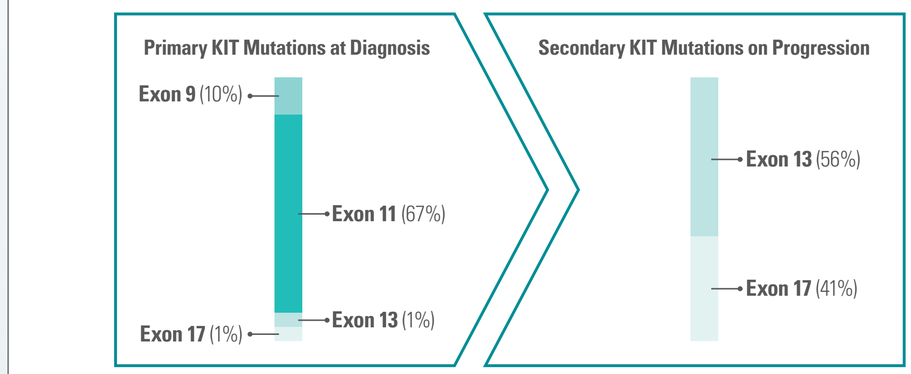
Evolution of GIST tumor post frontline therapy is primarily driven by secondary-resistance mutations[2]

KIT and PDGFRA mutations are the primary oncogenic drivers in GIST[3,4]



Most common KIT activating mutations in GIST are located in KIT exon 11[3]



Secondary KIT mutations develop in a nonrandom pattern clustered along exon 13 and exon 17[3]

Important Safety Information (cont)

Hepatotoxicity: Severe drug-induced liver injury with fatal outcome occurred in STIVARGA-treated patients across all clinical trials. In most cases, liver dysfunction occurred within the first 2 months of therapy and was characterized by a hepatocellular pattern of injury. In gastrointestinal stromal tumor (GIST), fatal hepatic failure occurred in 0.8% of patients in the STIVARGA arm.

Liver Function Monitoring: Obtain liver function tests (ALT, AST, and bilirubin) before initiation of STIVARGA and monitor at least every 2 weeks during the first 2 months of treatment. Thereafter, monitor monthly or more frequently as clinically indicated. Monitor liver function tests weekly in patients experiencing elevated liver function tests until improvement to less than 3 times the upper limit of normal (ULN) or baseline values. Temporarily hold and then reduce or permanently discontinue STIVARGA, depending on the severity and persistence of hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis.

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NCCN Preferred Category 1

Regorafenib (STIVARGA®) remains the ONLY 3L approved treatment for patients with GIST[1]

National Comprehensive Cancer Network® (NCCN®) Guidelines recommend regorafenib as a category 1, systemic agent for patients with progressive, unresectable, or metastatic GIST after imatinib and sunitinib.[1]

Potential treatment algorithms[1,*]

*For a complete listing of treatment options, see NCCN.org.

NCCN Categories of Evidence and Consensus

Category 1: Based upon hight-level evidence, there is uniform NCCN consensus that the intervention is appropriate

Appropriate and timely transition between lines of therapy is important over the course of GIST treatment[5]

Important Safety Information (cont)

Infections: STIVARGA caused an increased risk of infections. The overall incidence of infection (Grades 1-5) was higher (32% vs 17%) in 1142 STIVARGA-treated patients as compared to the control arm in randomized placebo-controlled trials. The incidence of grade 3 or greater infections in STIVARGA treated patients was 9%. The most common infections were urinary tract infections (5.7%), nasopharyngitis (4.0%), mucocutaneous and systemic fungal infections (3.3%) and pneumonia (2.6%). Fatal outcomes caused by infection occurred more often in patients treated with STIVARGA (1.0%) as compared to patients receiving placebo (0.3%); the most common fatal infections were respiratory (0.6% vs 0.2%). Withhold STIVARGA for Grade 3 or 4 infections, or worsening infection of any grade. Resume STIVARGA at the same dose following resolution of infection.

Hemorrhage: STIVARGA caused an increased incidence of hemorrhage. The overall incidence (Grades 1-5) was 18.2% in 1142 patients treated with STIVARGA vs 9.5% with placebo in randomized, placebo-controlled trials. The incidence of grade 3 or greater hemorrhage in patients treated with STIVARGA was 3.0%. The incidence of fatal hemorrhagic events was 0.7%, involving the central nervous system or the respiratory, gastrointestinal, or genitourinary tracts. Permanently discontinue STIVARGA in patients with severe or life-threatening hemorrhage and monitor INR levels more frequently in patients receiving warfarin.

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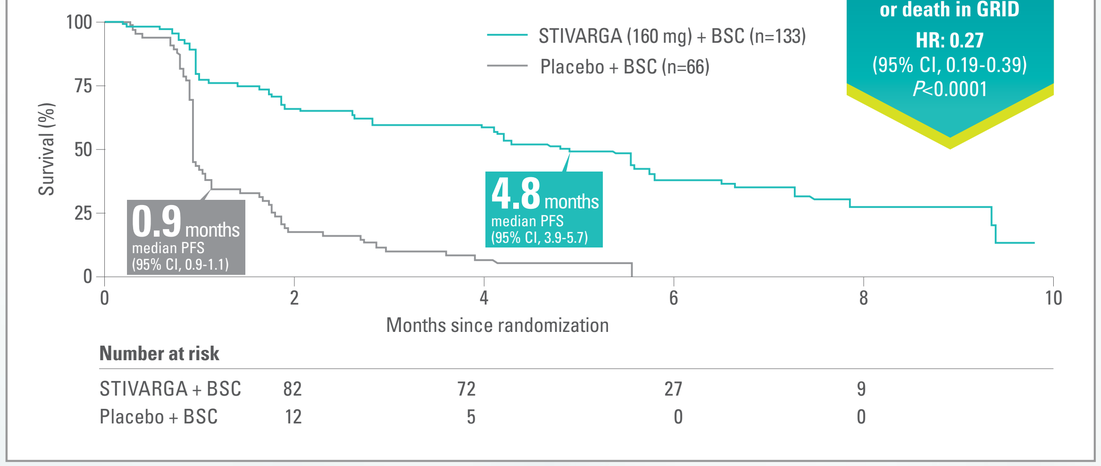
STIVARGA® (regorafenib) significantly improves PFS in previously treated patients with GIST[2,6]

STUDY DESIGN

STIVARGA was studied in patients with a high unmet need following disease progression on 2 prior TKIs in the GRID[5] trial: a phase 3, randomized, placebo-controlled trial in 199 patients with metastatic or unresectable GIST who had progressed after failure with at least imatinib and sunitinib or after intolerance to imatinib[2,6] with a primary endpoint of PFS (per modified RECIST 1.1).[5] Secondary endpoints included OS, time to progression, ORR, and DCR (defined as rate of complete response or partial response plus stable disease lasting for ≥12 weeks).[7]

PFS

Significant improvement in PFS in GRID[2,6]



- 82 of 133 STIVARGA patients (62%) vs 63 of 66 placebo patients (96%) experienced disease progression or died[6]
- At the time of disease progression as assessed by central review, the study blind was broken, and all patients were offered the opportunity to take STIVARGA at the investigator's discretion[6]

OS

- Median OS was 17.4 months for both STIVARGA (95% CI, 14.9-20.2) and placebo (95% CI, 12.3-21.0) with HR=0.91 (95%, 0.65-1.27) and *P* value* 0.5716[6]
- There was no statistically significant difference in OS at the final OS analysis, conducted at 162 OS events[6]

DCR

- 52.6% DCR achieved for STIVARGA (70/133 patients) vs 9.1% for placebo (6/66 patients)[6]
  - DCR was a secondary endpoint[2]
  - DCR is defined as the rate of complete response or partial response plus stable disease lasting for ≥12 weeks[2]

*A 2-sided *P* value by log-rank test stratified by line of treatment and geographical region.
CI=confidence interval; DCR=disease control rate; ECOG PS=Eastern Cooperative Oncology Group Performance Status; HR=hazard ratio; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors; TKI=tyrosine kinase inhibitor.

88% of patients in the placebo arm crossed over to open-label STIVARGA after disease progression[5]

Important Safety Information (cont)

Gastrointestinal Perforation or Fistula: Gastrointestinal perforation occurred in 0.6% of 4518 patients treated with STIVARGA across all clinical trials of STIVARGA administered as a single agent; this included eight fatal events. Gastrointestinal fistula occurred in 0.8% of patients treated with STIVARGA and in 0.2% of patients in the placebo arm across randomized, placebo-controlled trials. Permanently discontinue STIVARGA in patients who develop gastrointestinal perforation or fistula.

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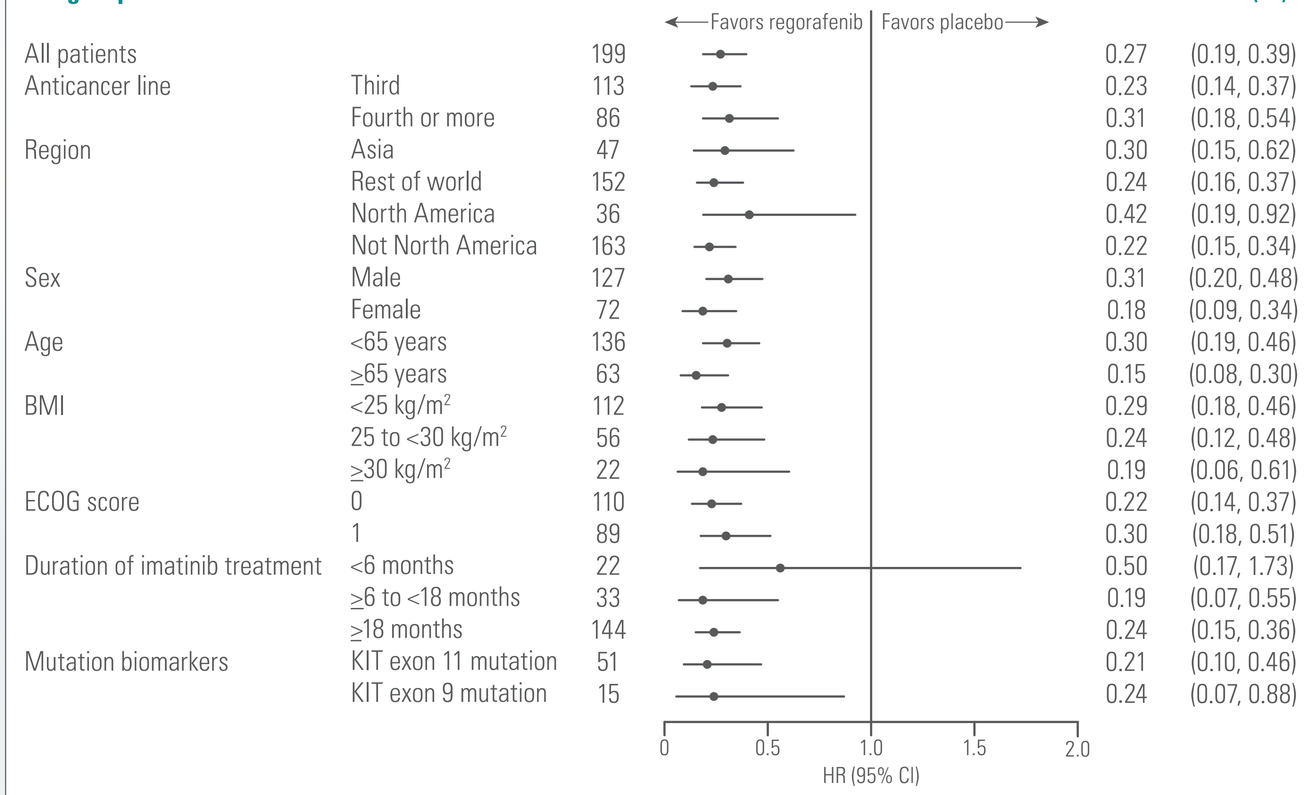
STIVARGA® (regorafenib) PFS based on exploratory, preplanned patient subgroup analyses in the GRID study[2]

- Prespecified subgroup analysis. Not powered to allow comparisons to be made across subgroups

PFS by subgroup in GRID[6]



BMI=body mass index.

Important Safety Information (cont)

Dermatological Toxicity: In randomized, placebo-controlled trials, adverse skin reactions occurred in 71.9% of patients with STIVARGA arm and 25.5% of patients in the placebo arm including hand-foot skin reaction (HFSR) also known as palmar-plantar erythrodysesthesia syndrome (PPES) and severe rash, requiring dose modification. In the randomized, placebo-controlled trials, the overall incidence of HFSR was higher in 1142 STIVARGA-treated patients (53% vs 8%) than in the placebo-treated patients. Most cases of HFSR in STIVARGA-treated patients appeared during the first cycle of treatment. The incidences of Grade 3 HFSR (16% vs <1%), Grade 3 rash (3% vs <1%), serious adverse reactions of erythema multiforme (<0.1% vs 0%), and Stevens-Johnson syndrome (<0.1% vs 0%) were higher in STIVARGA-treated patients. Across all trials, a higher incidence of HFSR was observed in Asian patients treated with STIVARGA (all grades: 72%; Grade 3: 18%). Toxic epidermal necrolysis occurred in 0.02% of 4518 STIVARGA-treated patients across all clinical trials of STIVARGA administered as a single agent. Withhold STIVARGA, reduce the dose, or permanently discontinue depending on the severity and persistence of dermatologic toxicity.

Hypertension: Hypertensive crisis occurred in 0.2% in STIVARGA-treated patients and in none of the patients in placebo arm across all randomized, placebo-controlled trials. STIVARGA caused an increased incidence of hypertension (59% vs 27% in GIST). The onset of hypertension occurred during the first cycle of treatment in most patients who developed hypertension (67% in randomized, placebo controlled trials). Do not initiate STIVARGA until blood pressure is adequately controlled. Monitor blood pressure weekly for the first 6 weeks of treatment and then every cycle, or more frequently, as clinically indicated. Temporarily or permanently withhold STIVARGA for severe or uncontrolled hypertension.

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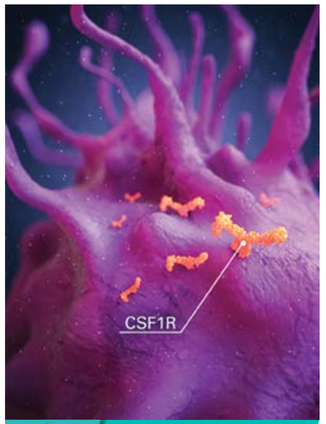
STIVARGA® (regorafenib) is a multikinase inhibitor (MKI) that targets normal cellular functions and pathological processes such as oncogenesis, tumor angiogenesis, metastasis, and tumor immunity

STIVARGA inhibits a large set of TKIs, resulting in multiple antitumor activities[6]

- In in vitro biochemical or cellular assays, STIVARGA or its major human active metabolites, M-2 and M-5, inhibited the activity of RET, VEGFR1, VEGFR2, VEGFR3, KIT, PDGFR-alpha, PDGFR-beta, FGFR1, FGFR2, TIE2, DDR2, TrkA, Eph2A, RAF1, BRAF, BRAF V600E, SAPK2, PTK5, Abl, and CSF1R at concentrations of STIVARGA that have been achieved clinically[6]
- In in vivo models, STIVARGA demonstrated antiangiogenic activity in a rat tumor model and inhibition of tumor growth in several mouse xenograft models, including some for GIST. STIVARGA also demonstrated antimetastatic activity in a mouse xenograft model and 2 mouse orthotopic models of human colorectal carcinoma[6]

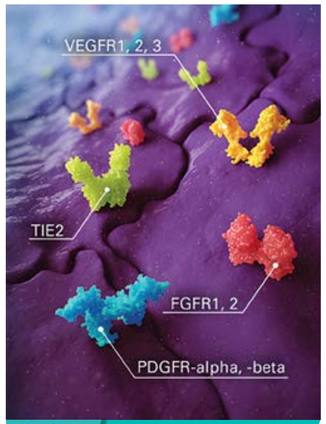
Target the tumor 4 ways through multikinase inhibition[7-14]

TUMOR IMMUNITY



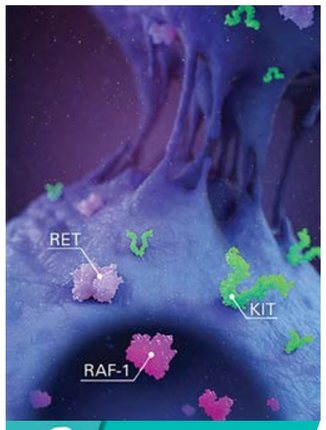
STIVARGA disrupts **tumor immunity** by inhibiting **CSF1R**, a receptor important for macrophage proliferation[6,9,10]

TUMOR ANGIOGENESIS



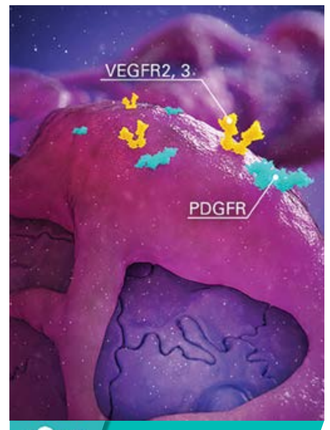
STIVARGA inhibits key angiogenic receptors: **VEGFR1, 2, and 3; TIE2; PDGFR-alpha and -beta; and FGFR1 and 2** via kinase inhibition[8,11,12]

ONCOGENESIS



STIVARGA potently blocks multiple protein kinases, including **KIT, RAF-1, and RET**, which are important in oncogenesis[6,11,12]

METASTASIS



STIVARGA inhibits **VEGFR2 and 3**, important mediators involved in endothelial cell proliferation and migration[5,11,12]

Blocks **PDGFR**, believed to play a role in cancer-associated, fibroblast-induced metastasis[6,14]

Abl=Abelson kinase; CSF1R=colony-stimulating factor 1 receptor; DDR=discoidin domain receptor; Eph2A=ephrin type-A receptor 2; FGFR=fibroblast growth factor receptor; PDGFR=platelet-derived growth factor receptor; PTK5=protein tyrosine kinase 5; RAF=rapidly accelerated fibrosarcoma; RET=rearranged during transfection; TIE2=tyrosine kinase with immunoglobulin-like and EGF-like domains; TrkA=tropomyosin receptor kinase A; VEGFR=vascular endothelial growth factor receptor.

Important Safety Information (cont)

Cardiac Ischemia and Infarction: STIVARGA increased the incidence of myocardial ischemia and infarction (0.9% with STIVARGA vs 0.2% with placebo) in randomized placebo-controlled trials. Withhold STIVARGA in patients who develop new or acute cardiac ischemia or infarction, and resume only after resolution of acute cardiac ischemic events if the potential benefits outweigh the risks of further cardiac ischemia.

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Regular monitoring is critical for the management of AEs

- Patients taking STIVARGA® (regorafenib) should be managed with frequent and proactive monitoring, especially during the first 2 to 4 weeks of treatment[7,15]

Adverse drug reactions (≥10%) reported in patients treated with STIVARGA in GRID and reported more commonly than in patients receiving placebo

- AEs that resulted in treatment discontinuation were reported in 2.3% of STIVARGA-treated patients compared to 1.5% of patients who received placebo[6]

Drug-related AEs occurring in ≥10% of patients treated with STIVARGA[6,*]

	STIVARGA (n=132)		Placebo (n=66)	
AEs	**All grades**	**Grade ≥3**	**All grades**	**Grade ≥3**
Skin and subcutaneous tissue disorders				
HFSR/PPE	67%	22%	12%	2%
Rash[†]	30%	7%	3%	0%
Alopecia	24%	2%	2%	0%
General disorders and administration site conditions				
Asthenia/Fatigue	52%	4%	39%	2%
Fever	21%	0%	11%	2%
Vascular disorders				
Hypertension	59%	28%	27%	5%
Hemorrhage	11%	4%	3%	0%
Gastrointestinal disorders				
Pain	60%	8%	55%	14%
Diarrhea	47%	8%	9%	0%
Mucositis	40%	2%	8%	2%
Nausea	20%	2%	12%	2%
Vomiting	17%	<1%	8%	0%

	(n=132)		(n=66)	
AEs	**All grades**	**Grade ≥3**	**All grades**	**Grade ≥3**
Respiratory, thoracic, and mediastinal disorders				
Dysphonia	39%	0%	9%	0%
Infections and infestations				
Infection[‡]	32%	5%	5%	0%
Metabolism and nutrition disorders				
Decreased appetite and food intake	31%	<1%	21%	3%
Hypothyroidism[§]	18%	0%	6%	0%
Nervous system disorders				
Headache	16%	0%	9%	0%
Investigations				
Weight loss	14%	0%	8%	0%
Musculoskeletal and connective tissue disorders				
Muscle spasms	14%	0%	3%	0%

*AEs graded according to NCI CTCAE v4.0.
[†]The term rash represents reports of events of rash, erythematous rash, macular rash, maculopapular rash, papular rash, and pruritic rash.
[‡]Fatal outcomes observed.
[§]Hypothyroidism incidence based on subset of patients with normal TSH and no thyroid supplementation at baseline.

AE=adverse event; HFSR=hand-foot skin reaction; NCI CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events; PPE=palmar-plantar erythrodysesthesia; TSH=thyroid-stimulating hormone.

Some AEs may occur early during treatment, so it's important to evaluate patients early and often[6]

Important Safety Information (cont)

Reversible Posterior Leukoencephalopathy Syndrome (RPLS): Reversible posterior leukoencephalopathy syndrome (RPLS), a syndrome of subcortical vasogenic edema diagnosed by characteristics finding on MRI, occurred in one of 4800 STIVARGA-treated patients across all clinical trials. Perform an evaluation for RPLS in any patient presenting with seizures, severe headache, visual disturbances, confusion, or altered mental function. Discontinue STIVARGA in patients who develop RPLS.

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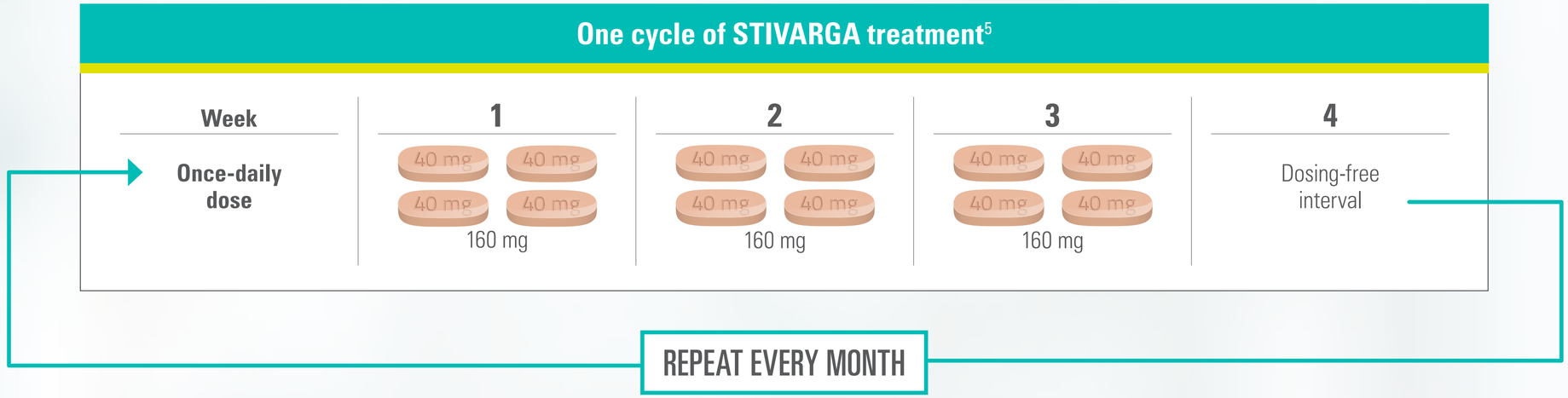
Standard starting dose with options for dose management[6]

STIVARGA® (regorafenib) dosing in the phase 3 GRID trial[2,6]

The recommended starting dose is 160 mg STIVARGA (four 40-mg tablets) taken orally once daily for the first 3 weeks, followed by a 1-week treatment break.[5]



Dosage and administration[6]

- Treatment should continue until disease progression or until unacceptable toxicity occurs
- STIVARGA should be taken whole with water after a low-fat meal that contains <600 calories and <30% fat at the same time each day
- Advise patients to take any missed dose on the same day, as soon as they remember, and that they must not take 2 doses on the same day to make up for a dose missed on the previous day

Dose modifications[6]

- In GRID trial, 50% of patients receiving STIVARGA had their dose reduced, and dose interruptions for adverse events were required in 58% of the patients
- No dose adjustment is recommended for patients with renal impairment
- The pharmacokinetics of STIVARGA have not been studied in patients who are on dialysis and there is no recommended dose for this patient population
- No dose adjustments are required based on mild (total bilirubin ≤upper limit of normal [ULN] and aspartate aminotransferase [AST] >ULN, or total bilirubin >ULN to ≤1.5x ULN) or moderate (total bilirubin >1.5 to ≤3x ULN and any AST) hepatic impairment. Closely monitor patients with hepatic impairment for adverse reactions. STIVARGA is not recommended for use in patients with severe hepatic impairment (total bilirubin >3x ULN), as STIVARGA has not been studied in this population

Important Safety Information (cont)

Wound Healing Complications: Impaired wound healing complications can occur in patients who receive drugs that inhibit the VEGF signaling pathway. Therefore, STIVARGA has the potential to adversely affect wound healing. Withhold STIVARGA for at least 2 weeks prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of STIVARGA after resolution of wound healing complications has not been established.

Embryo-Fetal Toxicity: STIVARGA can cause fetal harm when administered to a pregnant woman. There are no available data on STIVARGA use in pregnant women. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with STIVARGA and for 2 months after the final dose.

Nursing Mothers: Because of the potential for serious adverse reactions in breastfed infants from STIVARGA, do not breastfeed during treatment with STIVARGA and for 2 weeks after the final dose.

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Prepare a dose modification plan for treating your GIST patients with STIVARGA

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Dose modifications may help keep therapy manageable[6]

	Interrupt STIVARGA® (regorafenib) for the following	Reduce STIVARGA dose to 120 mg	Reduce STIVARGA dose to 80 mg	Discontinue STIVARGA permanently for the following
Hand-foot skin reaction (HFSR)	• Grade 2 HFSR that is recurrent or does not improve within 7 days despite dose reduction • Grade 3 HFSR (interrupt for a minimum of 7 days)	• First occurrence of Grade 2 HFSR of any duration • After recovery from Grade 3 HFSR	• Recurrence of Grade 2 HFSR at the 120-mg dose • After recovery from Grade 3 HFSR at 120-mg dose	• Failure to tolerate the 80-mg dose
Liver-function test abnormalities	• Grade 3 aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) elevation	• Grade 3 AST/ALT elevation. Resume only if the potential benefit outweighs the risk of hepatotoxicity		• Any occurrence of AST/ALT >20x upper limit of normal (ULN) • Any occurrence of AST/ALT >3x ULN with concurrent bilirubin >2x ULN • Recurrence of AST/ALT >5x ULN despite dose reduction to 120 mg
All other adverse events (AEs)	• Symptomatic Grade 2 hypertension • Any Grade 3 or 4 AE • Worsening infection of any grade	• After recovery from any Grade 3 or 4 AE except infection	• After recovery from any Grade 3 or 4 AE at the 120-mg dose (except hepatotoxicity or infection)	• Failure to tolerate the 80-mg dose • Any Grade 4 AE. Resume only if the potential benefit outweighs the risks

- If dose modifications are required, reduce the dose in 40-mg (1-tablet) increments
- The lowest recommended daily dose is 80 mg
- Resume STIVARGA at the same dose following resolution of infection

Important Safety Information (cont)

Most Frequently Observed Adverse Drug Reactions in GIST (≥30%): The most frequently observed adverse drug reactions (≥30%) in STIVARGA-treated patients vs placebo-treated patients in GIST, respectively, were: HFSR/PPE (67% vs 12%), pain (60% vs 55%), hypertension (59% vs 27%), asthenia/fatigue (52% vs 39%), diarrhea (47% vs 9%), mucositis (40% vs 8%), dysphonia (39% vs 9%), infection (32% vs 5%), decreased appetite and food intake (31% vs 21%), and rash (30% vs 3%).

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The power of patient support and expert assistance

$0 CO-PAY

NO monthly cap and up to $25,000 per year for privately insured patients.
Annual enrollment is required.

- $0 co-pay for privately insured patients*
- NO monthly cap
- Covers 100% of co-pays up to $25,000 per year per patient
- Patients cannot participate if:
  – Prohibited by their insurance company or applicable laws
  – Enrolled in any type of government insurance or reimbursement program
- If Prior Authorization determinations are delayed or denied, patients will be assessed for temporary patient assistance

3 WAYS TO ENROLL IN $0 CO-PAY

1. Directly via www.zerocopaysupport.com or call 1-647-245-5622
2. Call Access Services by Bayer™: 1-800-288-8374
3. Specialty Pharmacy Provider (SPP) Network

For more information, call us by phone: 1-800-288-8374

Nurse counselors: 9 AM-6 PM ET
A resource for patient education and support

- Answering questions, providing information, and offering patient assistance
- Education about potential AEs
- Patient educational materials/starter kits
- Refill reminders
- Outbound calls

Financial counselors: 9 AM-6 PM ET
A resource assisting with patient access

- Benefit verification, identification, and coordination of SPP
- $0 co-pay for privately insured patients*
- Alternative coverage research-referral to independent organizations that may assist qualified patients with their out-of-pocket expenses†

*Patients who are enrolled in any type of government insurance or reimbursement programs are not eligible. As a condition precedent of the co-payment support provided under this program, eg, co-pay refunds, participating patients and pharmacies are obligated to inform insurance companies and third-party payors of any benefits they receive and the value of this program and may not participate if this program is prohibited by or conflicts with their private insurance policy, as required by contract or otherwise. Void where prohibited by law, taxed, or restricted. Patients enrolled in Bayer's Patient Assistance Program are not eligible. Bayer may determine eligibility, monitor participation, equitably distribute product, and modify or discontinue any aspect of the Access Services by Bayer program at any time, including but not limited to this commercial co-pay assistance program.

†Patients do not automatically qualify for financial help from charitable organizations; eligibility criteria apply.

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CHOOSE STIVARGA® (regorafenib) FOR YOUR 3L GIST PATIENTS

Regorafenib (STIVARGA®) remains the ONLY 3L approved, NCCN recommended treatment option after imatinib and sunitinib in patients with GIST[1]

GRID EFFICACY[4,5]

- 4.8-month (95% CI, 3.9-5.7) median PFS in the phase 3 GRID trial (vs 0.9 months [95% CI, 0.9-1.1] with placebo)
- 73% reduction in risk of disease progression or death (HR: 0.27 [95% CI, 0.19-0.39]); *P*<0.0001
- 82 of 133 STIVARGA patients (62%) vs 63 of 66 placebo patients (96%) experienced disease progression or died
- 17.4 mo OS in both STIVARGA and placebo arms (no statistically significant difference noted)
- 88% of placebo patients crossed over to open-label STIVARGA after disease progression

DOSING MANAGEMENT[4]

- Recommended starting dose is 160 mg
- Plan for dose modification as certain AEs may be managed by dose reduction, interruption, or discontinuation

Indication

STIVARGA is indicated for the treatment of patients with locally advanced, unresectable or metastatic gastrointestinal stromal tumor (GIST) who have been previously treated with imatinib mesylate and sunitinib malate.

Important Safety Information

WARNING: HEPATOTOXICITY

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Please see additional Important Safety Information throughout this brochure and click for full Prescribing Information for STIVARGA, including the Boxed Warning.

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References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastrointestinal Stromal Tumors (GISTs). V1.2023. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed February 24, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. **2.** Demetri GD, Reichardt P, Kang Y-K, et al; on behalf of the GRID Study Investigators. Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet*. 2013;381(9863):295-302. **3.** Hemming ML, Heinrich MC, Bauer S, et al. *Annals of Oncology*. 2018;29: 2037-2045. **4**. Lopes LF, Bacchi CE. Imatinib treatment for gastrointestinal stromal tumour (GIST). *J Cell Mol Med*. 2010;14(1-2):42-50. doi:10.1111/j.1582-4934.2009.00983 **5.** Ahmed M. Recent advances in the management of gastrointestinal stromal tumor. *World J Clin Cases*. 2020;8(15):3142-3155. **6.** STIVARGA [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc; December 2020. **7.** Grothey A, George S, Van Cutsem E, et al. Optimizing treatment outcomes with regorafenib: personalized dosing and other strategies to support patient care. *Oncologist*. 2014;19:1-12. **8.** Zhao Y, Adjei AA. Targeting angiogenesis in cancer therapy: moving beyond vascular endothelial growth factor. *Oncologist*. 2015;20(6):660-673. **9.** Arai H, Battaglin F, Wang J, et al. Molecular insight of regorafenib treatment for colorectal cancer. *Cancer Treat Rev*. 2019;81:1-19. **10.** Grothey A, Blay J-Y, Pavlakis N, Yoshino T, Bruix J. Evolving role of regorafenib for the treatment of advanced cancers. *Cancer Treat Rev*. 2020;86:1-17. **11.** Zopf D, Fichtner I, Bhargava A, et al. Pharmacologic activity and pharmacokinetics of metabolites of regorafenib in preclinical models. *Cancer Med*. 2016;5(11):3176-3185. **12.** Wilhelm SM, Dumas J, Adnane L, et al. Regorafenib (BAY 73-4506): a new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. *Int J Cancer*. 2011;129(1):245-255. **13.** Schmieder R, Hoffmann J, Becker M, et al. Regorafenib (BAY 73-4506): antitumor and antimetastatic activities in preclinical models of colorectal cancer. *Int J Cancer*. 2014;135(6):1487-1496. **14.** Takigawa H, Kitadai Y, Shinagawa K, et al. Multikinase inhibitor regorafenib inhibits the growth and metastasis of colon cancer with abundant stroma. *Cancer Sci*. 2016;107(5):601-608. **15.** Krishnamoorthy SK, Relias V, Sebastian S, Jayaraman V, Wasif Saif M. Management of regorafenib-related toxicities: a review. *Therap Adv Gastroenterol*. 2015;8(5):285-297.

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PP-STI-US-1719-1 04/23

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