THE LANCET
Oncology

QINLOCK® (ripretinib) 50 mg tablets

HIGHLIGHTS FROM A PUBLICATION

Ripretinib in Patients with Advanced Gastrointestinal Stromal Tumours (INVICTUS): A Double-blind, Randomised, Placebo-Controlled, Phase 3 Trial[1]

INVICTUS

A global, multicenter, Phase 3, randomized, double-blind, placebo-controlled trial in 129 patients who had received ≥3 prior anticancer therapies in advanced GIST[1,2]

- Primary endpoint: progression-free survival (PFS) assessed by BICR
- Secondary endpoints: objective response rate (ORR) by BICR, overall survival (OS), time to progression (TTP), time to best response, PFS by investigator assessment, quality of life, and safety
- Included patients with KIT or PDGFRα mutations or wild-type GIST, among other characteristics

IMAGE: HISTOPATHOLOGIC IMAGE OF GIST OF THE STOMACH

BICR=blinded independent central review; GIST=gastrointestinal stromal tumor; KIT=KIT proto-oncogene receptor tyrosine kinase; PDGFRα=platelet-derived growth factor receptor α.

INDICATION

QINLOCK is a kinase inhibitor indicated for the treatment of adult patients with advanced gastrointestinal stromal tumor (GIST) who have received prior treatment with 3 or more kinase inhibitors, including imatinib.

SELECT SAFETY INFORMATION

There are no contraindications for QINLOCK.

Palmar-plantar erythrodysesthesia syndrome (PPES): In INVICTUS, Grade 1-2 PPES occurred in 21% of the 85 patients who received QINLOCK. PPES led to dose discontinuation in 1.2% of patients, dose interruption in 2.4% of patients, and dose reduction in 1.2% of patients. Based on severity, withhold QINLOCK and then resume at same or reduced dose.

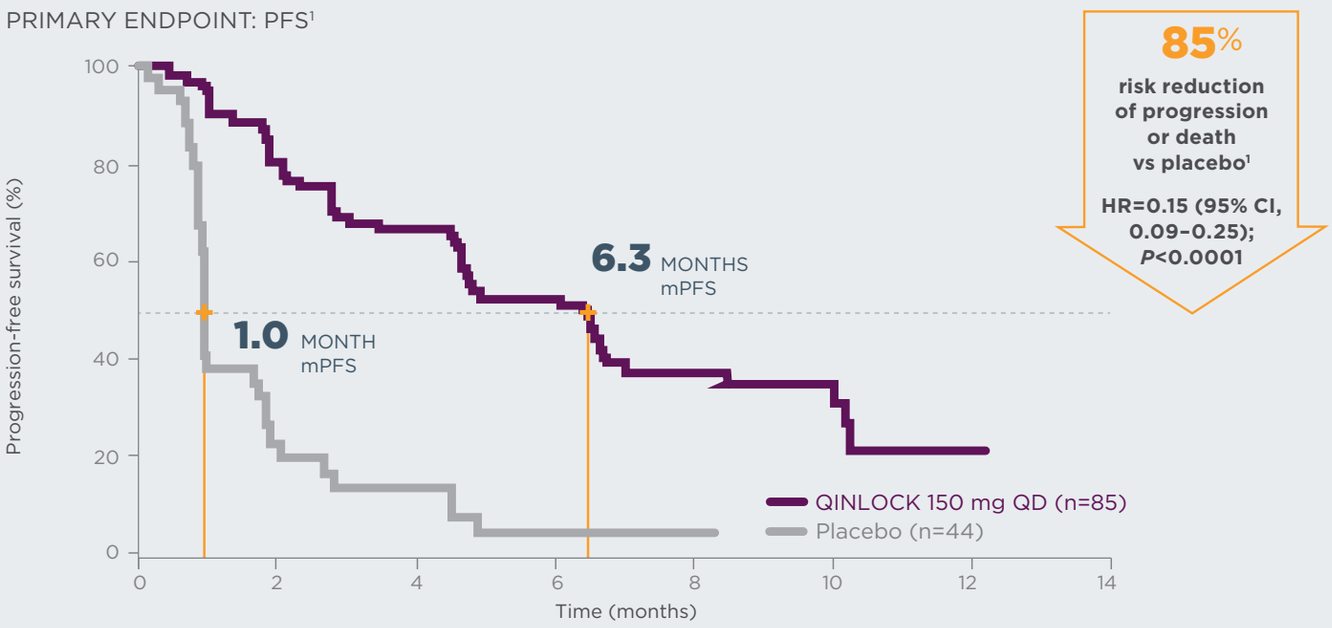
New Primary Cutaneous Malignancies: In INVICTUS, cutaneous squamous cell carcinoma (cuSCC) occurred in 4.7% of the 85 patients who received QINLOCK with a median time to event of 4.6 months (range 3.8 to 6 months). In the pooled safety population, cuSCC and keratoacanthoma occurred in 7% and 1.9% of patients, respectively. In INVICTUS, melanoma occurred in 2.4% of the 85 patients who received QINLOCK. In the pooled safety population, melanoma occurred in 0.9% of patients. Perform dermatologic evaluations when initiating QINLOCK and routinely during treatment. Manage suspicious skin lesions with excision and dermatopathologic evaluation. Continue QINLOCK at the same dose.

Please see additional Safety Information throughout and accompanying full Prescribing Information, including Patient Information.

QINLOCK® (ripretinib) DEMONSTRATED A POWERFUL PFS BENEFIT[1]

QINLOCK demonstrated superior median progression-free survival (mPFS) vs placebo: 6.3 months vs 1.0 month (*P*<0.0001)[1]*

PRIMARY ENDPOINT: PFS[1]



Number of patients at risk

QINLOCK	85	65	52	37	18	8	1	0
Placebo	44	7	4	1	1	0		

*Double blind period.

- QINLOCK PFS results were generally consistent across all assessed patient subgroups[1]

KEY SECONDARY ENDPOINT

Objective response rate (ORR) by BICR: 9.4% with QINLOCK vs 0.0% with placebo (*P*=0.0504)[1,2†]

- The median duration of response had not been reached at the study cutoff date[1]

†All responses were partial responses.

EXPLORATORY ANALYSIS

- 66% of QINLOCK-treated patients experienced stable disease ≥6 weeks vs 20% with placebo[1]

CI=confidence interval; HR=hazard ratio.

SELECT SAFETY INFORMATION

Hypertension: In INVICTUS, Grade 1-3 hypertension occurred in 14% of the 85 patients who received QINLOCK, including Grade 3 hypertension in 7% of patients. Do not initiate QINLOCK in patients with uncontrolled hypertension. Monitor blood pressure as clinically indicated. Based on severity, withhold QINLOCK and then resume at same or reduced dose or permanently discontinue.

Cardiac Dysfunction: In INVICTUS, cardiac failure occurred in 1.2% of the 85 patients who received QINLOCK. In the pooled safety population, cardiac dysfunction (including cardiac failure, acute left ventricular failure, diastolic dysfunction, and ventricular hypertrophy) occurred in 1.7% of patients, including Grade 3 adverse reactions in 1.1% of patients.

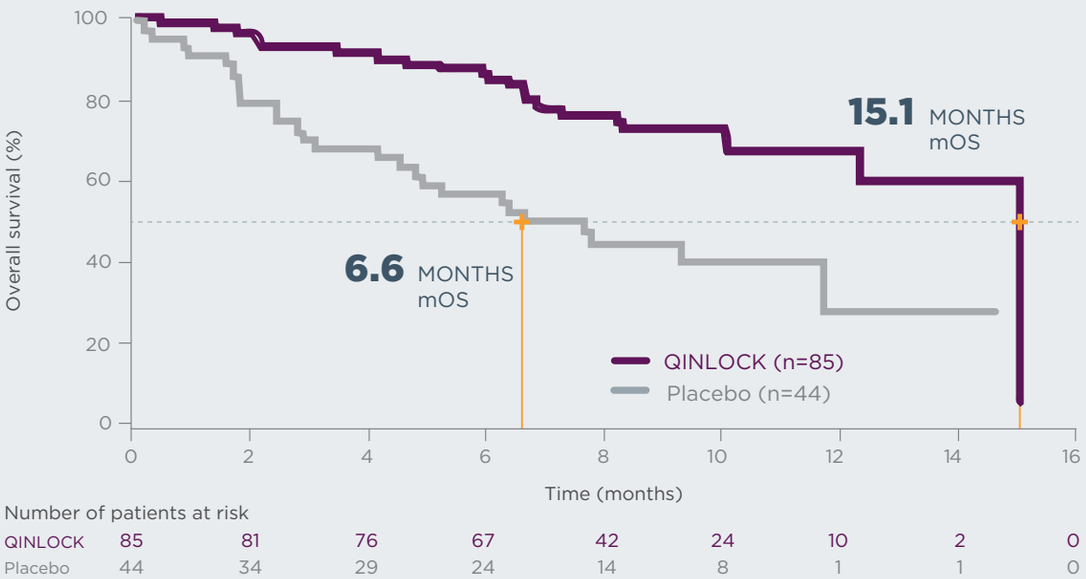
In INVICTUS, Grade 3 decreased ejection fraction occurred in 2.6% of the 77 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram. Grade 3 decreased ejection fraction occurred in 3.4% of the 263 patients who received QINLOCK and who had a baseline and at least one post-baseline echocardiogram.

In INVICTUS, cardiac dysfunction led to dose discontinuation in 1.2% of the 85 patients who received QINLOCK. The safety of QINLOCK has not been assessed in patients with a baseline ejection fraction below 50%. Assess ejection fraction by echocardiogram or MUGA scan prior to initiating QINLOCK and during treatment, as clinically indicated. Permanently discontinue QINLOCK for Grade 3 or 4 left ventricular systolic dysfunction.

Visit QinlockHCP.com to learn more

Overall survival (OS) with QINLOCK® (ripretinib): 15.1 months vs 6.6 months with placebo[1]*

SECONDARY ENDPOINT: OS[1]



Number of patients at risk

QINLOCK	85	81	76	67	42	24	10	2	0
Placebo	44	34	29	24	14	8	1	1	0

64%
risk reduction of death vs placebo[1]

HR=0.36 (95% CI, 0.21–0.62)*

*Not evaluated for statistical significance as a result of the sequential testing procedure used for the secondary endpoints of ORR and OS.[1]

Upon disease progression, patients on placebo could cross over to receive open-label QINLOCK. An exploratory analysis of OS in placebo crossover patients was conducted.[1,2†]

- Tumor assessments were conducted after each 4-week treatment cycle through the first 4 cycles
- At study cut-off date, 66% of patients had crossed over from placebo and received ≥1 dose of QINLOCK
- Median OS in patients who crossed over to QINLOCK was 11.6 months (95% CI, 6.3-NE) vs 1.8 months (95% CI, 0.9-4.9) in patients who did not cross over

"At 12 months, estimated overall survival was 65.4% (51.6–76.1) for the ripretinib group and 25.9% (7.2–49.9) for the placebo group."[1]

†This analysis was exploratory in nature; it did not control for type 1 error and was not powered to determine treatment effect in any subgroup.
mOS=median overall survival; NE=not estimable.

To read the INVICTUS trial paper, visit QinlockClinicalTrial.com

SELECT SAFETY INFORMATION

Risk of Impaired Wound Healing: QINLOCK has the potential to adversely affect wound healing. Withhold QINLOCK for at least 1 week 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 QINLOCK after resolution of wound healing complications has not been established.

Photosensitivity: QINLOCK may cause photosensitivity reactions. In 621 patients treated with QINLOCK in clinical trials, photosensitivity reactions occurred in 0.6% of patients. Advise patients to limit direct ultraviolet exposure during treatment with QINLOCK and for at least 1 week after discontinuation of treatment.

Please see additional Safety Information throughout.

INVICTUS SHOWS QINLOCK® (ripretinib), A NOVEL SWITCH-CONTROL KINASE INHIBITOR, PROVIDES A POWERFUL PFS BENEFIT IN ADVANCED GIST[1]

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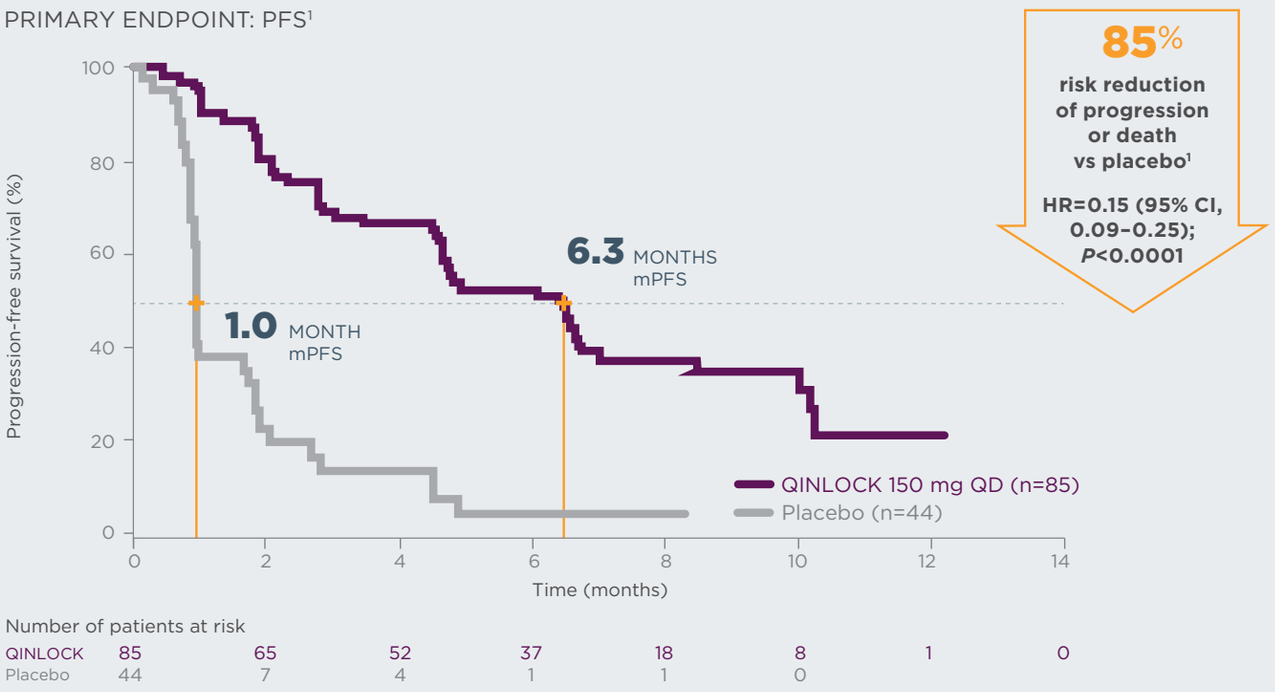
Significant improvement in median PFS with QINLOCK vs placebo: 6.3 months vs 1.0 month (*P*<0.0001)[1]*

PRIMARY ENDPOINT: PFS[1]



Number of patients at risk

QINLOCK	85	65	52	37	18	8	1	0
Placebo	44	7	4	1	1	0		

*Double blind period.

Most QINLOCK-treated patients were able to start and stay on the full indicated dose[2]

- 93% **did not** experience a dose reduction due to an adverse reaction
- 92% **did not** discontinue QINLOCK due to an adverse reaction

Serious and common adverse reactions[2]

- Serious adverse reactions occurring in >2% of patients were abdominal pain (4.7%), anemia (3.5%), nausea (2.4%), and vomiting (2.4%)
- The most common adverse reactions (≥20%) were alopecia (52%), fatigue (42%), nausea (39%), abdominal pain (36%), constipation (34%), myalgia (32%), diarrhea (28%), decreased appetite (27%), PPES (21%), and vomiting (21%). The most common Grade 3 or 4 laboratory abnormalities (≥4%) were increased lipase (7%) and decreased phosphate (5%)

SELECT SAFETY INFORMATION

Embryo-Fetal Toxicity: QINLOCK can cause fetal harm when administered to a pregnant woman. 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 and for 1 week after the last dose. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment and for 1 week after the last dose. QINLOCK may impair fertility in males of reproductive potential.

Adverse Reactions: The most common adverse reactions (≥20%) were alopecia, fatigue, nausea, abdominal pain, constipation, myalgia, diarrhea, decreased appetite, PPES, and vomiting. The most common Grade 3 or 4 laboratory abnormalities (≥4%) were increased lipase and decreased phosphate.

The safety and effectiveness of QINLOCK in pediatric patients have not been established.

Administer strong CYP3A inhibitors with caution. Monitor patients who are administered strong CYP3A inhibitors more frequently for adverse reactions. Avoid concomitant use with strong and moderate CYP3A inducers. If a moderate CYP3A inducer cannot be avoided, increase QINLOCK dosing frequency from the recommended dose of 150 mg once daily to 150 mg twice daily during the co-administration period. If the concomitant moderate CYP3A inducer is discontinued, resume QINLOCK dosage back to 150 mg once daily 14 days after the discontinuation of the moderate CYP3A inducer.

Please see accompanying full Prescribing Information, including Patient Information.

To report SUSPECTED ADVERSE REACTIONS, contact Deciphera Pharmaceuticals, LLC, at 1-888-724-3274 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

References: 1. Blay JY, Serrano C, Heinrich MC, et al. Ripretinib in patients with advanced gastrointestinal stromal tumours (INVICTUS): a double-blind, randomised, placebo-controlled, phase 3 trial. *Lancet Oncol.* 2020;21(7):923-934. **2.** Qinlock [package insert]. Waltham, MA: Deciphera Pharmaceuticals, Inc; 2022.

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