Nexavar® (sorafenib) – Stivarga® (regorafenib):
Improving survival in HCC

The most common form of primary liver cancer is hepatocellular carcinoma (HCC)[1]

>841,000 cases of liver cancer are diagnosed each year[2]

75 - 85% of liver cancers worldwide are HCC[3]

4th leading cause of cancer-related deaths globally[3]

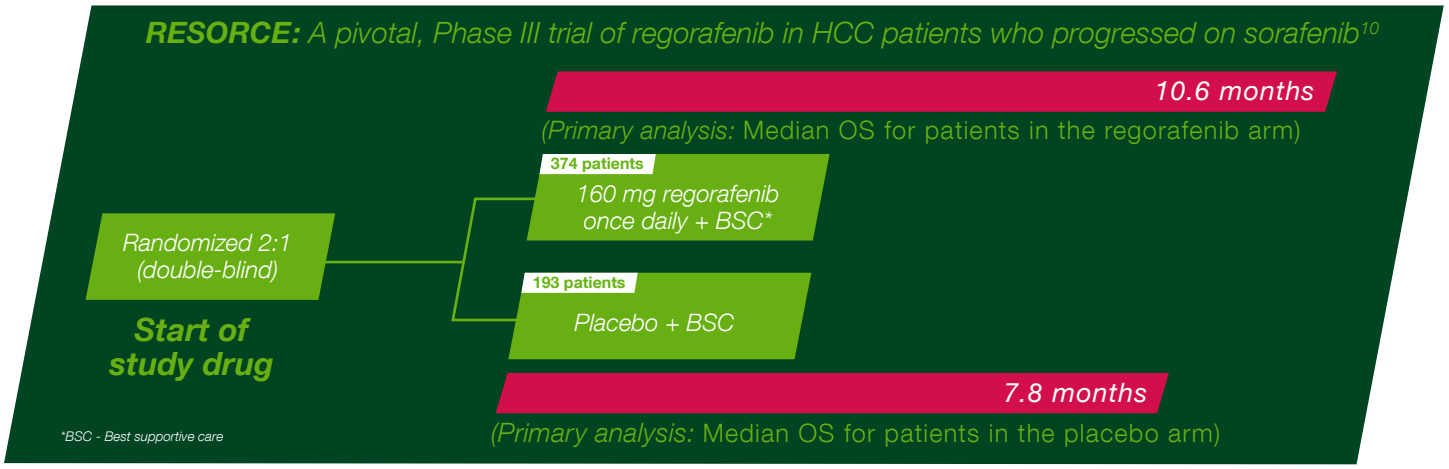
2007
Sorafenib (marketed as Nexavar®) is approved for the treatment of certain forms of unresectable HCC.[4,5]

2017
Regorafenib (marketed as Stivarga®) is approved for the second-line treatment of patients with HCC who have been previously treated with sorafenib.[6,7]

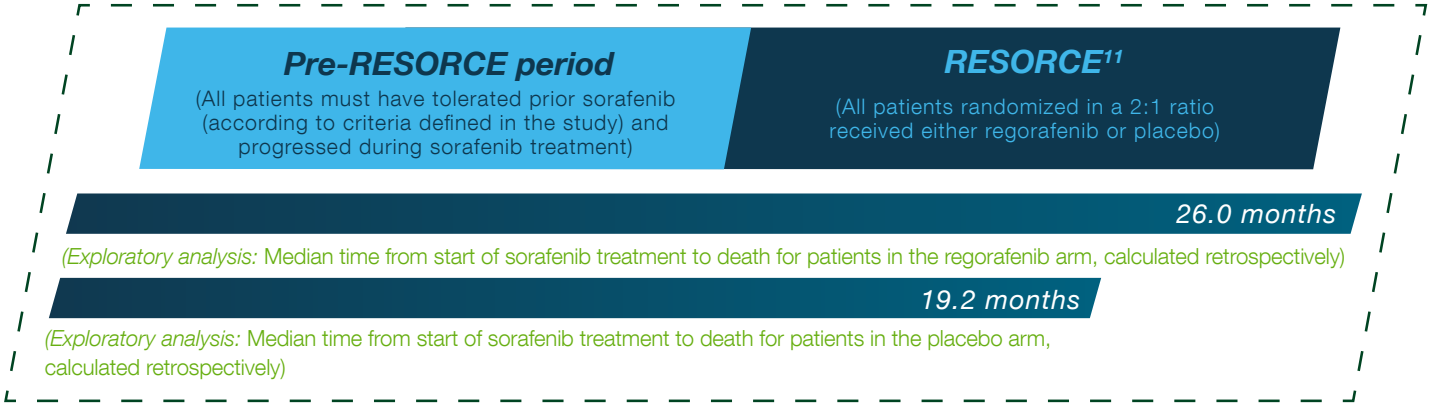
Regorafenib for second-line HCC is recommended by clinical guidelines worldwide, including **EASL*** in **Europe** and the **NCCN*** in the **U.S.**[8,9]

In the primary analysis of RESORCE, regorafenib significantly improved median OS (overall survival) in second-line HCC:

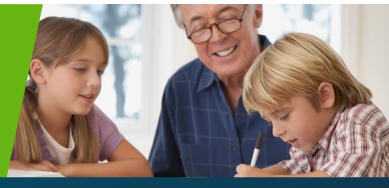
***RESORCE:** A pivotal, Phase III trial of regorafenib in HCC patients who progressed on sorafenib[10]*



Exploratory analysis on the sequence of sorafenib followed by regorafenib or placebo:[11]



Results from the exploratory, retrospective analysis based on the **pivotal Phase III RESORCE trial** suggests that patients with advanced HCC treated with **sorafenib followed by regorafenib** had a median time from the start of sorafenib treatment to death of **26.0 months**, compared with **19.2 months** for those treated with **sorafenib followed by placebo.**[11]



Safety Results: The safety and tolerability were generally consistent with the known profile of regorafenib.[11]

The most common adverse events (grade 3 or greater) occurring more frequently in the regorafenib group included hypertension, hand-foot skin reaction, fatigue, hypophosphatemia, lipase increase, platelet count decrease and diarrhea.[11]

*EASL - European Association for the Study of the Liver, NCCN - National Comprehensive Cancer Network

References: 1. American Cancer Society. Liver Cancer. 2019. Available at: www.cancer.org/cancer/liver-cancer/about/what-is-liver-cancer.html. Accessed August 2020. **2.** GLOBOCAN 2018: Liver Cancer Factsheet. Available at: http://gco.iarc.fr/today/data/factsheets/cancers/11-Liver-fact-sheet.pdf. Accessed August 2020. **3.** Bray F, Ferlay J, *et.al.* Global Cancer Statistics 2018: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2018 Nov;68(6):394-424. doi: 10.3322/-caac.21492. Epub 2018 Sep 1. **4.** Bayer HealthCare Pharmaceuticals Inc. Nexavar (Sorafenib). 2018. U.S. Food and Drug Administration website. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2018/021923s020lbl.pdf. Accessed August 2020. **5.** European Medicines Agency. 2020. Nexavar: Product information. 2019. Available at www.ema.europa.eu/en/medicines/human/EPAR/nexavar. Accessed August 2020. **6.** Bayer HealthCare Pharmaceuticals Inc. Stivarga (Regorafenib). 2018. U.S. Food and Drug Administration website. Available at: www.accessdata.fda.gov/drugsatfda_docs/label/2012/203085lbl.pdf. Accessed August 2020. **7.** European Medicines Agency 2020. Stivarga: Product information. 2019. Available at www.ema.europa.eu/en/medicines/human/EPAR/stivarga. Accessed August 2020. **8.** European Association for the Study of the Liver. EASL Clinical Practice Guidelines. J Hepatol 2018;69:182–236. **9.** National Comprehensive Cancer Network. NCCN Guidelines Version 5.2020. Hepatocellular Carcinoma. Available at: www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed August 2020. **10.** Bruix J, Qin S, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2017;389(10064):56–66. **11.** Finn RS, Merle P, et al. Outcomes of sequential treatment with sorafenib followed by regorafenib for HCC: Additional analyses from the phase III RESORCE trial. J Hepatol 2018;69(2):353–358.

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