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SWOG Study Shows Strong Long-Term Survival Rates for Patients with GIST

PORTLAND, OR – Nine years ago, SWOG researchers confirmed a new standard of care for patients with incurable gastrointestinal stromal tumors (GIST), who could survive by being treated with imatinib mesylate, the breakthrough drug marketed as Gleevec. SWOG researchers are back with long-term findings from that study, which estimate that nearly one in four patients treated with Gleevec will survive 10 years. Results are published in *JAMA Oncology*.

"This is a really exciting finding," said Dr. Michael Heinrich, a SWOG investigator and a professor of medicine and cell and developmental biology at Oregon Health & Science University, where SWOG is based. "Until Gleevec arrived on the scene 15 years ago, patients with advanced GISTs faced a life expectancy of 18 months. Now we've learned that some might live a decade or longer. And we've come to understand which class of patients benefit the most from Gleevec."

In new study results published in *JAMA Oncology*, researchers from SWOG, the international cancer research community supported by the National Cancer Institute, report a follow-up of patients originally enrolled in S0033, a SWOG-led trial supported by other groups in the NCI's National Clinical Trials Network (NCTN). This was a Phase III study that began in 2000. Initial results published in 2008 confirmed Gleevec as an effective treatment for advanced GIST patients, and recommended that therapy start with a 400 mg daily dose. The SWOG team decided to collect post-study data on S0033 patients, and from 2011 to 2015 gathered information. As part of their research, the team used next-generation DNA sequencing on some tumor tissue samples taken for S0033, which had been deposited in a biospecimen bank. The team reanalyzed tissue from 20 patients originally classified as having a wild-type tumor – one without any mutations of KIT, a gene implicated in 85 to 88 percent of all GISTs.

Analysis showed that of the 695 eligible patients originally enrolled in S0033, 189 survived eight years or longer, with a 10-year estimate of overall survival of 23 percent, or nearly one in four patients. DNA sequencing also showed that survival rates were significantly higher for patients with a KIT exon-11 mutant GIST, when compared with patients whose tumor had a KIT exon-9 mutation or with no KIT mutations or mutations in the platelet-derived growth factor receptor gene, or PDGFRA.

"Our findings show two things," Heinrich said. "One is that Gleevec has revolutionized treatment for patients with advanced GISTs. Our findings also highlight the importance of banked biospecimens to drive new scientific findings, and how tumor mutation testing can optimize treatment for cancer patients."

GISTs are different from more common types of gastrointestinal tumors because of the type of tissue in which they start. GISTs belong to a group of cancers called soft-tissue sarcomas. Soft-tissue sarcomas develop in the tissues that support and connect the body, including muscles, nerves, tendons, and joints. GIST is a rare cancer, with about 6,000 new cases diagnosed in the United States each year.

Researchers at Oregon Health & Science University have pioneered the treatment of GISTs. Dr. Brian Druker, director of the OHSU Knight Cancer Institute, conducted the most influential work in the development of Gleevec, and OHSU researchers have been part of major discoveries in the use of the drug to treat GISTs, as well as chronic myeloid leukemia (CML) and acute lymphoblastic leukemia (ALL).

Along with Heinrich, lead author of the *JAMA Oncology* article, the SWOG study team includes: Cathryn Rankin, MS, of Fred Hutchinson Cancer Research Center; Dr. Charles D. Blanke of Knight Cancer Institute; Dr. George Demetri of Dana-Farber Cancer Institute; Dr. Ernest Borden of Cleveland Clinic; Dr. Christopher Ryan of Knight Cancer Institute; Dr. Margaret von Mehren of Fox Chase Cancer Center; Dr. Martin Blackstein of Mount Sinai Hospital; Dr. Dennis Priebat of MedStar Hospital Research Center; Dr. William Tap of Memorial Sloan Kettering Cancer Center; Dr. Robert Maki of Norwell Health and Cold Spring Harbor Laboratory; Dr. Christopher Corless of Knight Cancer Institute; Dr. Jonathan Fletcher of Dana-Farber Cancer Institute; Kouros Owzar, PhD, of Duke University School of Medicine; John Crowley, PhD, of Cancer Research And Biostatistics; Dr. Robert Benjamin of University of Texas MD Anderson Cancer Center; and Laurence Baker, DO, of University of Michigan.

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SWOG is a global cancer research community of over 12,000 members in 47 states and six foreign countries who design and conduct publicly funded clinical trials. Since 1956, SWOG trials have led to the approval of 14 cancer drugs, changed more than 100 standards of cancer care, and saved more than 2 million years of human life. The group is a proud member of the NCI's National Clinical Trials Network and the NCI Community Oncology Research Program, and is a major part of the cancer research infrastructure in the U.S. and the world. Headquartered at the Knight Cancer Institute at Oregon Health & Science University in Portland, Ore., SWOG's Statistics and Data Management Center is based at Fred Hutchinson Cancer Research Center in Seattle, Wash. and its Operations Office is located in San Antonio, Texas. Learn more at swog.org.

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