

100 Questions & Answers About Gastrointestinal Stromal Tumor (GIST)

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PREFACE

Gastrointestinal stromal tumor (GIST) has emerged in recent years as one of the most tremendous success stories in cancer research and therapy. While GIST is an uncommon cancer, it has unique properties making it a model for a new frontier in cancer medicine called “targeted cancer therapy.” These days, patients whose GIST cannot be surgically cured are enjoying dramatically better chances of survival and control of their disease due to new breakthrough drugs. In addition to being far more effective than older forms of cancer therapy (chemotherapy), these new drugs have important practical benefits: they can be taken by patients at home as oral pills or capsules, and they are reasonably well tolerated so that patients can enjoy acceptable quality of life over the course of years of continuous treatment. The revolutionary advancements in the care of GIST patients are quite remarkable when we consider that even less than ten years ago, doctors lacked reliable methods to accurately diagnosis GIST, and worse yet, there was nothing at all in the arsenal of standard anti-cancer therapies that could treat GIST effectively. But with the arrival of imatinib in the first clinical trials for GIST in the year 2000 as the first targeted cancer therapy, and the introduction of sunitinib in 2002 as a second option for GIST patients if imatinib fails, the outlook for GIST patients has improved dramatically. This once “orphan disease” and overlooked cancer has gained wide recognition in recent years as the topic of plenary lectures at professional oncology conferences and as the subject of medical news stories in the popular news media.

A new GIST diagnosis brings to patients and their families not only many personal adjustments, but also the challenges of learning new medical concepts and making decisions about the best medical care. Patients and families want to retain some measure of control over their own situation and be their own advocates in the health care system. Gathering practical information and knowing enough to ask the right questions of your doctor and health care team are both aspects of dealing with cancer. We wrote *100 Questions & Answers About Gastrointestinal Stromal Tumor (GIST)* to give

our readers an overview of the major and sometimes novel concepts that have become very relevant to GIST patients in recent years. We have tried to provide simple yet accurate explanations about the biology of GIST and how targeted cancer therapies block the major defects that are responsible for the cancerous behavior of GIST cells. The advent of targeted therapies for GIST in recent years has also brought a new set of considerations for doctors and patients regarding the optimal way to manage the disease and how to evaluate the clinical response of GIST to these drugs. We appreciate that a GIST diagnosis brings many new psychological, social, and working concerns to a family's daily routine. We share with you some of the emotional insights and practical tips that might help you and your friends and relatives cope better with your diagnosis.

So what are important things for a newly diagnosed GIST patient to keep in mind? First, many patients with early GIST that is limited to one part of the body may still be cured by expert surgery alone. However, even when surgeons cannot cure a patient with more advanced GIST, this disease is now manageable as a long-term, chronic condition for many patients. GIST patients are able to lead fairly normal lives with only mild side effects from their targeted cancer therapy. Still we should point out that GIST remains a serious and potentially life threatening disease. Patients diagnosed with GIST need to be committed to take their oral cancer drugs, and to be vigilant about having routine medical check ups for many years to come.

The authors of this book represent the combined voices of a surgical oncologist, a GIST patient, and a medical oncologist. In addition, a registered nurse provided editorial guidance and additional material for this volume. Each of us brings to this project a unique perspective as either a health care professional or a GIST patient.

The Surgeon's Journey with GIST before and after Imatinib

Ronald DeMatteo, MD, became interested in GIST in 1998 because of the lack of effective therapies for it. In fact, surgery was used quite commonly at that time for patients with metastatic GIST since conventional chemotherapy was essentially ineffective. While he and his colleagues were

trying to develop a new approach using intraperitoneal chemotherapy for metastatic GIST, it became clear that a new agent then known as “STI571” (now called imatinib mesylate) was efficacious. Dr. DeMatteo went on to lead 2 national clinical trials of adjuvant imatinib after the resection of primary GIST. These trials are sponsored by the National Cancer Institute and Novartis Pharmaceuticals and are being led by the American College of Surgeons Oncology Group. He, along with a team of investigators at Memorial Sloan-Kettering Cancer Center, have contributed to our current understanding of the clinical management of patients with primary or metastatic GIST and the mechanism of imatinib resistance.

The Patient’s Journey with GIST before and after Imatinib

Marina Symcox, PhD, is a retired biochemist who was diagnosed at age 38 years with advanced terminal GIST in 1997. She fought a losing battle against GIST in the era of the late 1990’s before the arrival of effective therapies. At one point she spent eight months in hospice and came close to death. In 2000, she became one of the first patients in the world to receive imatinib as an experimental drug. Continuing with six years of successful imatinib therapy, she has recovered to lead a normal and active life. In the nine years since her diagnosis, Marina has been an active member of Internet support groups for patients. Marina has brought to *100 Questions & Answers About Gastrointestinal Stromal Tumor (GIST)* her insights regarding what patients on the Internet would like to know about GIST biology, treatments, and coping in the face of terminal disease.

The Medical Oncologist’s Journey with GIST before and after Imatinib

George Demetri, MD, has spent the majority of his professional career developing new drugs against solid tumors such as GIST and other sarcomas. Working with a network of colleagues across the world, Dr. Demetri’s team was the first to give imatinib to patients with GIST, and later followed similar scientific paths to successfully treat imatinib-resistant GIST patients with sunitinib. Dr. Demetri has brought together a coalition of investigators

and universities globally with support from large pharmaceutical firms including Novartis and Pfizer, smaller biotechnology firms such as Sugen and Infinity, as well as the U.S. National Cancer Institute and the philanthropic foundation of the Ludwig Trust for Cancer Research. The work from this team has formed the basis for the U.S. Food and Drug Administration (FDA) approval of imatinib and sunitinib as safe and effective therapies for GIST, and is also forming the foundation of future research to improve further the effectiveness of targeted cancer therapies.

We would like to extend a warm thank you to Chris Davis, Executive Publisher for the medical list at Jones and Bartlett Publishers, Inc. His unwavering encouragement for this project, from the time it was conceptualized 2 years ago, deserves recognition as the keystone between concept and implementation that has brought this book to GIST patients and their families.

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