the NIH Pediatric & Wildtype GIST Clinic

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Abstract

INTRODUCTION
Gastrointestinal stromal tumor (GIST) is a rare disorder and only a small fraction of affected patients are children. The rarity of this tumor, combined with biological differences between children and adults with GIST, have made it difficult to study the natural history of this disorder and to determine the best therapy for pediatric patients. In an effort to help answer this question, we developed the NIH Pediatric and wildtype GIST clinic. This clinic is a collaborative effort to bring together patients and medical specialists in an effort to better understand the pathogenesis of GIST and to develop the best treatment alternatives for these patients.

METHODS
Announcement of the clinic was posted on the websites of two GIST support groups, LifeRaft Group and GIST Support International. The first clinic took place on June 19th 2008.

RESULTS
Twenty-one patients registered on-line, of which 14 were seen in the inaugural clinic. Our patients included 10 females and 4 males. The average age of the patients was 21.5 (range 11-35, median 21), age at the time of first symptoms was 15.1 (range 9-21) and the age at the time of diagnosis was 16.4 (range 9-22). Histological subtype was available for 13 patients (1 epithelioid, 4 spindled, 8 mixed epithelioid and spindled). Eleven patients had sequencing of their tumor samples and all eleven had wildtype *KIT*.

CONCLUSIONS
These patients represent the largest cohort of children and young adults with GIST. We will present the results of what we have learned from this clinic. This includes histological, molecular, radiographic results and response to different treatment regimens.

What is CPGR

CPGR is the **C**onsortium for **P**ediatric and wildtype **G**IST **R**esearch. It is composed of basic science investigators, clinical researchers and patient advocates who have an interest in GIST. CPGR members attend the Pediatric and wildtype GIST clinics hosted by the NIH. This allows members to discuss the current state of pediatric GIST research and medicine and identify areas and initiatives to move the field forward. All clinicians and researchers with an interest in Pediatric or wildtype GIST are encouraged to join CPGR.

CPGR meets twice yearly, at the NIH. The 2nd Pediatric and wildtype GIST Clinic will take place on January 22nd and 23rd.

Our hope is to see all patients with Pediatric or wildtype GIST at one of these clinics.

CPGR Consortium for Pediatric and GIST Research

CPGR Members

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Introduction

The Pediatric and wildtype GIST clinic at the National Institutes of Health (NIH) is a collaborative effort between clinicians, research scientists and patient advocates, who share the goal of helping young patients with Gastrointestinal Stromal Tumor (GIST).

Our mission:

- Bring together all patients with Pediatric or wildtype GIST with health care providers in the field
- Utilize the resources of the NIH to bridge shortcomings in basic and clinical research
- Provide storage of tumor samples, that can then be accessed by researchers throughout the world
- Disseminate new information in the field of Pediatric and wildtype GIST
- Develop innovative treatment protocols

Our focus is to compile the medical histories of all patients with Pediatric or wildtype GIST seen in our clinic, in order to determine if there are any common elements in this rare group of patients. The goal is utilize this information to design rational therapeutic protocols. We have stressed to all clinic participants that we will immediately relay all of our information to the patient's primary oncologist.

As the first step towards this goal, we have established the **C**onsortium for **P**ediatric and wildtype **G**IST **R**esearch (CPGR)

We have also opened a website dedicated to Pediatric and wildtype GIST - **www.pediatricgist.cancer.gov**

Patients who wish to register for subsequent clinics at the NIH should contact - ncipediatricgist@nih.mail.gov

On clinic day 1, patients will have the opportunity to meet health care specialists in a variety of fields, such as dermatology, genetics, nutrition, pain management and psychosocial services. On clinic day 2, patients will meet with members of CPGR. Throughout the day, there will be a series of seminars that address subjects such as alternative/complementary approaches, nutrition tips, recreational/art therapy and relaxation techniques.

Results

Summary of patients on tyrosine kinase inhibitors (also described in Patient Characteristics section)
(excludes patients who have been on therapy for less than 6 months) (the doses that patients received also vary)

Nilotinib 2 patients with progressive disease have recently started Nilotinib (currently 2 and 7 months)
1 patient had stable disease (8 months), but then had abdominal complications possibly related to Nilotinib and discontinued
Sunitinib 1 patient with a second recurrence in the stomach has stable disease (currently 24 months)
3 patients progressed (6, 8 and 9 months) and 1 patient discontinued Sunitinib due to intolerance (6 months)
1 patient had stabilization of disease (22 months), but discontinued in order to monitor tumor status off therapy
Imatinib 2 patients appear to have slowing of progression of disease on Imatinib (currently 16 and 21 months)
2 patients with complete resection stopped (17 and 29 months), due to lack of data on the optimal duration of therapy
1 patient discontinued Imatinib due to intolerance (6 months)
Dasatinib 1 patient who progressed quickly through all three of the above tyrosine kinase inhibitors has recently started Dasatinib

In our first cohort, ten patients have isolated GIST
One patient has Carney's Triad (GIST, paraganglioma, pulmonary chondroma), two have GIST and pulmonary chondroma
One patient has Carney-Stratakis syndrome (CSS) which is the dyad of GIST and paraganglioma
- Dr Stratakis and others have shown that CSS is a familial disorder, and that these patients have germline mutations in subunits of the succinate dehydrogenase (*SDH*) gene
- In order to help define the biology that underlies GIST, all of the patients who participated in the first clinic consented to sequencing of *SDH* from blood samples to determine if patients with isolated GIST have *SDH* mutations

In this cohort, we advise against radical surgery such as complete gastrectomy. This is based on the high probability for severe gastrointestinal complications, with little potential that radical surgery alone will prevent recurrence.

Many members of CPGR have independently shown that patients with wildtype GIST have much higher levels of the insulin-like growth factor receptor 1 (IGF-1R) in their tumor samples, which has provided the impetus for a clinical trial.

Ongoing Projects

Assessment of germline mutations in subunits of the succinate dehydrogenase gene in isolated GIST and CSS patients
Longitudinal measurement of tumor size on radiographic scans to determine the rate of tumor growth in younger patients
Development of a treatment protocol using IGF-1R antibody in patients with wildtype GIST (PIs : Janeway, von Mehren)

Patient Characteristics

Gender	Age (yrs)	Age at first symptoms	Age at diagnosis	Years since diagnosis	Current therapy	Site - size	Multi focal	Metastatic sites	Sites of recurrence	Time to recurrence	Paragang liomas	Chond romas	Histology	Molecular	Surgery	Imatinib	Sunitinib	Nilotinib	Other	Radiology
M	11	9	9	2	none	stomach - 9cm	yes - 5	none	NED	n/a	no	no	mixed	wildtype	one	2 months trial				CT
F	15	11	11	4	none	abdomen	yes	stomach	never NED	n/a	yes	yes	spindled	wildtype	ten	29 months duration length				PET/CT
F	16	10	10	6	Sutent	stomach - 14cm	yes - 3	none	stomach x1 stomach x2	22 months 18 months	no	no	mixed	wildtype	two	5 months intolerance	24 months on now			PET/CT
M	18	11	12	6	none	stomach - 15cm	no	none	stomach, liver	24 months	no	no	spindled	wildtype	three					PET/CT
F	18	12	14	4	Nilotinib	abdomen	yes	abdominal	never NED	n/a	no	yes	mixed	wildtype	two	6 months intolerance	6 months intolerance	2 months on now		PET/CT
F	20	15	17	3	none	abdomen, pelvis, liver	yes	multiple	never NED	n/a	no	no	mixed	wildtype	four	2 months progressed	6 months progressed	8 months stabilized	2 months OSI-930	CT
M	20	18	18	2	none	stomach - 8cm	yes	none	NED	n/a	no	no	spindled	wildtype	one					PET/CT
F	22	13	16	6	none	stomach - 4cm	yes	none	stomach	38 months	no	maybe	mixed	wildtype	three	2 months no PET response	3 months trial			PET/CT
F	22	21	21	1	Dasatinib	stomach	yes	liver	never NED	n/a	no	no	not described	not performed	one	1 month progressed	8 months progressed	4 months progressed	2 months IPI-504	CT
F	23	16	18	5	Gleevac	stomach - 6cm	no	none	liver	41 months	yes	no	mixed	not performed	two	21 months on now			12 months placebo	PET/CT
F	23	20	22	1	none	stomach - 6cm	yes - 2	none	NED	n/a	no	no	epithelioid	not performed	one	17 months duration length				PET/CT
M	27	22	22	5	Gleevac	stomach - 6cm	yes	duodenum lymph node	lymph node	45 months	maybe	no	mixed	wildtype	one	16 months on now				PET/CT
F	31	20	20	11	Nilotinib	abdomen	yes	liver	never NED	n/a	no	no	mixed	wildtype	one	3 months intolerance	9 months progressed	7 months on now	19 months Gleevec/Rapa	CT
F	35	20	20	15	none	stomach - 3cm	no	none	liver	12 years	no	no	spindled	wildtype	one	18 months stabilized	22 months stabilized			MRI