2020 VIRTUAL MEETING

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The NEW HORIZONS GIST Patient Advocacy Roundtable:
Improving access to treatment and quality of care through global exchange.

For several years now NEW HORIZONS GIST is the most important global annual conference for GIST patient advocates. Due to the current coronavirus pandemic, the 2020 New Horizons GIST conference was held planned and held as a virtual conference – the first-ever virtual New Horizons GIST meeting.

With more than 60 people from more 30 countries around the globe attending, it was the largest New Horzions GIST meeting ever.

The 2020 conference was chaired and planned by a steering committee and Sarcoma Patients EuroNet e.V./Assoc.

- Piga Fernandez, Alianza GIST (Chile)
- David Josephy, Life Raft Group (Canada)
- Ginger Sawyer, GIST Support International (USA)
- Norman Scherzer, The Life Raft Group (USA)
- Markus Wartenberg, Deutsche Sarkom-Stiftung (Germany)
- Martin Wettstein, Swiss GIST Group (Switzerland)

- Supported by: Sara Rothschild, Laura Occhiuzzi (LRG, USA), Tanja Ullersberger (Deutsche Sarkom-Stiftung/German Sarcoma Foundation)
- Organised by SPAEN: Michi Geissler& Kathrin Schuster

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Acknowledgement

We would like to thank the following funders who supported NEW HORIZONS GIST 2020 with an unrestricted educational grant:

Initial Funder of NEW HORIZONS: NOVARTIS

Supporter: blueprint MEDICINES, decīphera

At the request of the Steering Committee, NEW HORIZONS GIST received grants from these three companies. This funding is not related to any objectives/content of the Virtual Conference 2020. The idea, planning, preparation, realization, management and the summary of the NEW HORIZONS GIST 2020 Conference are the responsibilities of the Steering Committee and Sarcoma Patients EuroNet (SPAEN) without any influence from the sponsors/funders. We are looking forward to continuing these open and transparent partnerships with the healthcare industry towards achieving our goal of collaboration among independent GIST patient organizations on an international level.

We also would like to thank our friends/colleagues from the medical GIST Expert Community. Thank you very much for agreeing to speak at NEW HORIZONS GIST 2020. We very much appreciate that you are taking time out of your very busy schedules to join us for our first Virtual NEW HORIZONS meeting. We are very grateful for the valuable, trustful and long-term partnership between leading medical GIST experts worldwide and the Global GIST patient advocacy community.

This report was written by members of the Steering Committee, the Life Raft Group and Sarcoma Patients EuroNet (SPAEN)

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New Horizons GIST 2020:
Report of the first-ever virtual NH GIST conference

The first-ever virtual New Horizons GIST Meeting was held from **Thursday September 10th to Saturday, September 12, 2020**. The meeting was originally planned for Berlin, Germany, but was reorganized to be held virtually due to the coronavirus pandemic.

At the New Horizons (NH) GIST conferences, participants traditionally focus on discussing critical information about GIST that impacts the global GIST patient and medical communities. Participants have opportunities to interact with leading GIST experts, learn new medical and scientific information about GIST, exchange best practices and discuss advocacy issues.

This year's New Horizons GIST Meeting was dedicated our dear friend, colleague in the SPAEN Board of Directors, GIST patient and patient advocate **Dr. Nikhil Guhagarkar**. Nikhil sadly passed away in May 2020.

Markus Wartenberg, of the German Sarcoma Foundation/SPAEN and NH Steering Committee Member, launched this 17th meeting of New Horizons GIST with a gracious welcome and opening notes: "We are delighted that we will have a very interesting programme over 3 half days with a great group of leading speakers providing their knowledge about diagnosis, treatment and care of GIST and the possibility to discuss the challenges and needs of the Global GIST Community."

But who are the participants of the New Horizons GIST 2020 virtual meeting? A short online survey revealed this:

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1. From which continent are you participating today?

Africa	(2) 4%
Antarctica	(0) 0%
Asia	(7) 16%
Australia	(0) 0%
Europe	(21) 47%
North America	(12) 27%
South America	(3) 7%
Alien. Sorry I'm not from this planet...	(0) 0%

2. Which group of people do you represent? I´m a (Mehrfachauswahl)

GIST patient	(11/45) 24%
GIST-Patient and Patient Advocate	(15/45) 33%
Caregiver/Relative	(5/45) 11%
Caregiver/Relative and Patient Advocate	(6/45) 13%
Patient Advocate	(16/45) 36%
Medical Expert / Physician	(4/45) 9%
Pharma Representative	(5/45) 11%
Am wrong here!	(1/45) 2%

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3. How many New Horizons Face to Face Meetings have you attended so far?

All 17 conferences (conference dinosaurs)	(1) 2%
13-16 meetings (conference dinosaurs)	(7) 16%
9 - 12 meeting (repeat offenders)	(2) 4%
5 - 8 meetings (repeat offenders)	(5) 11%
1 - 4 meetings (repeat offenders)	(13) 29%
This is my first meeting (conference virgin)	(17) 38%

Industry representatives of the conference sponsors Novartis, Blueprint Medicines, and Deciphera welcomed the GIST patient community as well, highlighting the important role patient advocacy plays especially in a rare disease like GIST and the fruitful collaboration between the patient community and the healthcare industry.

NOVARTIS

blueprint MEDICINES

decīphera

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The programme: 9 GIST Episodes

The programme for the New Horizons GIST conference encompasses 9 so-called "GIST Episodes" – one for each important topic and milestone throughout the journey with GIST. All 9 GIST Episodes have been recorded and have been made available here.

Special thanks to our dedicated speakers of New Horizons GIST 2020:


Dr. Albiruni Razak, Canada


Dr. David Josephy, Canada


Dr. Breelyn Wilky Denver, USA


Dr. Peter Reichardt, Germany


Dr. Gina D'Amato, USA


Dr. Ramesh Bulusu, UK


Dr. Jonathan Trent, USA


Dr. Robin Jones, UK


Prof. Hans Gelderblom, The Netherlands


Dr. Ruth Casey, UK

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Thursday, September 10, 2020

Day 1 was dedicated to an introduction and overview of the disease, basic knowledge on pathology, biology and genetics as well as the situation if the tumor is localized and operable.

Prof. Hans Gelderblom, The Netherlands

Dr. David Josephy, Canada

Dr. Peter Reichardt, Germany

GIST Episode 1: Introduction – Overview

The first session was moderated by **Martin Wettstein** from the **Swiss GIST group "GIST Gruppe Schweiz"**, GIST patient and advocate, and also a Steering Committee Member. **Prof. Hans Gelderblom**, a medical oncologist from **Leiden University Medical Center, The Netherlands**, addressed the following questions in his presentation "What is GIST?", "How is it treated?" and "What are the current developments?". He spoke about the frequency of GIST, its unique characteristics and clinical presentation as well as the structure and biology of c-KIT. He continued with a general review of treatments and molecular pathology.

View his talk here.
Download his presentation here.

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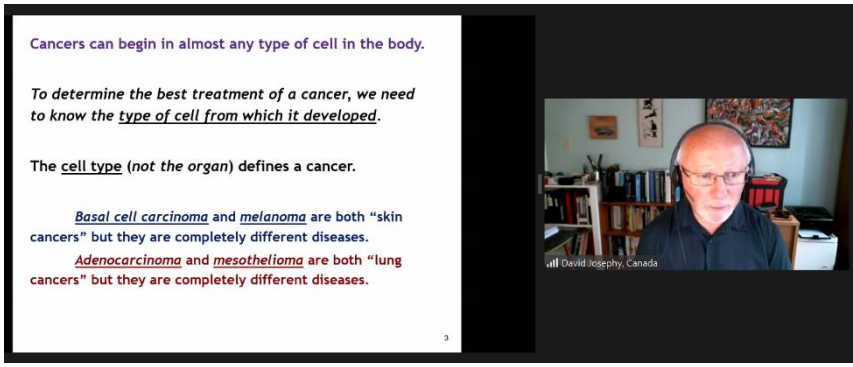
GIST Episode 2: Biology – Genetics – Pathology

In session two, **Dr. David Josephy** from the GIST Sarcoma **Life Raft Group Canada**, presented an overview of the biology, genetics and pathology of GIST. David Josephy was a Professor of Molecular and Cellular Biology at the University of Guelph in Ontario, Canada, until his recent retirement (2020). He is the author of a textbook, "Molecular Toxicology", and has published more than 100 scientific articles in the fields of biochemistry, toxicology, and cancer research.

Dr. Josephy explained the distinction between (common) carcinomas and (rare) sarcomas. GI tract physiology was discussed, explaining the role of peristalsis in digestion, and its coordination by the interstitial cells of Cajal (pacemaker cells), which are believed to be the cells of origin of GISTs. The fundamentals of molecular biology were presented, emphasizing the relationship between proteins and DNA (genes). The discovery of oncogenes raised the prospect of targeted therapy for cancer, but it took many years to bring this approach to clinical practice, with imatinib being one of the first successes. The biochemistry of tyrosine kinases and tyrosine kinase inhibitors were explained, with the role of KIT protein in GIST as the important example. Immunohistochemistry (IHC) and mutational testing are critically important tools for defining the biology and treatment of a GIST, but they are very different tests, addressing different questions and giving different answers. IHC verifies expression of KIT and DOG1, marker proteins that identify a tumour as a GIST. Mutational testing distinguishes between distinct forms of GIST driven by different classes of driver mutations, which can occur at many different sites in the KIT gene (exon 11, exon 9, etc.), affecting many different sites in the KIT protein, and GIST driver mutations can also occur in genes other than KIT: PDGFRA, SDH, BRAF, NTRK, etc. The structure of KIT gene and protein were outlined, explaining the terminology of exons and domains. Exon 11 encodes the juxtamembrane domain of KIT and is the most common site of mutations in GIST. Mutation terminology, as seen on pathology and gene-sequencing reports, was explained.



View his talk here.
Download his presentation here.

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GIST Episode 3: Localized, operable primary tumor

With the last session of day one, **Markus Wartenberg** of the **German Sarcoma Foundation** introduced a pre-recorded presentation by **PD Dr. Peter Reichardt, Sarcoma Center Berlin-Brandenburg, Germany**. Dr. Reichardt discussed therapy options and decisions in the situation of a localized and operable primary disease: After a brief history of the disease, Dr. Reichardt dove right into the various clinical decisions for the treatment of a GIST patient, ranging from surgery and the possibility of neo-adjuvant treatment and its aims to risk classification as basis for the initiation of adjuvant therapy. He highlighted recently published 10-year-data of a study that compared one year vs. three years of adjuvant GIST: "Three years of adjuvant imatinib is superior in efficacy compared to one year of imatinib. We found that about 50% of deaths can be avoided during the first 10 years of follow-up after surgery with the longer adjuvant imatinib treatment."

View his talk here.
Download his presentation here.

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Friday, September 11, 2020

Day two of the event began with LRG's Sara Rothschild facilitating.

Dr. Albiruni Razak
Toronto, Canada

Dr. Breelyn Wilky
Denver, USA

Dr. Jonathan Trent
Miami, USA

GIST Episode 4: Metastatic (advanced) disease

The first presentation of the day was held by **Dr. Albiruni Razak, Toronto, Canada** about "Initial Therapy in Metastatic Disease", moderated by **David Josephy**. Dr Albi Razak is a Staff Physician and Medical Oncology Sarcoma Site Lead, Princess Margaret Cancer Centre and Mount Sinai Hospital, Toronto, Canada and Associate Professor of Medicine, University of Toronto. His talk was summarized by David Josephy:

- The distribution of GISTs is approximately 60% stomach, 30% small bowel, and 10% other sites (oesophagus, rectum). GIST epidemiology: approximately 450 new cases per year in Canada; prevalence, 129 per million. GISTs may present with symptoms such as pain, bleeding, or weight loss, but many GISTs are discovered incidentally.
- In the metastatic setting, the liver and peritoneum are the most frequently involved organs.
- The treatment of choice for localised disease is surgery, but many patients suffer relapse. The main risk factors are tumour size and mitotic count.
- Dr Razak reviewed the early clinical trials and studies of imatinib therapy.
- Evaluation of GIST patients should be carried out, initially, every 2 or 3 months; the period can subsequently be extended.

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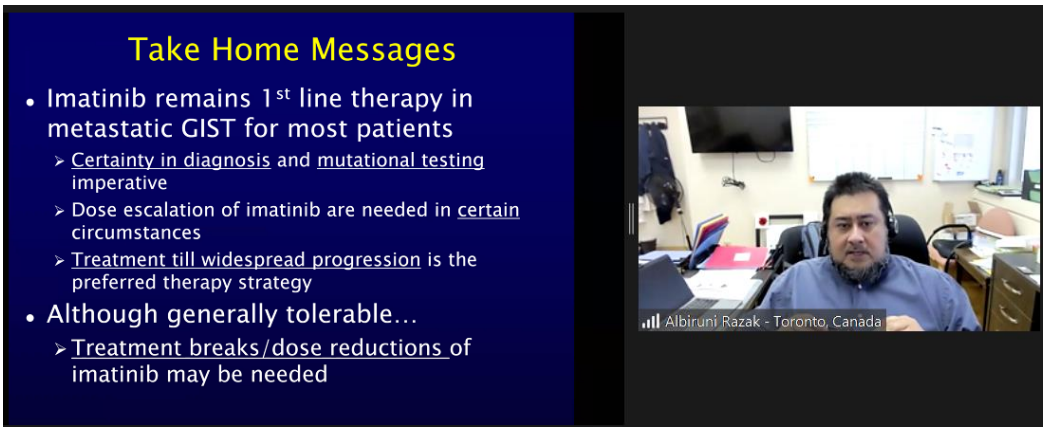
- Abdominal/pelvic CT with contrast is recommended for diagnosis and staging and is also useful for assessing common sites of metastasis (liver, peritoneum).
- Dr. Razak reviewed imatinib toxicities and dose management. Imatinib is metabolized via the P450 pathway, mainly involving CYP3A4 and CYP3A5. Interactions with other drugs and natural products are possible and should be checked with the physician and pharmacist. He noted that community hospitals may miss imatinib drug-drug interactions e.g. with PPIs (proton pump inhibitors), lipitor (statins).
- Dr. Razak reviewed the management of common imatinib toxicities. For GI side effect, antiemetic and anti-diarrhea medications can be prescribed and the doses can be split. For cramps/myalgia: increased fluid intake, salt supplements, analgesics. For rash, topical medication. If high grade toxicities prove intolerable despite supportive therapy, the dose can be reduced.
- Disease progression beyond imatinib: two type of progression can be distinguished, with different therapies. For limited or nodular progression, options include surgical resection, hepatic artery chemoembolization, hepatic radio-frequency catheter ablation, and radiation therapy of esophageal or rectal lesions. For widespread progression, imatinib dose can be increased, or switch to further lines of treatment: Sunitinib/ Regorafenib/ Ripretinib/ clinical trials.
- Dr. Razak stressed these take-home messages:
    - Imatinib remains the first-line therapy in metastatic GIST for most patients.
    - Certainty in diagnosis and mutational testing are imperative.
    - Dose escalation of imatinib is needed in some circumstances.
    - Treatment until widespread progression is the preferred therapy strategy.



View his talk here.
Download his presentation here.

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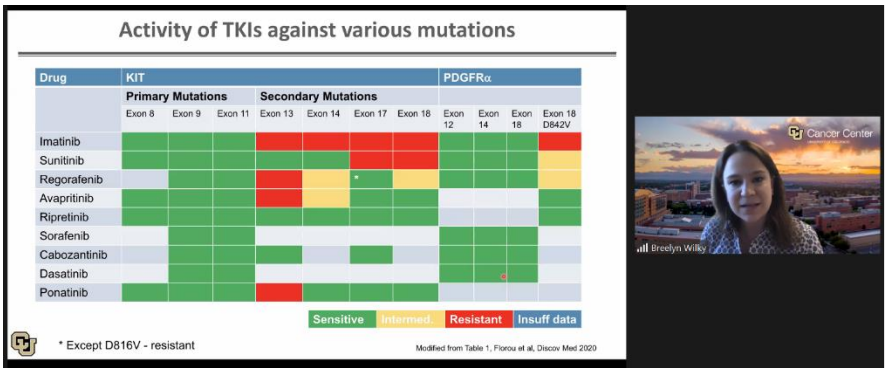
GIST Episode 5: Progression of metastatic disease under drug treatment

This session was moderated **Laura Occhuizzi, Life Raft Group**. **Dr. Breelyn Wilky, Director of Sarcoma Translational Research at the University of Colorado, USA** discussed treatment options for patients with progression.

Dr. Wilky began by discussing the overall biology of progression, and moved on to looking at KIT-resistant mutations, as well as tools to identify these biomarkers. She presented two case studies, each showing the need for personalized treatment decision making. Discussing the two types of progression, localized and widespread, she was able to illustrate that all progression is not equal. This further highlighted the need for patients to see a GIST expert whenever possible.

Finally, Dr. Wilky shared several alternative treatments for progression, explaining ablation and embolization among them. Outlining the protocol for making decisions on treatment for fifth line and beyond, she discussed the use of ctDNA (circulating tumor DNA) and genomic sequencing, sometimes involving repeating a tumor biopsy.



During questions from the audience, Dr. Wilky also spoke about the importance of side effect management, the importance of discussing side effects with your physician and making a decision together with the patient when it is time move to a different treatment line.

View her talk here.
Download her presentation here.

GIST Episode 6: Introducing new treatment options in GIST

Moderator **Sara Rothschild, Life Raft Group** introduced **Dr. Jonathan Trent, of Sylvester Comprehensive Cancer Center, University of Miami, USA**. Dr. Trent discussed the latest treatment options for GIST patients and emphasized the importance of mutational analysis, outlining the GIST subtypes driving treatment and stating that, “Patients waste valuable time and money often taking medication that has no effect on their tumors. Every single GIST patient needs to have mutational testing.”

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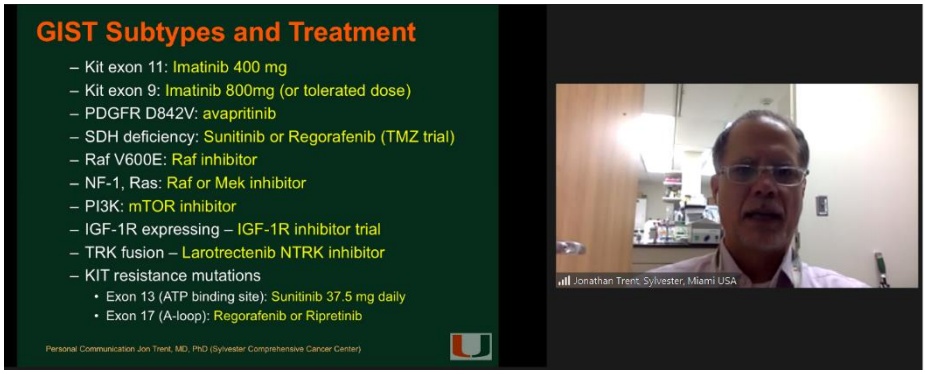

Dr. Trent showed data that indicates that only 30% of GIST patients are getting testing for KIT. He is currently studying the value of circulating DNA testing, especially for those who progress on TKIs. He went on to discuss in detail some of the more promising clinical trials, and emphasized the importance of personalized side effects management, using side effects profiles to help make decisions in prescribing medications.

Blueprint Medicines Navigator study showed high activity in Exon 18 incl. the D842V mutation, which led to approval in the US and most recently in the EU. There was definite activity in unselected patients with avapritinib in 4L and beyond. Deciphera Pharmaceuticals Invictus study showed ripretinib as statistically significant with PFS and OS. The data shows lots of stable disease in patients (some times out to 12 weeks). Ripretinib was approved in the US for 4th line therapy for GIST, in the EU the approval process is ongoing.

View his talk here.
Download his presentation here.

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Saturday, September 12, 2020


Dr. Ramesh Bulusu, UK


Dr. Ruth Casey, UK


Dr. Robin Jones, UK


Dr. Gina D'Amato, USA

GIST Episode 7: Challenges in approaching a non-KIT/PDGFR mutated GIST

Kicking off the third day of New Horizons 2020, **Jayne Bressington of GIST Support UK** introduced **Dr. Ramesh Bulusu, Addenbrooke's Hospital, Cambridge University Hospitals, UK,** and **Dr. Ruth Casey of Cambridge University Hospitals, UK**, who presented on the challenges of treating patients with rare subsets of GIST. Jayne Bressington is founder and head of PAWS GIST UK, a patient advocacy organization for "Paediatric and Wild-Type GIST" under the roof of GIST Cancer Support UK.

Dr. Bulusu began with an overview of GIST, moving on to the specifics of the 15% of patients who are not KIT or PDGFRa. He spoke about the term "wildtype," believing strongly that we should abandon that term, using instead specific mutational subtypes. He stated that SDH mutations are both "fascinating" and "challenging." The NF1 subtype is the most challenging to treat. New oncogenic drivers are being discovered all the time, with BRAF mutant GISTs, NTRK fusion GISTs, NF1 and FGFR pathways as well as succinate dehydrogenase (SDH) deficient GISTs being targeted. Descriptive terms for these include quadruple negative GISTs (KIT, PDGFRA, BRAF, wildtype and SDH preserved), and Quintuple negative GISTs (KIT, PDGFRA, BRAF, wildtype, SDH preserved, no NTRK fusion).

He outlined the standard of care for non-KIT PDGFRa GISTS, indicating that the oncogenic driver needs to be identified, e.g. BRAF would be treated with BRAF kinase inhibitors, NTRK fusion GIST with NTRK inhibitors. In terms of the standard TKIs: imatinib has no benefit, although there have been anecdotal reports of response that could be due to the natural history of GIST. Sunitinib has shown some activity in SDH-deficient GIST. Regorafenib has shown some response in SDH-deficient and in NF1 GISTs. There is concern about the long-term effects on younger patients.

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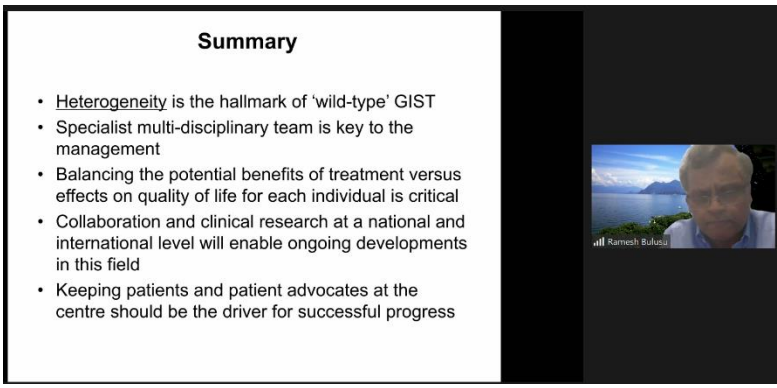
One exciting technique mentioned was the use of MRI spectroscopy in detecting succinate in tumors in vivo. Also, the use of SIRT therapy, injecting an agent directly into the tumor. This has been used in colon cancer. Dr. Bulusu shared helpful charts concerning asymptomatic SDHx carriers.

Dr. Casey's background in endocrinology and interest specifically in inherited (germline) GISTs aided her in providing an overview of SDH-deficient GIST. With SDHC epimutation, specifically Carney Triad, hypermethylation plays a role.

Screening protocol for patients with an SDHC epimutation was outlined stating it was not clear. Their recommendation was that screening for PPGL should follow similar guidelines as for SDHA germline mutations. No family screening is recommended.



Two takeaways from their presentation that are key: treat the patient to tolerance, not toxicity, and see a GIST specialist. Dr. Bulusu ended with a fervent cry for more collaboration.

View their talk here.
Download their presentation here.

GIST Episode 8: Following the research journey in GIST

The second session of the day was "Following the Research", moderated by **Pete Knox, Life Raft Group**. **Dr. Robin Jones, Institute for Cancer Research, London, UK** discussed potential treatments in the research pipeline. He provided a concise overview of the treatments available, both approved and off-label, indicating that in many cases the country you are from will determine availability of off-label medications.

As in previous sessions, Dr. Jones discussed the importance of side effects management. He then elaborated on current promising clinical trials as well as combination therapies and immunotherapy.

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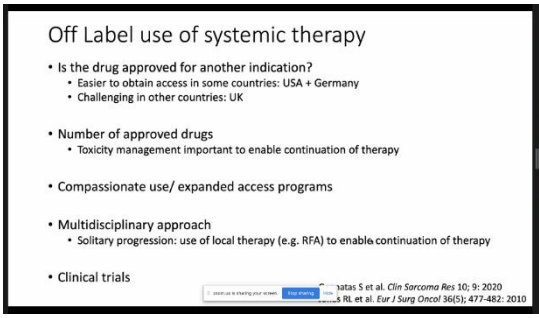

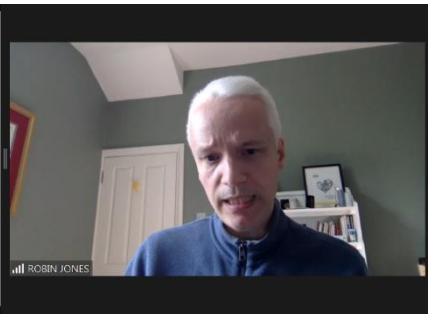

The patient/doctor relationship is at the heart of treatment success, requiring a careful discussion at every stage. He cited three main stages: Discussion of conventional options, discussion of clinical trials, and finally thinking "outside the box." Like some of his colleagues who spoke prior to his own presentation, Dr. Jones ended with a call for collaboration among oncologists, researchers, patient advocacy groups and regulatory agencies to unite for the welfare of patients. Dr. Jones answered a number of questions from the audience concerning worries about off-label treatments, drug access, and talking to your physician about an off-label treatment.

View his talk here.
Download his presentation here.

GIST Episode 9: Quality of diagnosis, treatment & care

The conference concluded with the ninth presentation, moderated by **Piga Fernández, Fundación GIST Chile and The Life Raft Group,** and **Ginger Sawyer, GIST Support International**, specifically designed for patients' needs. Piga Fernández introduced **Dr. Gina D'Amato**, noting that Dr. D'Amato is an **Associate Professor of Medicine at the Sylvester Comprehensive Cancer Center at the University of Miami, USA**. Dr. D'Amato also serves Sylvester as a Sarcoma Medical Oncologist, Assistant Director of Clinical Research, and Medical Director of the Comprehensive Treatment.

Dr. D'Amato stressed the necessity of quality professional care and correct diagnoses for GIST patients. She highlighted the need for a patient to have a mutation analysis conducted so that the specialist could best direct care and appropriate therapies. Her power point detailed the host of side effects to which patients may be subject when taking the various therapeutic drugs, giving recommendations and strategies for the best treatment of those side effects. A point that she stressed throughout her presentation was "hydrate, hydrate, hydrate," as a means for resolving issues of nausea, bowel disruptions, edema and other side effects of the inhibitors.

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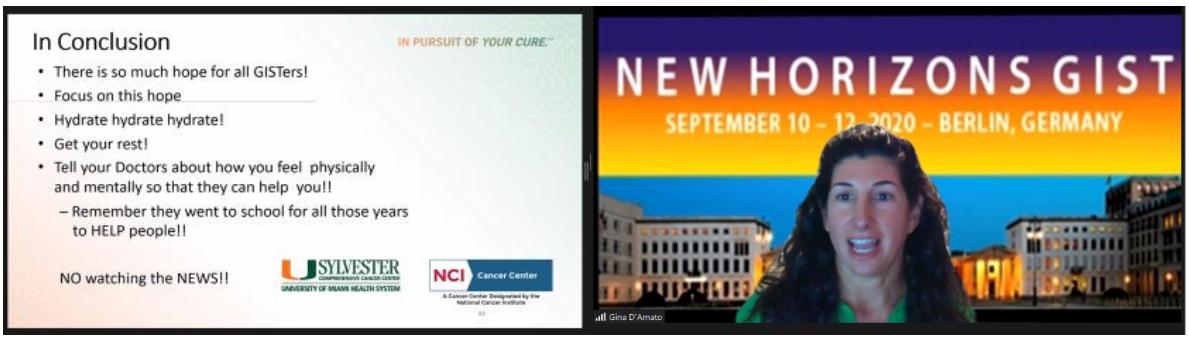
Additionally, Dr. D'Amato suggested numerous ways through which patients can reduce or eliminate fatigue and stress via exercise and moderation of activities. She gave examples of various activities that would be appropriate for GIST patients. Dr. D'Amato also urged the appropriate management of pain, anxiety, and stress and suggested various ways to care for the mind as well as the body.



Ginger Sawyer of GIST Support International and Piga Fernández helped close out the session by directing participants' questions to Dr. D'Amato. During the Q&A period, Dr. Amato highlighted the importance of not taking any alternative/complementary treatments that are not supported by scientific evidence. She also reminded all that caregivers have special needs that must also be considered along with the needs of the patients.

View her talk here.
Download her presentation here.

The NEW HORIZONS GIST Patient Advocacy Roundtable:
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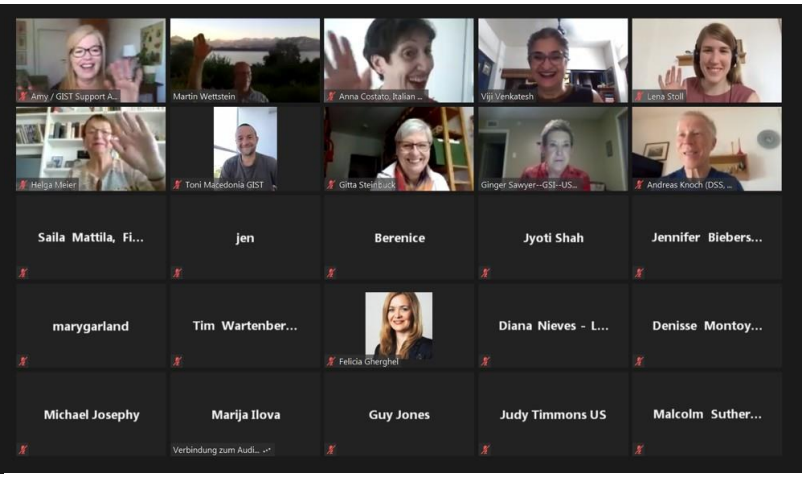
The End

The conference closed with remarks from Markus Wartenberg, who thanked everyone who made the conference possible, and shared his hope that we will meet in person in 2021. Norman Scherzer, Life Raft Group, stated that we had unfinished business: "To assure that all GIST patients received mutational analysis for accurate diagnosis, and had access to the best possible treatment for their individual disease."

The conference ended on a high note. The final sessions had over 60 people in attendance, from 27 countries, the highest attendance for any New Horizons meeting.



A very special thanks to all speakers and all participants for making this first-ever virtual New Horizons GIST conference such a success!

Visit our New Horizons GIST 2020 online library

on www.sarcoma-patients.eu

All presentations and recordings are available on this website.
