2023 New Horizons GIST Conference Report

Dublin, Ireland
May 13-14, 2023

The 2023 New Horizons GIST conference in Dublin, Ireland began on the afternoon of May 13th immediately after the conclusion of the SPAGN Annual Conference. This year was the first time the two conferences were scheduled together in order to maximize opportunities for networking and learning among participants of both conferences.

This year's conference, the 20th since the first New Horizons GIST meeting back in 2001 was also once again a hybrid event, allowing participants to join from all over the world. More than 50 people attended the conference either in person or virtually, with a little more than half present in Dublin. The hybrid set-up also allowed for some of our expert presenters to join virtually who would otherwise not have been able to contribute.

Piga Fernandez (Chile) and Martin Wettstein (Switzerland) of the 2023 New Horizons GIST Steering Committee welcomed participants to the conference.

Following this brief introduction, Piga introduced the first expert presenter and the conference began.

2023 New Horizons GIST Conference Report

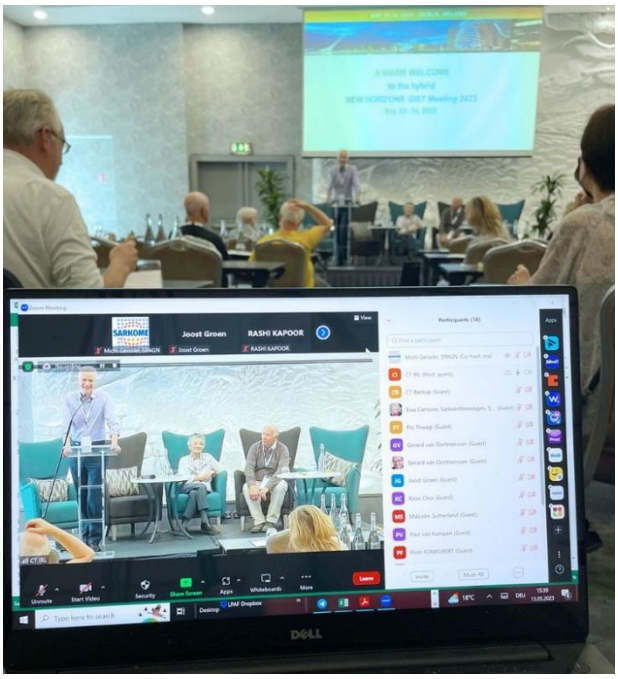
Dublin, Ireland
May 13-14, 2023

During this year's New Horizons GIST conference, we will explore:

- How to treat GIST (Gastrointestinal Stromal Tumors) today?
- Scientific evidence and expert evidence (= practical clinical experience)
- GIST patients urgently need innovative tools to improve survival and quality of life
- The use of precision oncology in treatment of GIST
- General overview of rare and very rare GISTs
- Where is the GIST research journey currently taking us?

How to treat qualified GIST conditions today

Dr. Robin Jones (UK) gave a presentation on how GIST treatment has changed compared to previous therapy algorithms, with an overview of changes and innovations. Below is a brief outline of his presentation, which you can watch here.



Overview, changes, and innovations

Activation of receptor tyrosine kinases (**RTK)** triggers GIST disease. About 80% are KIT and about 8% PDGFR mutations. There are many different subtypes.

Prof. Jones covered three stages: localized disease, metastatic disease, and progressive or advanced disease.

Regarding localized tumors, Prof. Jones said they are removed surgically whenever possible. If the tumor is more than 3 cm, Imatinib is recommended as adjuvant

therapy. A recent study examines whether adjuvant therapy over 5 years is more beneficial than 3 years. Results are expected in the next few years.

Regarding progressive or advanced disease, Prof. Jones said that the chronological order of the approved therapies for advanced GIST disease is fixed.

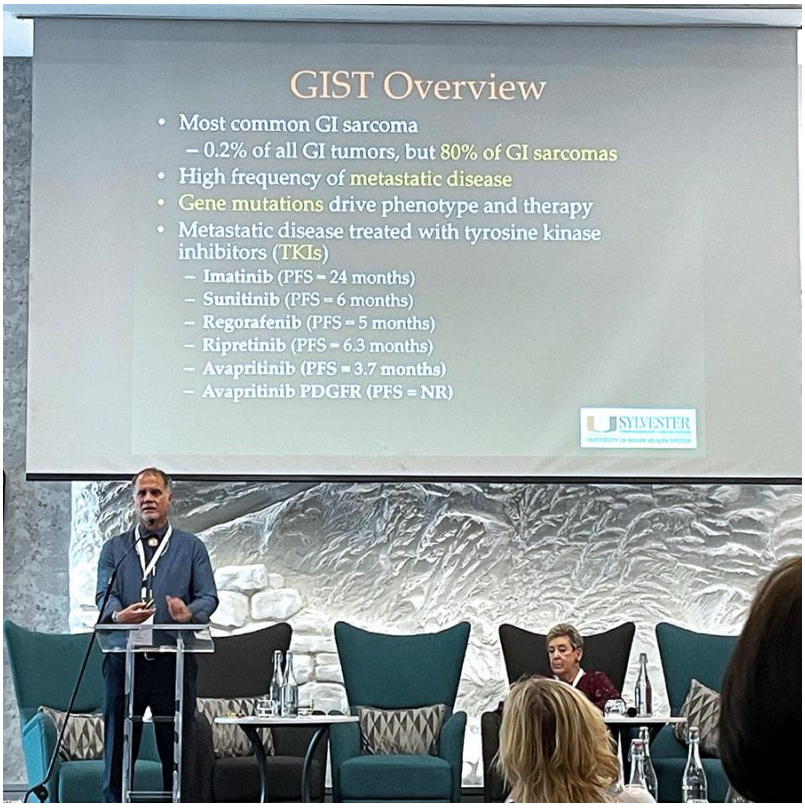
There are new therapy options currently being tested in clinical trials.

Clinical Experience with Two New GIST Therapies

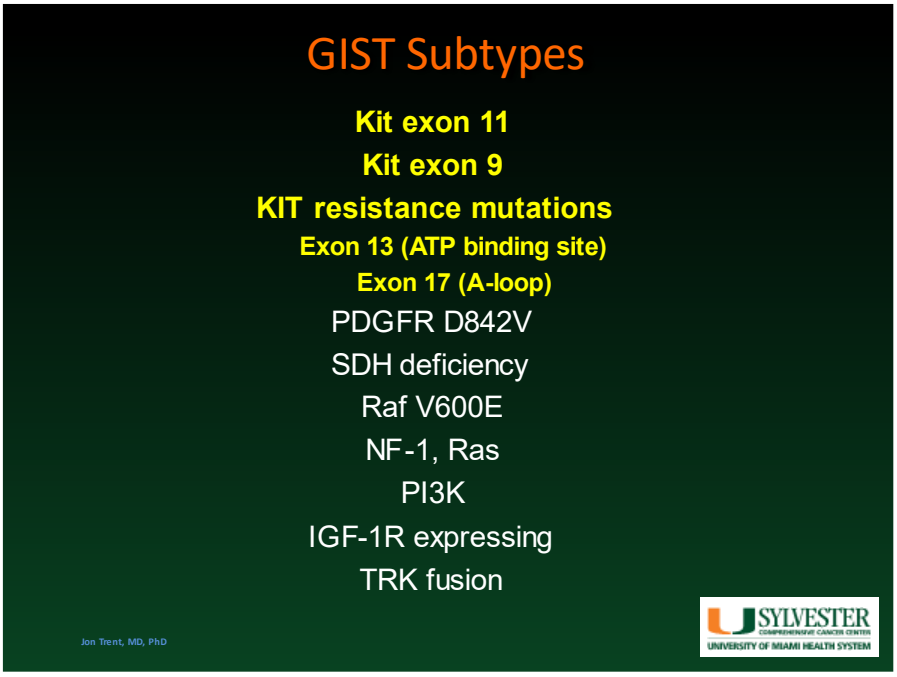
Dr. Jonathan Trent (USA) of the Sylvester Comprehensive Cancer Center, University of Miami, gave a presentation on precision oncology, covering some of the newer GIST therapies that have emerged in recent years. Below is a brief outline of his presentation, which you can watch here.

According to Dr. Trent, there is a whole range of targeted therapies for the treatment of GIST. These substances belong to the group of TKIs (tyrosine kinase inhibitors).

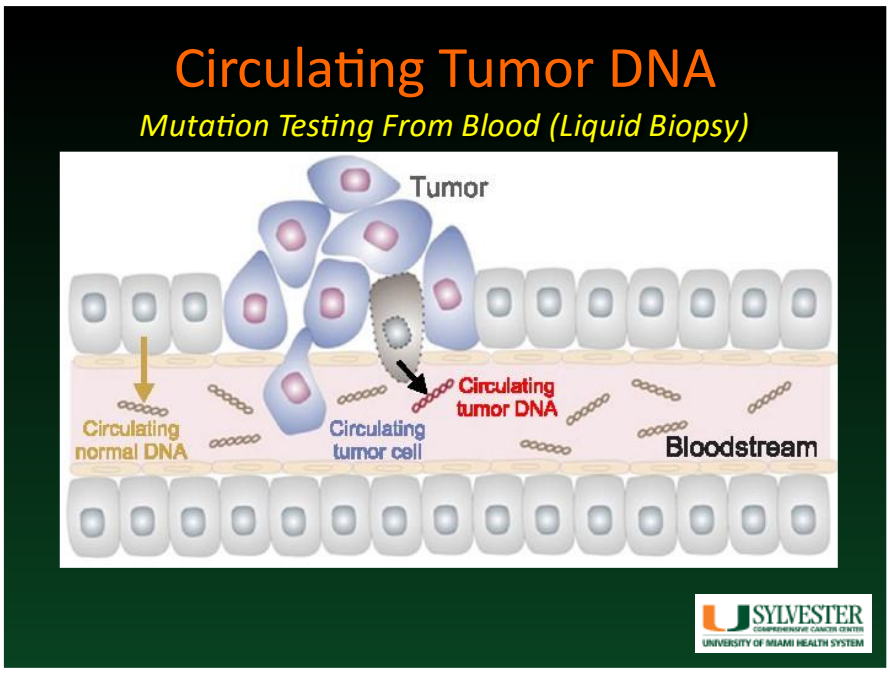
- Imatinib
- Sunitinib
- Regorafinib
- Ripretinib
- Avapritinib



Dr. Trent also emphasizes the importance of **mutation detection** in order to apply the best therapy but stresses that this practice is still a long way from being carried out systematically.

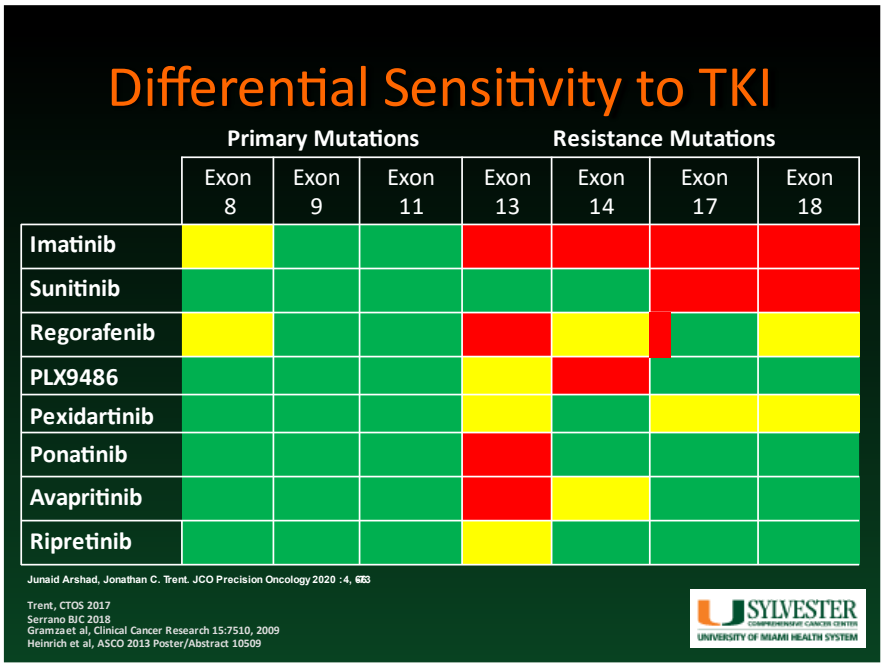


In the case of an advanced GIST disease, the mutation can now be determined with a liquid biopsy, however this method is still being explored further.

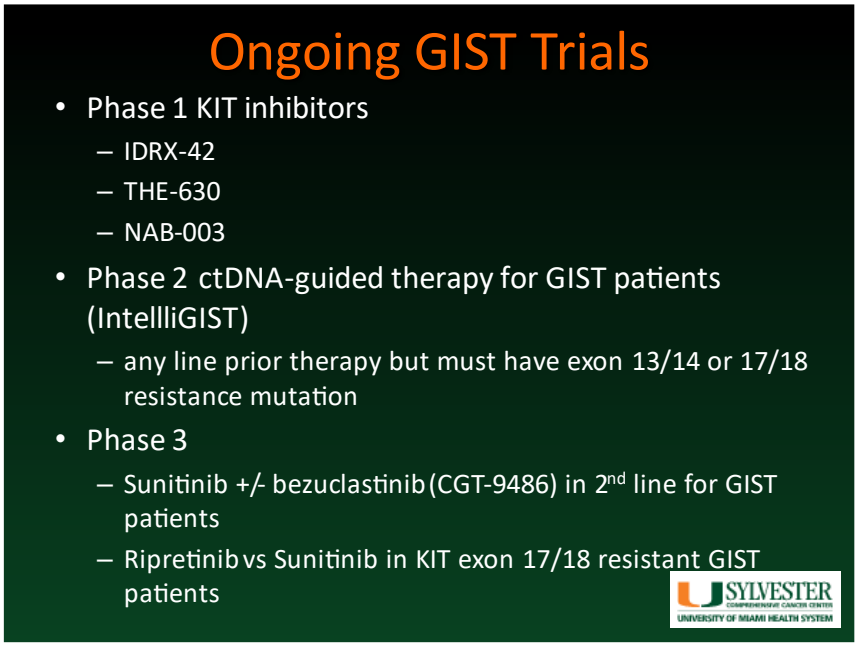


Dr. Trent stipulates that resistance mutations are mostly exon 17, or exon 13, which do not respond to Imatinib. The table gives an overview of the mutations and the responses of the different therapies.

Green indicates a good response; red indicates no response; and yellow indicates that the response is indeterminate.



Finally, Dr. Trent shared that several clinical trials with new drugs for GIST treatment are currently underway, including:



The most pressing questions from the patient's point of view about GIST diseases

Markus Wartenberg (Germany) and David Josephy (Canada) co-chaired a panel discussion featuring ***Dr. Peter Reichardt (Germany), Dr. Robin Jones (UK), Dr. Jon Trent (USA), and Dr. Marco Baia (Italy)*** who joined remotely to address the most frequently asked questions from patients.

The discussion is outlined below, which you can watch here.

1. *Can research be used to identify the reason for a person getting GIST?*

- Molecular changes in cells happen all the time, mostly without consequences. Why mutations in KIT or PDGFRA occur in certain people is unknown
- Very many people have "micro-GISTs", why some of them develop into malignant tumors remains unknown.

2. *Is GIST hereditary?*

- According to all experts, GIST is almost always sporadic, i.e., not hereditary.

3. *Can the ctDNA (liquid biopsy) method be used to determine whether GIST cells are still present in the body?*

- ctDNA techniques for GIST detection are not yet sufficiently sensitive for definitive conclusions to be made, but the technology is improving quickly.

4. How do you assess the risk of a recurrence of the disease?

- There are widely accepted methods for naming the risk of recurrence (high - low - intermediate). However, the current risk classification does not include the mutation status.

5. What is the recommended course of action for long-term adjuvant treatment?

- In the case of metastatic GIST, long-term therapy with imatinib is absolutely recommended.
- For exon 9 patients, the dosage is clearly 800 mg/d

6. What is the role of surgery in metastatic tumors?

- Surgical removal of a metastasis is rarely recommended. Consultation with a GIST expert is essential before any such surgery is undertaken

7. What is the order of treatment and what new substances may impact that protocol?

- The order of therapy is clearly defined (see above).
- However, there are a number of clinical studies underway that could possibly change these given therapies.
- A change in therapy must always be assessed very carefully and must never be made hastily.

- Combining different GIST drugs has been considered, and clinical trials have been conducted, but this strategy carries the risk of increased side effects. It is essential that a GIST expert oncologist be consulted before any GIST drugs are combined.

8. *What are the long-term side effects of the treatments?*

- Long-term side effects of imatinib therapy are well documented, including, for example, rare kidney problems.
- The fact that many GIST patients have been maintained on imatinib for long periods - even decades - is very positive news. We should be cautious not to assume that all long-term health effects are due to imatinib therapy; some changes may simply be due to the normal aging process.
- High blood pressure is also described as a side effect of certain medications, but this can usually be treated well.

Follow up question: How can we manage treatment of side effects systematically to improve quality of life?

- It is important to find a good balance between the stabilization of the tumor and unwanted side effects that impair the quality of life.
- This can be accomplished with an adjusted dosage and other measures.
- The first measure is generally to control the side effects and only then to reduce the dosage.

9. What are the benefits of plasma level testing?

- The physicians on the panel did not deem it to have therapeutic benefit; however, other global experts differ. Best to speak with your physician regarding this question.

10. After how many years can a patient be considered to have recovered?

- After five years without findings, a patient can be considered recovered.
- A follow-up examination should be conducted every 6 months, after 5 years the interval can be increased to 12 months.
- The standard examination is CT, or MRI. MRI may be preferable to CT scanning, since CT scans require exposure to ionizing radiation.

Rare GIST Mutations and Potential Treatments

Jayne Bressington (UK) chaired the session on rare GIST mutations; what they are; how they are treated; and how patients and experts have been working together, from both UK and USA perspectives; she also made a presentation, along with ***Dr. Florian Haller (Germany)***, ***Dr. Ramesh Bulusu (UK)***, and ***Dr. John Glod (USA***). Dr. Glod joined remotely

Dr. Florian Haller (Germany) of the University Hospital Erlangen, gave an overview of rare and very rare GISTs, biology, genetics, and profiles of the individual subtypes. Below is a brief outline of his presentation, which you can watch here.

- NF-1 mutation occurs mainly in the small intestine and does not respond to Imatinib.
- BRAF mutation occurs mainly in the small intestine and does not respond to Imatinib.
- RAS or PI3K mutation - very rare

- Fusion-positive GIST - very rare. Experts are discussing whether this fusion should still be counted among the GIST diseases.

Dr. Ramesh Bulusu (UK) of Cancer Research UK spoke about how to treat rare GISTs, with an examination of the molecular classification of GIST.

Dr. Bulusu spoke about several clinical trials currently being monitored for results, and the benefits of Selective Internal Radiotherapy (SIRT).

Watch here to view his full presentation.

Jayne Bressington (UK) spoke about her experience as the mother of a paediatric wild-type GIST patient and the founding of PAWS-GIST (Paediatric Adolescent Wild-Type Syndromic GIST), detailing the working partnership between patients and experts in the UK. Watch here to view her full presentation.

Since 2010, their achievements include:

- Developing infrastructure for GIST research in the UK
- Establishing the National GIST tissue bank and National GIST registry
- Opening the PAWS-GIST Clinic
- Funding research into NGS sequencing of Wild-type GISTs to identify therapeutic targets
- Funding research to review clinical course, genetics, epigenetics & metabolomics - SDH deficient GISTs
- Funding research to grow Cell lines from biopsies of PAWS GIST. (an ongoing effort)

Dr. John Glod (USA) of the National Cancer Institute joined the conference remotely to discuss the US perspective on patient-expert partnerships to develop effective therapies for patients with SDH-deficient GIST.

Below are some highlights from his presentation, which you can watch here.

- Helping local providers with diagnosis by offering pathology review and molecular analysis.
- Helping patients identify trials and resources outside the National Institute of Health (NIH).
- Identifying open clinical trials and clinicians with expertise in caring for patients with SDH-GIST and connecting patients to the programs they need through the NIH Pediatric and Wild-Type GIST Clinic.

Where does the GIST research journey take us?

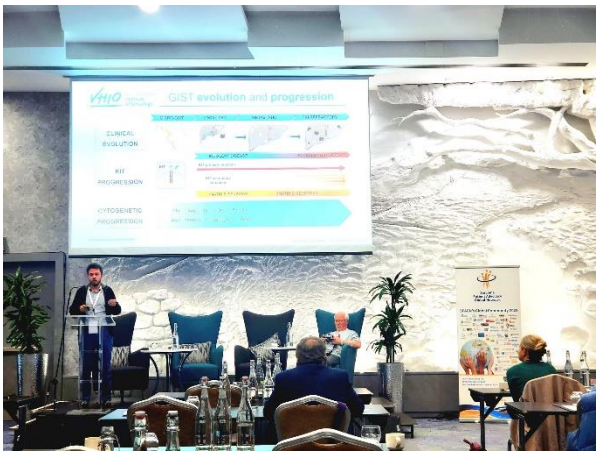
Dr. César Serrano (Spain) of the Vall D'Hebron Institute of Oncology in Barcelona presented on the latest discoveries in basic and clinical research. Listed below are highlights and conclusions from his presentation.

Basic Research

- Combination treatments targeting compensation mechanisms are required for GIST cell eradication. Better in the first line but need to balance toxicity & duration vs. QoL.
- Secondary mutations in KIT or PDGFRA are the main drivers of resistance to imatinib → the focus of drug development.

- ctDNA determination is feasible, detects GIST-relevant mutations and may guide therapeutic decisions.

Clinical Research in GIST



- Current TKIs (approved and on trials) do not inhibit the full spectrum of KIT primary and secondary mutations.
- The goal for the years to come would be to develop innovative approaches to abrogate durably and completely the oncogenic activation of KIT/PDGFRA.
- There is a need to innovate and identify novel targets outside of the KIT/PDGFRA axis.

Conclusion

Markus Wartenberg (Germany) and David Josephy (Canada) co-chaired the closing session of New Horizons GIST 2023 by facilitating a conversation on the main research questions and priorities from the perspective of GIST patients.

After a thoughtful conversation, Markus and David thanked all of the organizers and the conference was concluded.

For two decades NEW HORIZONS GIST is the most important global annual conference for GIST patient advocates. Once again, this conference was a great event for patients from the global GIST patient community to come together, to interact with top GIST experts, to have access to state-of-the-art medical and scientific information and to exchange best practice in patient advocacy among each other.

2023 New Horizons GIST Conference Report

Dublin, Ireland
May 13-14, 2023

2023 New Horizons GIST was a joint endeavor organized by:

Sarcoma Patient Advocacy Global Network

The Life Raft GROUP

Thank you from the New Horizons GIST Steering Committee!

Pictured LEFT to RIGHT: David Josephy (Canada), Martin Wettstein (Switzerland), Piga Fernandez (Chile), Sara Rothschild (USA), Ginger Sawyer (USA), Markus Wartenberg (Germany), Kathrin Schuster (Germany), and Michi Geißler (Germany).

The full playlist of recorded sessions from this hybrid conference can be accessed on the SPAGN YouTube channel by scanning the QR code here or visiting bit.ly/NHGiST23playlist.