



Welcome to the second edition of our Newsletter which has been designed to be as informative as possible to everyone affected by GIST Cancer.

It contains information about our most recent Patient / Carer meeting; a trial for a potential new drug and the GIST story of our most recent Trustee, Drewe Lacey. We are grateful to the contributors to this Newsletter and we would welcome more articles from you about your GIST journey and your fund-raising efforts or anything else of interest.

We are working on producing updated literature at the moment and hope to have it all already to distribute by the end of the year. We are always looking for more volunteers and Trustees, so please do contact me on the email below if you can help in any way.

Finally, a thank you from me to our Trustee, Ros Langford, for producing this Newsletter which I am sure you will all find a very interesting read.

Nic Puntis. (Chairman, GIST Cancer UK Board of Trustees)... nicp@gistcancer.org.uk

CLINICAL RESEARCH: **The Peak Study**

The Peak Study is a Phase 3 clinical research study evaluating an investigational study drug Bezuclastinib, - also known as CGT9486) in combination with Sunitinib in people with locally advanced, unresectable, or metastatic GIST who have previously received Imatinib (standard of care medication).

Sunitinib is an approved therapy for GIST often used after people have received Imatinib. Bezuclastinib is an investigational tyrosine kinase inhibitor that is designed to selectively and potently target a specific range of KIT mutations, including some mutations that Sunitinib does not work against. Using Bezuclastinib and Sunitinib together may have the potential to provide complementary coverage across several mutations in the KIT gene.

The study has multiple parts (Parts 1a, 1b and 2).

Part 1a : patients receive Bezuclastinib + Sunitinib (dose escalation lead-in to determine the dose of Bezuclastinib to be administered in parts 1b and 2). **Enrolment complete.**

Part 1b : patients are randomised 1:1 to receive either Bezuclastinib or Sunitinib as single agent for 2 weeks followed by Bezuclastinib + Sunitinib (evaluating the potential interaction between Sunitinib and Bezuclastinib). **Enrolment complete.**

Part 2 : patients are randomised 1:1 to receive either Bezuclastinib + Sunitinib or Sunitinib only. **Actively enrolling.**

* Crossover: Patients in the Sunitinib-only group who have centrally confirmed disease progression on study may be permitted to crossover to receive Bezuclastinib + Sunitinib.

For more information go to the Clinical Research & Trials section of the GIST Cancer UK website.

GIST Cancer UK is unique. We are the only charity focussing solely on GIST cancer for the benefit of patients, carers and clinicians in the UK.

The charity is run by volunteer trustees who are patients, carers or those with a special interest in GIST Cancer.



LEEDS

GIST Cancer UK Patient / Carer Meeting

Novotel, Whitehall Quay, Leeds. Friday 6th October 2023.

GCUK Chairman, Nic Puntis, welcomed everyone to the conference and introduced our first speaker, - **Dr Alex Lee**, a Consultant Medical Oncologist who works for the Greater Manchester and Oswestry Sarcoma Service. Dr Lee's presentation was entitled 'Side Effects Management'.

Dr Lee explained that typically, 80% of GIST cases express a deficiency in the KIT receptor, Tyrosine Kinase. (TK). TK transmits messages within the cell and a mutation of TK can cause the messages to be stuck in the 'ON' position which leads to cell growth, proliferation and cancerous behaviour. This abnormal behaviour can be 'treated' using small molecules called Tyrosine Kinase Inhibitors (TKIs) which are designed to turn-off the mutated TKs and thus prevent cancerous growth. The drugs Imatinib, Sunitinib and Regorafenib are three different types of TKIs and they each have different but often overlapping molecular TK targets.



Dr Alex Lee



Imatinib is a potent inhibitor of KIT & PDGFRA mutations, and has a high rate of durable response in treatment of advanced GIST and some early stage GIST. There are now many generic forms of Imatinib in routine use by the NHS e.g. Accord, Teva, Sandoz, AmaroX.

Imatinib is generally found to be a well-tolerated drug with limited negative impact on the 'quality of life'. Side effects vary from person to person. Dr Lee outlined some of the side effects which can be graded on a 1 – 5 scale.

Sunitinib is used to benefit those where imatinib has stopped working on an advanced GIST. It has a manageable toxicity profile but can often have some limited impact in the quality of life e.g. high blood pressure, Hand-Foot syndrome and affecting wound healing. Similarly **Regorafenib** (used when Sunitinib

becomes ineffective), can cause Hand –Foot syndrome, an increase in risk of infection due to a drop in white blood cells, and anaemia.

The general expectancy with TKIs is for some side effects but the goal should be to manage the toxicities / side effects so that it has little negative impact on daily life. Oncology care teams are the experts in supporting patients and the management of specific side effects, and should be involved at an early stage.

Our second speaker for the morning was **Professor Dan Stark** Professor of Teenage and Young Adult Cancer Research, Leeds University Institute Medical Research and Consultant in Cancer Medicine at Leeds Teaching Hospitals Trust. Professor Stark gave a very interesting talk about GIST Management (a brief history up to current clinical trials).

GIST was once considered an *obscure* tumour, and population studies in N. Europe show that they occur with an incidence of 14 – 20 per million people. The term GIST (gastro intestinal stromal tumour) was first coined in 1983 by Mazur and Clark who studied the histological origins of these tumours which developed in the walls of the Gastro-intestinal tract. Then in 1998 Hirota and colleagues discovered that GIST develops due to a mutation in the c-KIT gene. Since 1990, GIST cancer research, management and treatment have advanced rapidly.

Since the 1990's advances have been made that have substantially refined the diagnostic work-up, refined sub classification and risk assessment and improved clinical management. Typically 80% of GIST cases are now known to have mutations in the Kit gene, whereas about 10% of cases have the PDGFRA gene mutation and a further 10% are classified as 'wild type' as they do not harbour the mutation of either the KIT or PDGFRA genes.

continued

Professor Stark discussed the effectiveness of Imatinib on the survival of GIST patients of varying genotypes. He explained that studies using continuous versus interrupted treatment with TKIs shows that interrupted treatment slightly lowers the chance of survival, but these chances can be improved once the patient returns to TKI treatment. Studies have shown that treatment of KIT positive, high risk patients with adjuvant Imatinib over 12 months reduces the risk of death by 45%, whereas treatment for 3 years can reduce the risk of death by 66%. A similar pattern was shown with continuous v intermittent treatment with Sunitinib.



Differential Sensitivity to TKI

	Primary Mutations			Resistance Mutations			
	Exon 8	Exon 9	Exon 11	Exon 13	Exon 14	Exon 17	Exon 18
Imatinib	Green	Green	Green	Red	Red	Red	Red
Sunitinib	Green	Green	Green	Green	Yellow	Green	Yellow
Regorafenib	Green	Green	Green	Red	Yellow	Green	Yellow
PLX9486	Green	Green	Green	Yellow	Red	Yellow	Yellow
Pexidartinib	Green	Green	Green	Green	Green	Green	Green
Ponatinib	Green	Green	Green	Red	Yellow	Green	Green
Avapritinib	Green	Green	Green	Red	Yellow	Green	Green
Ripretinib	Green	Green	Green	Yellow	Green	Green	Green

Junaid Anshad, Jonathan C. Trent. JCO Precision Oncology 2020 4, 66-73
Trent, CTOS 2017, Serrano BJC 2018
Gramza et al. Clinical Cancer Research 15:7510, 2009
Heerich et al. ASCO 2013 Poster/Abstract 10509

Ripretinib is also considered to be a life-extending treatment, but unfortunately, despite being proven to be effective when advanced GIST gets worse, it has as yet not been accepted by NICE on economic grounds. Organisations including GCUK have lobbied the manufacturers to see if costs can be reduced.

Selective Internal Radiotherapy (SIRT) is now being used to treat metastases on the liver. Prof. Stark said that four patients in the UK have so far received this treatment.

Members then had the opportunity to ask questions, and these were answered by Judith Robinson, (GCUK Honorary Vice Chairman), Prof. Dan Stark, Dr Alex Lee and Nic Puntis (GCUK Chairman).

After a wonderful lunch in the Novotel restaurant the conference continued with a presentation on 'The Psychological Impact of Diagnosis and Treatment of GIST' by Clinical Psychologist, - **Marion Oliver** . Feedback from patients felt that her presentation was very relevant and



Judith Robinson, Prof Dan Stark , Dr Alex Lee, Nic Puntis.



Marion Oliver & Nic Puntis

that they could resonate with most of the feelings she outlined as being common when being diagnosed or living with GIST. Her opening statement was that 'You are the expert, - no one knows more about you do than you do'! She talked about the physical symptoms, psychological symptoms and behavioural impact that GIST can have both on patient, carers, family and friends. It is normal to have feelings of despair, loneliness, anger and resentment and there is no 'norm' on how you should respond. She concluded her talk by saying: 'Just remember ... **You are normal – it is the situation that isn't!**

The afternoon concluded with feedback by Mark Atlay (GCUK Secretary), on the recent patient GCUK patient survey (further information on page 5 &6), and then discussion groups amongst patients and carers which as usual was found to be very useful.

The next GIST Cancer UK patient / carers meeting will be held on

FRIDAY 12th April 2024



CARDIFF

Can YOU help?

The Board of Trustees are in need of help with the following....

- Administrative Support
- New Trustees
- Local / Regional Coordination
- Helpline
- Reviewer of materials/ resources/website
- Fundraising support
- Reviewer of research applications

If interested, - contact us on: admin@gistcancer.org.uk for a discussion and to find out further information.

A PATIENT'S STORY: My Cancer Journey in 2023

With symptoms in March of loss of weight, some fatigue and sensitivity around my stomach I decided to go to the local GP on 22nd March .The next day I developed a high temperature and returned to my GP on the 24th when my blood tests revealed anaemia and now an infection. I was admitted to hospital 4 hours later where the following morning a scan showed a 'large mass' in the lower intestine. After various delays, the operation, took place on the 2nd April when the surgeons removed a 10.5cm tumour from the lower intestine. Thank God for the blessing of NO STOMA as they had managed to resect my intestine, and I returned home on the 7th April. The Surgeon thought it could be a GIST and for the first time CANCER was mentioned, and a few weeks later I found out that they also removed two lymph nodes. The second wait was to get the results of the histology tests which confirmed that the tumour was a GIST cancer with a high mitotic rate, but that they had seemingly been successful in removing the entire tumour. My first meeting with the Oncologist was on 3rd May, but they were awaiting the tissue to be sent to a specialist hospital, (in this case Birmingham) for mutational analysis which would take a further 4 weeks. At my next meeting on the 28th June, a written report had not been received so the oncologist had phoned Birmingham and obtained the main points regarding the position of tumour, its size. I was told it had a high mitotic count with a high risk of the re-occurrence . It was a GIST with an Exon 11 mutation and thus Imatinib could be taken with a good chance it would either prevent re-occurrence or slow down the process of tumour growth.

Side Effects experienced so far, -

- Fatigue – resulting from discomfort in the stomach and poor sleep and possibly from attempting to do too much. I was advised to take a daily rest as is necessary and preferably before 3pm. I normally set the alarm for anything from 60 to 90 minutes depending on how I feel.
- Diarrhoea -not severe but every 3 days or so. I have been prescribed a tablet to take only when needed.
- Rash on part of my back, shoulders and chest. Not severe and use creams.
- Occasional cramps in calves, thighs and hands.

I took the decision on leaving hospital to re-instate physical activity immediately - primarily walking, and after one month I also decided to re-instate all of my voluntary activities which in effect are full time. I also became a Trustee of GIST Cancer UK. After the first two or so weeks of treatment, I felt very low at the sudden realisation that I needed to live with this for at least three years, and accepted a referral to a psychologist.

Advice Note : - simply say YES to offers of assistance and learn from those experiences.

The side effects and uncertainty about re-occurrence are skirmishes and sometimes battles; the war you need to win is to stay positive and continue to lead your lives in whatever ways mean normality and give you the best quality.

Drewe Lacey (GCUK Trustee and GIST patient for 6 months)



GCUK Survey findings

In early summer GCUK conducted a survey patients and carers to ask about aspects of the charity's work and future priorities. Our thanks to the 75 GIST patients and 12 carers who completed the survey. The key outcomes are outlined below. The website was important and trusted with the majority of respondents (64%) reporting monthly, weekly or daily use. The most important areas (in order) were:

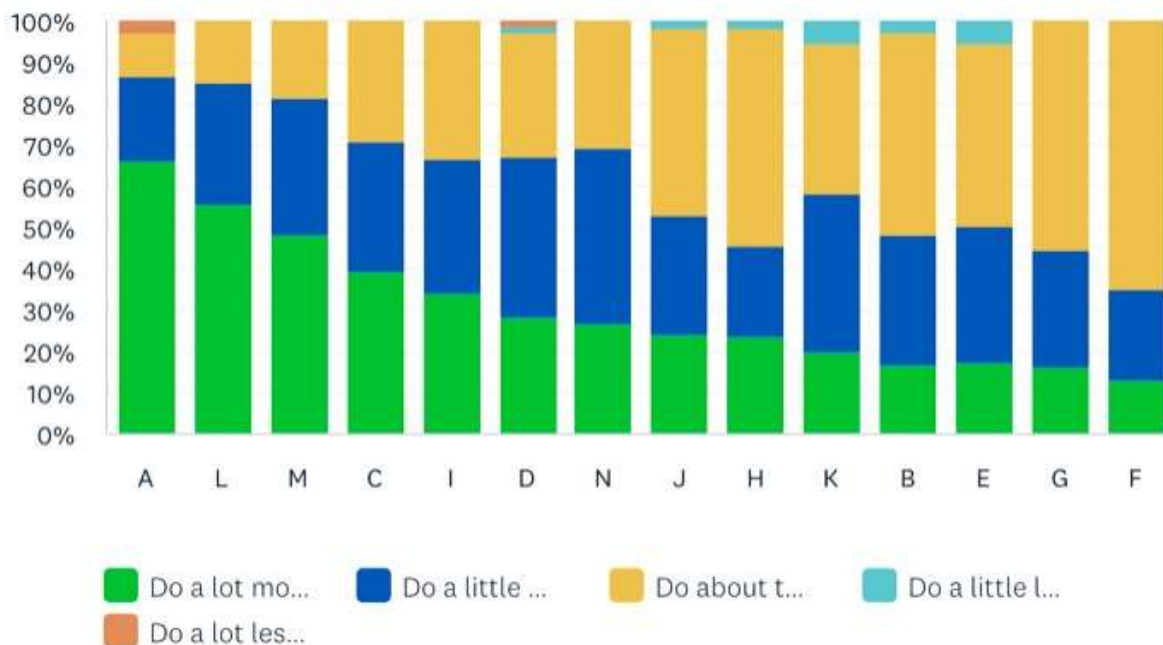
1. Information on GISTs
2. Patient stories
3. Forthcoming events
4. Research
5. Videos
6. Clinical trials

You identified some areas for improvement including: adding more recent patient stories and provide audio recordings to make more personal, revise the Research section to include links to relevant research publications, refreshing the Clinical trials section to give a broader background to clinical trials planned and how to get involved.

Expect some significant changes to the website over the next few months as we respond to your suggestions.

The online Forum (Listserve) provides an opportunity for communication between patients. 78% of respondents said they used the forum but a significant minority found it 'somewhat' or 'very difficult' to use. You wanted to see the possibility of themed discussions and explorable archives as with some other discussion tools. We're exploring these possibilities and associated costs. 79% of respondents said they had read the booklets GCUK produces and all found them useful. They were a valued resource and needed to be refreshed and updated. Suggested further topics included: more coverage of mutational analysis, nutritional issues and external sources of support.

The final section asked about future priorities for GCUK. The results are shown in the following graphic.....



You identified the following priority areas for GCUK to work on (in order):

- A: Researching treatments
- L Working with oncologists
- M: Working with health care practitioners such as nurses

cont. page 5

- C: Supporting the mental health of patients and carers
- I: Working with other cancer charities to lobby on behalf of patients and carers
- D: Providing online support for patients and carers (e.g. regular webinars - online meetings)
- N: Providing support for carers
- J: Providing a helpline for people to call
- H: Supporting PAWS-GIST patients
- K: Regular newsletter
- B: Providing face-to-face patient/carer meetings
- E: Supporting regional events and activities
- G: Supporting fundraising activities
- F: Producing written resources

Conference videos now available.

The videos from the meeting are now available on **YouTube** on GIST Cancer UK and will shortly be available on the website at: <https://www.gistcancer.org.uk/patient-meetings-2023/>

The Board of Trustees have used the survey’s findings to inform their strategic planning for the period from 2024 – 2026 and we will report further on developments in future Newsletters.

Mark Atlay (Secretary GCUK) MarkA@gistcancer.org.uk

FUND RAISING : For Research & Patient Support

Charity event raised £6k for GIST Cancer UK! (Sept. '23)

Dr Ramesh Bulusu Network GIST Lead at Cambridge University Hospitals receiving a cheque for £6,000 from **Scott Currie**, a GIST patient and his partner **Caoimhe** in front of the Waggon and Horses pub in Griston village, Norfolk. Scott and Caoimhe raised the money through a charity event in the village.

Scott had his GIST operation at Addenbrooke’s hospital in Cambridge and is very grateful for the specialist care he received from Mr Emanuel Huguet, HPB surgeon and GIST Oncologist, Ramesh Bulusu.



£13,000 raised for GCUK by completing the Three Peaks Challenge!



Huge congratulations to **Darren (Daz) Oliver, Josh Scott and Liam Louth** who successfully completed the Three Peaks Challenge and also raised a whopping **£13,000 for GIST Cancer UK** in memory of Daz's Mum who died from GIST cancer.

Well done guys and thank you SO much for supporting GCUK. You are utterly AMAZING and a huge thank you to everyone who has supported them and made generous donations. A further £10,000 was pledged by another contact making an amazing **total of £23,000**

Their challenge in numbers:

3 mountains.

19 days camping.

Zero hotels during the challenge.

500 miles or 804km total with around 25-30 miles being covered each day, sometimes more.

3,000 m Total elevation

Carrying 18-26kg depending on location and availability of shops.

Countless blisters and bites.



Congratulations to **Dan Stevens** who did a skydiving jump in Portsmouth on 28th August raising money for GCUK. We salute you Dan!



Joe Jordan passed away suddenly last year with GIST Cancer aged 32. His mother Fran Mclean and a group of friends decided to do something in his memory. Joe was at university in Swansea and was also a dedicated Arsenal fan and seasonal ticket holder. The group raised money by cycling 420kms from Swansea to Arsenal over 4 days.

To date they have raised over £8000 for GIST Cancer UK. You are all amazing; - thank you for all of your support!



Annual Scottish Patient / Carer Meeting

Friday 1st December 2023

at the COSLA Conference Centre,
Edinburgh EJ12 5BH

To book a place, please email
meetings@gistcancer.org

PAWS-GIST CLINIC

1st December 2023

Addenbrook's Hospital
Cambridge, CB2 0QQ

To book a place please email
jayne@pawsgistclinic.org.uk



Two of the GCUK Trustees stood down from the Board recently due to work commitments. ...



Terry Wheldon

Terry Wheldon provided excellent support for patients on the GCUK email forum and telephone helpline. He also represented GCUK at local and international conferences. Thank you Terry for all your hard work and time given on behalf of GCUK.

Jane Means has done an excellent job of managing the GCUK Social Media pages on Facebook, Instagram and Twitter and we thank her for all her hard work and wish her well for the future.



Jane Means

NOBODY WANTS GIST TUMOURS WE DO... NATIONAL GIST TISSUE BANK

GIST RESEARCH WILL PROGRESS FASTER IF THERE IS A GOOD SUPPLY OF GIST TISSUE

Gastro Intestinal Stromal Tumours (GIST) are rare. Around 850 new patients are diagnosed with GIST cancer in the UK each year.

The National GIST Tissue Bank is based at The Royal Marsden, London.

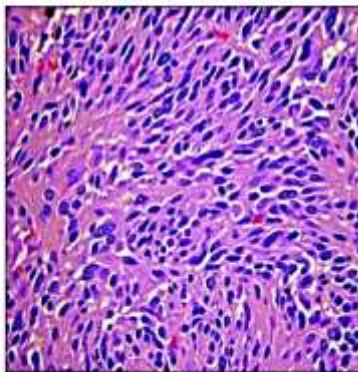
What does this mean for you?

- This tissue bank is a valuable resource that supports GIST cancer research locally, nationally and internationally.
- It provides researchers with a diverse selection of high-quality GIST tumour specimens and clinical data obtained by dedicated tissue bank staff who follow strict procedures and ethical guidelines.
- Research will progress faster if there is a good supply of GIST tissue upon which to test potential treatments and develop new diagnostic tests.

How does the Tissue Bank Operate?

Operating within the Royal Marsden in London, the National GIST Tissue Bank coordinates the collection, storage and distribution of a variety of biospecimens including fresh, frozen and paraffin blocks in addition to blood samples and clinical data.

Working in collaboration with pathologists, medical oncologists, surgeons and other hospital personnel, specially trained staff obtain patient consent, collect samples and assemble clinical information about each donor and their corresponding specimens.



YOU CAN HELP BY DONATING TISSUE ...

If you are a GIST patient who is preparing to have a GIST tumour removed and your GIST type is other than exon 11.

Please contact gistbiobank@rmh.nhs.uk and copy jayne.bressington@nhs.net or phone 0207 8118395 in good time to make arrangements for your tissue donation.

CONTACT INFORMATION

Website: gistcancer.org.uk/national-gist-tissue-bank/
Contact: gistbiobank@rmh.nhs.uk
Address: Tissue Manager
National GIST Tissue Bank
Royal Marsden Hospital,
Fulham Road, London,
SW3 6JJ

Phone: 0207 8118395

NATIONAL GIST TISSUE BANK

- Members of the GIST Cancer UK Medical Advisory Board have been working with the National Cancer Registration and Analysis Service (NCRAS) to further understand the molecular sub-groups of GIST.
- Since 2016, NCRAS have been collecting and recording molecular diagnostic tests on tumours. This includes mutational status information from GIST Cancer patients.
- They have lots of data about EXON 11 Tissue types but are in need of samples of other GIST types.
- GIST is rare and not all hospitals are familiar with the existence of the National GIST Tissue Bank.
- If you are preparing to have an operation and know your GIST type is other than EXON 11, please contact the gistbiobank@rmh.nhs.uk or phone 02078118395 in good time to make arrangements for your tissue to be donated to the National GIST Tissue Bank.