Paediatric Adolescent Wild type & Syndromic (PAWS) GIST Clinic United Kingdom

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PAWS-GIST

- Paediatric
- Adolescent
- Wild-type
- Syndromic
  - **SDH GISTs**
  - Neurofibromatosis 1 GISTs

The Eagle Pub in Cambridge

Victoria Arms-Marston Oxford

- PAWS-GIST – idea born in a pub in
- Oxford in 2011
- Patient & Carer led initiative

UK PAWS GIST Consortium Members

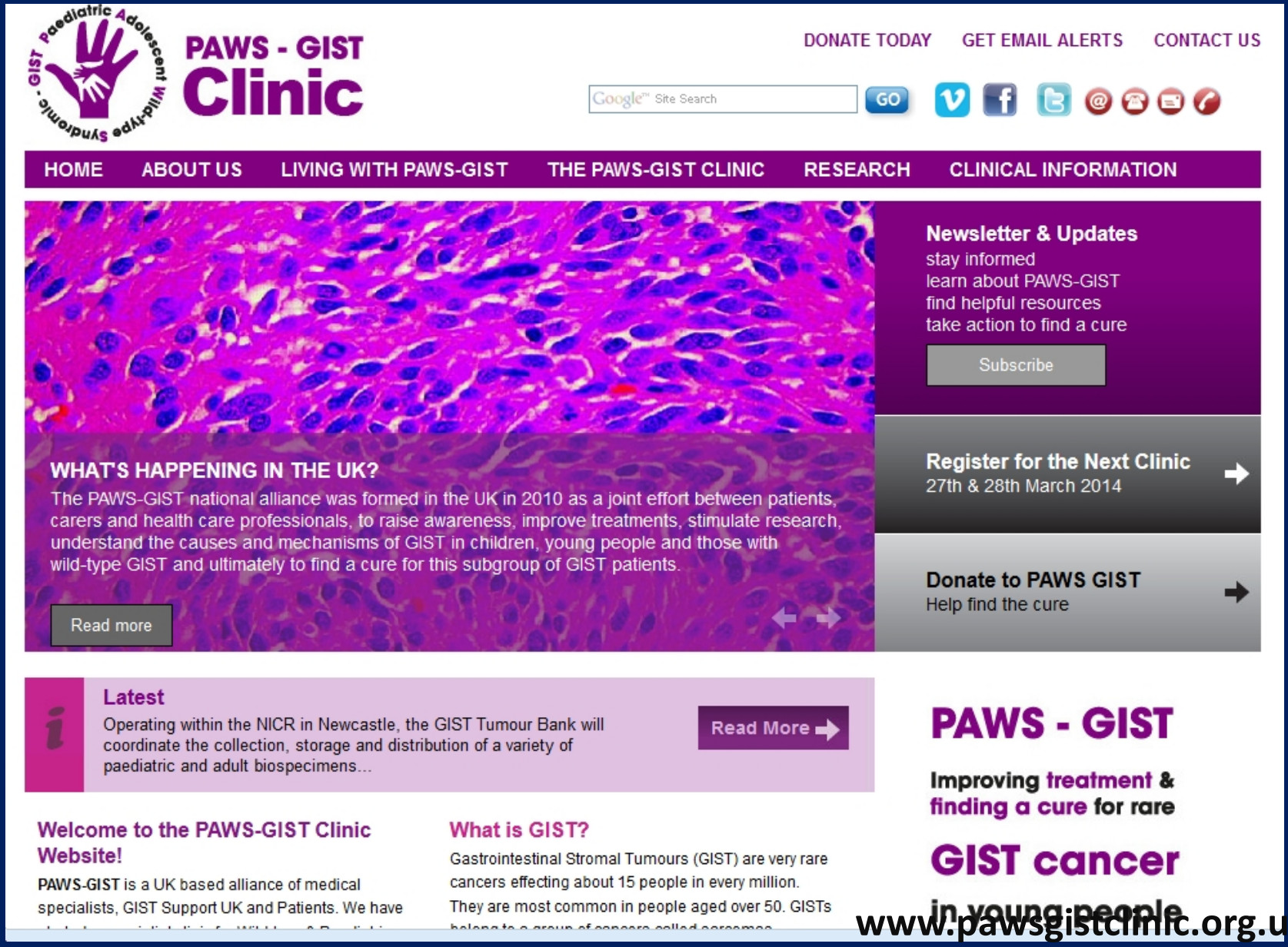








www.pawsgistclinic.org.uk



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Register for the Next Clinic

Title: First Name: Surname:

Address: City: Postcode:

Telephone: Mobile:

Email:

NHS No: DOB:

Age at Diagnosis: Year diagnosed:

Primary Tumour location: GIST tumour type: Wildtype Unknown

Hospital:

Oncologist Name: Email address: Tel No:

Can we contact oncologist?: Yes No

Surgeon Name: Email address: Tel No:

Can we contact surgeon?: Yes No

I am happy for my details to be shared with the Patient Director of the PAWS-GIST Initiative: Yes No

Submit details


Fundraising for PAWS-GIST
THANK YOU
FOR
gist

PAWS GIST-Clinical data

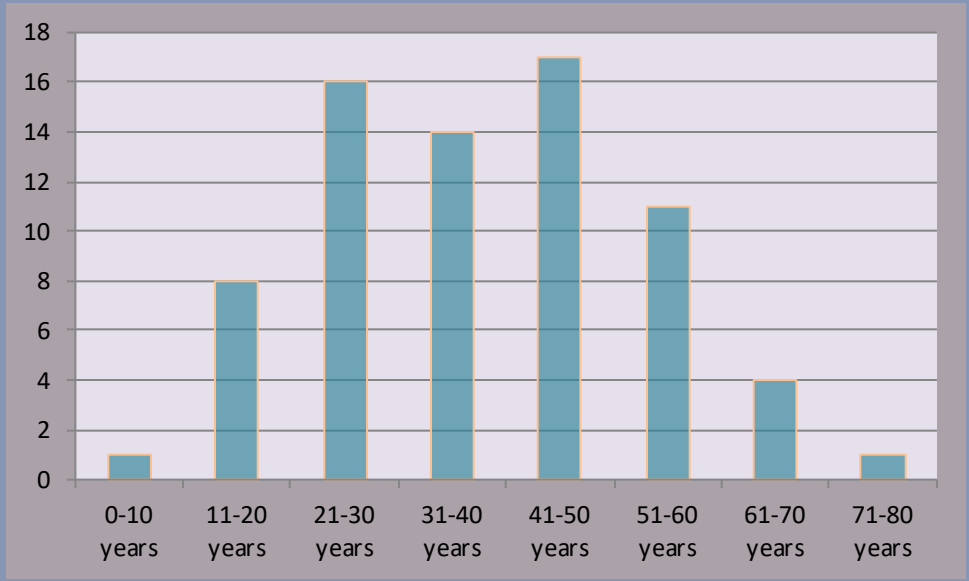
- 21 Clinics so far
- 110 pts
- Male:Female 1:2
- Median age 38 yrs Range 14-76 yrs
- Heterogeneity is the hallmark
  - SDH Deficient
  - Quadruple Negative
  - NF1 GISTs
  - KIT/PDGFRA mutant GISTs !

Results

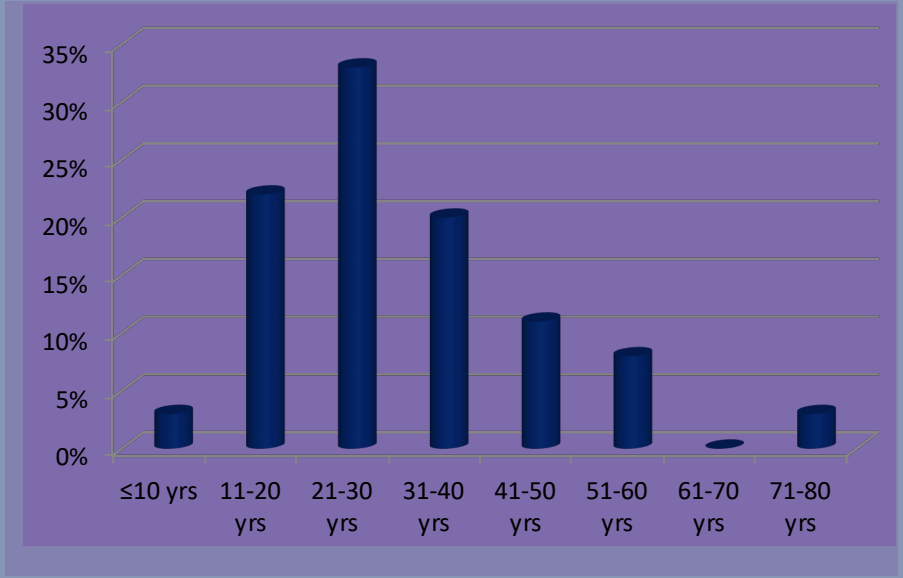
- N=110 pts
- Age at diagnosis range 9-76 years Median 36 yrs
- Gender Male:Female 26:54
- Clinical presentation
  - Anaemia 47%
  - GI bleed 28%
  - Abd pain/mass 24%
- 25% had metastases at diagnosis
- 50% had metastases at the time of clinic attendance

Age Distribution (Age when GIST was firs diagnosed)

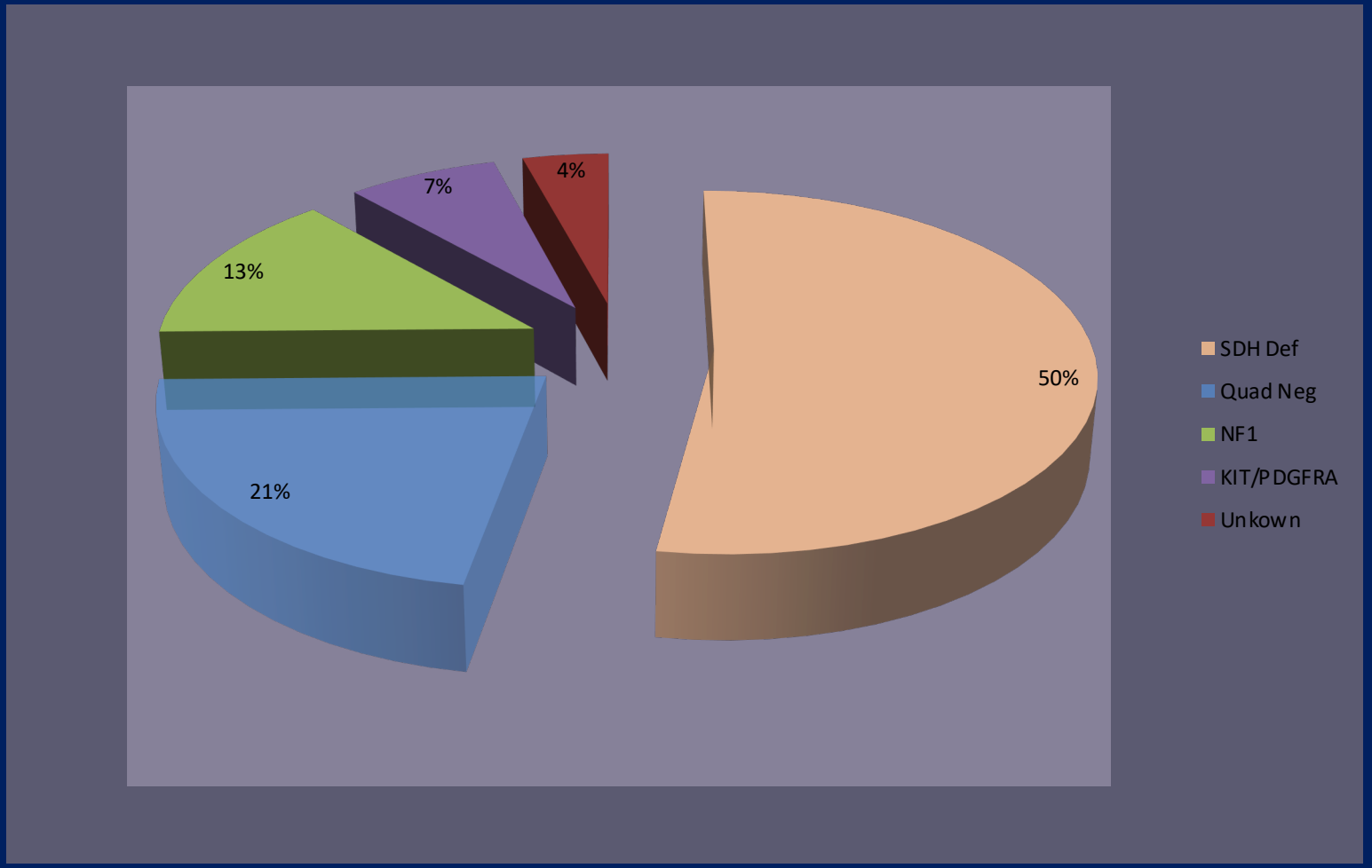
All PAWS GIST patients



SDH deficient GIST cohort



PAWS GIST-molecular subtypes



- 6 SDH deficient and 8 Quadruple negative GISTS tested for NTRK Fusion
- NONE found so far

Clinical Interventions

- 80% had primary GIST resected
- 30% had emergency resections
- 65% had been treated with at least one TKI
- 3 pts had SIRT for liver metastases
- 4 pts had palliative radiotherapy
- 2 pts had selective embolization of liver mets
- 3 pts entered into clinical trials (not GIST specific)

Research Focus in PAWS GIST

- Collaboration
- GIST Tumour bank established for researchers
- GIST Registry in collaboration with Public Health England
- Cell line development—work in progress
  - Sheffield and Nottingham research groups
- Better understanding of the biology
- Clinical trials

Basic/Translational Research outcomes from the PAWS GIST Clinic

- Preferential MGMT hypermethylation in SDH deficient wild- type GIST
  - Manuscript submitted to Clinical Pathology
  - Can discuss off line
- Exploring the utility of miRNA signatures as a tumour biomarker in patients with dSDH GIST and PPGL

Slide Courtesy Ruth Casey & Olivier Giger

Clinical Research in PAWS GIST Clinic
Work in progress—no data

- Radiolabeled Gastrin Releasing Peptide Receptor (GRPR) antagonists in GRPR expressing GISTs
- Diagnostic phase
  - Drug: [68Ga]-NeoB
  - [68Ga]-NeoB radioactive diagnostic agent
- Therapeutic phase
  - Drug: [177Lu]-NeoB
  - [177Lu]-NeoB: peptide receptor radionuclide therapy

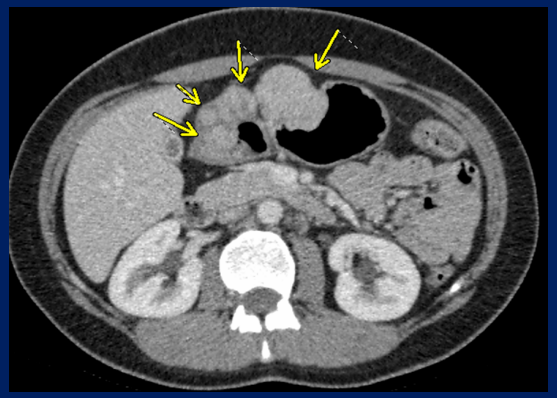
Yttrium 90 Selective Internal Radiotherapy (SIRT) in SDH Deficient GISTs

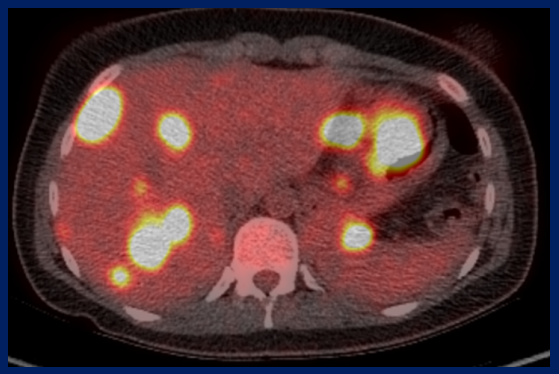
- International recommendations for personalised selective internal radiation therapy of primary and metastatic liver diseases with yttrium-90 resin microspheres: European Journal of Nuclear Medicine and Molecular Imaging volume 48,1570–1584 (2021). H Levillain et al.

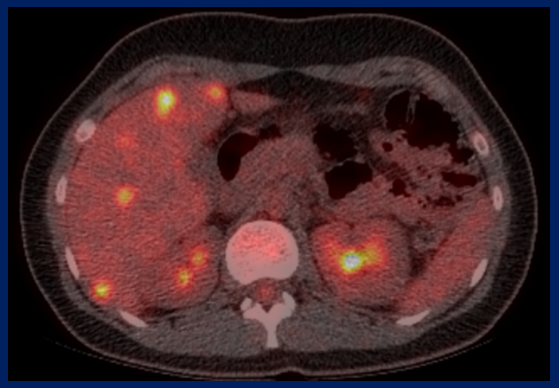
- Rationale for using Yttrium SIRT in SDH Def GISTS
- 3 patients treated in UK, 3 in USA and 1 in Germany
- Manuscript in preparation
- A potential option for patients with SDH Deficient GIST with liver only or liver predominant metastatic disease

SIRT in SDH Def GIST pt

- 25 year old female presented in 2016 with severe Fe def anaemia Hb 50
- Upper GI endoscopy and CT showed multiple gastric tumours
- EUS biopsy April 2016 mixed epithelioid/spindle cell GIST
- No activating mutations in KIT/PDGFRA
- CT/PET CT multifocal gastric gist and multiple liver metastases and peri gastric nodal met
- Imatinib 400 mg od commenced, discontinued 6 months later due to ongoing side effects
- Serial imaging showed slow progression over 3 years
- Mx options discussed with patient

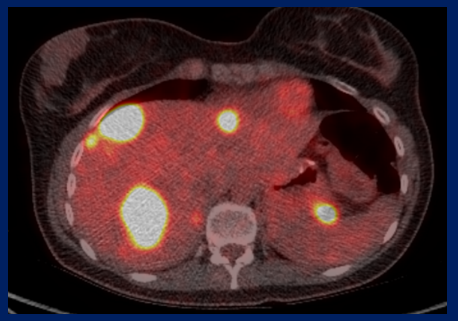


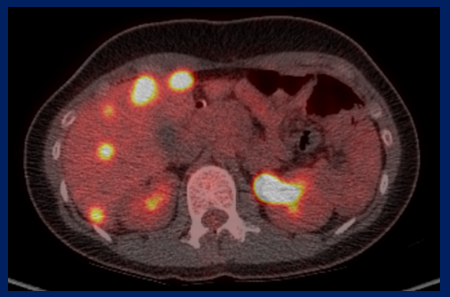


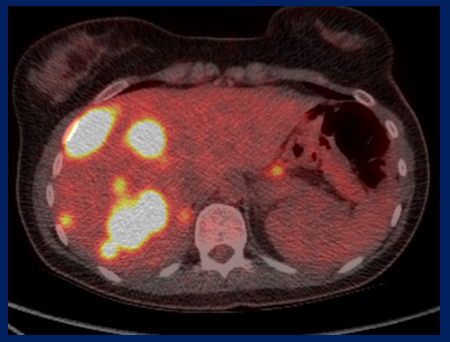


Ongoing surveillance CT & FDG PET CT

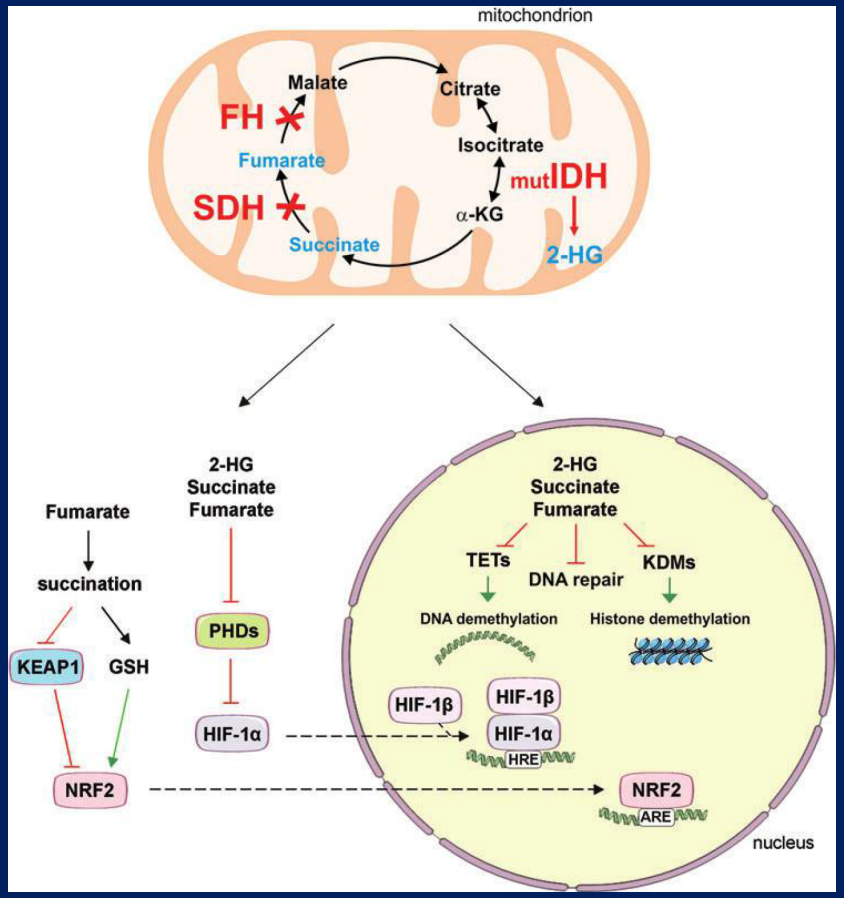
- Gastric GISTs symptomatic
  - Increasing pain
  - Anaemia
- Discussed in the PAWS GIST Clinic—Referred to Royal Marsden for debulking surgery for symptomatic multifocal gastric gists
- Partial gastrectomy Mar 2017 by Mr Dirk Strauss with excellent symptomatic benefit
- Germline sequencing no mutations in SDH complex
- SDHC promotor hypermethylation
- Continued surveillance
- Rpt PET CT Jan 2019 showed further progression liver mets
- Management options discussed in detail
  - ***PRIMUM NON NOCERE***







Rationale for SIRT



Metabolism and Epigenetic Interplay in Cancer: Regulation and Putative Therapeutic Targets Frontiers in Genetics 2018

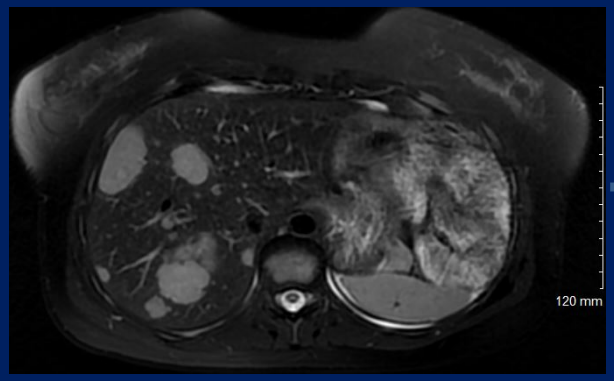
*Vera Miranda-Gonçalves[1], Ana Lameirinhas[1,2], Rui Henrique[1,3,4] and Carmen Jerónimo[1,4]**

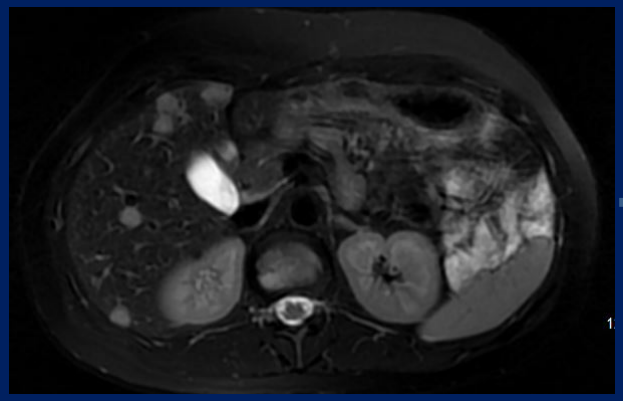
Long-term results of selective internal radioembolization (SIRT) to control progressive liver metastases of gastro-intestinal stromal tumors (GIST) beyond treatment with tyrosine kinase inhibitors (TKI). P Hohenberger ASC0 2015 updated in 2020

Conclusions: 90Y radioembolization (SIRT) offers a safe and effective treatment for patients with liver metastases of GISTs being the dominant site of tumor progression and with no drug treatment options available. In patients known to have no mutation in *KIT/PDGFRA* (wt, also NF-1 associated) it looks whether the results might be even more promising and SIRT could be used in early treatment lines.

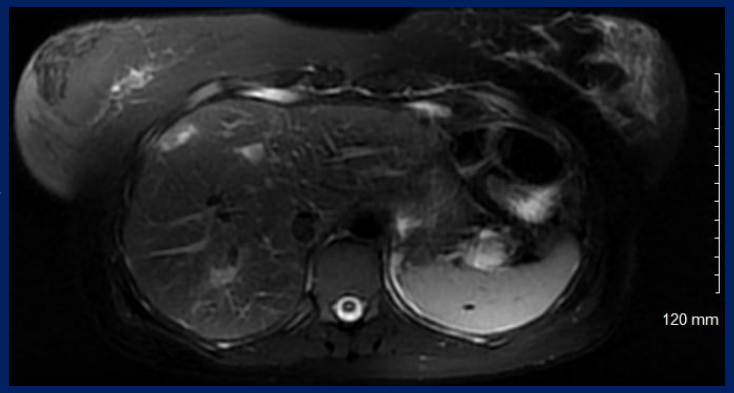
Yttrium 90 SIRT in SDH Deficient GIST

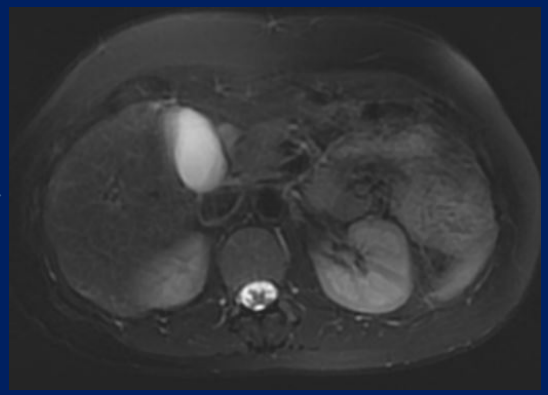
Baseline pre SIRT Sept 2019 Axial T2 wt MRI





32 months post SIRT June 2022 Axial T2 wt MRI





What next ?

- Collaboration—I am not tired of using this word
- Go back to basic question—should we call this tumour a GIST or SDH Deficient Cancer???
- My personal opinion is get this cancer out of GIST box
- Opens up other avenues
- Multinational/multi institute clinical trials
- Consensus/position statements from experts
- Collaborate/combine data sets

Position paper from the United Kingdom's Paediatric, Adolescent, Wild-type and Syndromic (PAWS) GIST consortium

Consortium members:
Dr V Ramesh Bulusu – *Chairman*
Ms Jayne Bressington – *Patient Director PAWS-GIST, Vice Chair GIST Cancer UK, Patient Advocate and mother of a PAWS-GIST patient.*

Dr Ruth Casey Dr Olivier Giger Professor Robin Jones Dr Charlotte Benson Mr Richard Hardwick Dr Nicholas Carroll Mr Myles Smith Dr Palma Dileo Dr Stephen Lowis Professor Andrew Hall Professor Ian Judson Professor Eammon Maher
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www.pawsclinic.org.uk

This document provides practical guidance for clinicians involved in the day-to-day management of PAWS-GIST patients.

We also hope that it will provide a platform for future engagement with national / international researchers to improve understanding of the biology and stimulate effective treatments.

Thank you to

- GIST Cancer UK
- Cambridge University hospital
- PAWS GIST Admin team

- Jayne Bressington
- Patients and families and carers who made this possible
- Fund raisers