

Imatinib in GIST patients
The Beatson West of Scotland Cancer
Centre experience

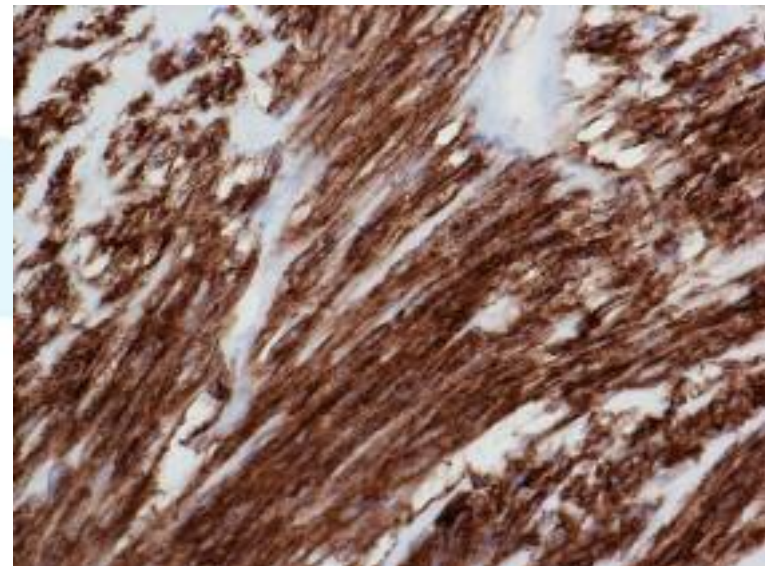
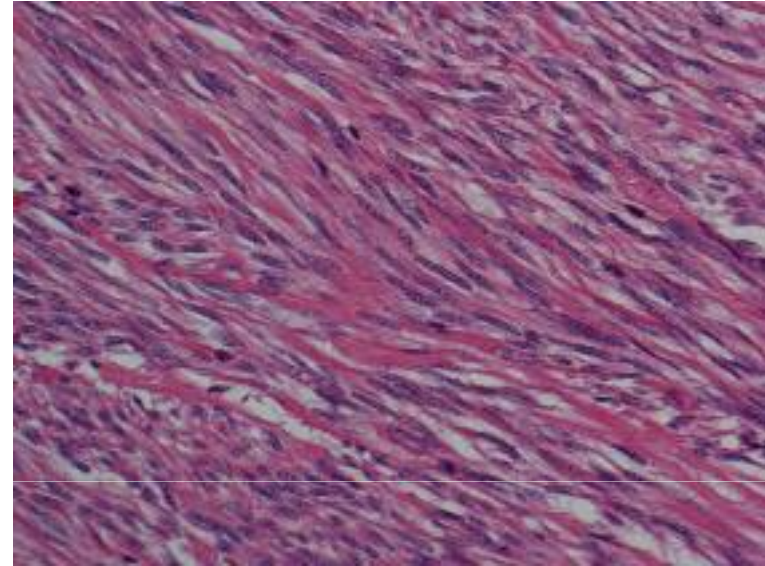
Dr Jens Samol
SpR Medical Oncology

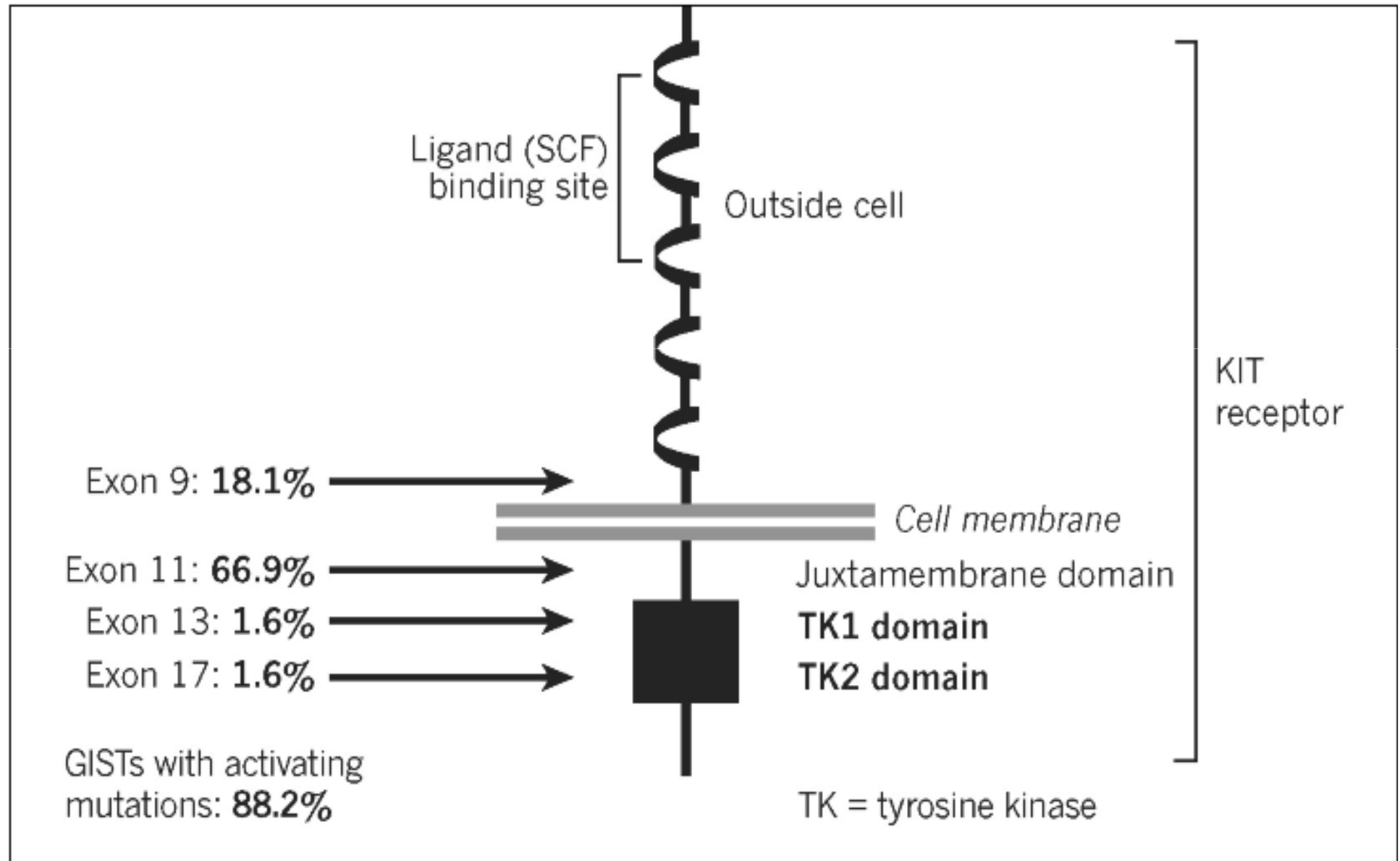
GIST's

- Rare, ~ 2% of GI cancers
- Most express c-KIT mutations in ICC – CD117+
- Incidence 10-20/million
- Surgery is mainstay of treatment
- Radioresistant and relatively chemoresistant
~7% RR with adriamycin
- Imatinib is standard treatment in unresectable/
metastatic disease
 - EORTC & NCI Phase III RCT. PFS 18-20 months and
median overall survival time exceeds 55 months

GIST-Histology

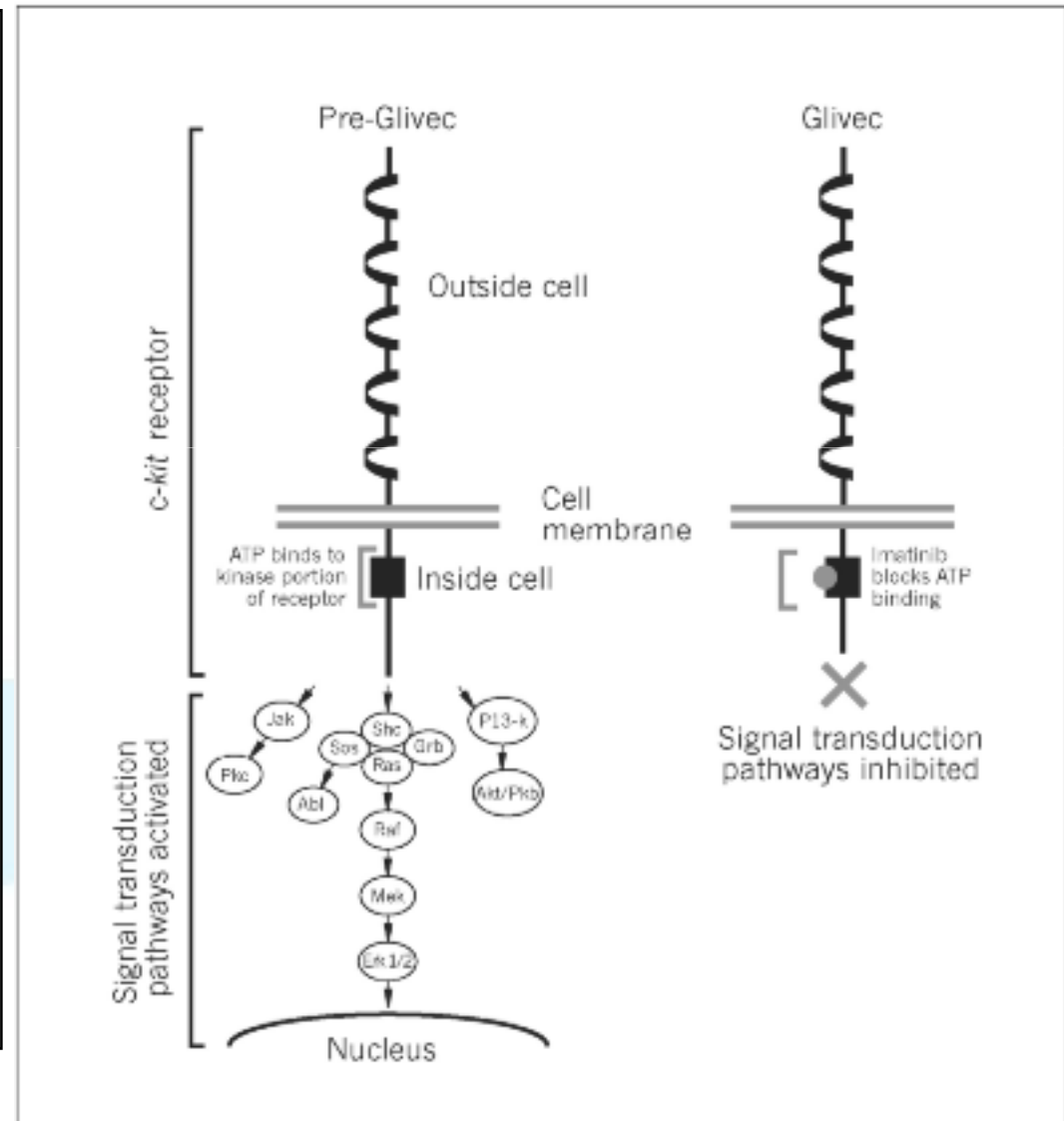
- Spindle cell (70%), epithelioid / round-cell variants (30%)
- **CD117**- Receptor tyrosine kinase for cytokine stem cell factor (SCF), also known as c-KIT ligand





Imatinib

- Initially 400mg/day
- Assess response after 3 months
- If no response \uparrow to 800mg/day or consider Sunitinib
- Assess every 3 months
- No drug holiday in responders



Method

- 39 patients with proven GIST, who received Imatinib were selected
- Time of diagnosis: Mar 1996 to July 2008 (>12 y)
- Time of starting Imatinib: Oct 2001 to July 2008 (~7 y)
- West of Scotland Cancer Centre Network
- Data sources: patient records, pharmacy records, pathology reports
- Data were collated retrospectively
- SPSS was used for data analysis

CHARACTERISTICS OF PATIENTS

		<u>No of Pts (%)</u>
Sex	Male	20 (51%)
	Female	19 (49%)
Age	Median	60
	Range	32 to 87
Surgery	No	17 (44%)
	Yes	22 (56%)
	-curative surgery	18 (81%)
	-palliative surgery	4 (19%)
CD 117	Positive	39 (100%)
CD 34	Positive	19 (49%)
	Negative	13 (33%)
	NA	7 (18%)
ECOG PS	0/1	36 (92%)
	2	2 (5%)
	3	1 (3%)
Original tumour site	Stomach	14 (36%)
	Duodenum	4 (10%)
	Small bowel	8 (20%)
	Rectum	3 (8%)
	Others	10 (26%)
Mutational analysis	Exon 13	3
	Exon 17	1
	Monosomy 14&22	1
	1p del + monos 22	1

PS in phase III trials

- PS 0 46%
- PS 1 40%
- PS 2 10%
- PS 3 4%

- PS 0-2 96%

– Verweij et al Lancet,
2004, 364, pp1127

- PS 0-2 96%
- PS 3 4%

– Blanke et al, JCO,
2008, 26, pp626

Patients receiving Imatinib

- Metastatic 26
- Locally advanced 6
- Neo-adjuvant 4
- Adjuvant 3

Dose reductions

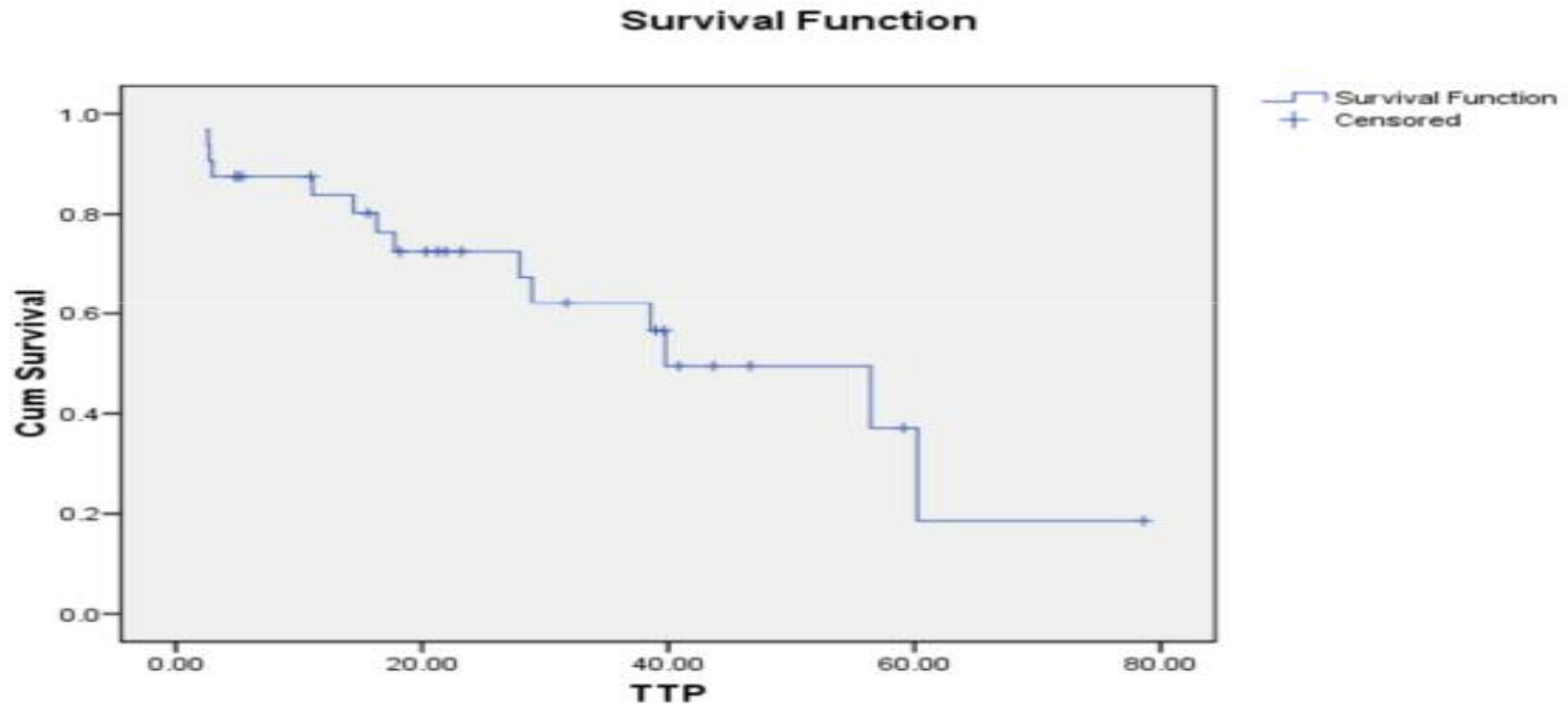
- 1 skin toxicity
- 1 myelosuppression
- 2 had skin toxicity and diarrhoea
- 1 had diarrhoea and fluid retention
- 1 had fluid retention and skin toxicity
- 1 had diarrhoea and periorbital oedema
- 3 stopped prior to surgery

- No significant toxicity was documented in remaining patients

Outcome of dose reductions

- Dose reduction was maintained in 5 patients – toxicity did not improve
- 1 patient re-escalated to 300mg OD
- 1 patient re-escalated to 400mg OD
- 1 surgical patient discontinued after surgery, whereas other 2 re-started 400mg OD

Progression free survival from start of Imatinib

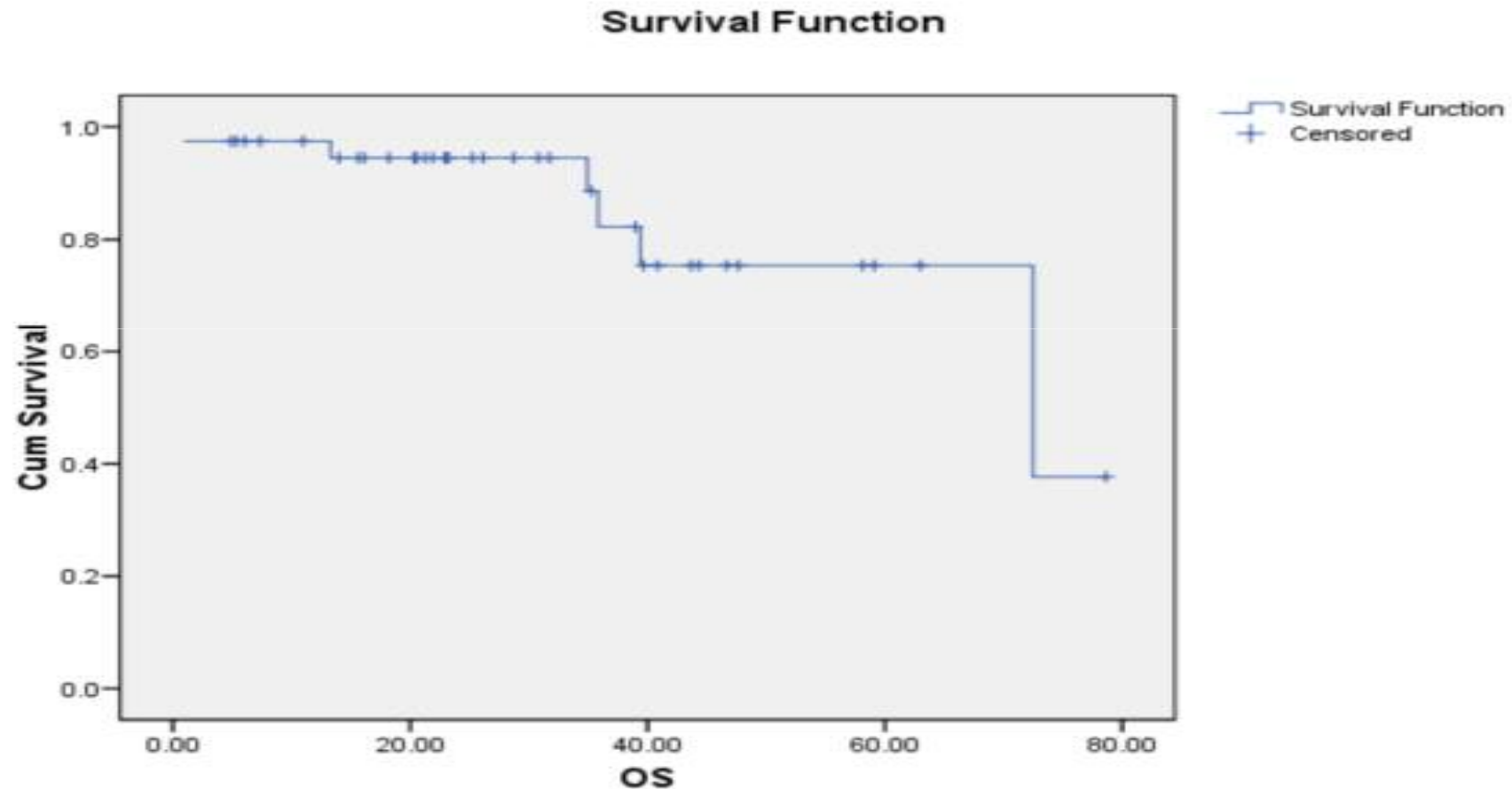


Median PFS 39 months (CI 19 – 60months)

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Overall Survival from start of Imatinib

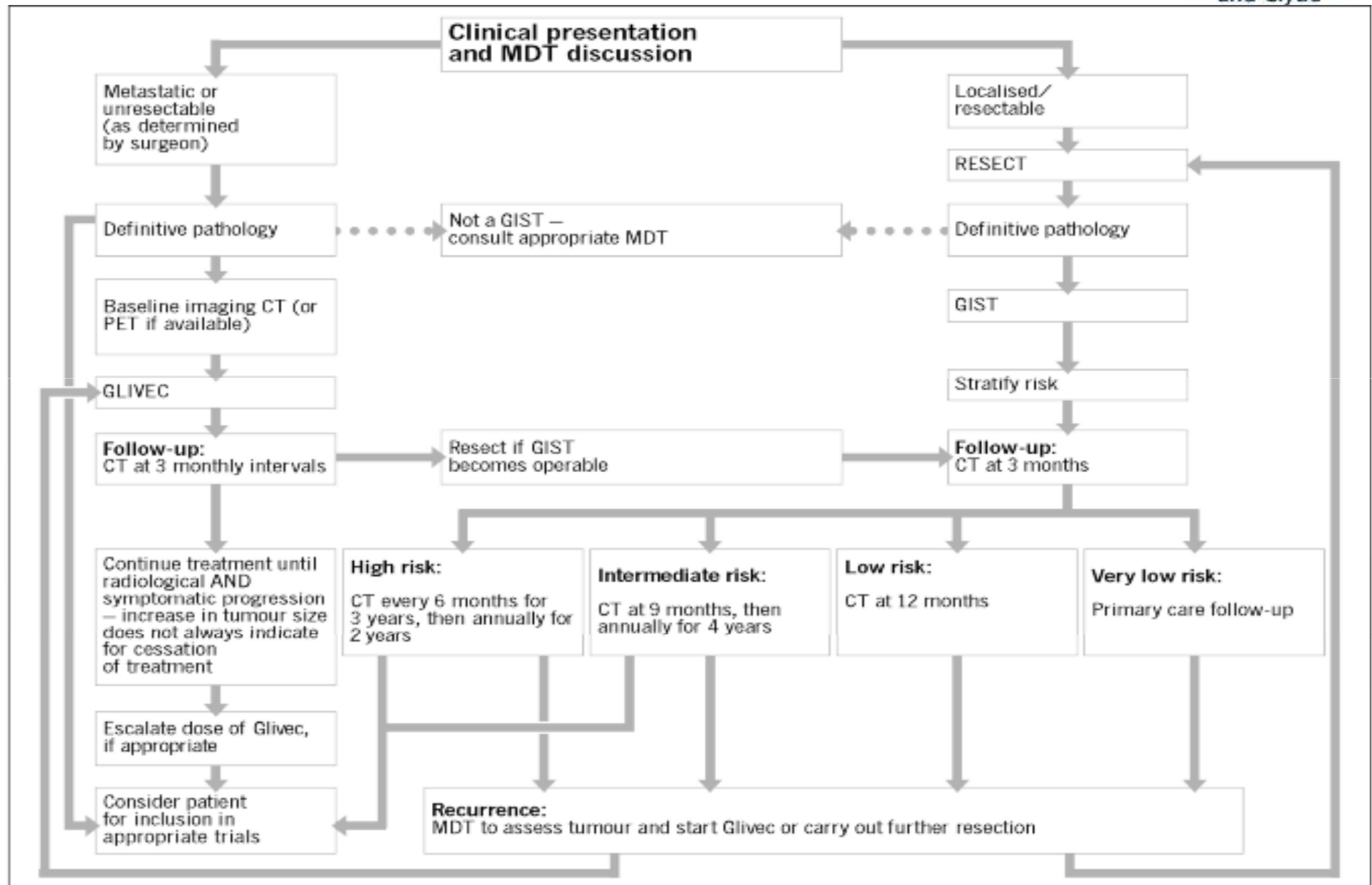


Median OS 72 months (CI 25 – 119 months)

Univariant analysis for PFS

- Between gender (p=0.46)
- When comparing NIH prognostic score (p=0.51)
- For initial PS (p=0.74)
- For dose reductions (p=0.2)

Scottish GIST Guidelines (2006)



SURGERY AFTER GLIVEC - PATIENTS CHARACTERISTICS

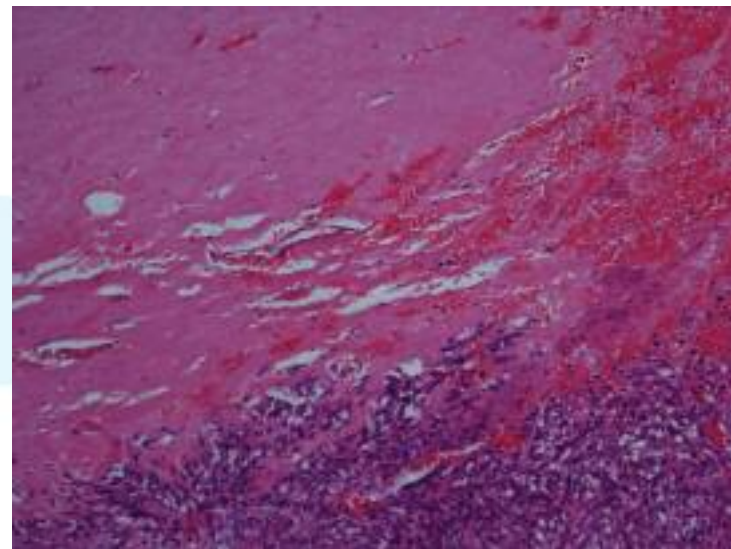
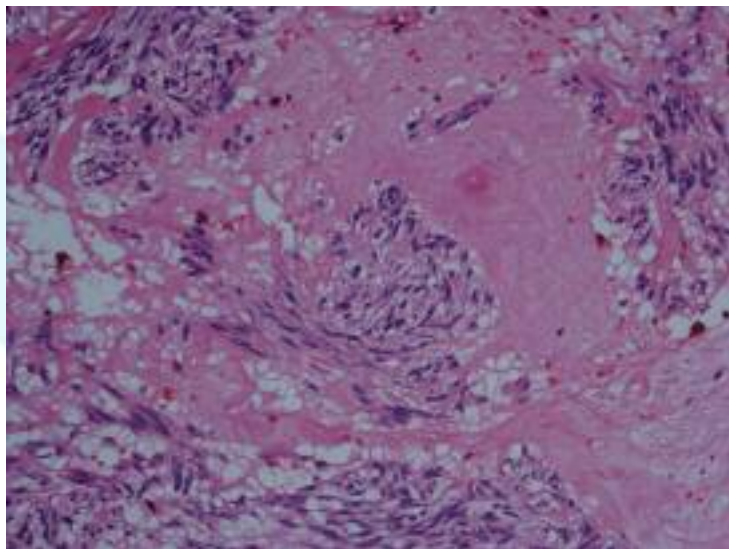
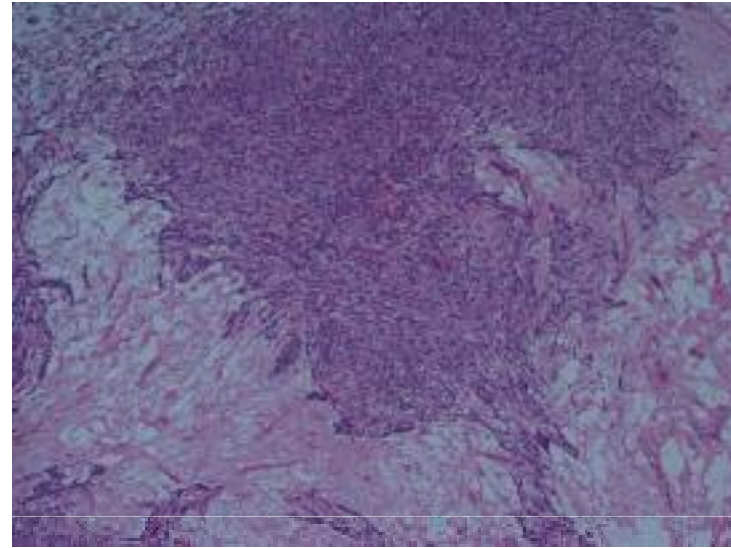
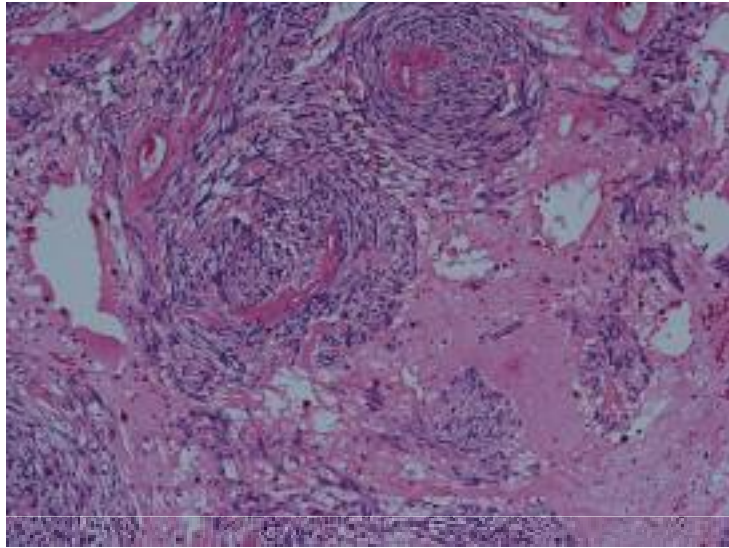
		<u>No of Pts (%)</u>
Sex	Male	5 (56%)
	Female	4 (44%)
Age	Median	58
	Range	35 to 69
Surgery	neo-adjuvant	2 (22%)
	Salvage	7 (78%)
ECOG PS	0/1	9 (100%)
Neutrophils	$< 5 \times 10^9/l$	7 (78%)
	$\geq 5 \times 10^9/l$	2 (22%)
Haemoglobin	$< 11.3g/l$	6 (67%)
	$\geq 11.3g/l$	3 (33%)
Albumin	$< 35g/l$	5 (56%)
	$\geq 35g/l$	4 (44%)
Pathological response	Yes	7 (78%)
	No	1 (11%)
	Not commented	1 (11%)

Pathological descriptions for Imatinib response:

Cystic and/or fibrotic degeneration with or without haemorrhage or necrosis

Hyalinised areas with or without fibrosis

Patchy foci of viable tumour



Lines of treatment post salvage surgery

- 2nd line
 - 1 (Imatinib 400mg second time round)
 - 1 (Sunitinib 37.5mg)
 - 1 (dose escalation to Imatinib 800mg)
- 3rd line
 - 1 (Imatinib 800mg vs Sunitinib trial)
- 6 pts had no further treatment after salvage therapy

Conclusion

- Patients characteristics reflect typical GIST patients
- PFS and OS after Imatinib are longer in this cohort
- Improved PFS and OS likely to be due to adherence to guidelines
- Side effects are mild and acceptable
- Patients on Imatinib post surgery are too few to perform statistical analysis
- This study highlights the need for a national GIST database to look at:
 - prognostic factors
 - who should have surgery
 - what 2nd line treatment + defining optimal treatment

Acknowledgement



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THANK YOU!

Any Questions?