

Education and Training Team Collaborative Stage Data Collection System Version 2.02



# What are GISTs?

- Rare type of soft tissue sarcoma - 4500-6000 adults (2009) - all sites
- Different from carcinomas
- Develop in muscle layer of gut rather than mucosa
   Grow outward (exophytic)
- Described as a distinct entity in 1998
- Umbrella term for most mesenchymal tumors of stomach and intestine
- Most tumors historically called leiomyosarcoma are now classified as GISTs

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	% GISTs	% Prim Site
Esophagus	5%	<u>&lt;</u> 1%
Stomach	55%	1-3%
Small intestine	30%	20%
_arge intestine	2%	<1%
Rectum	5%	<1%
Other (very rare	)	_
- Peritoneum, me	, sentery, omen	tum, liver, pancre



- behaviors
- Separate reportability rules apply

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	GIST Tumor Size
000	No mass/tumor found
001-988	001 - 988 millimeters (code exact size in millimeters)
989	989 millimeters or larger
990	Microscopic focus or foci only, no size of focus given
991	< 1 cm
992	< 2 cm, or > 1 cm, or "between 1 cm and 2 cm" Stated as T1, NOS
993	< 3 cm, or > 2 cm, or "between 2 cm and 3 cm"
994	< 4 cm, or "> 3 cm, or "between 3 cm and 4 cm"
995	< 5 cm, or > 4 cm, or "between 4 cm and 5 cm" Stated as T2, NOS
996	Stated as T3, NOS
997	Stated as T4, NOS
<b>999</b>	Unknown; size not stated Not documented in patient record



# **GIST CS Extension**

- · Varies by primary site
- Very similar to carcinoma schema for same site (depth of invasion)

  - Slight differences in wording
     Elimination of T subcategories (T1a, T1b, ...)
  - Carcinoma polyp codes generate error in TNM7
- TNM7 mapping driven by tumor size, not depth of invasion

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# **GIST CS Lymph Nodes**

- Nodal metastases rare in GISTs
  - If no information on nodes, assume negative and code as 00
- Schemas vary by primary site
- · Similar to carcinoma schema for same site
  - No N2, N3 codes
  - No tumor deposit codes
  - Slight differences in wording

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## Mets at Dx-Metastatic Sites

· 4 new fields

- Bone excluding marrow
- Lung excluding pleura and pleural fluid

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- Brain excluding spinal cord and other CNS
   Liver
- Code 0 when CS Mets at Dx is 00
- Code structure
  - 0 No 1 Yes
  - 8 Not applicable
  - 9 Unknown

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- Mitotic count
- Kit immunohistochemistry
- Kit gene mutation
- PDGFRA gene mutation
- Tumor multiplicity
- Location (SSF #) varies by primary site

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Mitotic Count (1)		
Code	Description	
000	0 mitoses per 50 HPF 0 mitoses per 5 square millimeters (mm <sup>2</sup> ) Mitoses absent No mitoses present	
001-008	.18 mitoses per 50 HPF .18 mitoses per 5 mm <sup>2</sup>	
009	.9 mitoses per 50 HPF .9 mitoses per 5 mm <sup>2</sup> Stated as < 1 mitosis per 50 HPF Stated as < 1 mitosis per 5 mm <sup>2</sup>	
010-100	1-10 mitoses per 50 HPF 1-10 mitoses per 5 mm <sup>2</sup>	
110	11 or more mitoses per 50 HPF 11 or more mitoses per 5 mm <sup>2</sup>	



Code	Description			
988	Not applicable: information not collected for this case			
990	Specific number not stated, described as ≤ 5 mitoses per 50 HPF Specific number not stated, described as ≤ 5 mitoses per 5 mm <sup>2</sup>			
995	Specific number not stated, described as > 5 mitoses per 50 HPF Specific number not stated, described as > 5 mitoses per 5 mm <sup>2</sup>			
999	Unknown Not stated Not documented in patient record			



KIT IHC		
Code	Description	
010	Positive	
020	Negative/normal; within normal limits	
030	Borderline; undetermined whether positive or negative	
988	Not applicable; information not collected for this case	
997	Test ordered, results not in chart	
998	Test not done (test was not ordered and was not performed)	
999	Unknown or no information Not documented in natient record	



# **KIT Gene Mutation**

- Source: specialty/reference lab report
- C-kit gene regulates cell growth and differentiation
- 85-90% of GISTs contain oncogenic mutations
  - of KIT receptor tyrosine kinase gene – Mutations primarily of exon 11 and 9, and rarely of exons 13 and 17
  - Exon: A segment of a gene that contains instructions for making a protein
- Specific exon mutation may indicate potential response to targeted therapy drugs
  - Imatinib mesylate (Gleevec) and Sutent

	KIT Gene Mutation				
Code	Description				
000	KIT gene test performed, negative for mutations				
010	KIT gene test performed, positive for mutation of exon 9				
020	KIT gene test performed, positive for mutation of exon 11				
030	KIT gene test performed, positive for mutation of exon 13				
040	KIT gene test performed, positive for mutation of exon 17				
800	KIT gene test performed, positive for other specified mutation				
810	KIT gene test performed, positive for more than one mutation				
850	KIT gene test performed, positive NOS; specific mutation(s) not stated				
988	Not applicable; information not collected for this case				
997	KIT gene test ordered, results not in chart				
998	KIT gene not done (test not ordered and not performed)				
<b>999</b>	Unknown; Not documented in patient record				





PDGFRA Gene Mutation		
Code	Description	
010	PDGFRA gene test performed, positive for mutations	
020	PDGFRA gene test performed, negative for mutations	
988	Not applicable: information not collected for this case	
997	PDGFRA gene test ordered, results not in chart	
998	PDGFRA gene test not done (test was not ordered and no performed)	
999	Unknown Not documented in patient record	
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## GIST Peritoneum SSF 10 Location of Primary Tumor

Code	Description	Stage Table
010	Mesentery Mesoappendix Mesocolon	GISTSmallIntestine
020	Omentum	GISTStomach
030	Pelvic Peritoneum	GISTSmallIntestine
040	Rectouterine pouch Cul de sac Pouch of Douglas	GISTSmallIntestine
988	Not applicable for this schema (may be used when AJCC staging is not derived)	
998	Other specified peritoneal site	GISTSmallIntestine
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# What Do Neuroendocrine Cells Do?

- Dual roles in both endocrine system and nervous system
- Functions

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- Produce large variety of biologically active substances
- Regulate neighboring cells (paracrine regulation) by excreting biologically active amines and hormones

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- Regulate numerous processes in body

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- Other sites that develop carcinoids
- 👷 and small cell carcinomas
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# Carcinoids and NETs in AJCC 7<sup>th</sup> Ed. and CSv2

Staging/Coding

- GI tract
  - Carcinoid: separate staging by site: stomach, small intestine, colon, rectum, ampulla of Vater
     Need size and/or depth of invasion
  - Small cell/large cell NET: stage with carcinoma
- Pancreas: stage with carcinoma
- Lung: stage with carcinoma
- Skin: separate classification for Merkel cell carcinoma

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# GI Carcinoids (NET) Mapping to T Category in AJCC 7<sup>th</sup> Ed.

Appendix Tumor size and location (organ)

Small Intestine Depth of invasion, tumor size, and segment involved

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Stomach Depth of invasion, tumor size

Large Intestine Tumor size, depth of invasion







# **Carcinoid Histologies**

- Enterochromaffin (EC) cell carcinoid (8241)

   Produces serotonin (associated with carcinoid syndrome)
  - Most common in appendix
- ECL cell tumor (Entero-Chromaffin-Like) (8242)
  - Non-peptide secreting tumor of gastric fundus/ body mucosa
  - Multiple, polypoid presentation
- Atypical carcinoid tumor (8249)
  - A.k.a moderately differentiated NET
  - More aggressive than a typical carcinoid
- Uncommon in gastrointestinal tract



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CS Common Tables for NETs
Tumor Size

Slight wording differences from solid tumors

TS/Ext Eval

LN Eval
Nodes Pos
Nodes Exam

Mets Eval

#### **General Notes for NET Schemas**

- Note 1: Only well-differentiated neuroendocrine tumors staged.
   – Grade code not needed to select the correct schema (code in 6<sup>th</sup> digit of morphology code)
- Note 2: NET schemas used for carcinoid
- tumors and malignant gastrinomas
- Note 3: NET histologies not staged in AJCC 6th Ed.
  - CSv2 algorithm will not derive 6<sup>th</sup> Ed T, N, M or stage group

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<b>CS</b> Tumor	Size
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Code	Description
000	No mass/tumor found
001-988	001 - 988 millimeters (code exact size in millimeters)
989	989 millimeters or larger
990	Microscopic focus or foci only, no size of focus given
991	Described as "less than or equal to 1 cm"
992	Described as "greater than 1 cm"
993	Stated as T1, NOS with no other information on size
994	Stated as T2, NOS with no other information on size
999	Unknown; size not stated Not documented in patient record
	CS manual



# **CS** Extension – **NET**

- Ampulla of Vater
  - Similar to carcinoma schema for site
  - No code 000
  - Separate codes for "Stated as T\_, NOS"

#### • Appendix

- Substantial differences from new carcinoma schema for appendix

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- No code 000, 050
- No polyp codes
  New T1 subcategories
- No T4 subcategories
- 50

# **CS Extension – NET**

Stomach

- Similar to carcinoma schema for site - No subcategories for T1, T4
- Small Intestine
  - Similar to carcinoma schema for site
  - No code 000, 050
  - Code 450 split to 460 and 470
  - No subcategories for T1, T4
  - Separate codes for "Stated as T\_, NOS"





- Small Intestine Appendix Colon Rectum Similar to carcinoma schema for site
  - No tumor deposits code
  - No N2
- Stomach

   Similar to carcinoma schema for site
   No N2, N3
- Ampulla of Vater
   No differences from carcinoma schema for site

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# CS Mets at Dx – NET

- Ampulla of Vater Stomach Small Intestine – No differences from carcinoma schema for site
- Colon Rectum
  - NET schema not subdivided into M1a and M1b codes
  - Similar to colon schema in CS version 1
- Appendix
  - Subdivided into mucinous and non-mucinous criteria
  - Subdivided into M1a and M1b codes

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- T combination of tumor size and location/ level of invasion
- N all involved regional lymph nodes map to N1 (no N2, N3)
- M all distant mets map to M1 (no M1a or M1b subcategories)
- Stage Grouping different from carcinoma schema for site

	Clin Assess Reg LN	CEA	Serum Chromo- granin	Urine 5-HIAA	Mitotic Count
Stomach	x	Not used	x	x	х
Sm Intest	Not used	Obsolete	x	x	х
Colon	x	Obsolete	x	x	х
Appendix	x	Obsolete	x		
Rectum	x	Obsolete	x	x	x
Ampulla	Not used	Not used	x	x	x



# **Clinical Assessment of Regional LN**

Code	Description	Stomach	Colon/Rectum
000	Nodes not clinically evident		
100	Mets in LN deter- mined clinically	1 to 6	1 to 3
200	Mets in LN deter- mined clinically	7 to 15	4 or more
300	Mets in LN deter- mined clinically	15 or more	
400	Clinically positive r	egional nodes	, NOS
988	Not applicable: Infe	ormation not c	ollected for this case
999	Unknown if nodes a	are clinically ev	vident





Mitotic Count (1)					
Code	Description				
000	0 mitoses per 10 HPF (40x field) 0 mitoses per 2 square millimeters (mm <sup>2</sup> ) Mitoses absent No mitoses present				
001-008	.18 mitoses per 10 HPF (40x field) .18 mitoses per 2 mm <sup>2</sup>				
009	.9 mitoses per 10 HPF (40x field) .9 mitoses per 2 mm <sup>2</sup> Stated as < 1 mitosis per 10 HPF (40x field) Stated as < 1 mitosis per 2 mm <sup>2</sup>				
010-500	1-50 mitoses per 10 HPF (40x field) 1-50 mitoses per 2 mm <sup>2</sup>				
510	0 51 or more mitoses per 10 HPF (40x field) 51 or more mitoses per 2 mm <sup>2</sup>				



Code	Description
988	Not applicable: information not collected for this case
990	Specific number not stated, described as < 2 mitoses per 10 HPF (40x field) Specific number not stated, described as < 2 mitoses per 2 mm <sup>2</sup>
995	Specific number not stated, described as 2 – 20 mitoses per 10 HPF (40x field) Specific number not stated, described as 2 – 20 mitoses per 2 mm <sup>2</sup>
997	Specific number not stated, described as > 20 mitoses per 10 HPF (40x field) Specific number not stated, described as > 20 mitoses per 2 mm <sup>2</sup>
999	Unknown; not stated Not documented in patient record



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Chromogranin A				
Code	Description			
000	0 ng/ml			
001	1 or less ng/ml			
002-979	002-979 ng/ml			
980	980 or greater ng/ml			
988	Not applicable: information not collected for this case			
997	Test ordered, results not in chart			
998	Test not done (test was not ordered and was not performed)			
999	Unknown or no information Not documented in patient record			
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• Source: clinical laboratory report (urine test)

- Other names
  - 5-hydroxyindoleacetic acid (5-HIAA); quantitative 5-HIAA urine
- Carcinoids release excessive serotonin (a vasoconstrictor)
  - Metabolized to 5-HIAA and excreted in urine
- Reference range: 2-8 mg/24 hours – Results > 25/24 hours indicate carcinoid
  - Many drugs can also affect 5-HIAA results

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## Urinary 5-HIAA Lab Value Level

Description			
0 ng/ml			
1 or less mg/24hours			
002-979 mg/24hours			
980 or greater mg/24hours			
Not applicable: information not collected for this case			
Test ordered, results not in chart			
Test not done (test was not ordered and was not performed)			
999 Unknown or no information Not documented in patient record			

## **NET/Carcinoid Treatment**

#### Surgical resection

- If primary is localized and resectable, 70-90% 5 year survival
- If metastatic at diagnosis, 2 year median survival
- No known effective adjuvant therapy for positive nodes
- · For distant metastases
  - Liver: wedge resections, RFA, cryosurgery, chemoembolization
  - Palliation: combination chemotherapy or radiation

3 (Marine 1997)

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Reading Lab Results								
Number	Prefix	Written	Unit	Abbrev.				
1,000,000	Mega-	М	Liter	L, I				
1000	Kilo-	k	Unit	U				
10	Deka-	da	Meter	m				
1 (baseline)		Unit-of-	Mole, mol					
1/10	Deci-	d	Gram	ar				
1/100	Centi-	c	milli-	mEq				
1/1000	Milli-	m	Equivalent	III-4				
One millionth	Micro-	μ, u, or mc	Femtomole	fmol				
One billionth	Nano-	n	Microgram ugr meg ugr					
One trillionth	Pico-	р	Milliliter	mi, mi				
One quadrillionth	Femto	f		R and areas				





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