AIGOM
ASSOCIAZIONE ITALIANA
GRUPPI ONCOLOGICI MULTIDISCIPLINARI

GIST AVANZATI:
il valore della gestione multidisciplinare del paziente

VERONA - 15 gennaio 2025

Crowne Plaza Hotel

Responsabile Scientifico
Dr.ssa Stefania Gori

Con il Patrocinio di

GIST:
dati epidemiologici

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IRCCS Ospedale Sacro Cuore Don Calabria
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Disclosures

- Advisory Board: AstraZeneca, MSD
- Speaker Honoraria: Amgen, AstraZeneca, MSD, Novartis, Roche
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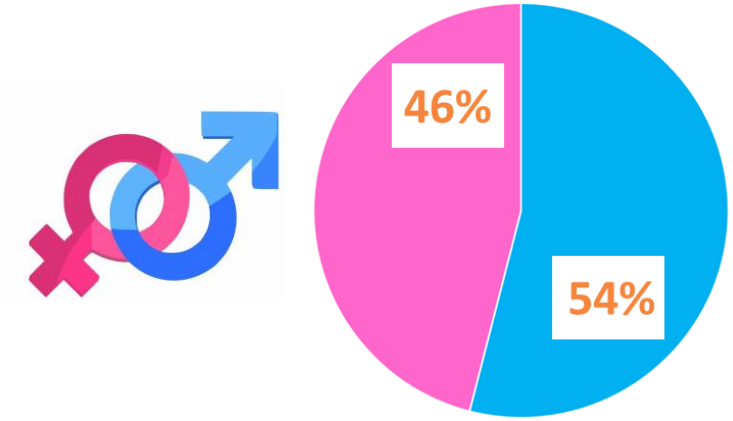
- Travel support: Amgen, AstraZeneca, Sanofi

GIST: dati di incidenza

GIST

1-1.5 nuovi casi / 100.000 / anno

600-900 nuovi casi / anno

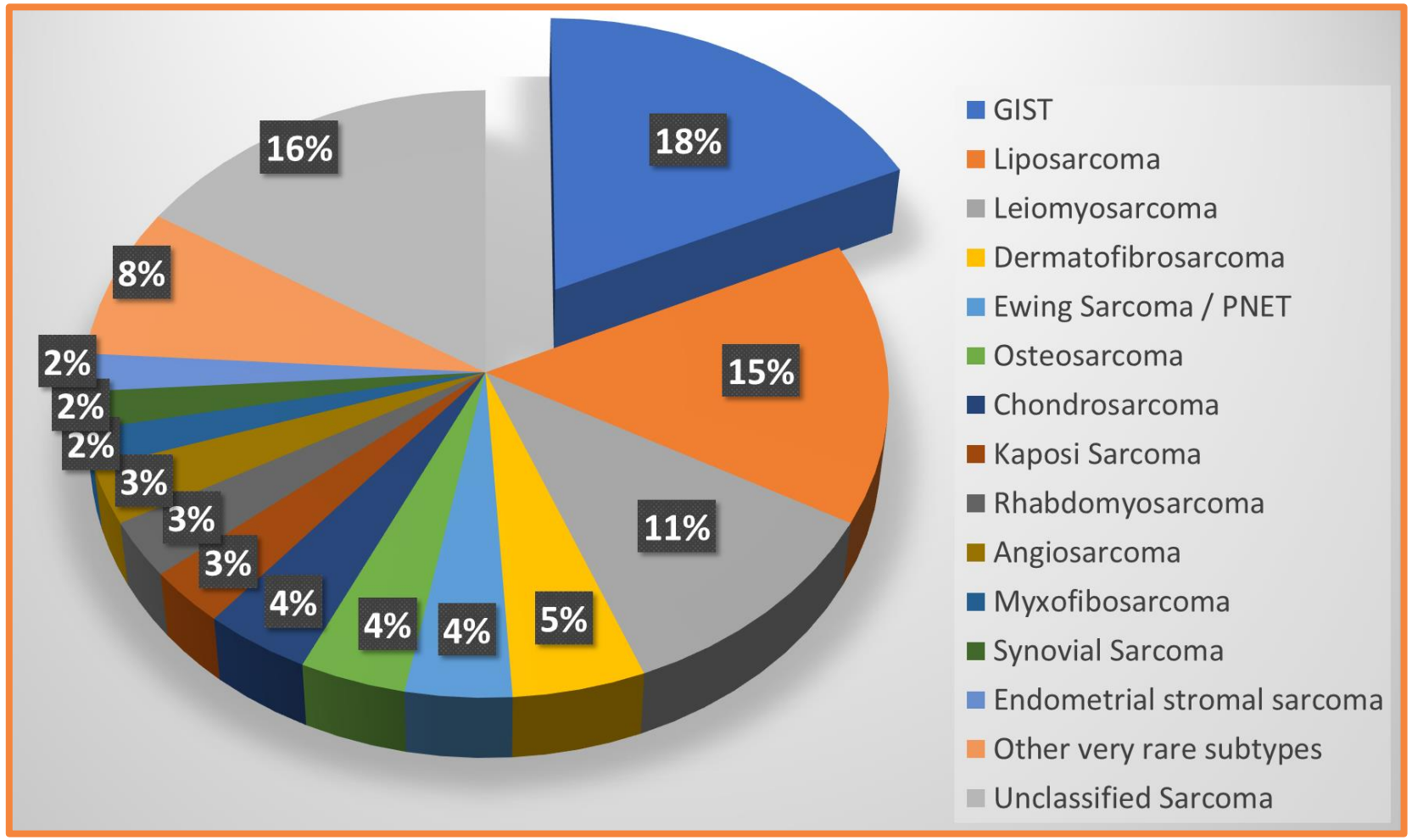


AGE **≈ 60-65 anni**

1. Nilsson B et al. Cancer 2005;103(4):821-9. 2. Søreide K et al. Cancer Epidemiol 2016;40:39-46.
3. Demetri GD et al. J Natl Compr Canc Netw 2010;8 Suppl 2(0 2):S1-41. 4. Casali PG et al. Ann Oncol 2022;33(1):20-33.
5. Alvarez CS et al. JAMA Netw Open 2024;7(8):e2428828.

Incidenza GIST/Sarcomi

I GIST rappresentano il sarcoma più frequente (18%)*

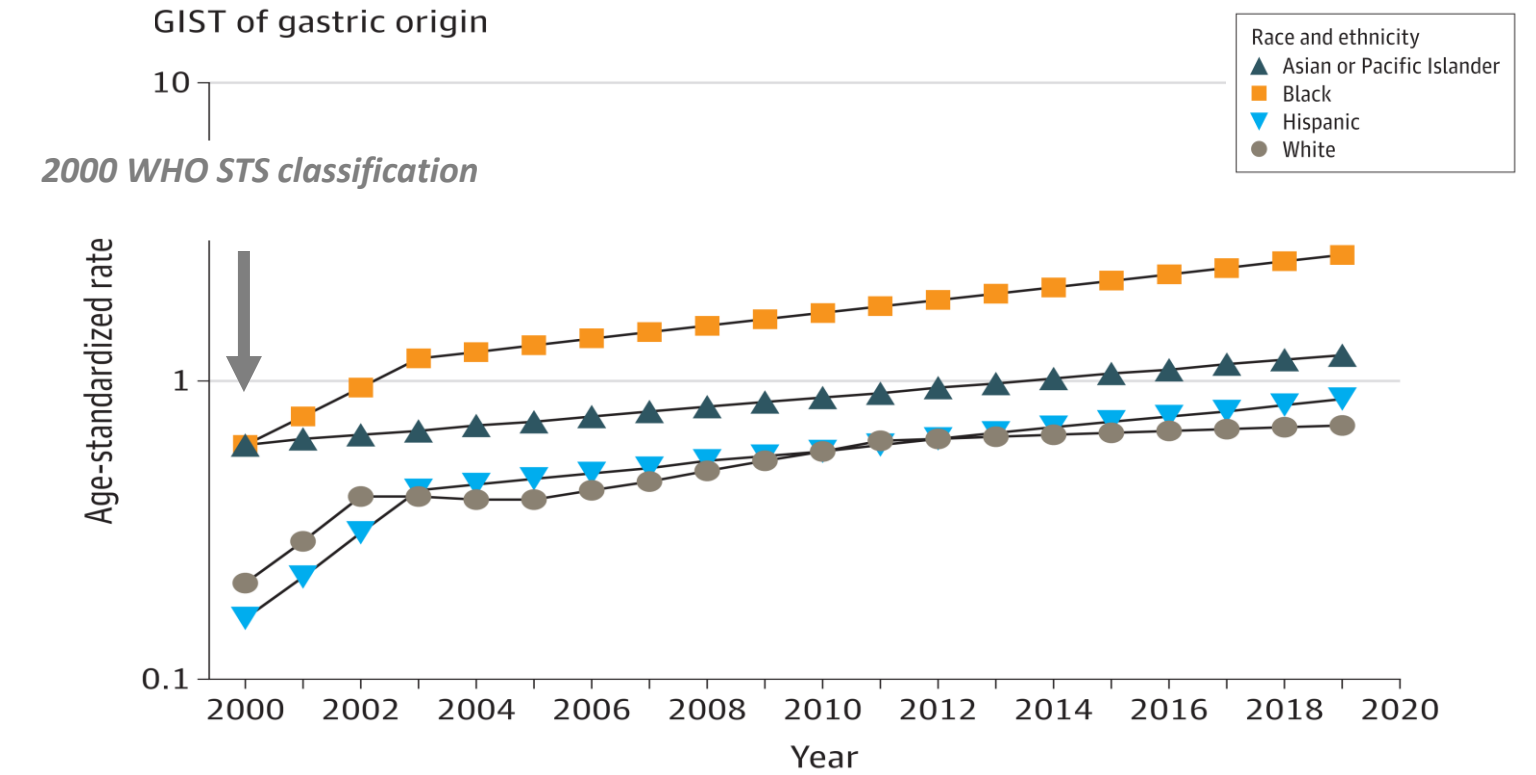


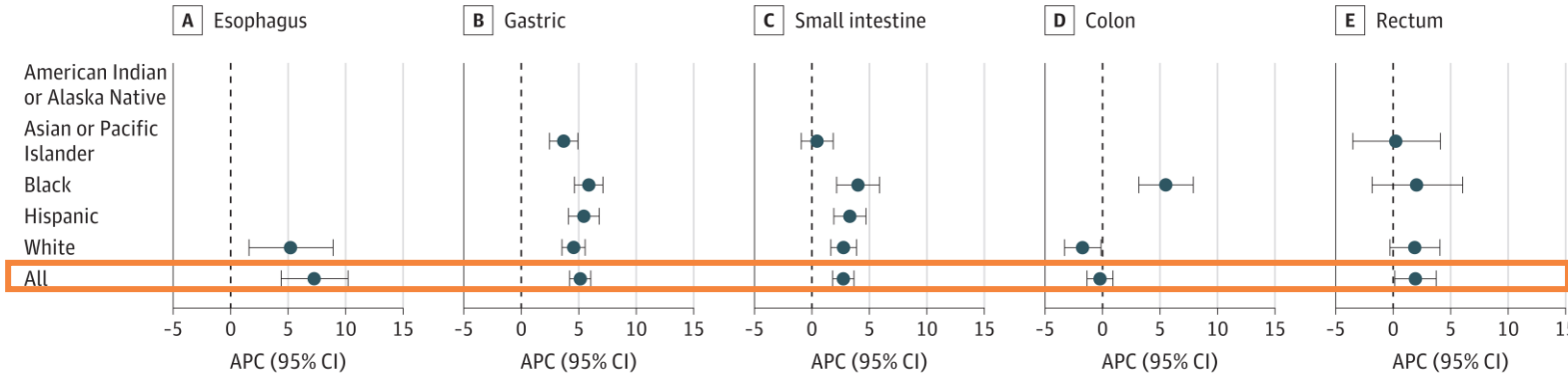
** Dati provenienti da studio epidemiologico francese su 784 sarcomi diagnosticati dal 2005 al 2007*

Modified from: Ducimetière F, et al. PLoS One 2011;6(8):e20294.

Incidenza: Variazioni temporali

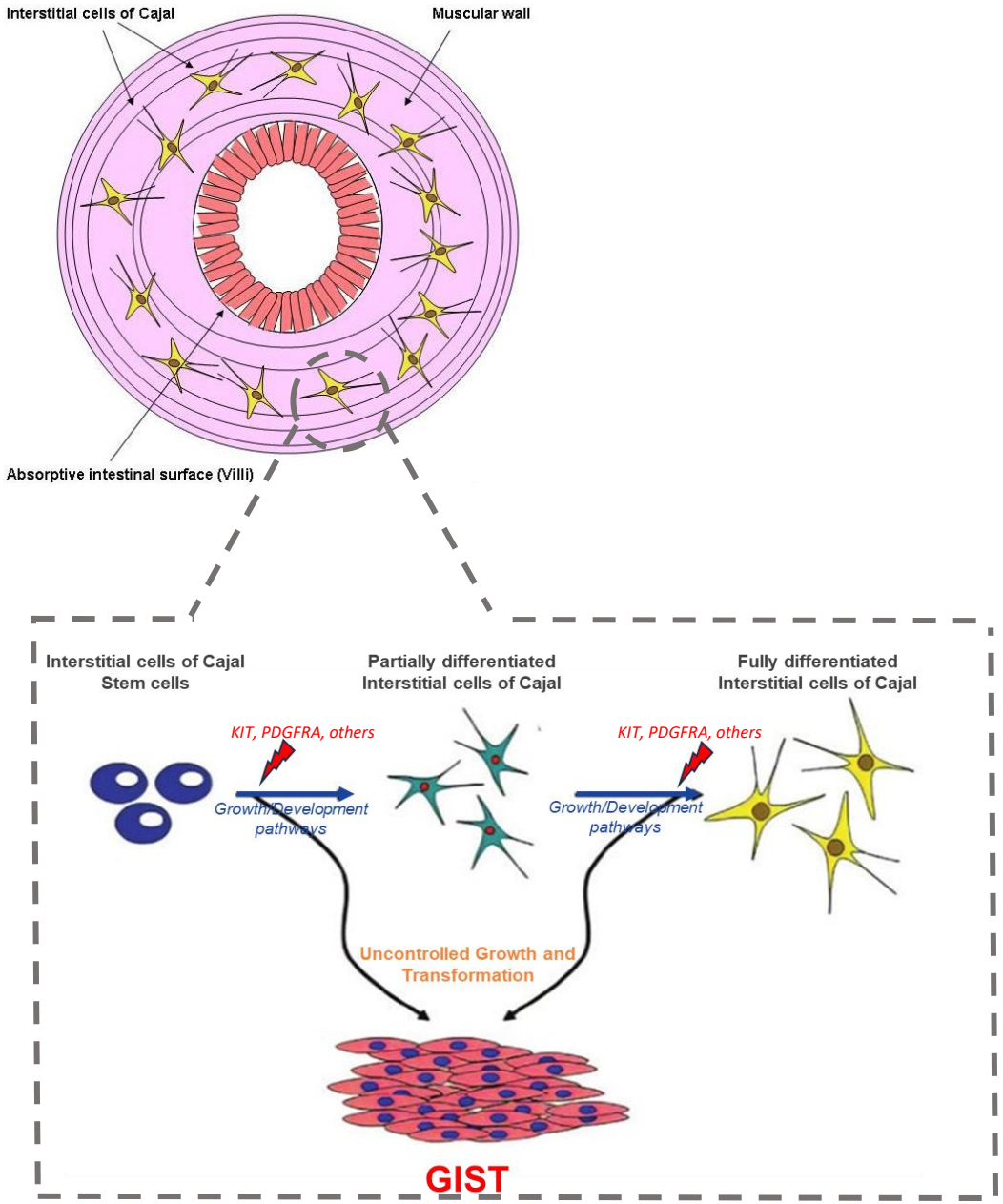
- Data from a NCI – SEER study including 23,001 patients aged ≥ 20 with GISTs diagnosed between 2000-2019
- Age-adjusted incidence rates increased between 2% and 7% in two decades, mainly early stages
- Overall incidence rates of GISTs increased substantially over time for all organ sites but the colon
- Increasing incidence cannot fully be explained by coding reclassification and advances in diagnostic technologies.
- Future research should explore lifestyle-related (i.e. obesity) or environmental factors



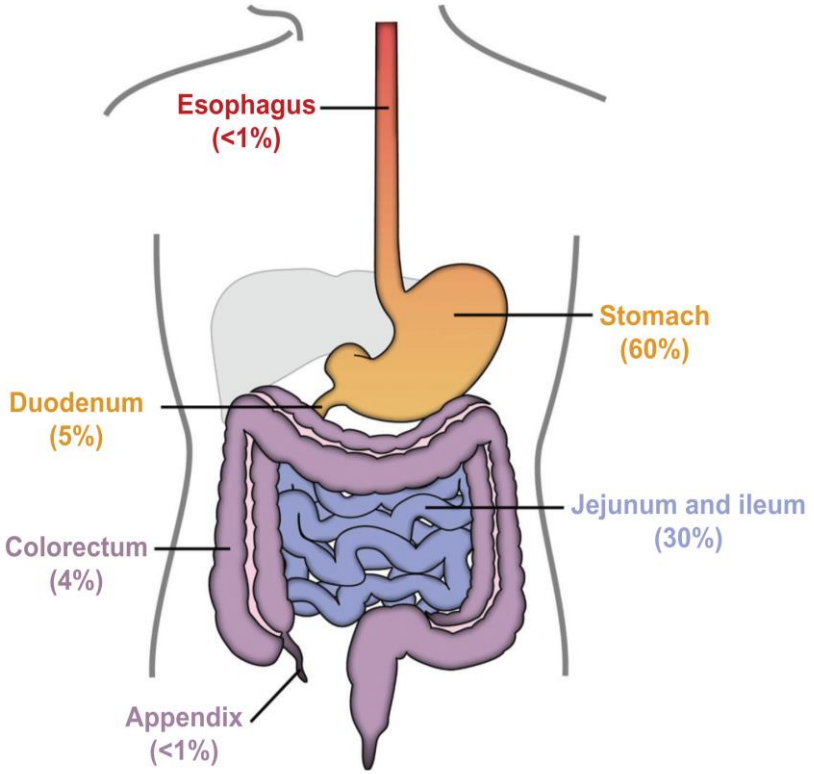


Alvarez CS et al. JAMA Netw Open 2024;7(8):e2428828.

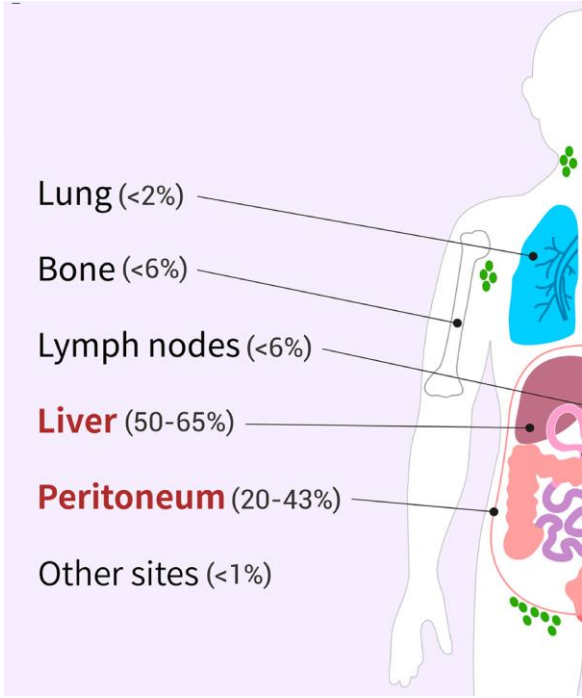
Patogenesi e distribuzione dei GIST



Primary sites

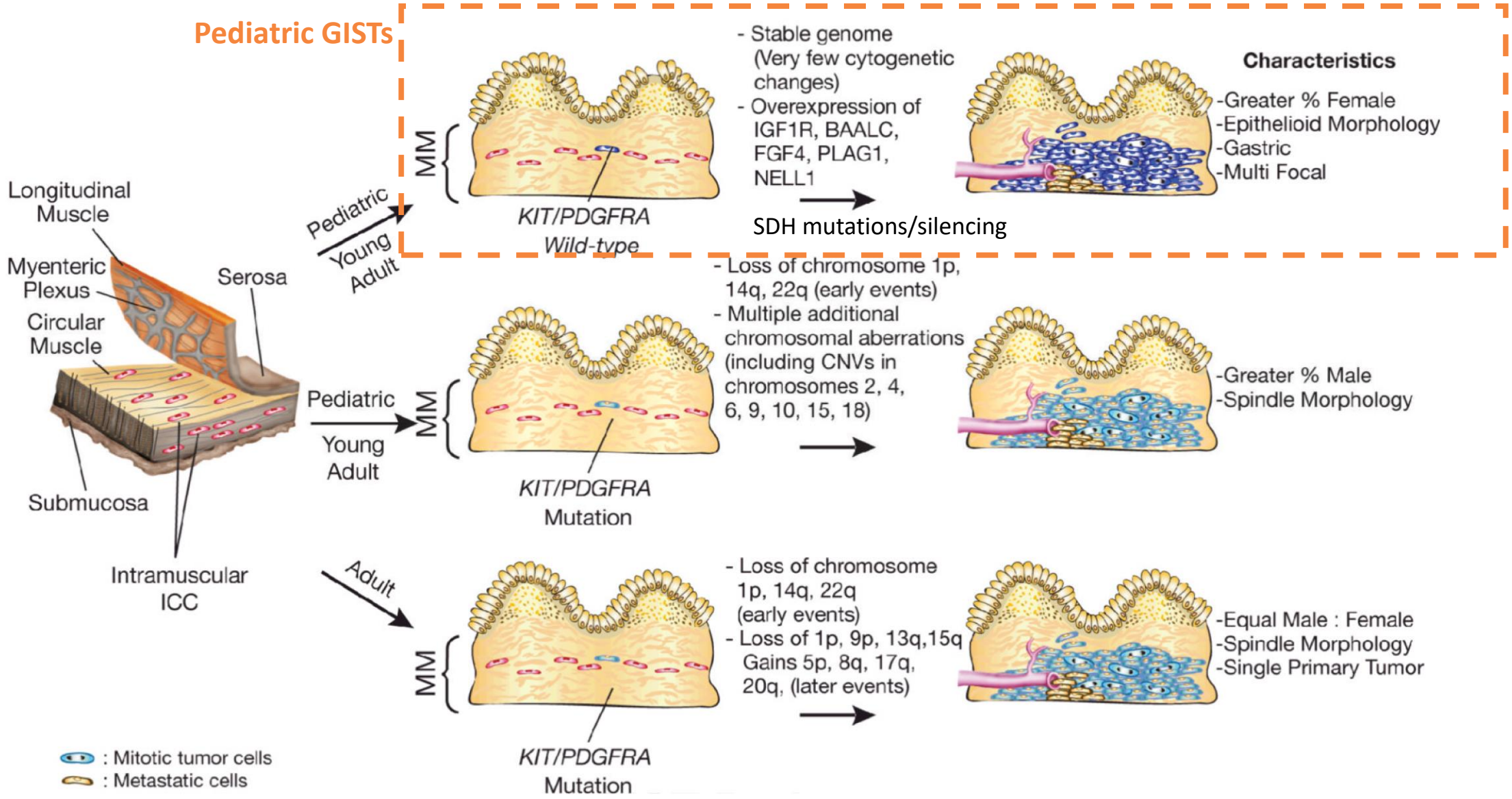


Metastasis sites



1. Sircar K et al. Am J Surg Pathol 1999;23(4):377-89.
2. Miettinen M et al. Hum Pathol 1999 Oct;30(10):1213-20.
3. Morey AL et al. Pathology. 2002;34(4):315-9.
4. Søreide K et al. Cancer Epidemiol 2016;40:39-46.

GIST pediatrici



Rink L, Godwin AK. Curr Oncol Rep 2009;11(4):314-21.

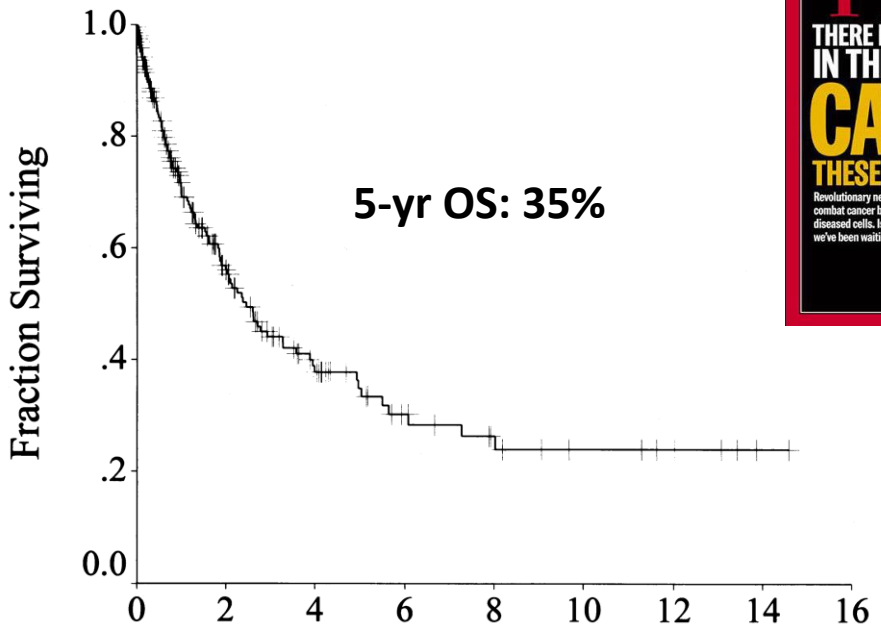
Sindromi associate a GIST

Syndrome	Molecular signature	Clinical features
Carney triad	*SDH-C* gene hypemethylation	Multifocal gastric GISTs, paraganglioma, pulmonary chondroma. Onset in the teenage years Female predominance
Carney-Stratakis	Germline mutation of one of the *SDH* subunit genes (A, B, C or D)	Multifocal gastric GIST and paraganglioma Onset from late teenage years to the 30s No gender predominance Lymph node metastatic potential
Type 1 neurofibromatosis	Germline mutation of *NF1* gene	Multicentric GISTs (in small bowel)
Familial KIT-mutant	Germline autosomal dominant *KIT* mutation	Multiple GISTs at early age Pigmented skin macules, urticaria pigmentosa and diffuse hyperplasia of the Cajal cells
Familial PDGFRA-mutant	Germline *PDGFRA* mutations	Multiple gastric GISTs Inflammatory fibroid polyps, hand deformities

1. Zhang L, et al. Am J Surg Pathol 2010;34(1):53-64. 2. Gaal J, et al Mod Pathol 2011;24(1):147-51.
3. Miettinen M, et al. Am J Surg Pathol 2006;30(1):90-6. 4. Maeyama H, et al. Gastroenterology 2001;120(1):210-5. 5. Manley PN, et al. Hum Pathol 2018;76:52-57.

Prognosi dei GIST

Pre-Imatinib

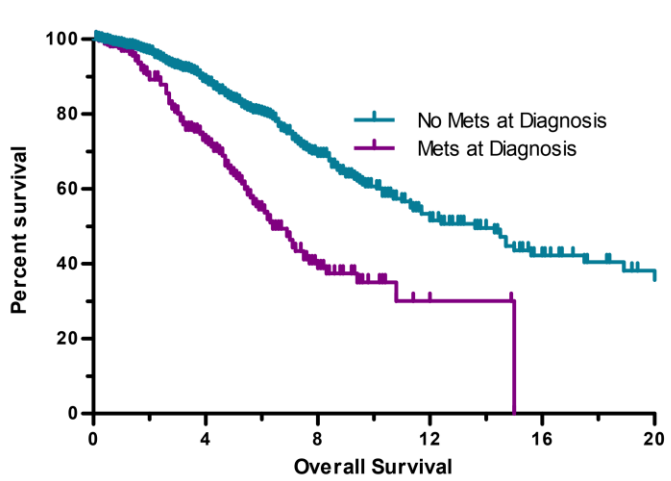


5-yr OS: 35%

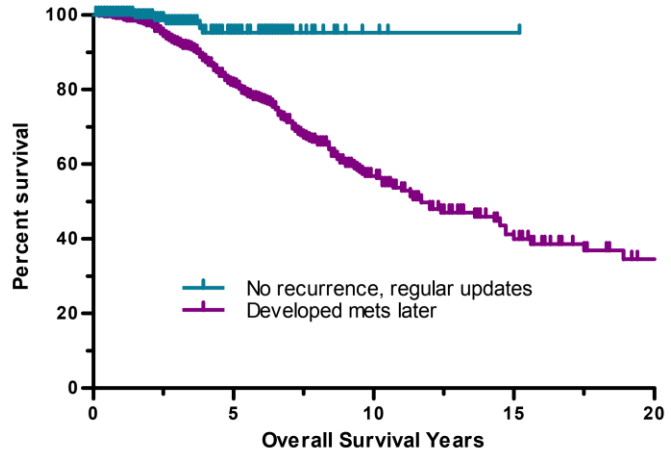
Presentation	n	Median Survival (months)	Complete Resection n	Complete Resection % of Row Total
Primary	93	60	80	86
Metastatic	94	19	28	30
Metastasis only	51	22	16	31
Primary tumor + metastasis	26	23	8	31
Local recurrence + metastasis	17	9	4	24
Locally recurrent	13	12	6	46

DeMatteo RP, et al- Ann Surg 2000;231(1):51-8.

Post-Imatinib



	Median OS
Metastatic disease at diagnosis* (n= 276)	6.4 years
Primary disease only at diagnosis (n=891)	13.6 years
P value	<0.0001
Hazard Ratio	3.075
*This group represents an easily defined group that is most similar to published results for metastatic imatinib trials. Patients less than 18 years old at diagnosis were excluded.	



	Median OS
Later had a recurrence* (n= 487)	11.7 years
No recurrence, regular updates (n=205)	Undefined
P value	<0.0001
Hazard Ratio	2.623
Both groups exclude patients diagnosed below the age of 18. *This group presented with primary disease only and later had a recurrence.	

Call J, et al. BMC Cancer 2012;12:90.

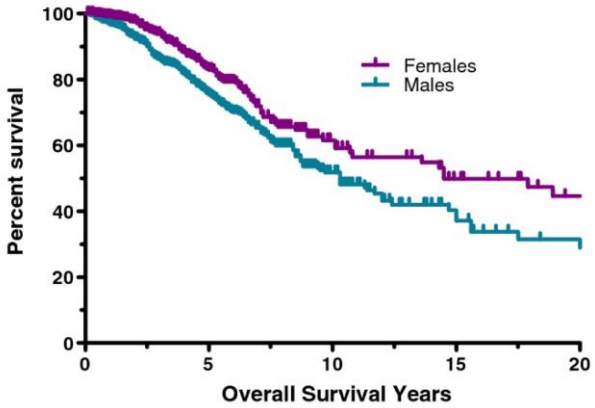
Fattori prognostici

Stage

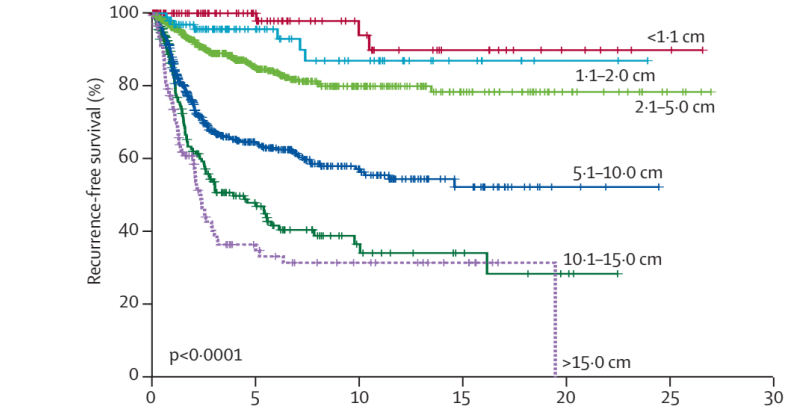
Gender

T-size
T-site
Mitoses
Rupture

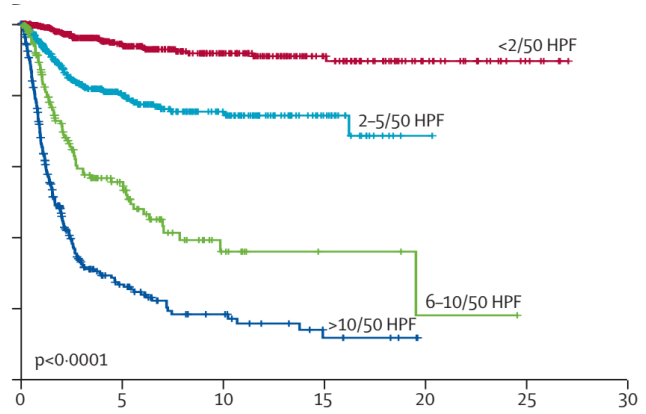
For resected GISTs



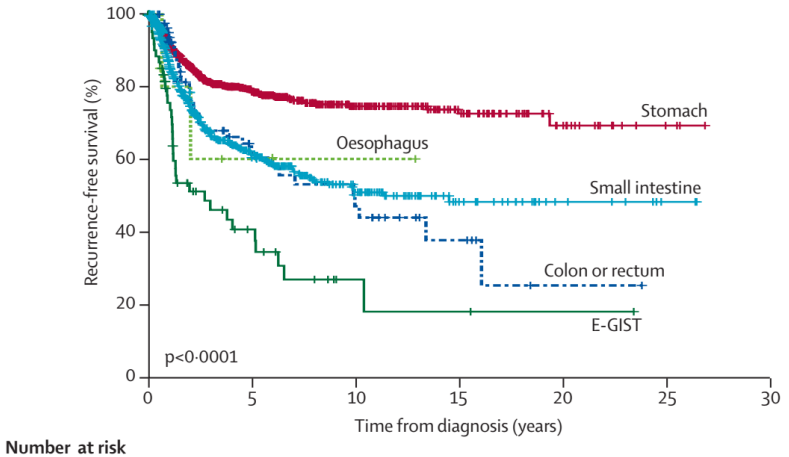
	MedianOS
Males (n=668)	10.3 years
Females (n=527)	14.5 years
Pvalue	0.0012
Hazard Ratio	1.456
Medianfollow-up	5.2 years



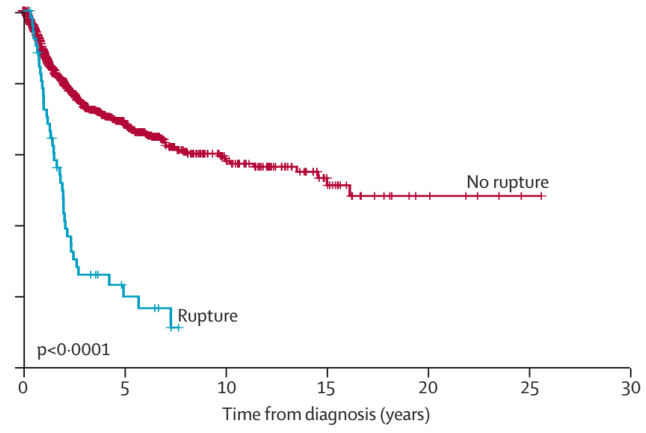
Number at risk							
≤1·0 cm	94	14	4	0	0	0	0
1·1–2·0 cm	114	41	23	8	2	0	0
2·1–5·0 cm	586	226	88	39	15	4	0
5·1–10·0 cm	491	159	68	23	3	0	0
10·1–15·0 cm	176	47	14	7	3	0	0
>15·0 cm	115	22	13	7	0	0	0



Number at risk							
<2 per 50 HPF	545	254	134	65	26	5	0
2–5 per 50 HPF	491	164	68	23	1	0	0
6–10 per 50 HPF	167	45	10	3	1	0	0
>10 per 50 HPF	290	42	15	6	0	0	0



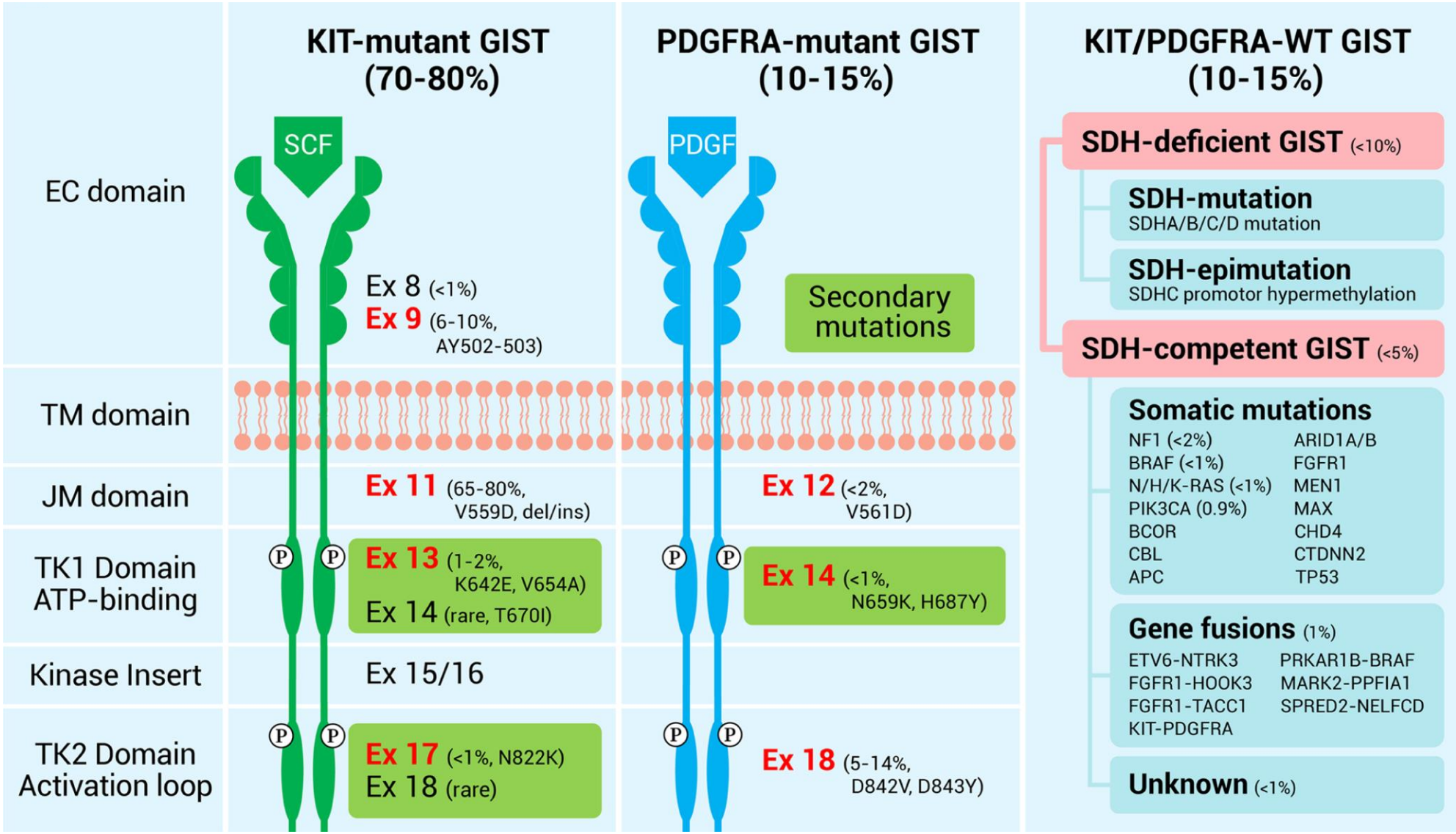
Number at risk							
Stomach	956	345	146	64	19	3	0
Small intestine	515	162	70	26	8	2	0
Oesophagus	8	2	2	0	0	0	0
Colon or rectum	84	32	15	6	1	0	0
E-GIST	61	13	3	2	1	0	0



Number at risk							
No rupture	1004	270	81	25	6	1	0
Rupture	57	6	0	0	0	0	0

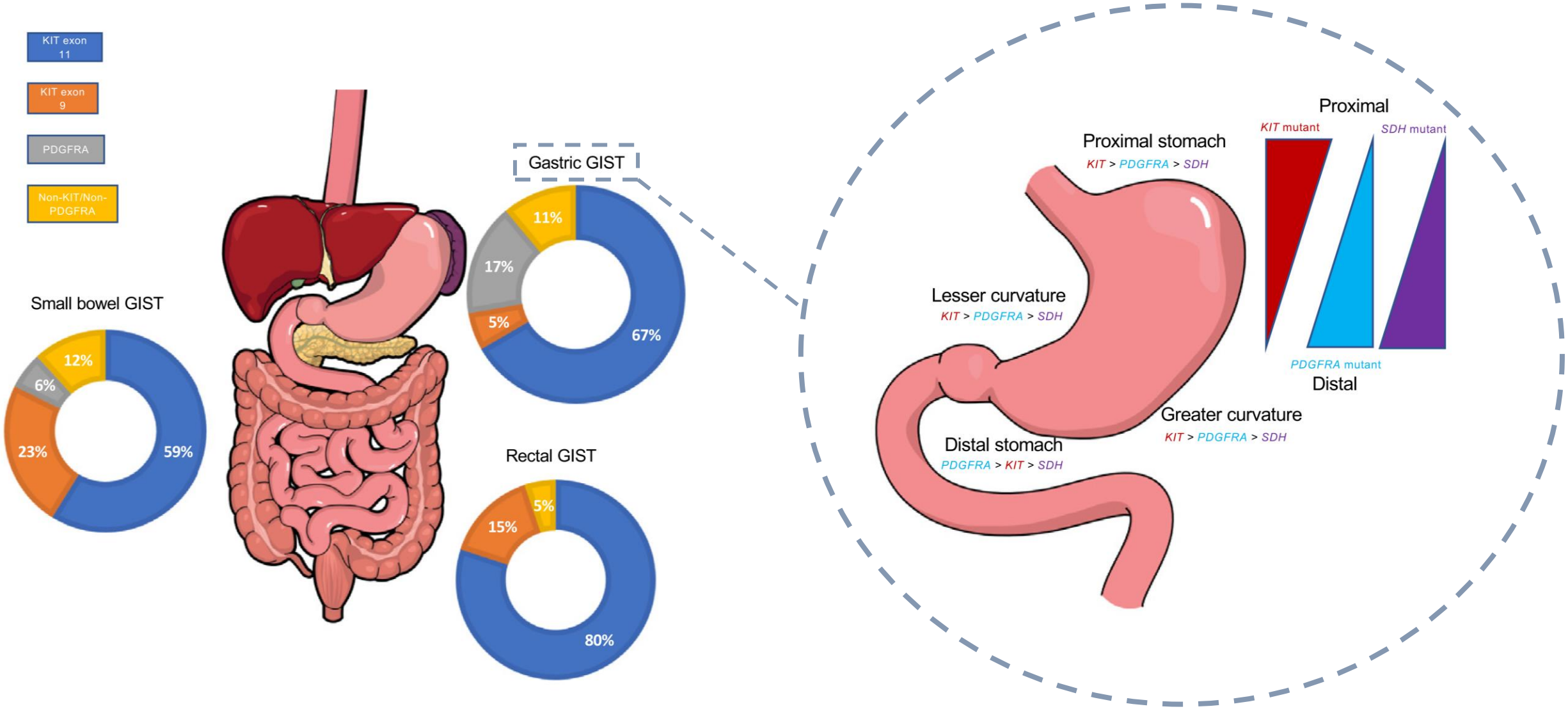
1. Call J, et al. BMC Cancer 2012;12:90. 2. Joensuu H, et al. Lancet Oncol.2012;13(3):265-74.

Caratterizzazione molecolare dei GIST



1. Li B, et al. Mol Cancer 2023;22(1):71. 2. Boikos SA, et al. JAMA Oncol 2016;2(7):922-8.

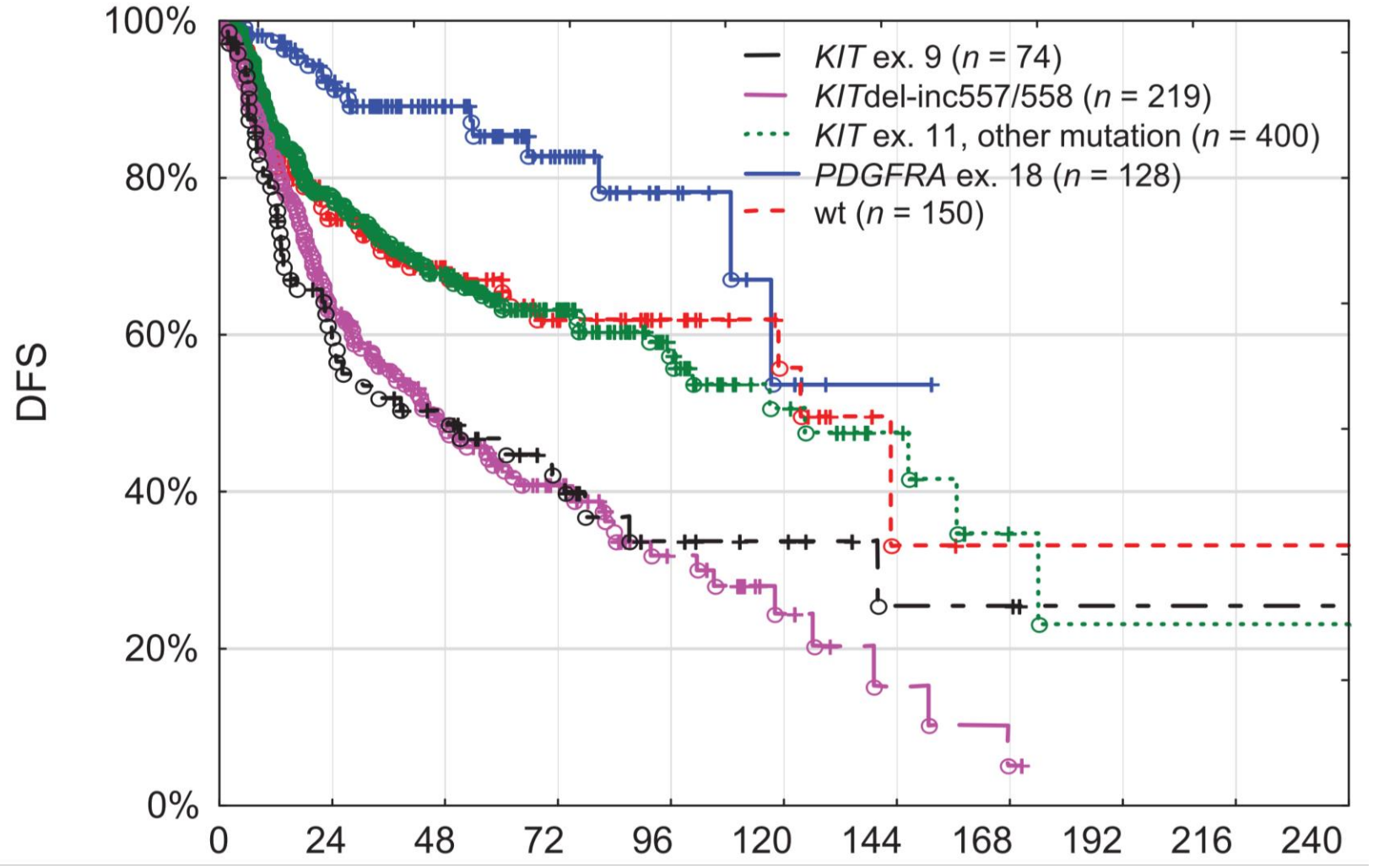
Distribuzione anatomica delle alterazioni molecolari



Fontebasso AM et al. Surg Oncol Clin N Am 2024;33(2):387-408.

Ruolo prognostico delle alterazioni molecolari

Data from 1,056 patients with localized, operable GIST of gastric origin (ConticaGIST registry)



KIT exon 11 point mutations:
good prognosis

KIT exon 11 deletions (including codons 557/558), or exon 9 point mutations:
worse prognosis

PDGFRA exon 18:
good prognosis (for primary GISTs)

Wozniak A et al. Clin Cancer Res 2014;20(23):6105-16.

Ruolo predittivo delle alterazioni molecolari

Dermawan JK, et al. Annu Rev Pathol 2022;17:323-344

Conclusioni

- Tumori rari (1.5/100.000/yr)… ma in aumento negli ultimi 20 anni
- La terapia target ha cambiato radicalmente la storia naturale della malattia (nei GIST avanzati: mOS da 19 mesi a 6,4 anni)
- Non una sola patologia… ma diversi sottotipi molecolari (KIT m, PDGFRA m, KIT/PDGFRA wt) con differenti prognosi e risposte alle terapie
- Paradigma di oncologia di precisione

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Sacro Cuore Don Calabria
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