AIGOM
ASSOCIAZIONE ITALIANA GRUPPI ONCOLOGICI MULTIDISCIPLINARI

VERONA - 15 gennaio 2025

GIST AVANZATI:
il valore della gestione

Crowne Plaza Hotel
Responsabile Scientifico
Dr.ssa Stefania Gori

# GIST quale follow-up?

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ISTITUTO ONCOLOGICO VENETO

OECI
COMPREHENSIVE Cancer Centre

European Reference Network

ESMO
Designated Centers of Integrated Oncology and Palliative Care

Regione del Veneto

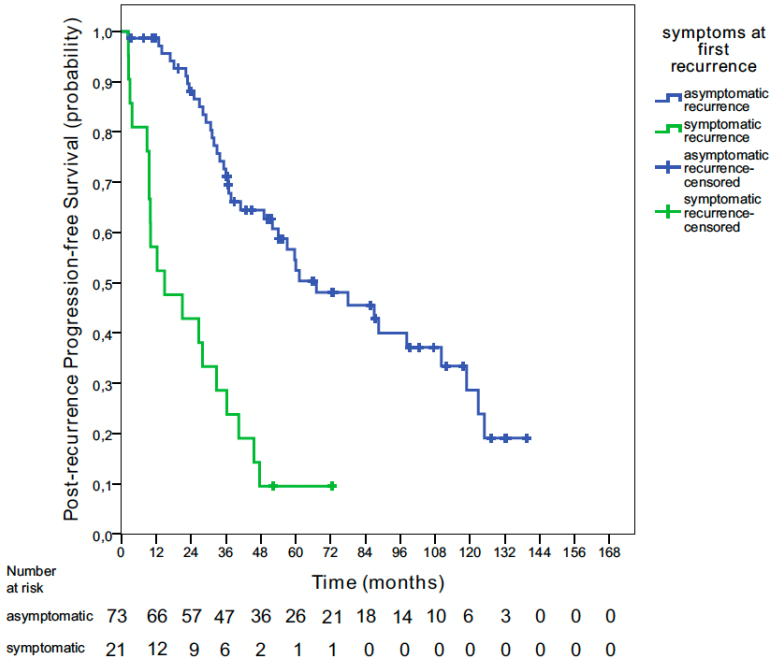
# Disclosures

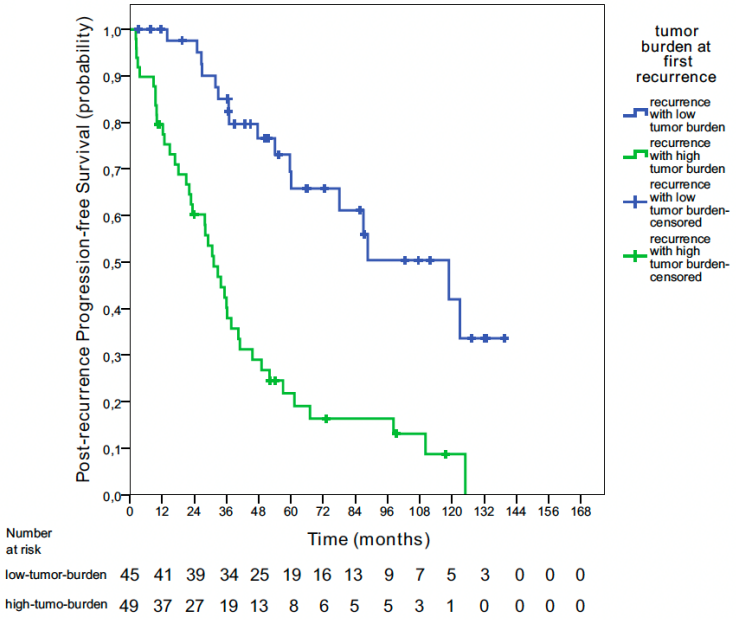
| | |
|---|---|
| **Honoraria** | **Boehringer Ingelheim, Deciphera, GSK, Pharmamar** |
| **Travel expenses** | **Istituti Gentili, Pharmamar** |

# MALATTIA LOCALIZZATA

# Il follow-up è utile?

Nei pazienti con GIST operato, il follow-up evidenza recidive ad uno stadio più precoce, con verosimile ricaduta in termini di migliori outcomes




*D'Ambrosio L et al, Eur J Cancer 2017*

# Quale follow-up?

- Dopo intervento chirurgico per GIST non vi è consenso sul tipo di follow-up da adottare.
- Non esistono protocolli di follow-up basati su prove di efficacia.

Modello di follow-up modulato sulla **categoria di rischio** e sul **tempo intercorso** dall'intervento.

# RFS nella malattia a basso/intermedio rischio

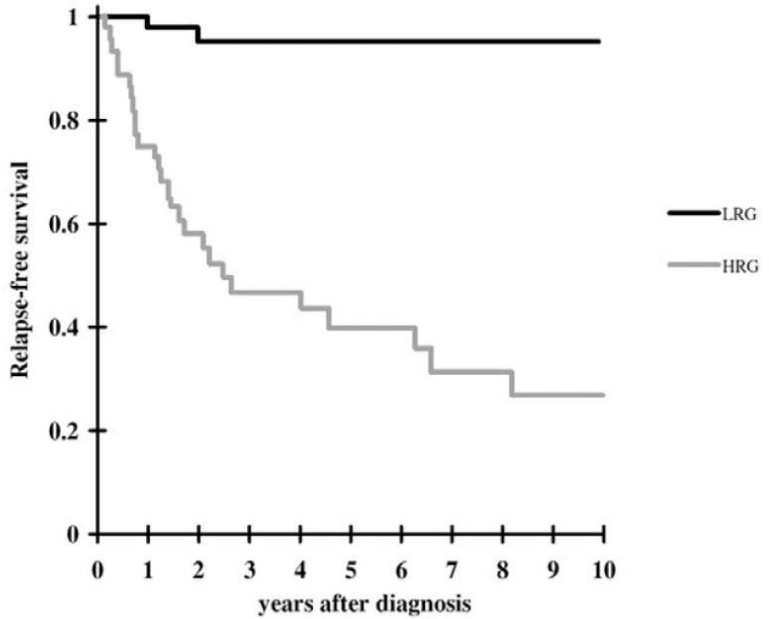
N=97 pts

LR: very low (N 18), low (N 16), intermediate (N 17)
HR: N 46

Years 1991-2004

RFS@10 yrs 95% Vs 40%

RFS@10 yrs



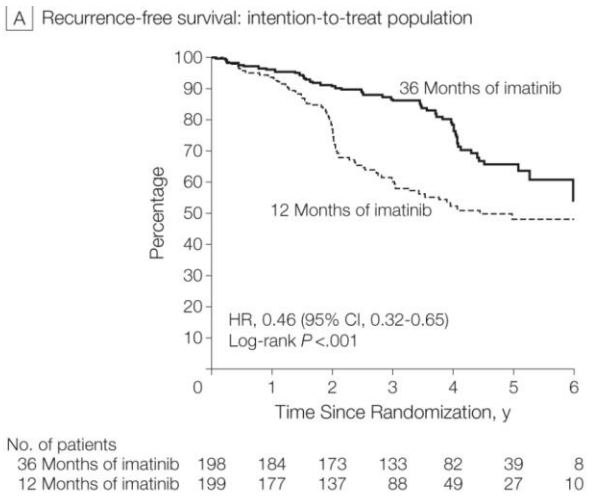

*Mucciarini C et al, BMC Cancer 2007*

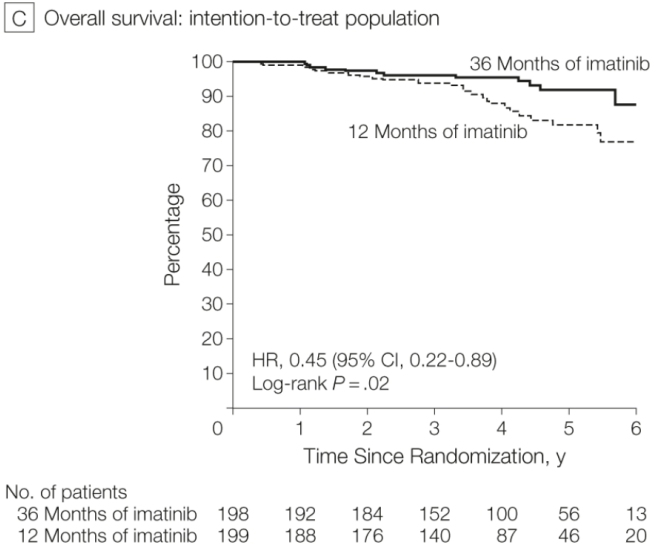
# Quali indicazioni dalle LG? AIOM

## Malattia localizzata ad alto rischio

Studio SSG XVIII/AIO:

- tasso di recidiva **in corso di trattamento adiuvante** con imatinib è basso
- >20% dei pazienti ha **recidiva nei 2 anni successivi al termine** di tale trattamento.




*Joensuu H et al, JAMA 2012; Joensuu H et al, JAMA Oncol 2020*

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## Malattia localizzata ad alto rischio

Studio SSG XVIII/AIO:

- tasso di recidiva **in corso di trattamento adiuvante** con imatinib è basso
- >20% dei pazienti ha **recidiva nei 2 anni successivi al termine** di tale trattamento.

- TC ogni 6 mesi durante terapia adiuvante
- TC ogni 3-4 mesi per 2 anni dopo l'interruzione della terapia adiuvante, successivamente ogni 6-12 mesi fino a 10 anni dal termine della terapia adiuvante

*Joensuu H et al, JAMA 2012; Joensuu H et al, JAMA Oncol 2020*

# Quali indicazioni dalle LG? AIOM

Il follow-up radiologico standard nei pazienti operati per GIST localizzato prevede l'esecuzione di **imaging dell'addome (TC / RM)**

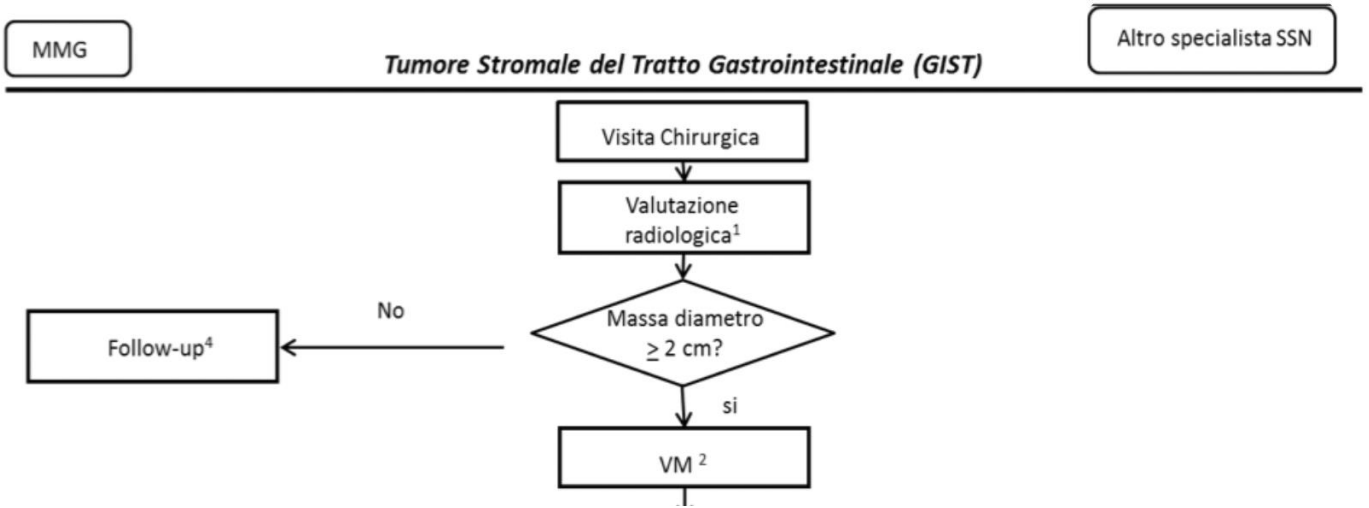
→ Non raccomandato nel follow-up di pazienti asintomatici imaging del torace

# Quali indicazioni dalle LG? AIOM

## Malattia localizzata a basso rischio NON OPERATA

- Approccio standard in caso di GIST gastro-duodenali <2 cm e con potenziale maligno minimo o assente: eco-endoscopia & TC dell'addome completo con mdc alla stadiazione
- In assenza di caratteristiche eco-endoscopiche suggestive di alto rischio, follow-up endoscopico/eco-endoscopico ogni 6-12 mesi, riservando l'escissione ai pazienti il cui tumore aumenti di dimensioni e/o diventi sintomatico.
- Salvo variazioni del quadro clinico, monitoraggio da parte del gastroenterologo.

# PDTA Veneto: Malattia localizzata a basso rischio NON OPERATA




- Essendo complessa la biopsia per lesioni < 2 cm, l'approccio suggerito è valutazione con eco-endoscopia (noduli delle alte vie digestive) o con RMN con mdc (noduli di altre sedi).
- In assenza di un'indicazione basata sull'evidenza, può essere ragionevole una prima rivalutazione a 3 mesi e allungare i tempi dei successivi controlli in caso di stabilità.

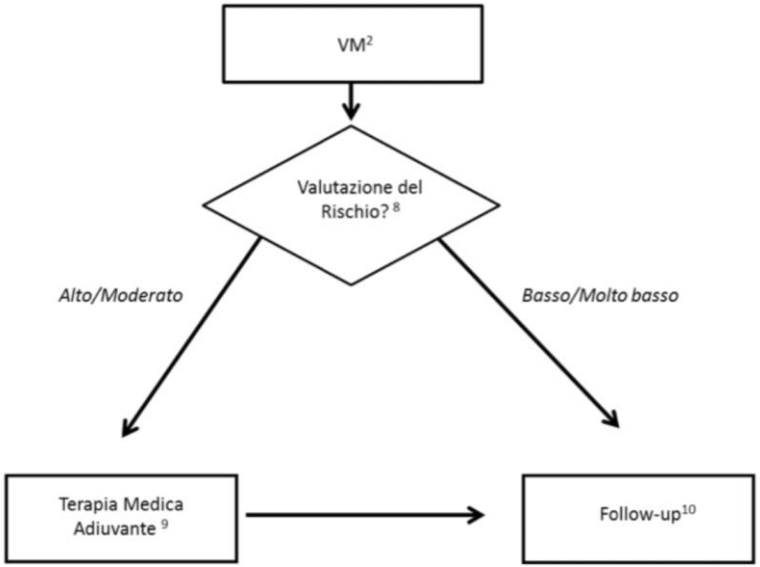
# Quali indicazioni dalle LG? AIOM

## Malattia localizzata a basso rischio OPERATA

- Nel GIST operato a basso rischio, non ci sono dati circa l'utilità o meno di un follow-up strumentale.

- In caso si opti per l'esecuzione del follow-up: TC o RMN ogni 6-12 mesi per 5 anni.

# Malattia localizzata a basso rischio OPERATA




- Non vi è consenso sul tipo di follow-up da adottare dopo intervento per GIST.
- Si suggerisce TC o RM dell'addome ogni 3-6 mesi per i primi 2-3 anni, poi ogni 6 mesi e quindi annuale dopo i 5 anni.
- La cadenza temporale va comunque orientata sulla base del livello di rischio.
- La PET non è da utilizzare nel normale follow-up dei GIST, ma può essere utile in caso di quadro dubbio all'imaging morfologico

# Quali indicazioni dalle LG? NCCN

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

## Gastrointestinal Stromal Tumors

Version 2.2024 — July 31, 2024

NCCN.org

NCCN recognizes the importance of clinical trials and encourages participation when ap
Trials should be designed to maximize inclusiveness and broad representative

**Follow-up**

- For completely resected primary disease, perform CT abdomen/pelvis with contrast and/or MRI with and without contrast every 3–6 months for 3–5 years, then annually
  - Less frequent imaging surveillance may be acceptable for low-risk or very small tumors (<2 cm)
  - More frequent imaging surveillance may be required for patients with high-risk disease who discontinue TKI therapy
- For incompletely resected disease or discovery of metastatic disease during surgery, perform CT and/or MRI every 3–6 months
- Progression may be determined by CT or MRI with clinical interpretation; FDG-PET/CT may be used to clarify if CT or MRI is ambiguous
- After treatment for progressive disease, reassess therapeutic response with CT or MRI
  - Consider FDG-PET/CT only if CT/MRI results are ambiguous

# Quali indicazioni dalle LG? ESMO

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

## Gastrointestinal stromal tumours: ESMO—EURACAN—GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up☆

P. G. Casali[1,2], J. Y. Blay[3], N. Abecassis[4], J. Bajpai[5], S. Bauer[6], R. Biagini[7], S. Bielack[8], S. Bonvalot[9], I. Boukovinas[10], J. V. M. G. Bovee[11], K. Boye[12], T. Brodowicz[13], A. Buonadonna[14], E. De Álava[15,16], A. P. Dei Tos[17], X. G. Del Muro[18], A. Dufresne[19], M. Eriksson[20], A. Fedenko[21], V. Ferraresi[22], A. Ferrari[23], A. M. Frezza[1], S. Gasperoni[24], H. Gelderblom[25], F. Gouin[26], G. Grignani[27], R. Haas[28,29], A. B. Hassan[30], N. Hindi[31], P. Hohenberger[32], H. Joensuu[33], R. L. Jones[34], C. Jungels[35], P. Jutte[36], B. Kasper[32], A. Kawai[37], K. Kopeckova[38], D. A. Krákorová[39], A. Le Cesne[40], F. Le Grange[41], E. Legius[42], A. Leithner[43], A. Lopez-Pousa[44], J. Martin-Broto[31], O. Merimsky[45], C. Messiou[46], A. B. Miah[47], O. Mir[48], M. Montemurro[49], C. Morosi[50], E. Palmerini[51], M. A. Pantaleo[52], R. Piana[53], S. Piperno-Neumann[54], P. Reichardt[55], P. Rutkowski[56], A. A. Safwat[57], C. Sangalli[58], M. Sbaraglia[17], S. Scheipl[43], P. Schöffski[59], S. Sleijfer[60], D. Strauss[61], S. J. Strauss[41], K Sundby Hall[12], A. Trama[62], M. Unk[63], M. A. J. van de Sande[64], W. T. A. van der Graaf[60,65], W. J. van Houdt[66], T. Frebourg[67†], A. Gronchi[68] & S. Stacchiotti[1], on behalf of the ESMO Guidelines Committee, EURACAN and GENTURIS*

# Quali indicazioni dalle LG? ESMO

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

SPECIAL ARTICLE

**Gastrointestinal stromal tumours: ESMO—EURACA**
**Practice Guidelines for diagnosis, treatment and fo**

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There are no published data to indicate the optimal routine follow-up policy for surgically treated patients with localised disease. Relapses occur more often to the liver and/or peritoneum. Bone lesions and other sites of metastases may be less rare along the course of metastatic disease treated with several lines of therapy. The mitotic rate likely affects the speed at which relapses take place. Risk assessment based on the mitotic count, tumour size and tumour site may be useful in choosing the routine follow-up policy. High-risk patients often have a relapse within 1-3 years from the end of adjuvant therapy. Low-risk patients may have a relapse later.

# Quali indicazioni dalle LG? ESMO

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

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Routine follow-up schedules differ across institutions. The optimal follow-up schedules are not known. As an example, at some institutions, high-risk patients undergo a routine follow-up with an abdominal CT scan or MRI every 3-6 months for 3 years during adjuvant therapy (with a tighter clinical follow-up due to the need to manage the side-effects of adjuvant therapy), unless contraindicated, then on cessation of adjuvant therapy every 3 months for 2 years, then every 6 months until 5 years from stopping adjuvant therapy and annually for an additional 5 years.[70]

For low-risk tumours, the usefulness of a routine follow-up is not known; if selected, this may be carried out with abdominal CT scan or MRI, for example, every 6-12 months for 5 years.

Very low-risk GISTs probably do not require routine follow-up, although the risk is not zero. X-ray exposure is a factor to consider, especially in low-risk GIST, with abdominal MRI being an alternative procedure.[71]

# Follow-up nella malattia localizzata a basso rischio

JAMA Network Open™

Original Investigation | Oncology

## Guideline-Based Follow-Up Outcomes in Patients With Gastrointestinal Stromal Tumor With Low Risk of Recurrence

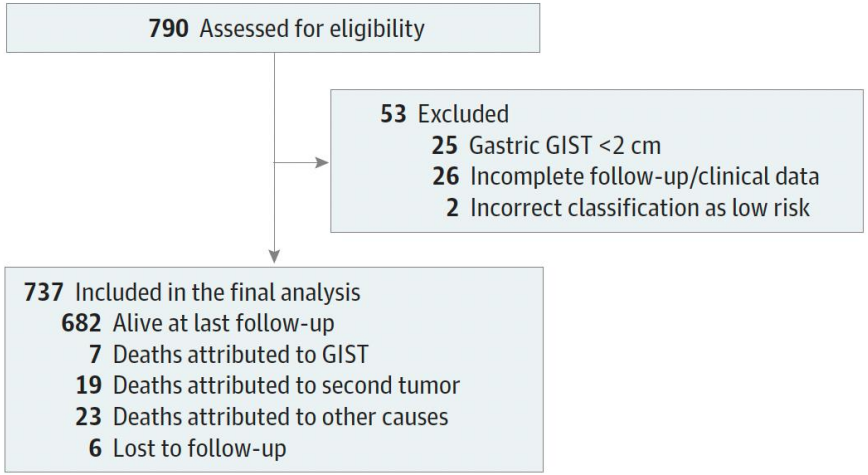
### A Report From the Italian Sarcoma Group

Lorenzo D'Ambrosio, MD, PhD; Elena Fumagalli, MD; Tommaso Martino De Pas, MD; Margherita Nannini, MD; Alexia Bertuzzi, MD; Silvia Carpano, MD; Antonella Boglione, MD; Angela Buonadonna, MD; Danila Comandini, MD; Silvia Gasperoni, MD; Bruno Vincenzi, MD; Antonella Brunello, MD; Giuseppe Badalamenti, MD; Elena Maccaroni, MD; Giacomo Giulio Baldi, MD; Alessandra Merlini, MD, PhD; Andrea Mogavero, MD; Francesca Ligorio, MD; Elisabetta Pennacchioli, MD; Fabio Conforti, MD; Giulia Manessi, MD; Sandra Aliberti, MD; Francesco Tolomeo, MD; Marco Fiore, MD; Marta Sbaraglia, MD; Angelo Paolo Dei Tos, MD; Silvia Stacchiotti, MD; Maria Abbondanza Pantaleo, MD; Alessandro Gronchi, MD; Giovanni Grignani, MD; for the Italian Sarcoma Group

*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

Figure 1. Patient Flowchart




*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

Table. Patient Demographic Characteristics

| Characteristic | No. (%) |
|---|---|
| Patients eligible for analyses | 737 (100) |
| Age at diagnosis, y | |
| Median (range) | 63 (18-86) |
| <65 | 402 (54.5) |
| ≥65 | 335 (45.5) |
| Sex | |
| Male | 377 (51.2) |
| Female | 360 (48.8) |
| Race[a] | |
| White or Caucasian | 737 (100) |
| Tumor site | |
| Stomach | 502 (68.1) |
| Duodenum | 68 (9.2) |
| Small bowel | 143 (19.4) |
| Large bowel or rectum | 16 (2.2) |
| Other | 8 (1.1) |
| Tumor size, cm | |
| <5 | 576 (78.2) |
| >5-10[b] | 161 (21.8) |
| Mitotic count (per 50 HPF) | |
| ≤5 | 713 (96.7) |
| 6-10 | 24 (3.3) |
| Symptoms at diagnosis | |
| No | 362 (49.1) |
| Yes | 281 (38.1) |
| Not reported | 94 (12.8) |
| Bleeding at diagnosis | |
| No | 520 (70.6) |
| Yes | 182 (24.7) |
| Not reported | 35 (4.7) |

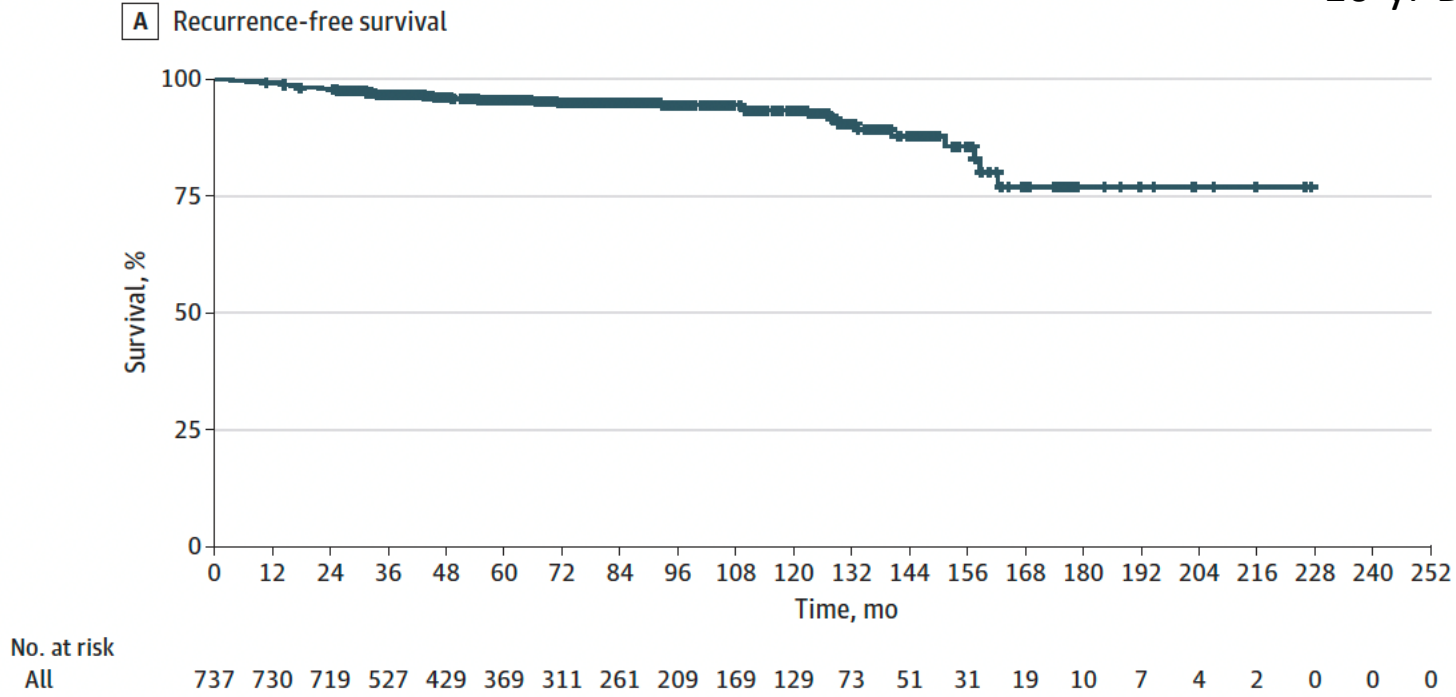
Table. Patient Demographic Characteristics

| Characteristic | No. (%) |
|---|---|
| Type of surgery | |
| Laparoscopic | 214 (29.0) |
| Laparotomic | 435 (59.0) |
| Endoscopic | 48 (6.5) |
| Not reported | 40 (5.4) |
| Radicality of surgery | |
| R0 | 699 (94.8) |
| R1 | 38 (5.2) |
| Second tumors | |
| Overall | 187 (25.4) |
| Before GIST | 80 (10.8) |
| Synchronous with GIST | 51 (6.9) |
| After GIST | 56 (7.6) |
| Mutations[c] | |
| Available mutational data | 294 (39.9) |
| *KIT* ex11 | 102 (34.7) |
| *KIT* ex11del | 53 (18.0) |
| *KIT* ex9 | 22 (7.5) |
| *KIT* ex13 | 8 (2.7) |
| *KIT* ex17 | 3 (1.0) |
| *PDGFRA* D842V | 61 (20.7) |
| *PDGFRA* non-D842V | 28 (9.5) |
| Other | 17 (5.8) |

*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

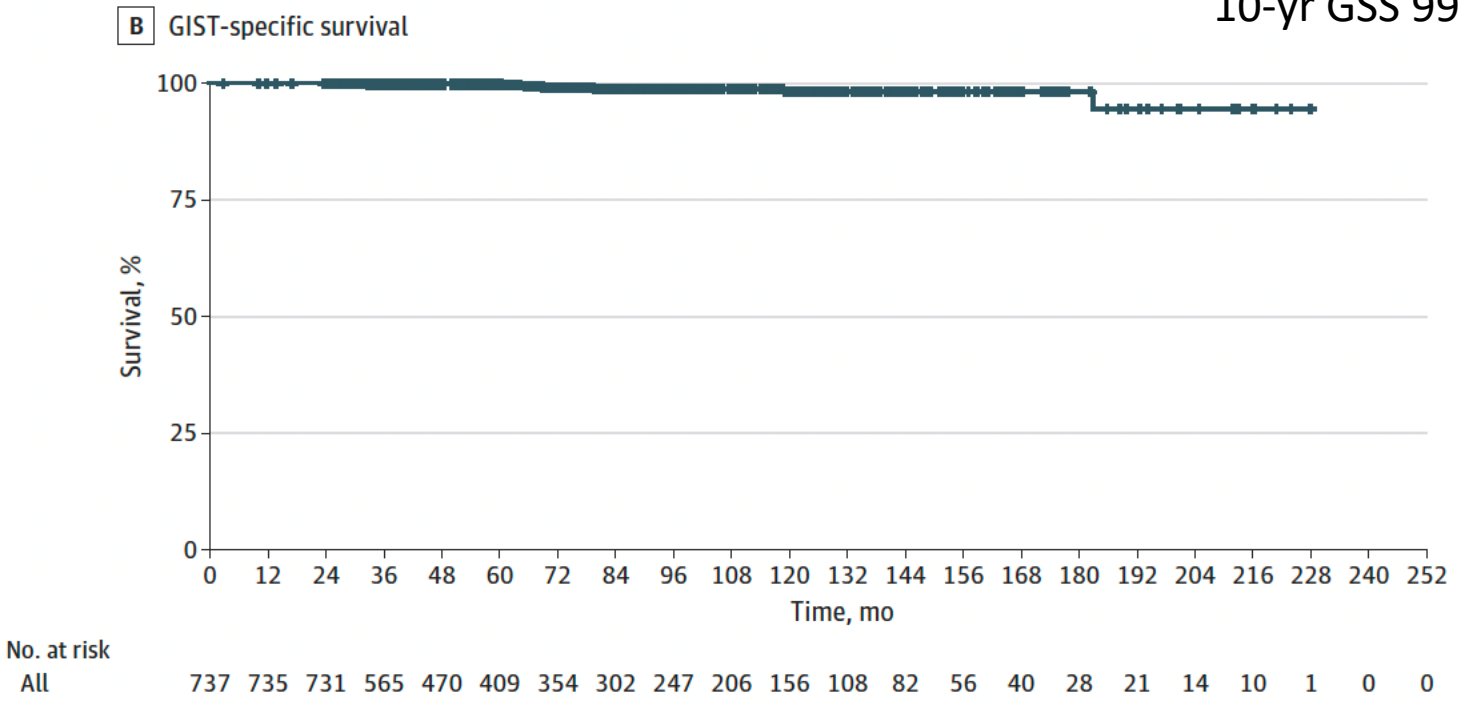
10-yr DFS 93.4%




*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

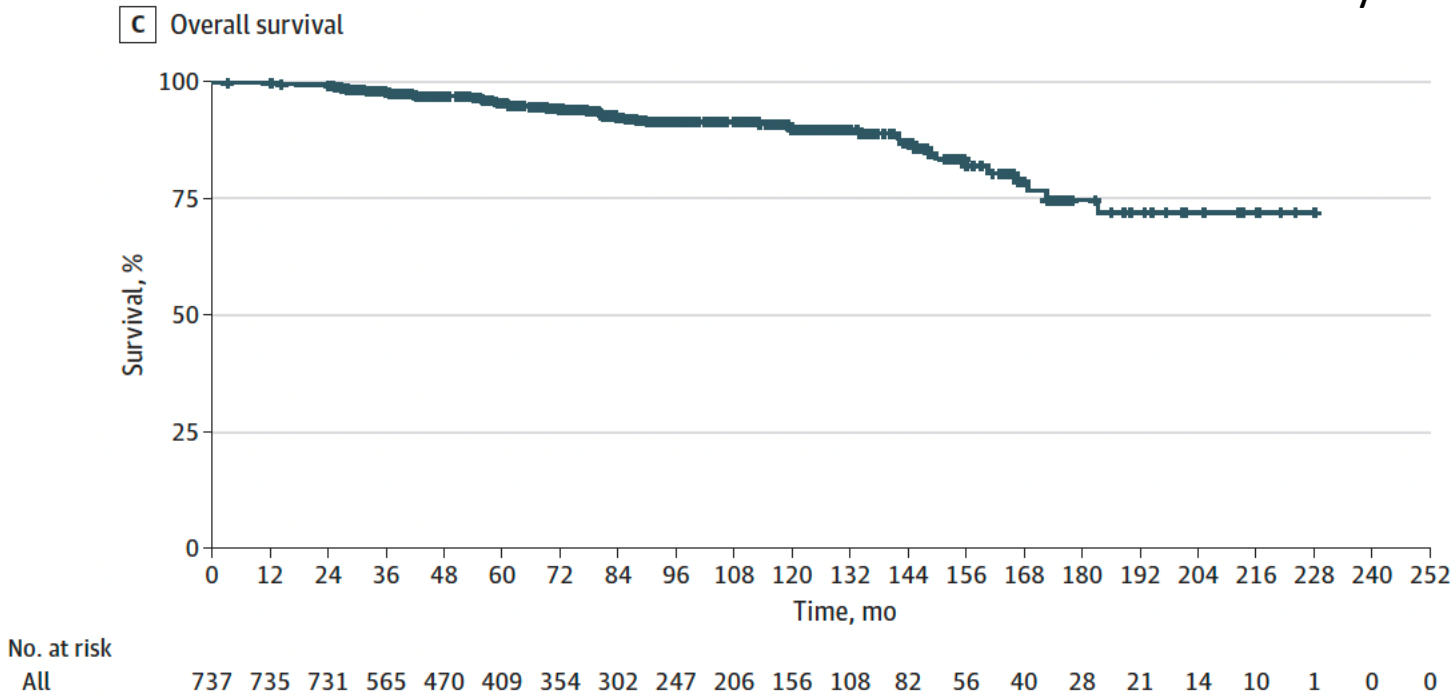
10-yr GSS 99.1%




*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

10-yr OS 91%




*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

5.7% (42 paz) → recidiva durante il follow-up (9 locale, 31 a distanza, 2 entrambe)
→ 9 rilevate oltre i 10 anni

→ Circa 1 recidiva rilevata per 170 TC effettuate (esposizione media a radiazioni di 80 mSv per paziente)

→ Maggior rischio di recidiva per **GIST non gastrico** (HR 2.09; 95%CI, 1.14-3.83; p = .02), e presenza di **mutazioni di KIT** (HR, 2.77; 95%CI, 1.05-7.27; p = .04)

*D'Ambrosio L et al, JAMA Network Open 2023*

# Follow-up nella malattia localizzata a basso rischio

Secondi tumori: 187 pazienti (25%).

- 80 diagnosticati prima del GIST
- 51 sincroni
- 56 durante il follow-up (28 riscontri incidentali durante i controlli di follow-up)

Decessi attribuibili a secondi tumori superiori a decessi per GIST (19 vs 7 eventi)
→ principale causa di morte (39% di tutti gli eventi)

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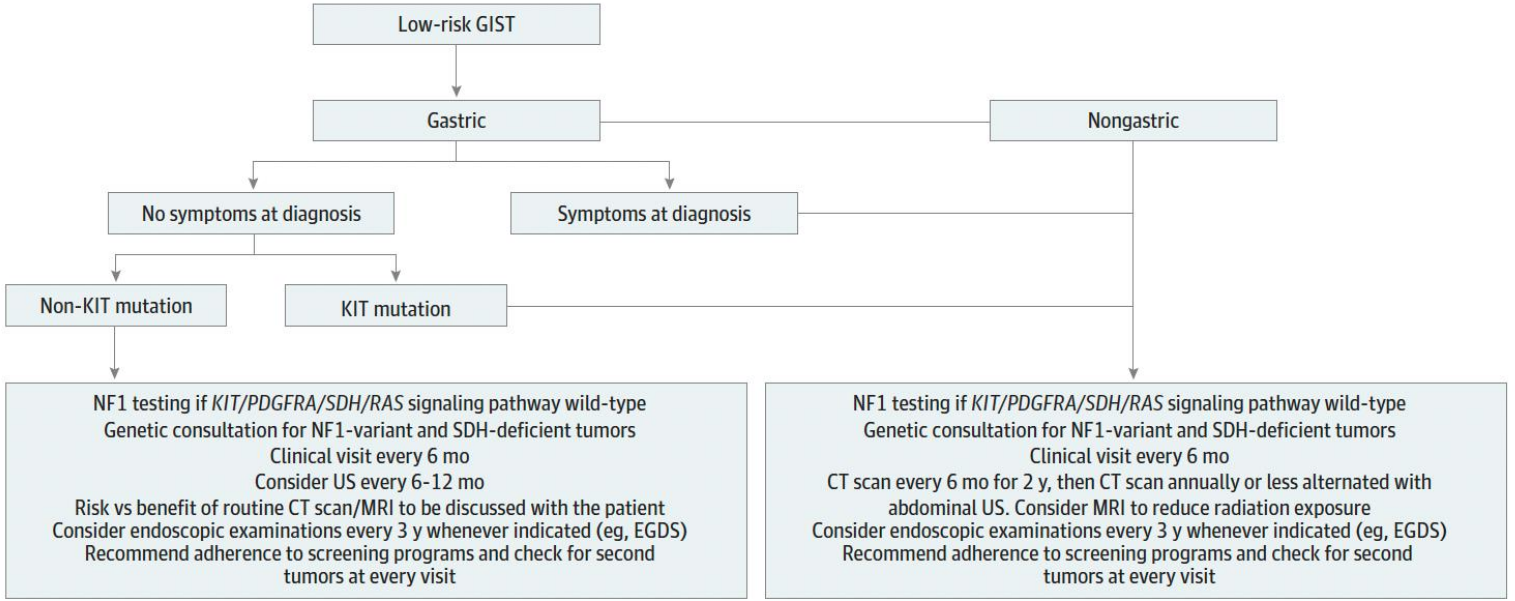
# Follow-up nella malattia localizzata a basso rischio

Figure 4. Revised Surveillance Algorithm

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# MALATTIA AVANZATA

# Rivalutazione nella malattia avanzata

- Baseline: TC addome e/o RM; imaging del torace; PET-TC se si prevede rivalutazione precoce con tale metodica o in caso di imaging morfologico dubbio

- Rivalutazioni: TC addome e/o RM ogni 8-12 settimane
  → FDG-PET/TC può servire per valutazione precoce di attività TKI dopo 2-4 settimane di terapia se necessaria rapido re-assessment, o per chiarire esiti ambigui di TC / RM
  → NB: FDG-PET/TC, non è sostitutiva di TC diagnostica!

- Imaging del torace intermittente

# The Italian health data system is broken

The Lancet Regional Health - Europe 2025;48: 101206
https://doi.org/10.1016/j.lanepe.2024.101206

The population of Italy is projected to decrease by approximately 8% by 2050, falling from 59 million in 2022 to 54.4 million, due to increased ageing and a declining birth rate. By 2050, more than 35% of Italians will be older than 65 years, while children younger than 14 years will represent only 11.7% of the population. Without reforms, this demographic shift will strain health-care and social systems.

A major weakness of the health-care system in Italy is the fragmented health data infrastructure: there is no unified, centralised system for documenting and sharing electronic health records (EHRs), hospital data, and general practitioner records.

The root cause is extensive regional autonomy, with 20 regions operating independently and implementing differing policies and technologies, creating regulatory fragmentation and inefficiencies. Poor interoperability between regions and hospitals, in addition to the lack of automatic data upload systems in private clinics, undermines the effectiveness of the Fascicolo Sanitario Elettronico—Italy's national EHR system designed to track patients' health histories—rendering it largely ineffective due to these structural flaws.

Compounding this is the absence of a national policy to allocate resources equitably to all regions or establish standardised protocols for data collection and transfer. Many hospitals and facilities continue to rely on outdated, incompatible systems, making the transfer of patient records and diagnostic images manual and labour-intensive, even within the same region or city. The absence of standardisation prevents the creation of national registries, hampering effective care, and crisis management.

The consequences of this fragmented system are profound. During the COVID-19 pandemic, it delayed the identification of links between comorbidities and infection severity, exacerbating regional disparities in health-care capacity and outcomes. A better-integrated system could have enabled broader analyses, generalisable insights, and supported a more effective, coordinated national response.

systems, hospitals in the north often cannot access patient records, resulting in repeated diagnostic tests and delayed care. This duplication inflates costs—interregional health-care mobility alone accounts for around €3.3 billion annually—and undermines patient outcomes.

The fragmented health data system in Italy also presents considerable challenges for research. Without a central platform, researchers must apply to the ethics and privacy committees of individual institutions, which can deny requests without substantive scientific justification. Since 2009, the percentage of authorised studies out of the total has fallen to 15%, marking a significant decline. Furthermore, data collection is often manual and of poor quality, making multi-centre, high-quality studies nearly impossible to conduct, severely hindering the generation of impactful, generalisable findings.

In 2022, Italy spent €1.8 billion on digital health care, a 7% increase from the previous year. However, it remains unclear whether these funds have been fully utilised and how they were spent, particularly in relation to EHRs and the integration of regional and national health systems, since only 42% of clinics reported having an active electronic data capturing system in all departments.

Public distrust in the government exacerbates the issue, with over 90,000 Italians refusing to share their health data due to privacy concerns—a sentiment amplified during the COVID-19 pandemic. While Europe has embraced so-called legitimate interest legal basis, allowing health data to be used for research and innovation without relying solely on individual consent, Italy's restrictive legislation and regional fragmentation hinder these efforts, failing to balance privacy rights with the public interest to improve health care.

A newly proposed reform threatens to worsen the situation even further. The autonomia differenziata law, if passed, will further decentralise health-care governance, deepening the fragmentation and disparities between regions instead of fostering harmonised data

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