Verona,15 Gennaio 2025

GIST AVANZATI:

Il valore della gestione multidisciplinare

Linee guida nazionali ed europee. Prospettive future

Giovanni Grignani

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Candiolo Cancer Institute, FPO - IRCCS

ISTITUTO DI CANDIOLO

CANDIOLO Fondazione del Piemonte per l'Oncologia

Disclosure

- Pharmamar: Honoraria + Institutional grant
- Bayer: Honoraria + Institutional grant
- Lilly: Honoraria
- Deciphera: Honoraria
- Incyte: Honoraria
- Merck: Honoraria
- Glaxo: Honoraria
- Novartis: Honoraria
- Gentilini: Honoraria
- Boehringer: Honoraria

Oncology today: between guidelines and personalized medicine

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The incredible evolution of GIST therapy

Driver	Mutation	Cell Line	IM	SU	RE	Rip	Ava	NIN	Bezu	IDRX	NB003
KIT	ECD	T1-AY	115	4	164	84	88	4	>1000	7	7
	JMD	GIST-T1	18	9	34	8	15	2	38	1	1
	AP	GIST882 (K642E)	103	26	211	99	330	72	252	26	6
		T1-V654A	747	15	314	71	77	42	>1000	16	4
		T1-T670I	>1000	28	106	714	349	6	>1000	681	149
	AL	T1-D816A	346	>1000	218	16	57	114	107	14	17
		T1-D820A	642	>1000	440	8	18	39	16	26	27
		T1-N822K	>1000	>1000	366	22	14	74	121	34	70
		T1-A829P	>1000	>1000	437	26	84	53	97	60	43
		T1-AY-N822K	931	>1000	157	16	185	161	144	48	83
	AP/AL	T1-V654A+D816A	>1000	>1000	>1000	>1000	140	>1000	>1000	482	197
		T1-V654A+D820A	>1000	59	>1000	>1000	36	49	>1000	295	269
		T1-V654A+N822K	>1000	199	>1000	>1000	70	81	>1000	>1000	247
		T1-V654A+A829P	>1000	82	>1000	>1000	46	18	414	276	175
PDGFRA	AL	T1-a-D842V	>1000	>1000	673	>1000	15	244	>1000	>1000	317
	AP/AL	T1-a-D842V+V658A	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
		T1-a-D842V+T674R	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000
GIST48B (KIT-negative)			>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000	>1000

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The “dog chain” of our clinical daily practice

Linee guida

SARCOMI DEI TESSUTI MOLLI E GIST

Edizione 2024

Aggiornata al 17/04/2024

In collaborazione con

Associazione Italiana Radioterapia e Oncologia clinica

Italian Sarcoma Group

Società Italiana di Chirurgia

SICO SOCIETÀ ITALIANA DI CHIRURGIA ONCOLOGICA

SIGO SOCIETA' ITALIANA DI GINECOLOGIA E OSTETRICIA

Società Italiana di Radiologia Medica e Interventistica

AIOM ASSOCIAZIONE ITALIANA ONCOLOGIA MEDICA

ISTITUTO DI CANDIOLO

Why narrowing treatment personalization?

NICE clinical guidelines:

“Recommendations on how healthcare and other professionals should care for people with specific conditions”

Agenda

Diagnosis

- **Pre-op diagnosis (most of the time)**
- **Genotype (not mandatory, but …)**
- **“Wild-type” (Reference Centers do exist)**

Surgery

- **Margins (GISTs are different from sarcomas)**
- **The tinier, the better**
- **If metastasis/ses: stop surgeons**
- **Rectal GIST: let’s talk about it**

Therapy

- **You must genotype (always!)**
- **The AIFA label is clear (not rational)**
- **New actors (avapritinib and ripretinib)**
- **Oligo-progressions and tumor board**
- **Re-challenge/s**

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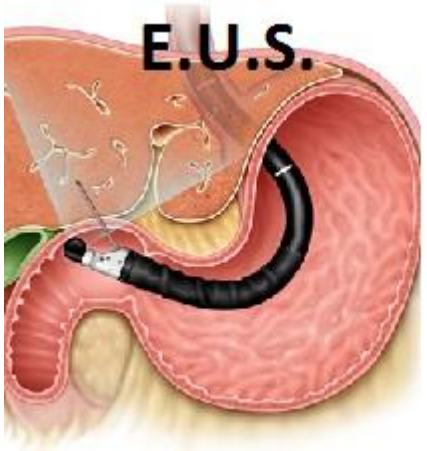
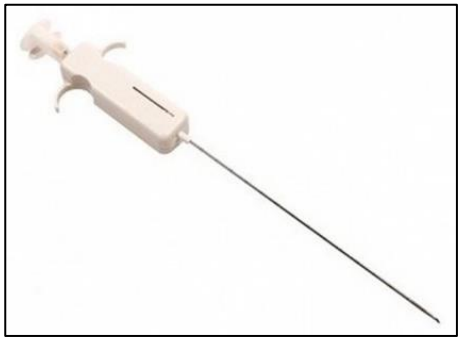
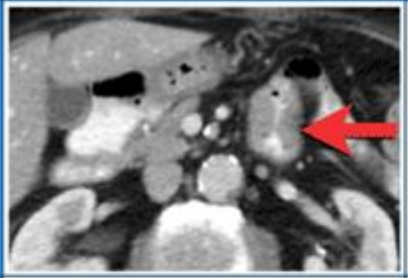
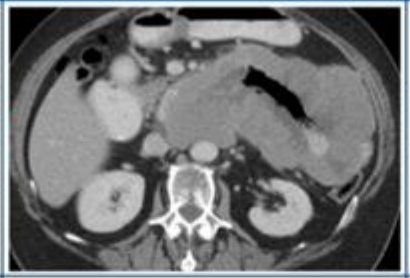
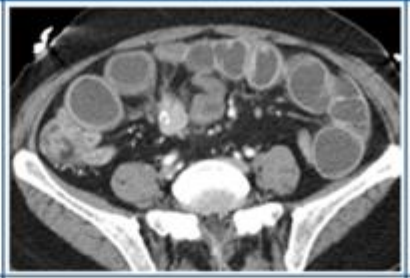
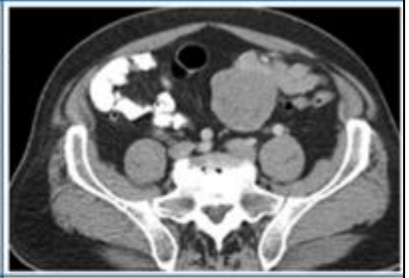
Gastro-enterolo**GIST** and Radiolo**GIST**



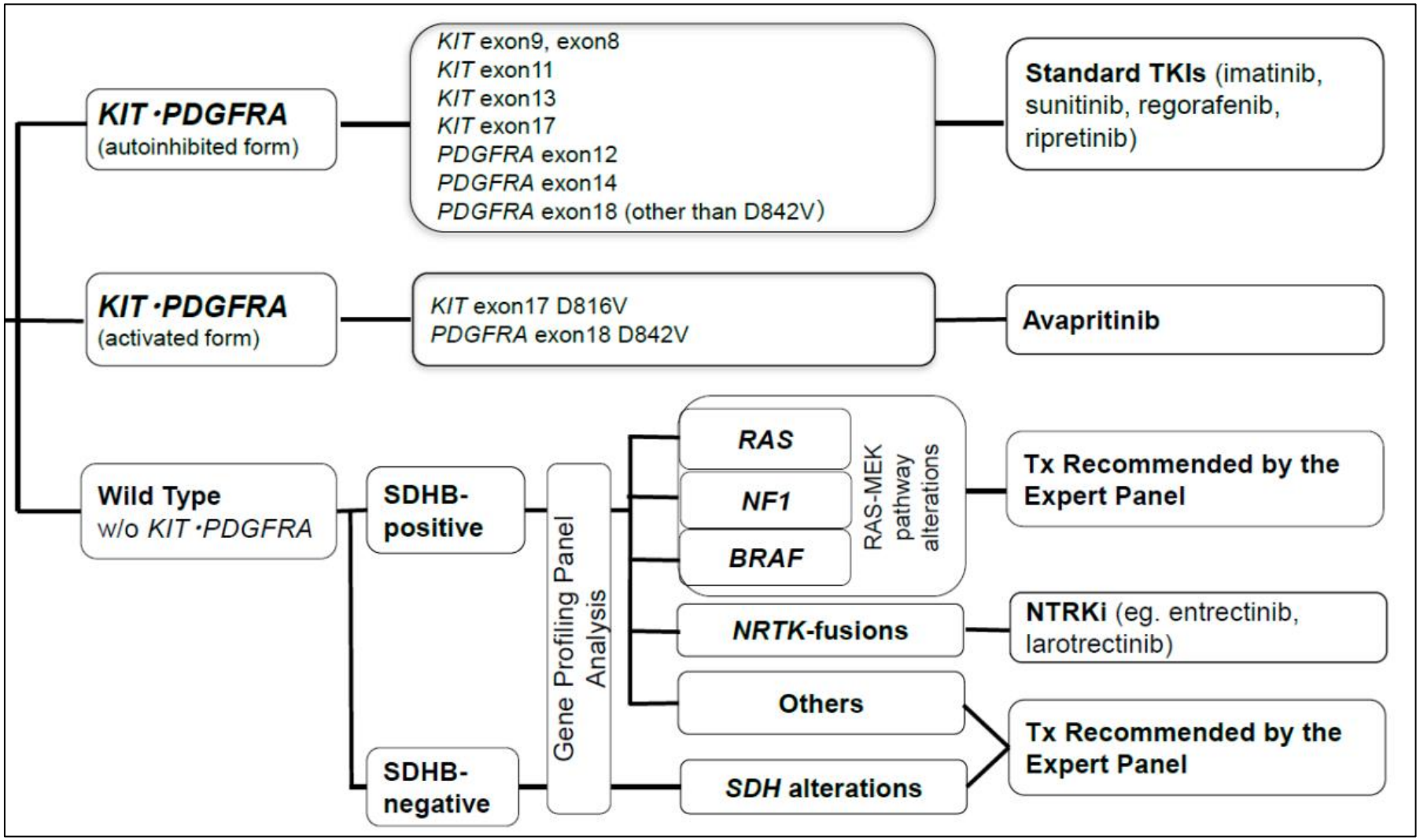


When a putative GIST is not a GIST

	Adenocarcinoma	Lymphoma	Carcinoid	GIST
				
Risk factors	HNPCC Familial adenomatous polyposis Peutz-Jeghers Celiac disease. Crohn's disease	Celiac disease Crohn's disease, SLE Immunocompromised state Post-Chemotherapy Extra-intestinal lymphoma		
Location	Duodenum > Jejunum > ileum	Terminal ileum	Distal ileum appendix	Stomach >> Small bowel
Key feature	Focal circumferential mass with shouldered borders	Thick walled infiltrating mass with aneurysmal dilatation	Transmural hypervascular mass Mesenteric mass with Ca++ Desmoplastic reaction Bowel wall thickening.	Well defined exophytic mass
Enhance-ment	Moderate and heterogeneous	Homogeneous	Hypervascular	Heterogeneous
Associated features		Splenomegaly Mesenteric and retroperitoneal lymphadenopathy	Carcinoid syndrome (<10 %) Liver metastases	Hypervascular liver metastases. No lymph node metastases. Mesenteric metastases often in recurrent disease
Diff. Diagn.	Large lymphoma	Large adenocarcinoma	Sclerosing mesenteritis	Lymphoma

https://radiologyassistant.nl/abdomen/bowel/small-bowel-tumors

Does GIST diagnosis mandate genotyping?



Cancers 2021, 13, 3158. https://doi.org/10.3390/cancers13133158

GIST genotype carries information

-KIT mutations are different: exon 11 del 557-558 *vs.* exon 11 del 560

-GIST SDH-deficient: lymph node metastases

-PDGFR-α: poor uptake FDG tracer

-NF1 GIST: multiple GISTs

-……..

Diagnostic (not research) genotyping

https://stores.biotecnika.org/products/molecular-biology-techniques-hands-on-training-internship-program-jan-2025

“Referring” a tumor specimen is easy

SARCOMI DEI TESSUTI MOLLI E GIST

LINEE GUIDA 2024

L’analisi mutazionale dei geni KIT e PDGFR-α costituisce parametro sia prognostico che predittivo di risposta ai farmaci inibitori dei recettori ad attività tirosin-chinasica (TKI). Nonostante la sempre maggiore importanza rivestita dallo stato mutazionale nella risposta ai diversi trattamenti impiegati nei GIST, ad oggi tale dato non è stato inserito in alcuna classificazione del rischio poiché non sembra correlare significativamente con il rischio di recidiva. Esso ha però un significato predittivo della risposta al trattamento con TKI e pertanto l’effettuazione dell’analisi mutazionale a complemento della diagnosi di GIST è sempre indicata intraprendendo una terapia medica (1-11).

Good practice statement:

- *La diagnosi istopatologica di GIST deve includere l’indice mitotico e le dimensioni, e dovrebbe essere chiaramente espressa la sede anatomica di manifestazione. La rottura della capsula tumorale e/o il sanguinamento della lesione sono un evento prognostico sfavorevole e dovrebbero essere sempre riportato nell’atto operatorio (8).*
- *L’analisi mutazionale a complemento della diagnosi di GIST deve essere effettuata sempre e va verificata in Centri di riferimento in caso di KIT e PDGFR-α wild type.*

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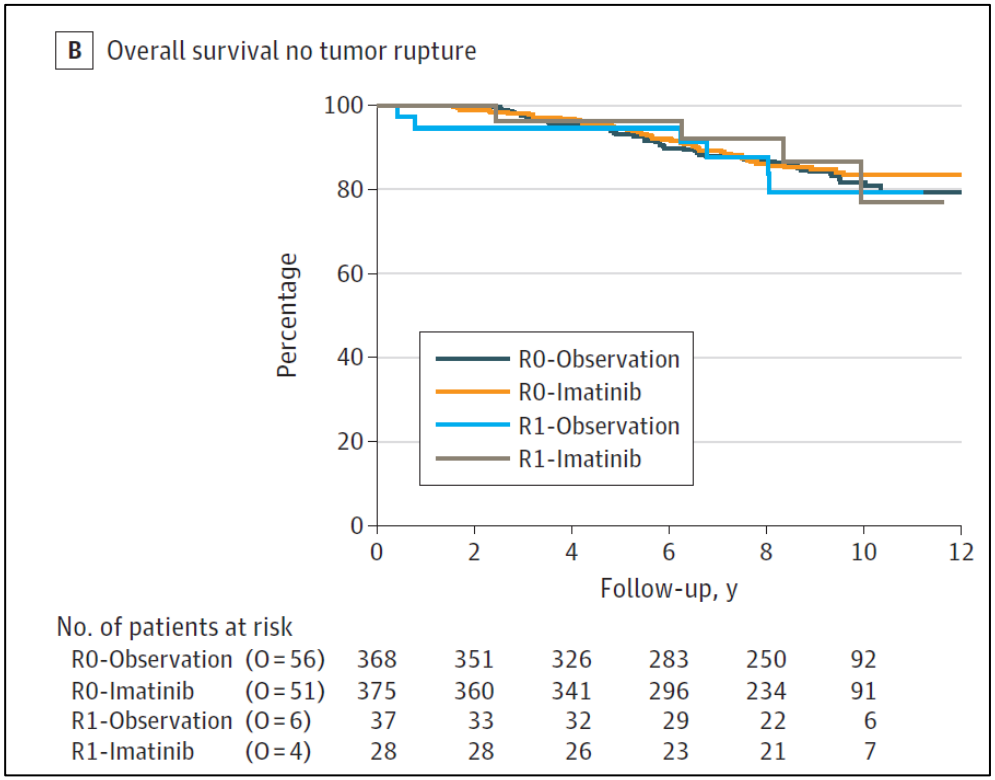
GIST treatment strategy: tumor board

Surgical margins: GIST are not “sarcomas”

JAMA Surgery | Original Investigation

Quality of Surgery and Outcome in Localized Gastrointestinal Stromal Tumors Treated Within an International Intergroup Randomized Clinical Trial of Adjuvant Imatinib



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GIST surgery: principles

-Complete

-Not multivisceral

-No lymph node dissection (see genotype)

-Avoiding contamination/rupture (≈ M1)

-Resectable metastatic GIST: TKI first!

A plea: do not touch rectal GIST

R1 surgery worsens prognosis (mesorectal & distal margin)

Any mistake causes abdomino-perineal amputation

Biopsy and genotype to set pre-op treatment

To be discussed within a tumor board (experienced!)

Agenda

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GIST medical treatment: be precise!

Imatinib

Progression-free survival in gastrointestinal stromal tumours with high-dose imatinib: randomised trial

Jaap Verweij, Paolo G Casali, John Zalcberg, Axel Le Cesne, Peter Reichardt, Jean-Yves Blay, Rolf Issels, Allan van Oosterom, Ronnan CW Hogendoorn, Matthew Van Glabbeke, Rossella Bertoldi, Ian Judson, for the EORTC Soft Tissue and Bone Sarcoma Group, the Italian Sarcoma Group, and the Australasian Gastrointestinal Trials Group*

Summary

Background Imatinib is approved worldwide for use in gastrointestinal stromal tumours (GIST). We aimed to assess dose dependency of response and progression-free survival with imatinib for metastatic GIST.

Methods 946 patients were randomly allocated imatinib 400 mg either once or twice a day. Those assigned the once a day regimen who had progression were offered the option of crossover. The primary endpoint was progression-free survival. Analysis was by intention to treat.

Findings At median follow-up of 760 days (IQR 644–859), 263 (56%) of 473 patients allocated imatinib once a day had progressed compared with 235 (50%) of 473 who were assigned treatment twice a day (estimated hazard ratio 0·82 [95% CI 0·69–0·98]; p=0·026). Side-effects arose in 465/470 (99%) patients allocated the once daily regimen compared with 468/472 (99%) assigned treatment twice a day. By comparison with the group treated once a day, more dose reductions (77 [16%] *vs* 282 [60%]) and treatment interruptions (189 [40%] *vs* 302 [64%]) were recorded in patients allocated the twice daily regimen, but treatment in both arms was fairly well tolerated. 52 (5%) patients achieved a complete response, 442 (47%) a partial response, and 300 (32%) stable disease, with no difference between groups. Median time to best response was 107 days (IQR 58–172).

Interpretation If response induction is the only aim of treatment, a daily dose of 400 mg of imatinib is sufficient; however, a dose of 400 mg twice a day achieves significantly longer progression-free survival.

Introduction

Gastrointestinal stromal tumours (GIST) are a subgroup of soft-tissue sarcomas with an estimated prevalence of 15–20 per 1 000 000.[1,2] These tumours are thought to arise from Cajal cells in intestinal walls, which are important for intestinal motor function.[3,4] GIST were previously classified as leiomyoma, leiomyoblastoma, or leiomyosarcoma. They are insensitive to conventional chemotherapy[5] and are generally characterised by a gain-of-function mutation of the KIT receptor[6] and, occasionally, of the platelet-derived growth factor receptor α.

The clinical activity of imatinib—a small-molecule tyrosine-kinase inhibitor active against BCR-ABL, KIT, and platelet-derived growth factor—has been confirmed in GIST, both in an EORTC (European Organisation for Research and Treatment of Cancer) phase I study,[7] in which the highest feasible dose of imatinib was identified as 400 mg twice a day, and in phase II studies with doses of 400–800 mg daily.[8,9] Imatinib is approved worldwide for use in GIST, with a usual recommended dose of 400 mg daily. However, we still do not know whether the highest feasible daily dose yields a higher initial response rate or a better progression-free survival than the recommended dose. For this reason, we did a randomised trial to compare imatinib 400 mg once a day with 400 mg

Patients and methods

Patients

Between February, 2001, and February, 2002, we recruited patients from 56 hospitals in 13 countries from Europe, Australia, New Zealand, and Singapore into our study. Eligibility criteria included histologically proven advanced or metastatic GIST characterised by c-KIT expression (assessed by DAKO immunohistochemical assay). Patients were not required to have measurable disease, and we did not need histological re-confirmation of malignant disease. Previous chemotherapy was accepted but should have been discontinued for more than 4 weeks. Other eligibility criteria included: age 18 years or older; WHO performance status less than 4; absolute neutrophil count greater than $1·5 \times 10^9$/L; platelet count greater than 100×10^9/L; serum creatinine up to 1·5 times the upper limit of normal (average 180 μmol/L); and total bilirubin less than 1·5 times the upper limit of normal (average 30 μmol/L). The study protocol was approved by institutional review boards according to applicable laws in all participating countries. All patients gave written informed consent.

Procedures

Within 14 days before we started treatment, we did a physical examination and complete blood count, including differential, platelet, and serum chemistry

Sunitinib

Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial

George D Demetri, Allan T van Oosterom, Christopher R Garrett, Martin E Blackstein, Manisha H Shah, Jaap Verweij, Grant McArthur, Ian R Judson, Michael C Heinrich, Jeffrey A Morgan, Jayesh Desai, Christopher D Fletcher, Suzanne George, Carlo L Bello, Xin Huang, Charles M Baum, Paolo G Casali

Summary

Background No effective therapeutic options for patients with unresectable imatinib-resistant gastrointestinal stromal tumour are available. We did a randomised, double-blind, placebo-controlled, multicentre, international trial to assess tolerability and anticancer efficacy of sunitinib, a multitargeted tyrosine kinase inhibitor, in patients with advanced gastrointestinal stromal tumour who were resistant to or intolerant of previous treatment with imatinib.

Methods Blinded sunitinib or placebo was given orally once daily at a 50-mg starting dose in 6-week cycles with 4 weeks on and 2 weeks off treatment. The primary endpoint was time to tumour progression. Intention-to-treat, modified intention-to-treat, and per-protocol analyses were done. This study is registered at ClinicalTrials.gov, number NCT00075218.

Findings 312 patients were randomised in a 2:1 ratio to receive sunitinib (n=207) or placebo (n=105); the trial was unblinded early when a planned interim analysis showed significantly longer time to tumour progression with sunitinib. Median time to tumour progression was 27·3 weeks (95% CI 16·0–32·1) in patients receiving sunitinib and 6·4 weeks (4·4–10·0) in those on placebo (hazard ratio 0·33; p<0·0001). Therapy was reasonably well tolerated; the most common treatment-related adverse events were fatigue, diarrhoea, skin discolouration, and nausea.

Interpretation We noted significant clinical benefit, including disease control and superior survival, with sunitinib compared with placebo in patients with advanced gastrointestinal stromal tumour after failure and discontinuation of imatinab. Tolerability was acceptable.

Introduction

Gastrointestinal stromal tumours are a form of sarcoma and the most common mesenchymal tumour of the gastrointestinal tract, distinguishable from other soft-tissue neoplasms by histology and immunohistochemistry.[1] The tumour probably arises from mutations in precursor cells that normally give rise to the interstitial cells of Cajal. Like these cells, most gastrointestinal stromal tumours express the protein product of the *KIT* proto-oncogene, a transmembrane receptor tyrosine kinase for which activity would normally be regulated by binding of its ligand. A subset of these tumours are overtly malignant, and greater than 40% are thought to be metastatic.[1–4] About 85–90% of gastrointestinal stromal tumours are associated with gain-of-function *KIT* gene mutations that lead to constitutive activation of KIT kinase activity.[5–7] A much smaller proportion (5%) are associated with analogous gain-of-function mutations in *PDGFRA*, the gene encoding platelet-derived growth factor receptor α (PDGFRα); less than 10% contain no identified receptor tyrosine kinase mutations.[5–7] Activating mutations of *KIT* and *PDGFRA* have been defined as the driving force behind development and maintenance of the malignant phenotype in most cases of gastrointestinal stromal tumours.

Understanding the molecular pathophysiology of this condition has allowed rational development of agents that target these signalling aberrations in the cancer cell. Traditional cytotoxic treatment is ineffective.[8,9] Imatinib mesylate, a selective inhibitor of the kinase activities of KIT and PDGFR, has substantially improved clinical outcomes for patients with advanced disease.[10–12] However, in a pivotal study of imatinib in advanced gastrointestinal stromal tumour, 5% of patients showed primary resistance to imatinib and another 14% developed early resistance.[11] Secondary or acquired resistance develops after a median of about 2 years of treatment with the drug.[12] Such resistance can develop through various mechanisms, the most common being secondary KIT mutations in clonally expanded cancer cells.[13–15] Since its approval in 2002, imatinib has been the only effective treatment for advanced gastrointestinal stromal tumour. Effective alternative treatments for use after failure of imatinib therapy were therefore an important unmet medical need justifying the development of alternative agents.

Sunitinib malate (SUTENT, previously known as SU11248; Pfizer, New York, USA) is an oral multitargeted receptor tyrosine kinase inhibitor that has shown antiangiogenic and antitumour activities in several in-vitro and in-vivo tumour models.[16–18] These effects were associated with the blockade of receptor tyrosine kinase

Regorafenib

Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (GRID): an international, multicentre, randomised, placebo-controlled, phase 3 trial

George D Demetri, Peter Reichardt, Yoon-Koo Kang, Jean-Yves Blay, Piotr Rutkowski, Hans Gelderblom, Peter Hohenberger, Michael Leahy, Margaret von Mehren, Heikki Joensuu, Giuseppe Badalamenti, Martin Blackstein, Axel Le Cesne, Patrick Schöffski, Robert G Maki, Sebastian Bauer, Binh Bui Nguyen, Jiaxiang Xu, Toshirou Nishida, John Chung, Christian Kappeler, Iris Kuss, Dirk Lorenz, Paolo G Casali, on behalf of all GRID study investigators*

Summary

Background Until now, only imatinib and sunitinib have proven clinical benefit in patients with gastrointestinal stromal tumours (GIST), but almost all metastatic GIST eventually develop resistance to these agents, resulting in fatal disease progression. We aimed to assess efficacy and safety of regorafenib in patients with metastatic or unresectable GIST progressing after failure of at least imatinib and sunitinib.

Methods We did this phase 3 trial at 57 hospitals in 17 countries. Patients with histologically confirmed, metastatic or unresectable GIST, with failure of at least previous imatinib and sunitinib were randomised in a 2:1 ratio (by computer-generated randomisation list and interactive voice response system; preallocated block design (block size 12); stratified by treatment line and geographical region) to receive either oral regorafenib 160 mg daily or placebo, plus best supportive care in both groups, for the first 3 weeks of each 4 week cycle. The study sponsor, participants, and investigators were masked to treatment assignment. The primary endpoint was progression-free survival (PFS). At disease progression, patients assigned placebo could crossover to open-label regorafenib. Analyses were by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT01271712.

Results From Jan 4, to Aug 18, 2011, 240 patients were screened and 199 were randomised to receive regorafenib (n=133) or matching placebo (n=66). Data cutoff was Jan 26, 2012. Median PFS per independent blinded central review was 4·8 months (IQR 1·4–9·2) for regorafenib and 0·9 months (0·9–1·8) for placebo (hazard ratio [HR] 0·27, 95% CI 0·19–0·39; p<0·0001). After progression, 56 patients (85%) assigned placebo crossed over to regorafenib. Drug-related adverse events were reported in 130 (98%) patients assigned regorafenib and 45 (68%) patients assigned placebo. The most common regorafenib-related adverse events of grade 3 or higher were hypertension (31 of 132, 23%), hand-foot skin reaction (26 of 132, 20%), and diarrhoea (seven of 132, 5%).

Interpretation The results of this study show that oral regorafenib can provide a significant improvement in progression-free survival compared with placebo in patients with metastatic GIST after progression on standard treatments. As far as we are aware, this is the first clinical trial to show benefit from a kinase inhibitor in this highly refractory population of patients.

Funding Bayer HealthCare Pharmaceuticals.

Introduction

Gastrointestinal stromal tumours (GIST) are the most common sarcomas arising in the gastrointestinal tract. Worldwide, the annual incidence of GIST is about 10 cases per million people,[1] corresponding to at least 8000 new cases per year in Europe. Early-stage disease can be surgically resected, but more than 40% of cases recur and metastasise.[2]

Cytotoxic chemotherapy, although active in other subtypes of sarcomas, is ineffective in metastatic GIST.[3,4] Elucidation of GIST molecular pathophysiology as a this malignancy.[5] About 85% of GIST are caused by gain-of-function mutations in the proto-oncogene *KIT*,[6] which encodes a tyrosine-kinase receptor. These mutations result in constitutive ligand-independent activation of KIT intracellular signalling.[7,8] Roughly 8% of metastatic GIST are associated with gain-of-function mutations in the structurally similar tyrosine-kinase receptor gene *PDGFRA*, encoding the platelet-derived growth factor receptor α.[6,9] Other rare subtypes of GIST exist that harbour no mutations in *KIT* or *PDGFRA*, but are probably driven by other mutations

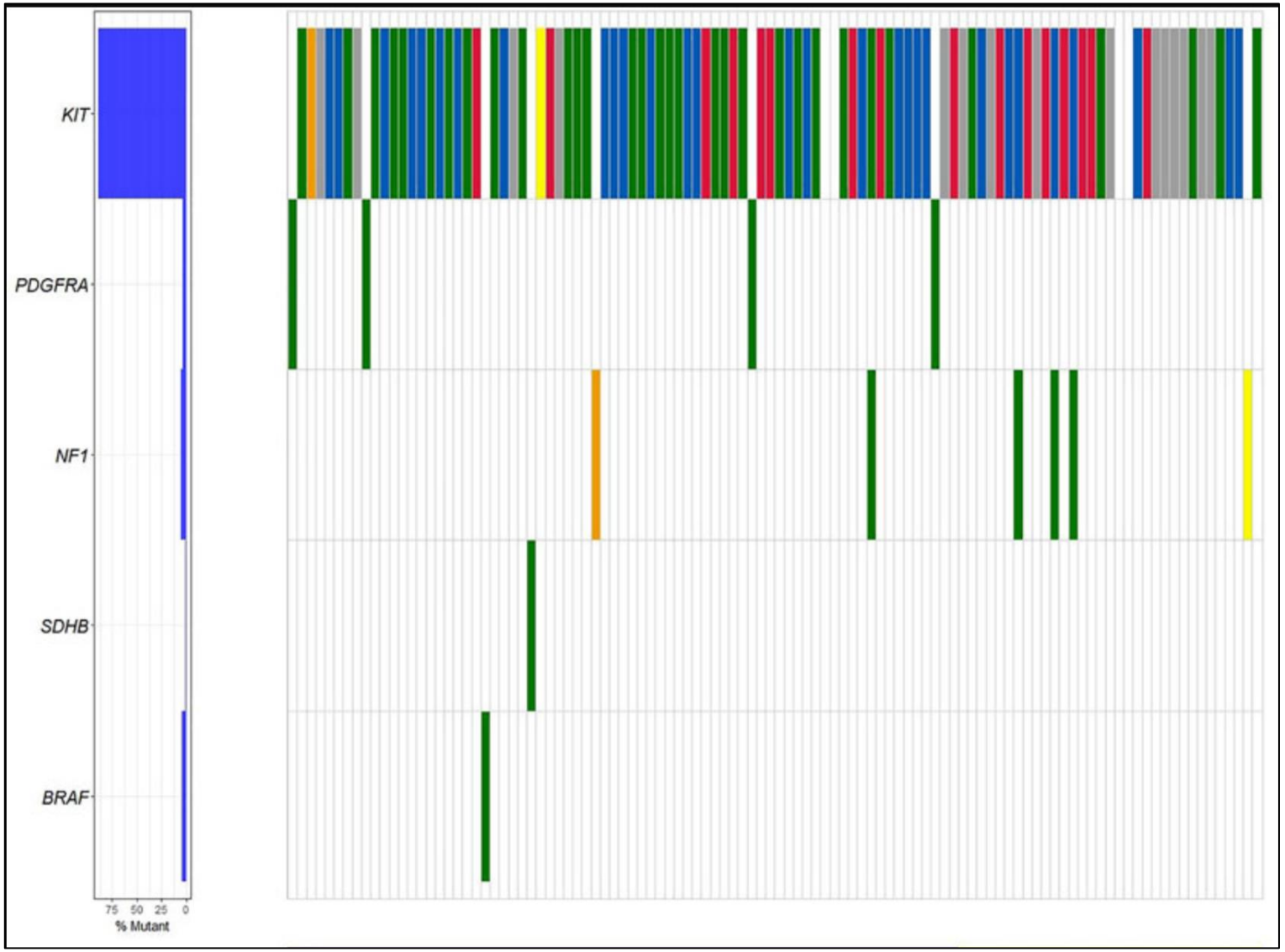
median-PFS = 20 months

median-PFS = 6.3 months

median-PFS = 4.8 months

ISTITUTO DI CANDIOLO

Likely kit-mutated, but not always



Rare
Very-rare
Ultra-rare

ISTITUTO DI CANDIOLO

https://doi.org/10.3389/fgene.2022.864499

AIFA label is “boring” and a bit irrational


GAZZETTA UFFICIALE
DELLA REPUBBLICA ITALIANA
Atto Completo
Avviso di rettifica Errata corrige
Lavori Preparatori
Direttive UE recepite
AGENZIA ITALIANA DEL FARMACO
COMUNICATO

Imatinib e' indicato per: il trattamento di pazienti adulti con tumori stromali gastrointestinali maligni (GIST) non resecabili e/o metastatici positivi a Kit (CD 117).

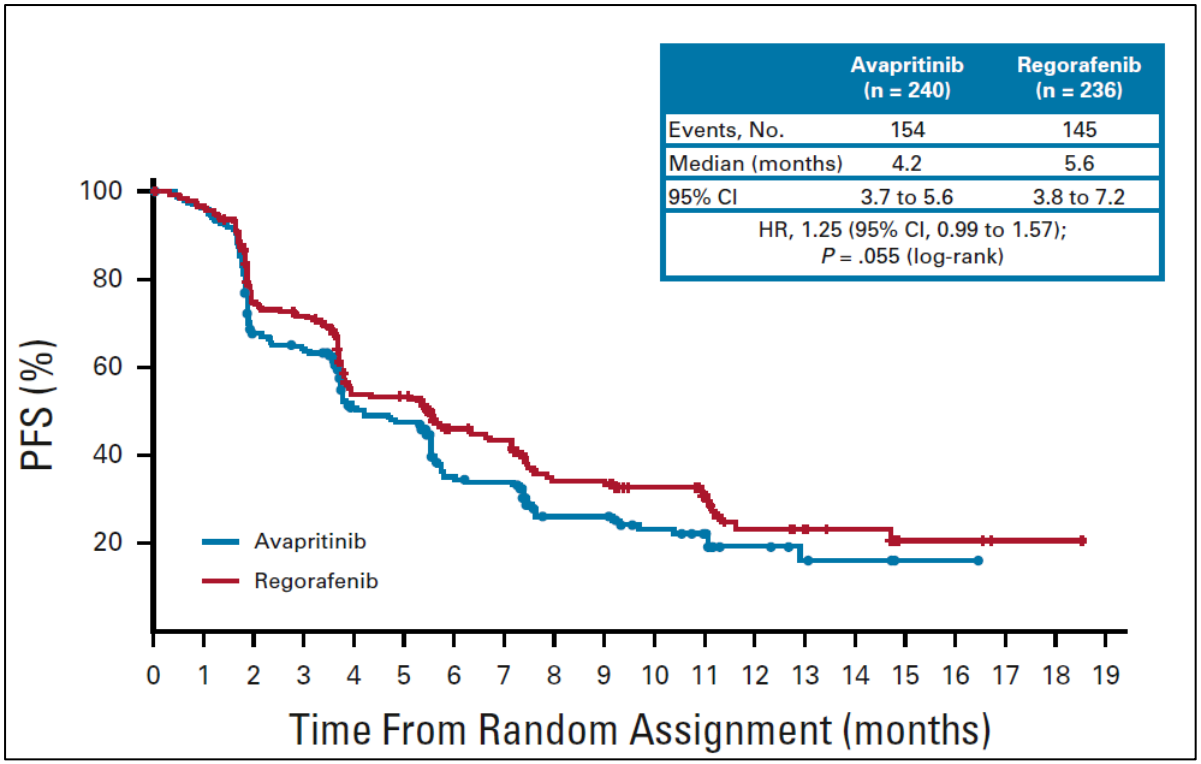
Sunitinib è indicato nel tumore stromale del tratto gastrointestinale (GIST) nei casi in cui l’imatinib (un altro medicinale antitumorale) non ha più effetto o non può più essere assunto.

Regorafenib è indicato nei tumori stromali gastrointestinali (gastrointestinal stromal tumors, GIST) non resecabili o metastatici, dopo progressione di malattia o intolleranti al trattamento precedente con imatinib e sunitinib.

Equally active, but off-label (toxic+expensive)

Avapritinib Versus Regorafenib in Locally Advanced Unresectable or Metastatic GI Stromal Tumor: A Randomized, Open-Label Phase III Study

Yoon-Koo Kang, MD, PhD[1]; Suzanne George, MD[2]; Robin L. Jones, MD[3]; Piotr Rutkowski, MD, PhD[4]; Lin Shen, MD, PhD[5];



ISTITUTO DI CANDIOLO

Take into account initial mutation

VOLUME 26 · NUMBER 33 · NOVEMBER 20 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Primary and Secondary Kinase Genotypes Correlate With the Biological and Clinical Activity of Sunitinib in Imatinib-Resistant Gastrointestinal Stromal Tumor

From the Oregon Health and Science University Cancer Institute and Portland Veterans Affairs Medical Center, Portland,

Michael C. Heinrich, Robert G. Maki, Christopher L. Corless, Cristina R. Antonescu, Amy Harlow,

Secondary kinase mutations were significantly more common in GISTs with primary KIT exon 11 mutations than in those with exon 9 mutations (73% *vs.* 19%; p= .0003).

Sunitinib might work better in exon 9 GISTs

Later TKIs may exhaust the patient

E	*Campo obbligatorio ai fini dell'eleggibilità*	**QINLOCK (RIPRETINIB) - GIST**	
O	*Campo obbligatorio*		
QINLOCK è indicato per il trattamento di pazienti adulti con tumore stromale gastrointestinale (GIST) avanzato che hanno ricevuto un trattamento precedente con tre o più inibitori della chinasi, incluso imatinib.			
	1- Scheda Registrazione paziente (RP)		
E	Età	≥18	
	2- Scheda Eleggibilità e Dati Clinici (EDC)		
O	Data di valutazione	../../....	
O	Data della prima diagnosi di GIST	mese/anno	
O	Sede GIST:	Stomaco	
		Digiuno	
		Ileo	
		Duodeno	
		Colon	
		Retto	
		Loc…	
O	Stadio di malattia		
O	Se metastatico, indicare le sedi di malatti…		
		…e	
		Encefalo	
		Fegato	
		Surrene	selezione multipla
		Ossa	
		Linfonodi	
		Altro	
E	Il paziente è andato in progressione oppure è risultato intollerante (malgrado le riduzioni di dose) a precedenti terapie con imatinib, sunitinib e regorafenib?	Sì	
		No	***blocco***

Ripretinib is in label!

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A parsimonious use of TKIs: tumor board

GIST deposits destruction: an effective strategy

Surgery:

Long-term follow-up of patients with GIST undergoing metastasectomy in the era of imatinib – Analysis of prognostic factors (EORTC-STBSG collaborative study)☆

S. Bauer [a,*], P. Rutkowski [b], P. Hohenberger [c], R. Miceli [d],

Radiofrequency (and the likes):

Meeting Abstract: 2004 ASCO Annual Meeting

FREE ACCESS | Sarcoma | July 15, 2004

Safety and efficacy of percutaneous radio-frequency ablation (RFA) in patients (pts) with metastatic gastrointestinal stromal tumor (GIST) with clonal evolution of lesions refractory to imatinib mesylate (IM)

Authors: P. Dileo, R. Randhawa, E. Vansonnenberg, S. Shankar, J. Desai, J. A. Morgan, K. Tuncali, A. Van Den Abbeele, S. G. Silverman, and G. D.

Radiotherapy:

Radiotherapy for GIST

Radiotherapy for GIST progressing during or after tyrosine kinase inhibitor therapy: A prospective study

Heikki Joensuu [a,*], Mikael Eriksson [b], Juhani Collan [a], Marja H. Balk [c], Serge Leyvraz [d], Michael Montemurro [d]

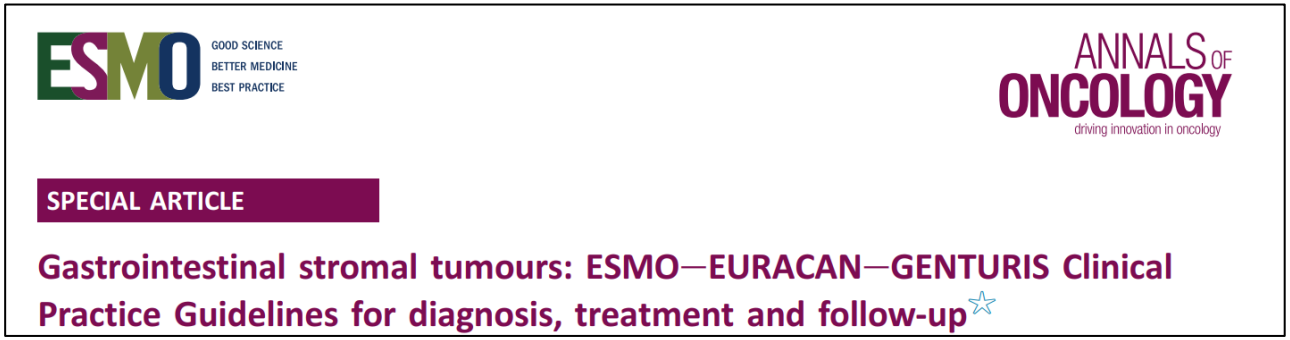
Embolization:

Hepatic Artery Embolization for Liver Metastasis of Gastrointestinal Stromal Tumor Following Imatinib and Sunitinib Therapy

Haruyuki Takaki · Tess Litchman · Ann Covey · Franois Cornelis ·

1. DOI:https://doi.org/10.1016/j.ejso.2013.12.020
2. https://doi.org/10.1200/jco.2004.22.90140.902
3. http://dx.doi.org/10.1016/j.radonc.2015.07.025
4. doi: 10.1007/s12029-014-9663-2.

When tumor board is mandatory



"**Surgical excision of progressing disease** has not been beneficial in published retrospective series, but surgery of focal progression, such as the 'nodule within a mass', up to one or few nodules/masses when the rest of the disease is still responding, has been associated with a PFS in the same range as for any furtherline treatment. Therefore this may be an option for the individual patient with limited progression, while continuing imatinib at the same dose [IV, C]. **Nonsurgical procedures** [e.g. local treatment, such as ablations or radiotherapy (RT)] may be selected"

GIST treatment strategy: final steps

SARCOMI DEI TESSUTI MOLLI E GIST

LINEE GUIDA 2024

Per i pazienti con GIST avanzato si deve prendere in considerazione la partecipazione a studi clinici con nuove terapie o combinazioni di farmaci. Sulla base dell'esperienza clinica e delle conoscenze biologiche della malattia, ci sono evidenze che indicano come il **re-challenge con imatinib** possa dare qualche beneficio e rallentare l'evoluzione di una malattia in franca progressione.

Do not stick to, but remember guidelines

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