UNIVERSITÄTS KLINIKUM FRANKFURT

Update Gastrointestinale Stromatumoren (GIST) 2024

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DGHO Fortbildung Update Sarkome, Basel 12.10.2024

Conflicts of interest

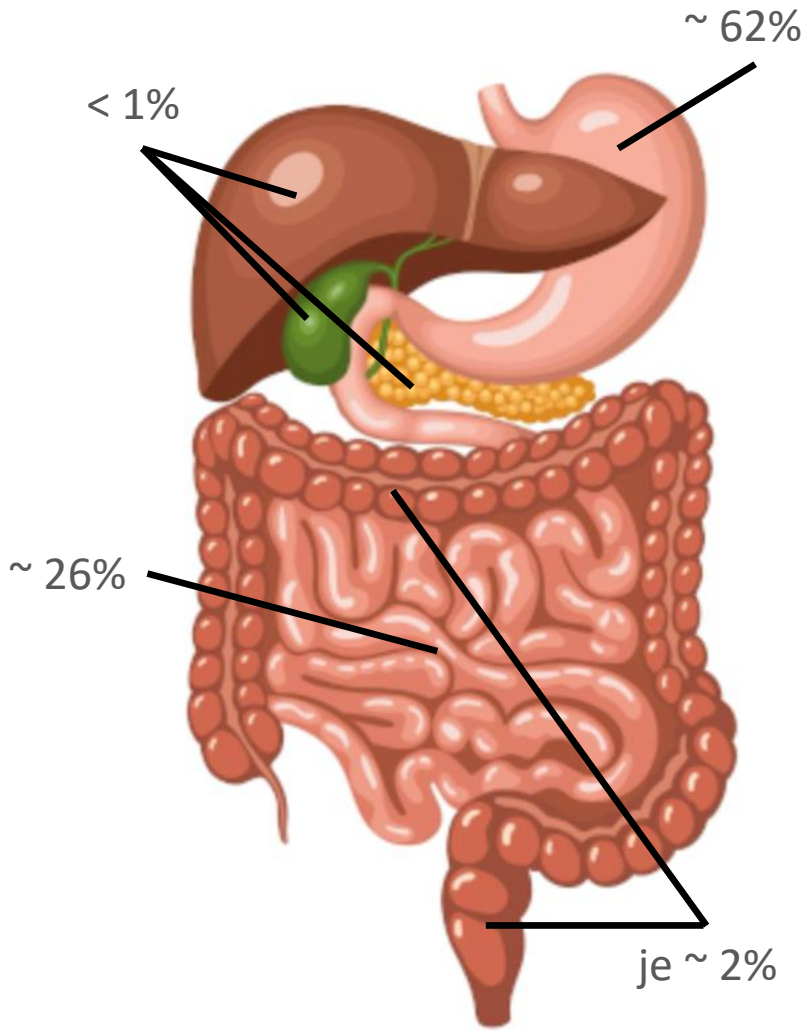
- Kongresseinladungen:
  - Deciphera, Merck, Pfizer
- Beratungsverhältnisse:
  - Apogepha, Blueprint, Boerhinger Ingelheim, Deciphera, PharmaMar

Übersicht

- **Hintergrund**
- **Lokalisierte GIST**
  - (Neo-) adjuvante Therapie
- **Metastasierte GIST**
  - **Therapielandschaft**
    - **KIT/PDGFR-Mutationen**
    - **PDGFR D842V Mutation**
- **Studien und Neuigkeiten**

Hintergrund

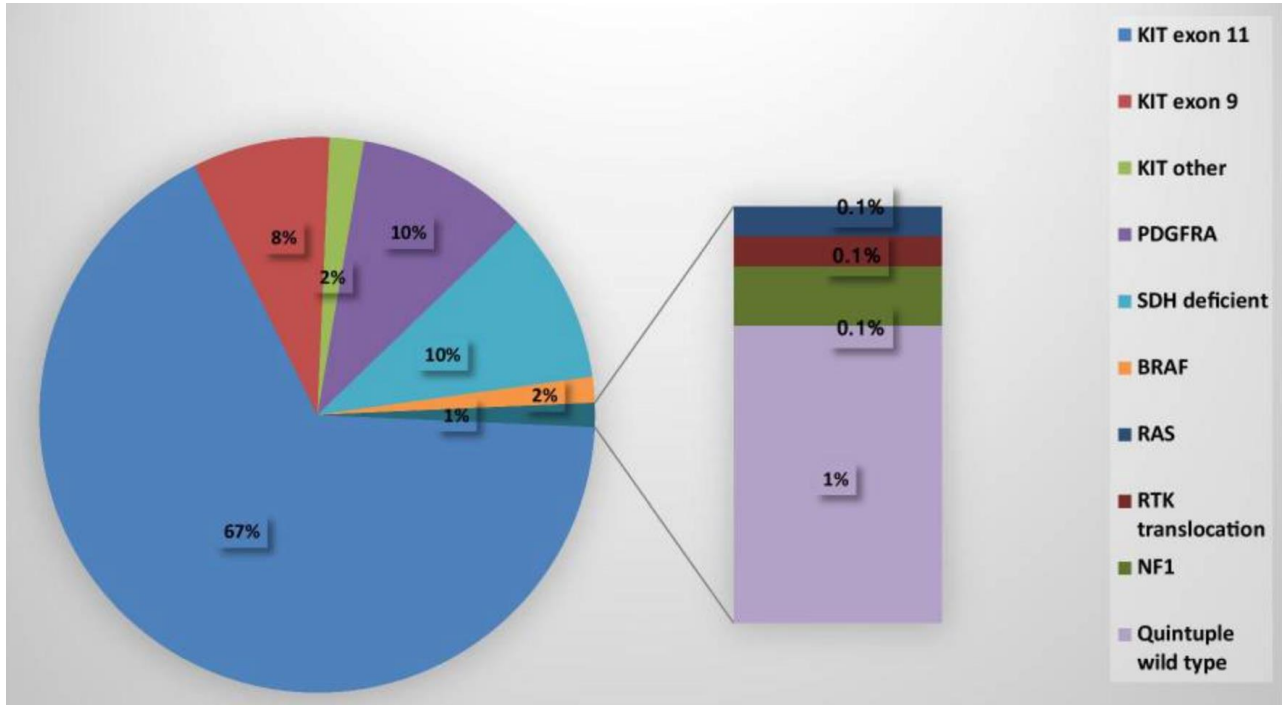
- Gastrointestinale Stromatumoren (GIST) = häufigste mesenchymale Tumoren im Gastrointestinaltrakt
- Inzidenz: 0.4-2 Fälle / 100.000 Einwohner / Jahr[1]
- Lokalisation: Meist Magen oder Dünndarm[1,2]
- Männer und Frauen etwa gleich häufig betroffen[1]
- Erkrankungsgipfel : ~ 60-65 Jahre[3]



[1] Ducimetiere et al. Plos One 2011, Sørejde et al. Can Ep 2016, [2] Aus Onkopedia Leitlinie 2019, [3] Casali et al. Ann Oncol 202

Hintergrund

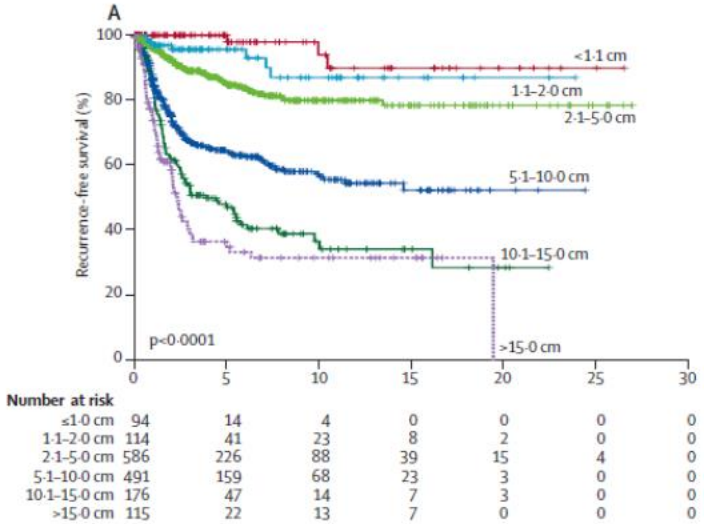
- Mehrheit der GIST zeigen ***gain of function Mutationen*** in KIT oder PDGFRa
- Molekulare Veränderungen wichtig für therapeutische Entscheidungen und Therapiemanagement
- **Molekulare Aufarbeitung** vor Einleitung einer medikamentösen Therapie



Kelly et al J Hematol Oncol 2021Graphik modifiziert nach Falkenhorst et al. Trillium 2016

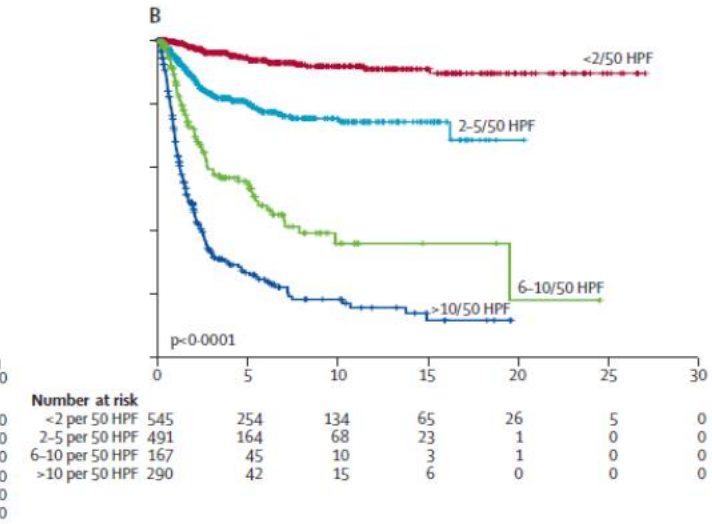
Staging und Risikoklassifikation

Size



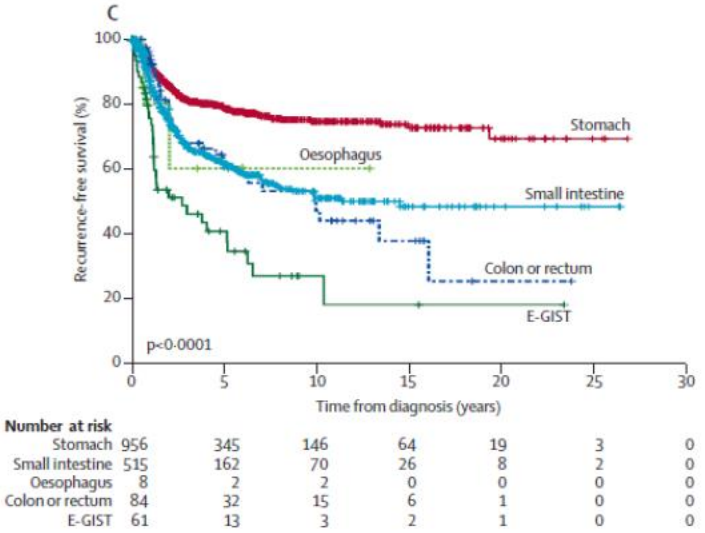
Number at risk							
≤1·0 cm	94	14	4	0	0	0	0
1·1–2·0 cm	114	41	23	8	2	0	0
2·1–5·0 cm	586	226	88	39	15	4	0
5·1–10·0 cm	491	159	68	23	3	0	0
10·1–15·0 cm	176	47	14	7	3	0	0
>15·0 cm	115	22	13	7	0	0	0

Mitosis



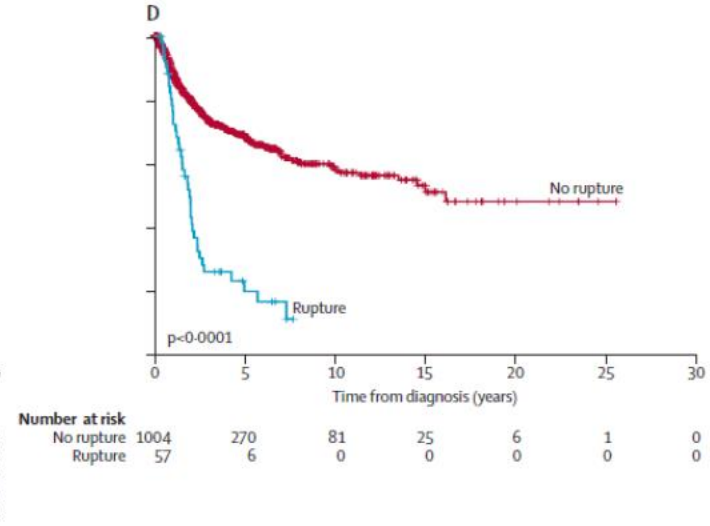
Number at risk							
<2 per 50 HPF	545	254	134	65	26	5	0
2–5 per 50 HPF	491	164	68	23	1	0	0
6–10 per 50 HPF	167	45	10	3	1	0	0
>10 per 50 HPF	290	42	15	6	0	0	0

Location



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

Rupture



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

BARCELONA 2024 ESMO congress

Joensuu et al, Lancet Oncol 2012

Serrano et al. presented at ESMO 2024

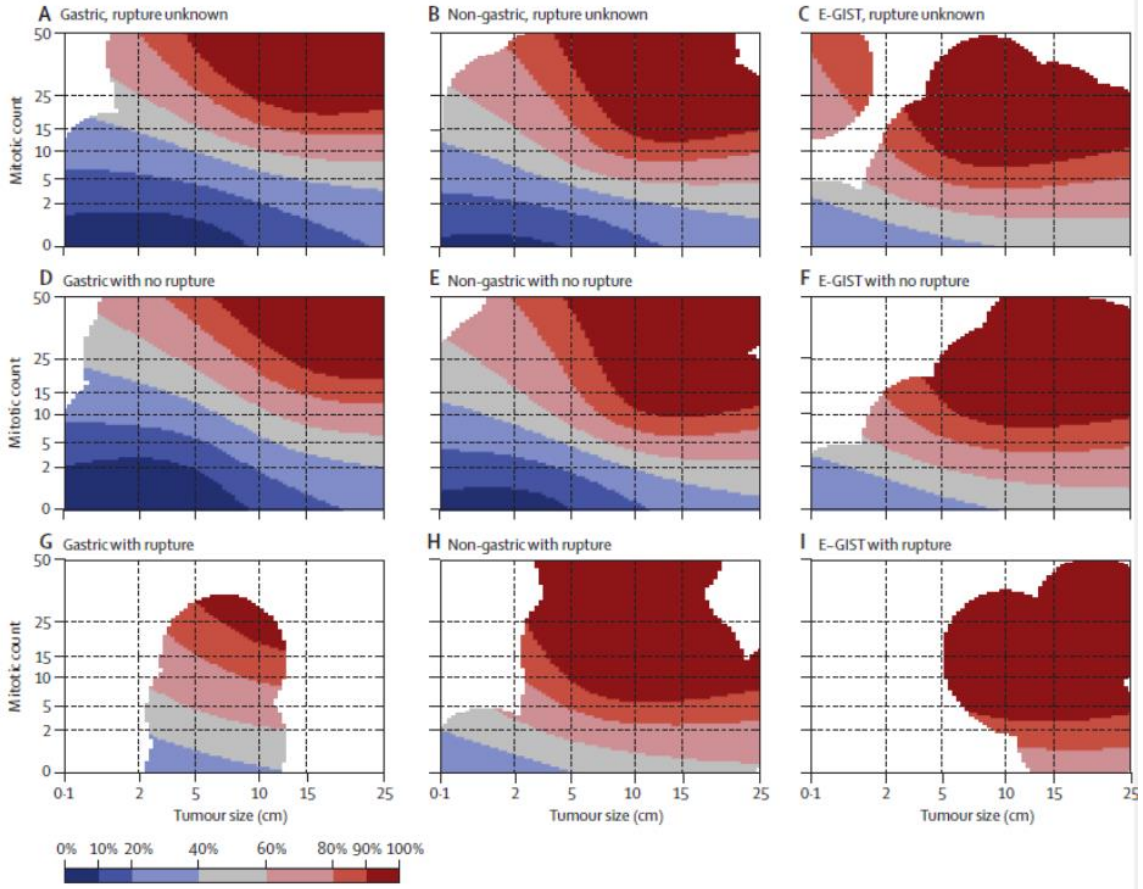
Staging und Risikoklassifikation

► NIH consensus modified

Risk Category	Tumor Size, cm	Mitotic Index Per 50 High-Power Fields	Primary Tumor Site
Very low risk	< 2.0	≤ 5	Any
Low risk	2.1-5.0	≤ 5	Any
Intermediate risk	2.1-5.0	> 5	Gastric
	5.1-10.0	≤ 5	Gastric
High risk	Any	Any	Tumor rupture
	> 10	Any	Any
	Any	> 10	Any
	> 5.0	> 5	Any
	2.1-5.0	> 5	Nongastric
	5.1-10.0	≤ 5	Nongastric

Joensuu H, Hum Pathol 2008

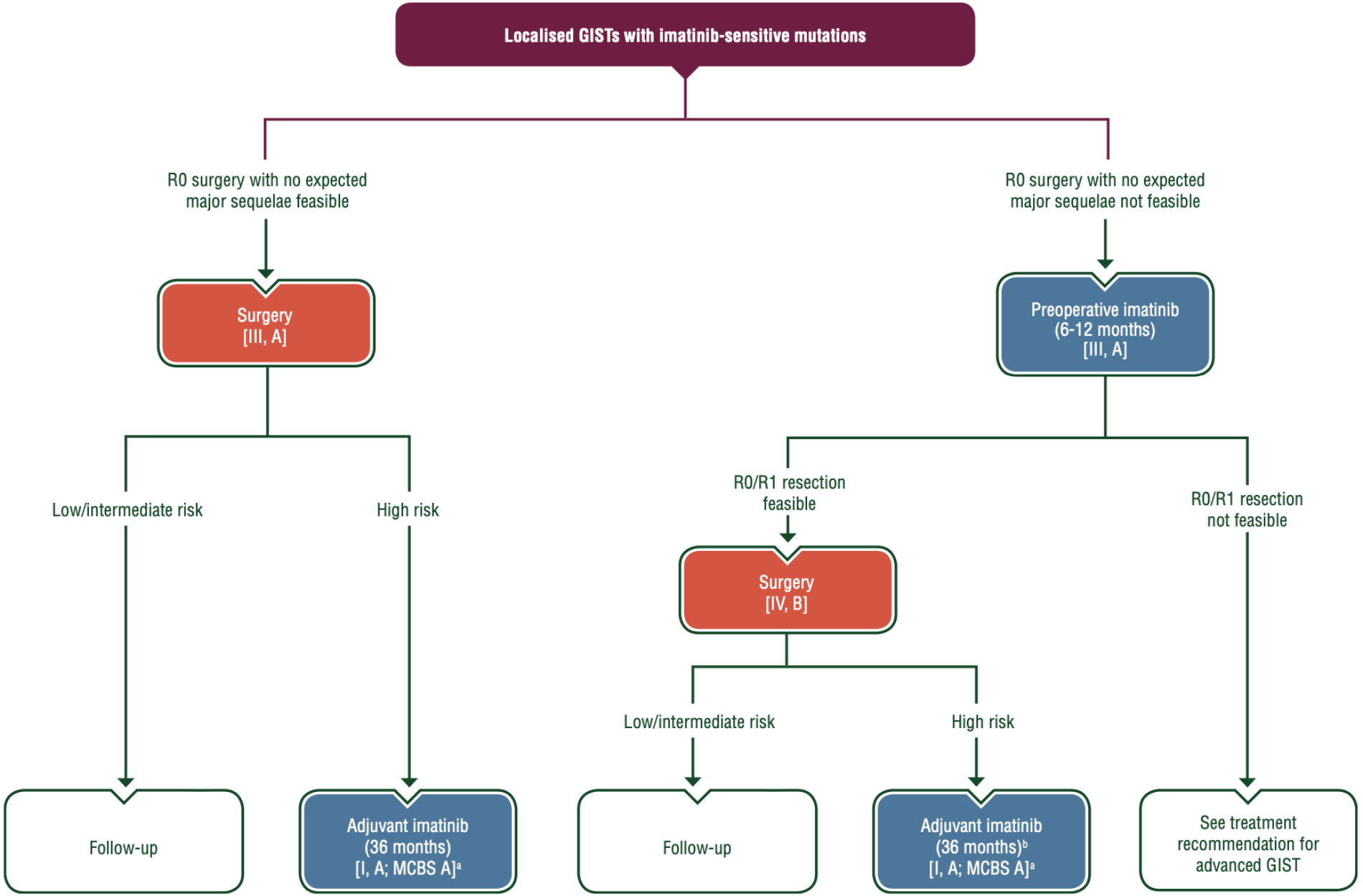
► Heatmaps



Joensuu et al, Lancet Oncol 2012

Serrano et al. presented at ESMO 2024

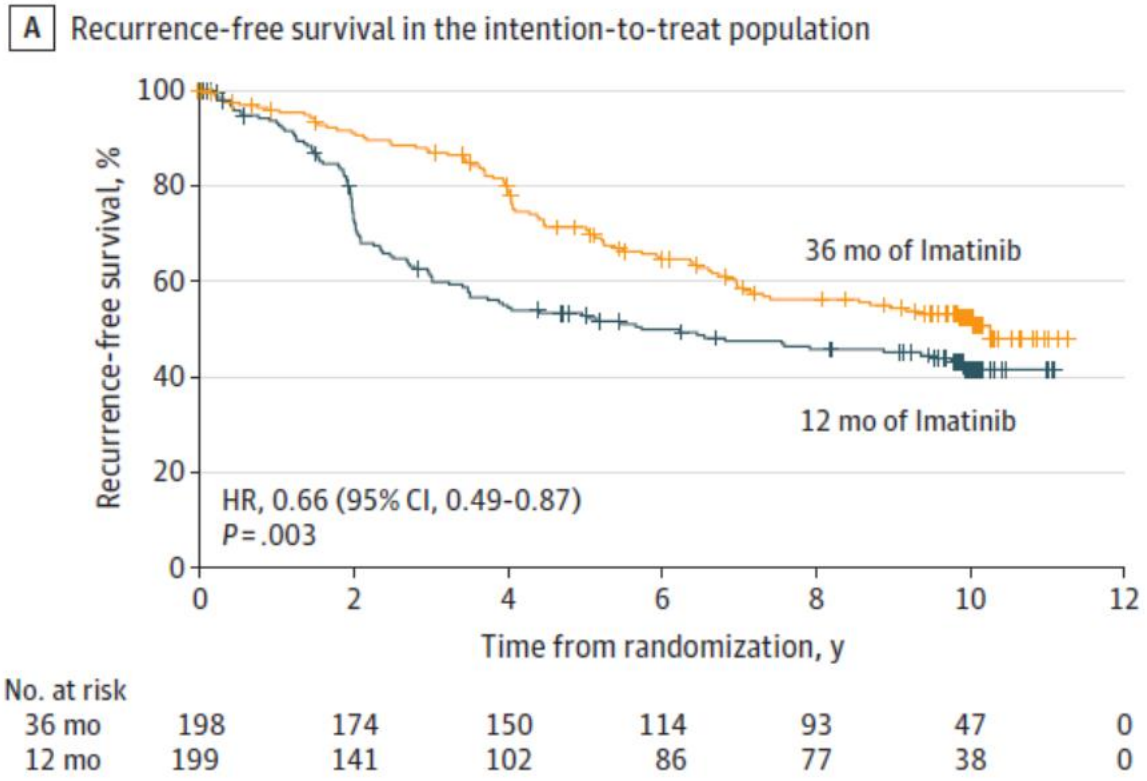
Lokalisierte Erkrankung

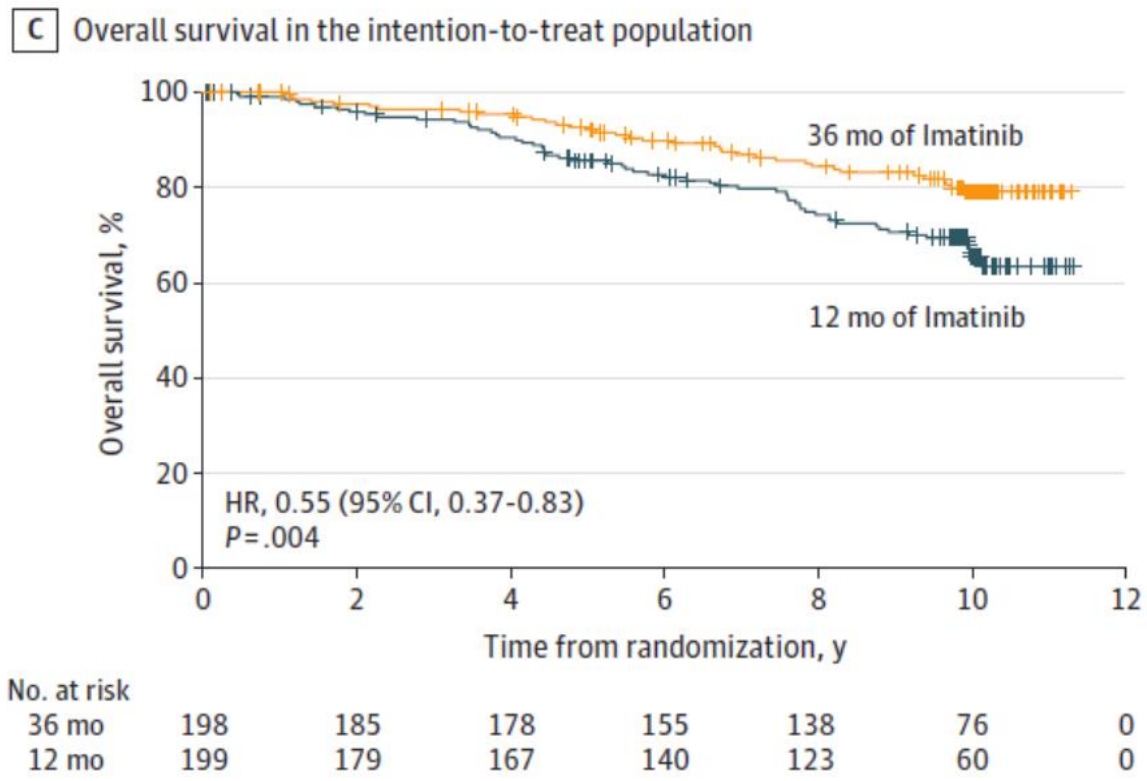


ESMO guidelines GIST 2021

Adjuvante Therapie

- **Adjuvante Therpie mit Imatinib muss mindestens 3 Jahre laufen**





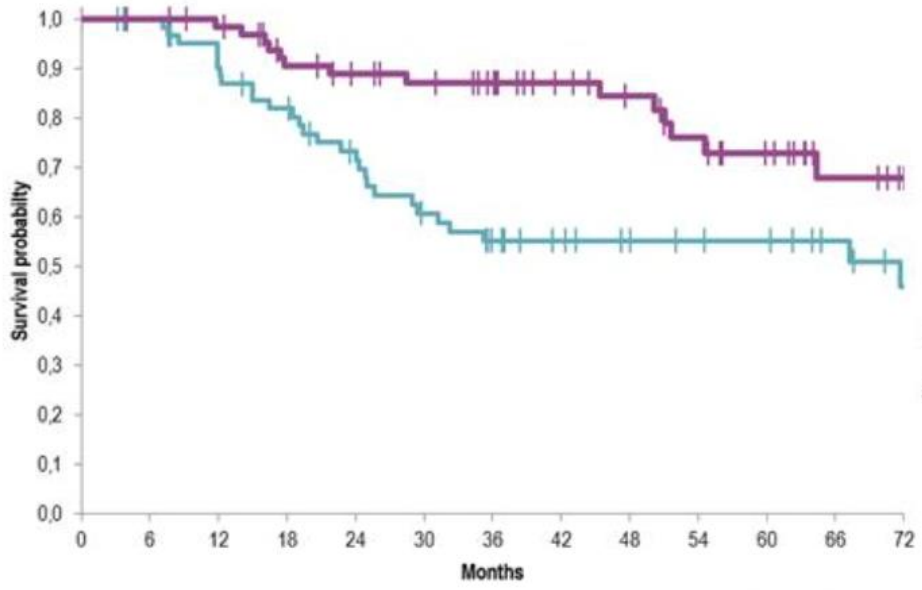
Joensuu et al, JAMA Oncol 2020

IMADGIST - Adjuvante Therapie

A randomized study of 6 *vs* 3 years of adjuvant imatinib in patients with localized GIST at high risk of relapse.

J-Y. Blay 1, C. Schiffler 1, Olivier Bouché 2, Mehdi Brahmi 1, F Duffaud 3, M Toulmonde 4, B. Landi 5, W. Lahlou 5, D. Pannier 6, E. Bompas 7, F. Bertucci 8, L. Chaigneau 9, O. Collard 10, M. Pracht 11, C. Henon 12, I. Ray-Coquard 1, K. Armoun 2, S. Salas 3, M. Spalato-Ceruso 4, A. Adenis 6,12, B. Verret 13, N. Penel 6, C. Moreau-Bachelard 7, A. Italiano 4, A. Dufresne1, S. Metzger 1, S. Chabaud 1, D. Perol 1, A. Le Cesne 12.

PRIMARY ENDPOINT : DISEASE FREE SURVIVAL



	Interruption arm	Maintenance arm
Events/Total	28/65 (43.1%)	15/71 (21.2%)
3-yr DFS	55% (42-67)	87% (76-93)

HR (95% CI)	0.4 (0.20-0.67)
Logrank p-value	0.008

6 Jahre adjuvante Therapie mit Imatinib verlängern das DFS signifikant

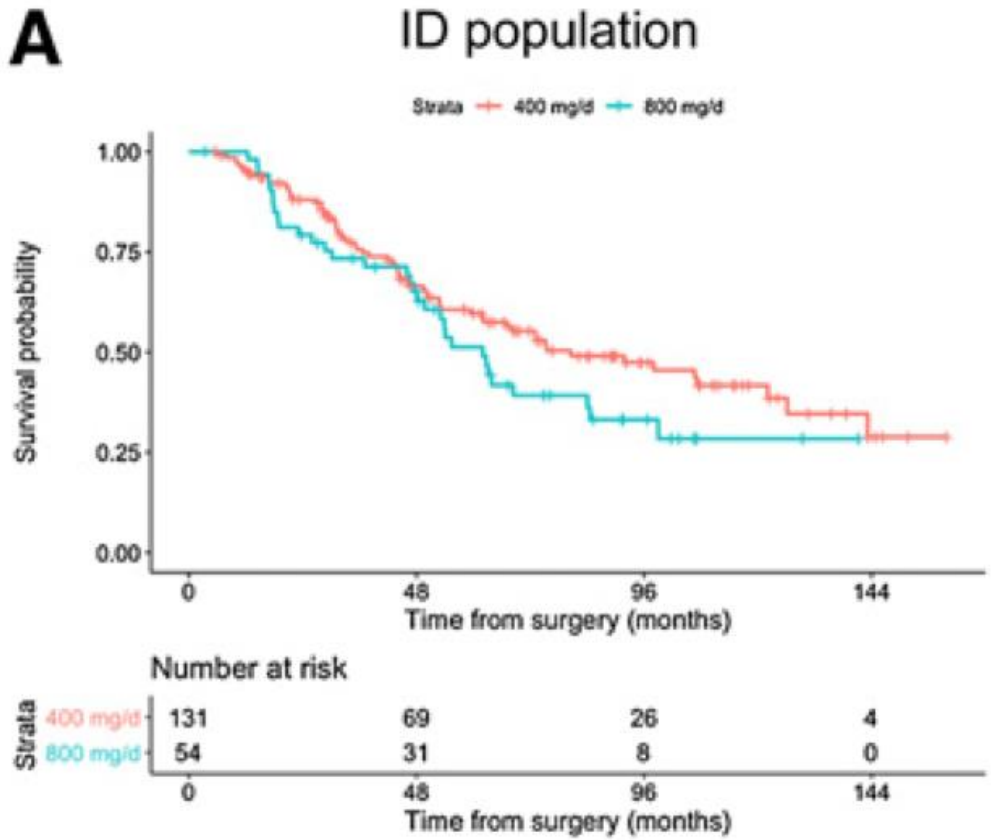
Blay et al, Ann Oncol 2024, Serrano et al. presented at ESMO 2024

Adjuvante Therapie Exon 9

CLINICAL CANCER RESEARCH | TRANSLATIONAL CANCER MECHANISMS AND THERAPY

Adjuvant Imatinib in Patients with GIST Harboring Exon 9 KIT Mutations: Results from a Multi-institutional European Retrospective Study

Bruno Vincenzi[1], Andrea Napolitano[1,2], Marta Fiocco[3], Olivier Mir[4], Piotr Rutkowski[5], Jean-Yves Blay[6], Peter Reichardt[7], Heikki Joensuu[8], Elena Fumagalli[9], Spyridon Gennatas[2], Nadia Hindi[10], Margherita Nannini[11], Mariella Spalato Ceruso[12], Antoine Italiano[12,13], Giovanni Grignani[14], Antonella Brunello[15], Silvia Gasperoni[16], Tommaso De Pas[17], Giuseppe Badalamenti[18], Maria A. Pantaleo[11], Winan J. van Houdt[19], Nikki S. IJzerman[20,21], Neeltje Steeghs[21], Hans Gelderblom[22], Ingrid M.E. Desar[23], Johanna Falkenhorst[24], Marianna Silletta[1], Marta Sbaraglia[25], Giuseppe Tonini[1], Javier Martin-Broto[10], Peter Hohenberger[26], Axel Le Cesne[4], Robin L. Jones[2,27], Angelo P. Dei Tos[25], Alessandro Gronchi[28], Sebastian Bauer[24], and Paolo G. Casali[9,29]



- **Kein Unterschied unter 400mg oder 800mg Imatinib**

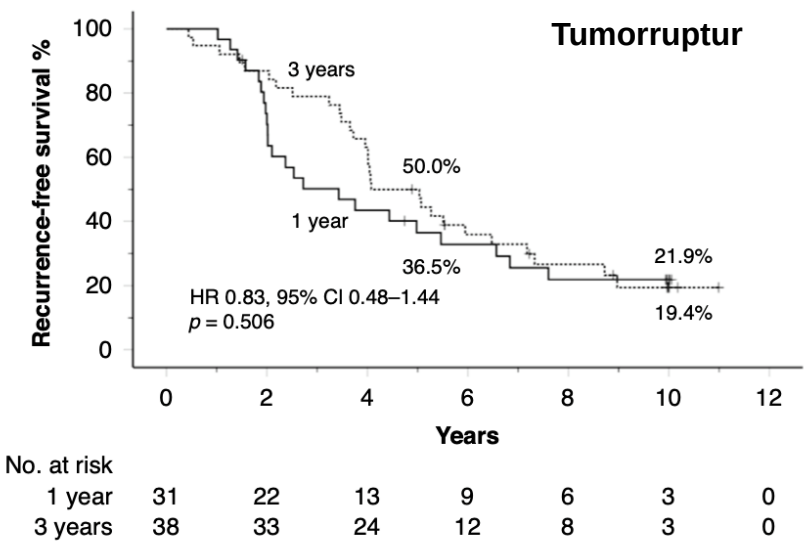
Vincenzi et al, Clin Cna Res 2022

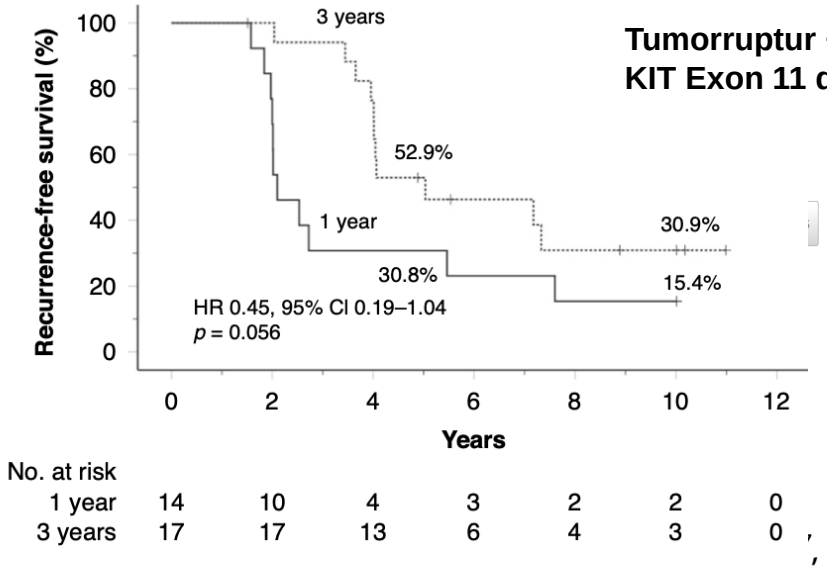
Adjuvante Therapie bei Tumorruptur

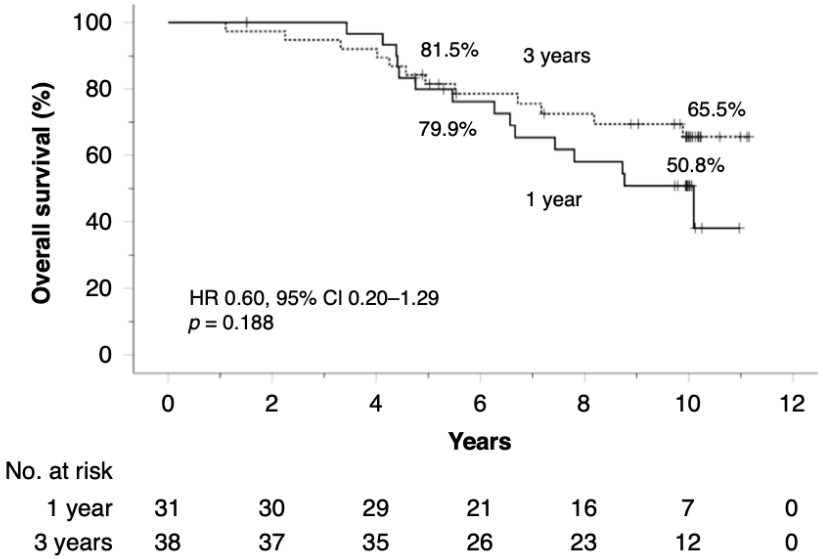
SSG XVIII/AIO

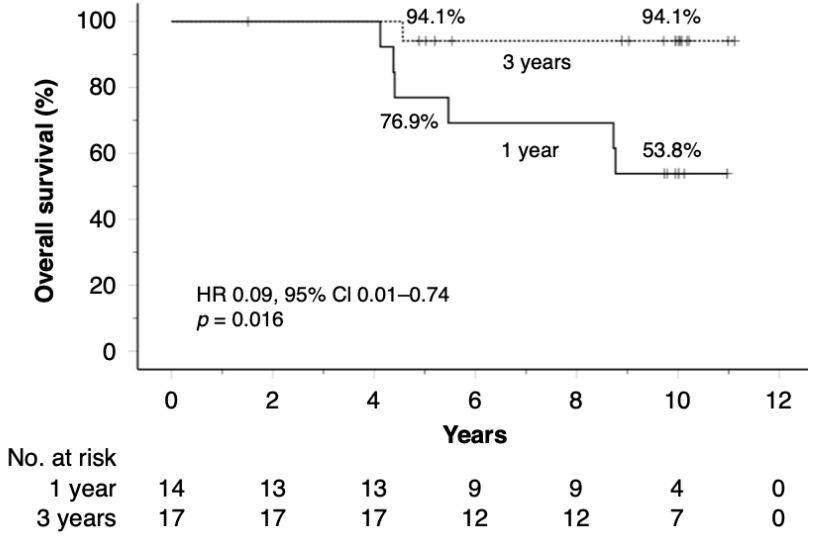
Besseres **OS** bei Pat. mit **Tumorruptur + KIT Exon 11 del/indel** unter **3 Jahren Imatinib**

Benefit auch bei längerer Adjuvanz?



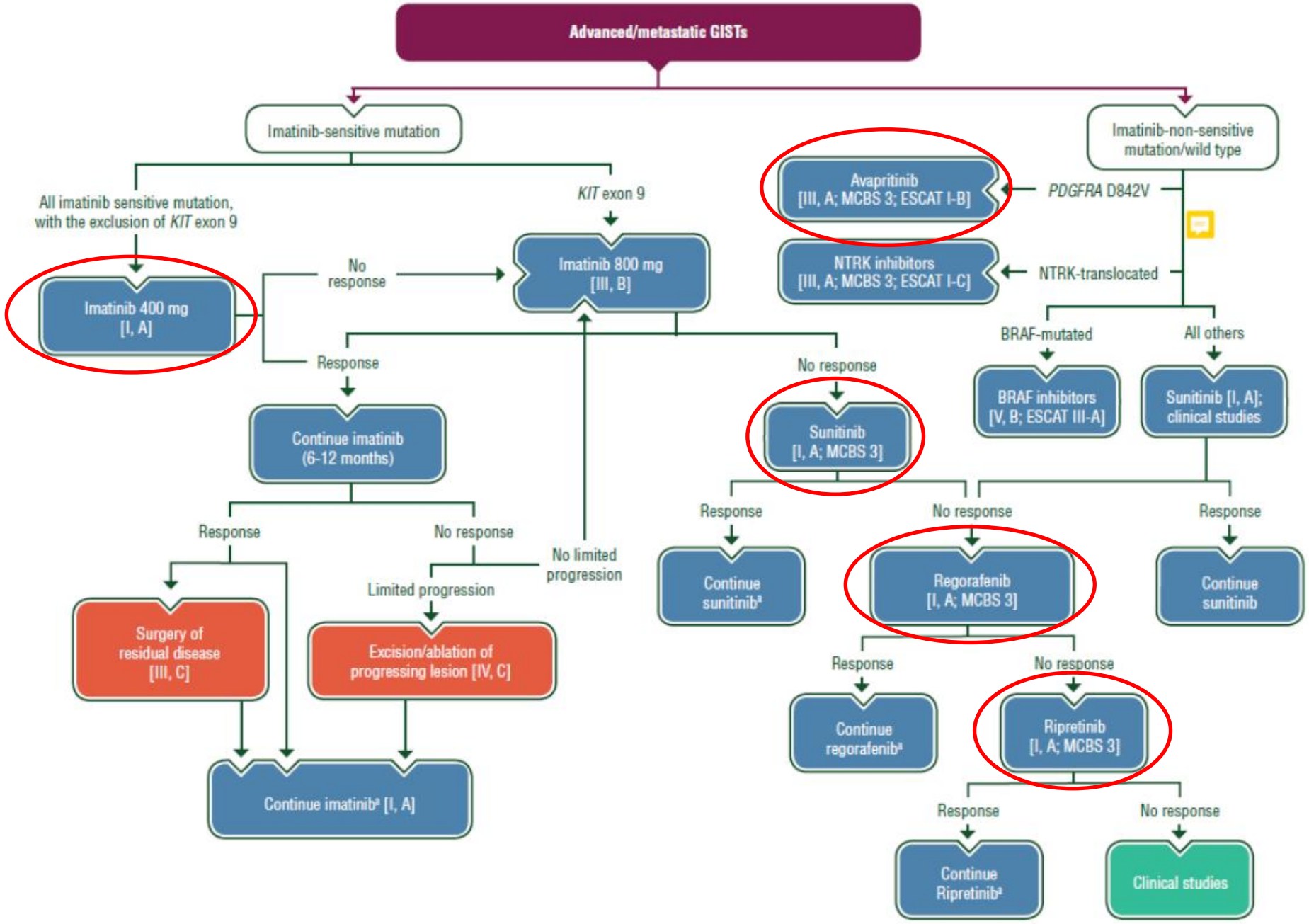






Joensuu et al, BJC 2024

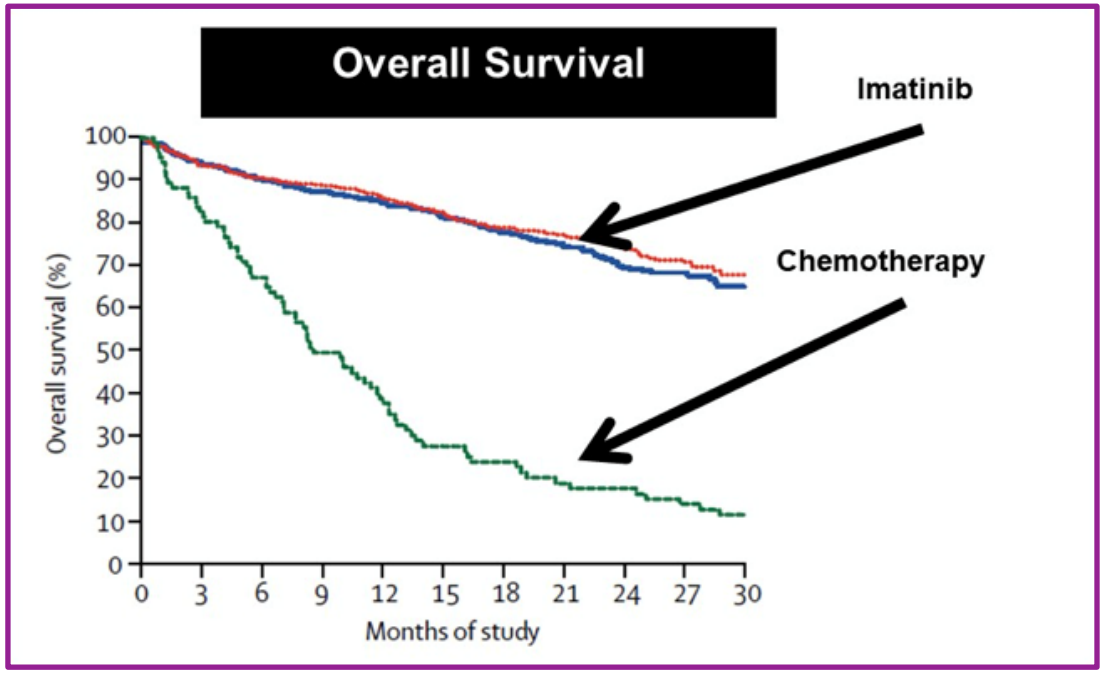
Metastasierte Erkrankung



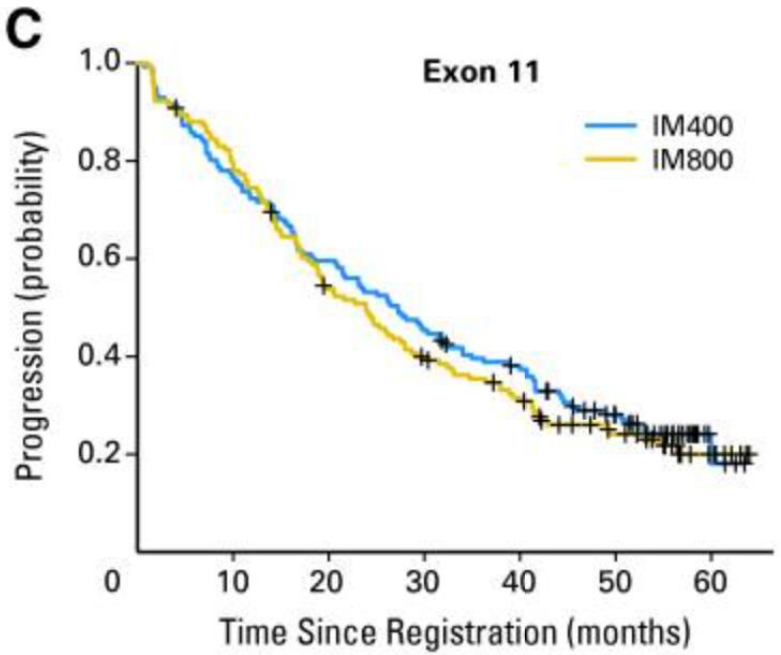
ESMO guidelines GIST 2021

KIT/PDGFRA mutierte GIST

Erstlinientherapie GIST: IMATINIB



IMATINIB
mPFS 20 mo
ORR 68.1%



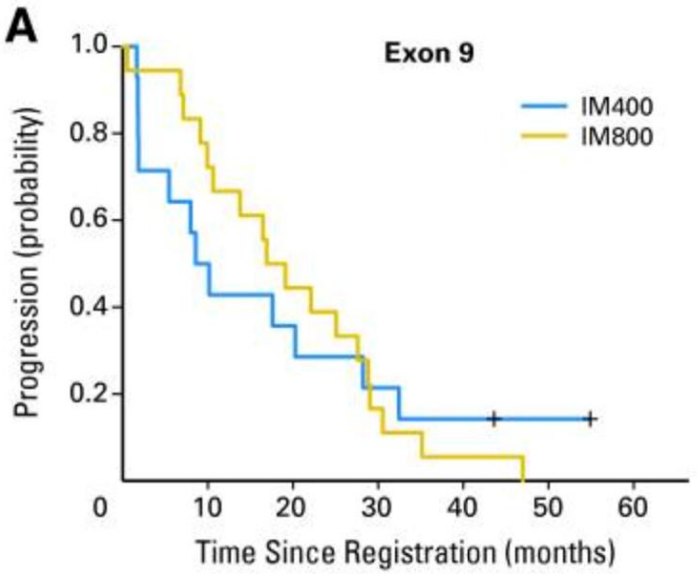
- Imatinib is the standard first-line treatment for locally advanced, inoperable and metastatic patients, except for GIST without KIT/PDGFRA mutations or with a *PDGFRA* exon 18 D842V mutation [I, A]. The standard dose of imatinib is 400 mg daily [I, A].

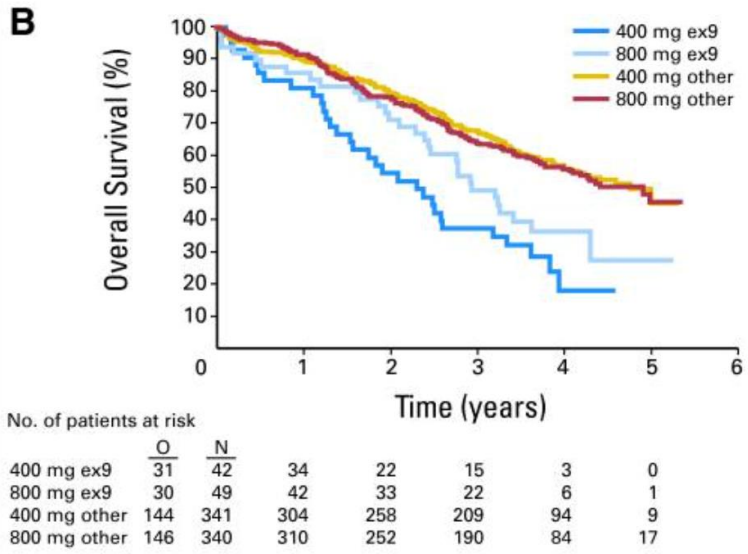
Blanke et al. JCO 2008, Heinrich et al. JCO 2003, Demetri et al. NEJM 2002, Debiec-Rychter et al. EJC 2006, ESMO guidelines GIST 2021

KIT/PDGFRA mutierte GIST

Erstlinientherapie GIST: IMATINIB

IMATINIB 400mg vs. 800mg Exon 9?



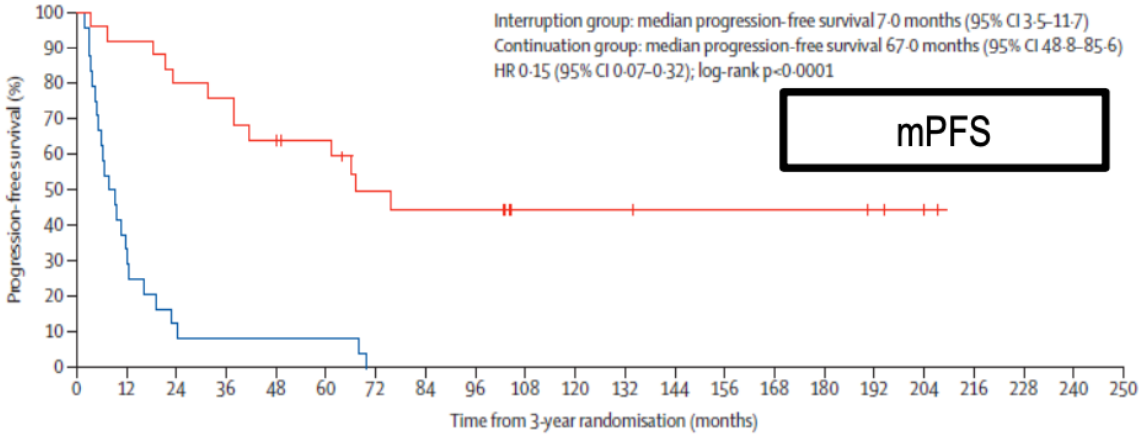


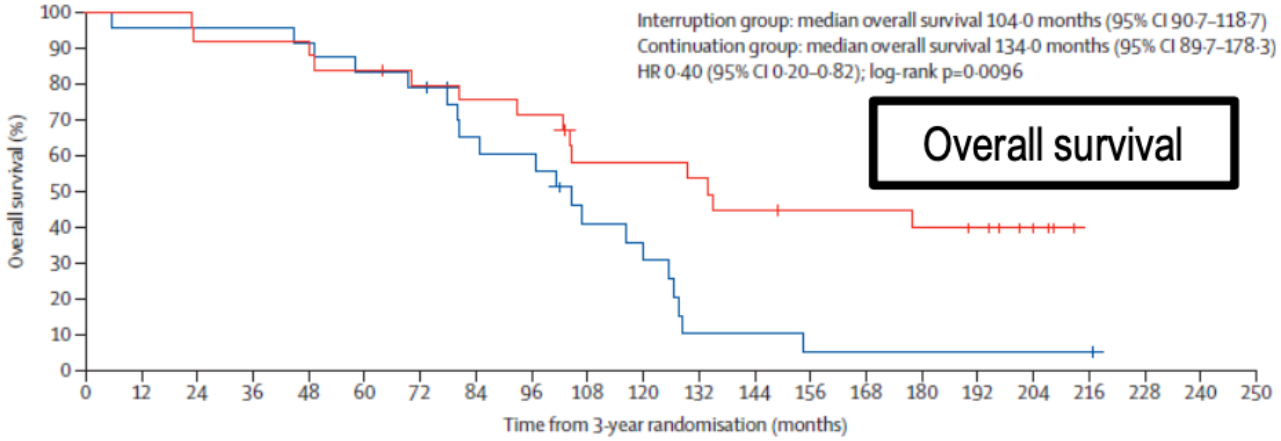
- Standard first-line treatment for patients with *KIT* exon 9 mutation is imatinib 800 mg daily [III, B; ESCAT score: I-A].

Van Glabbekk et al. JCO 2010, Heinrich et al. JCO 2003, Debiec-Rychter et al. EJC 2006, ESMO guidelines GIST 2021

KIT/PDGFRA mutierte GIST

Erstlinientherapie GIST: IMATINIB





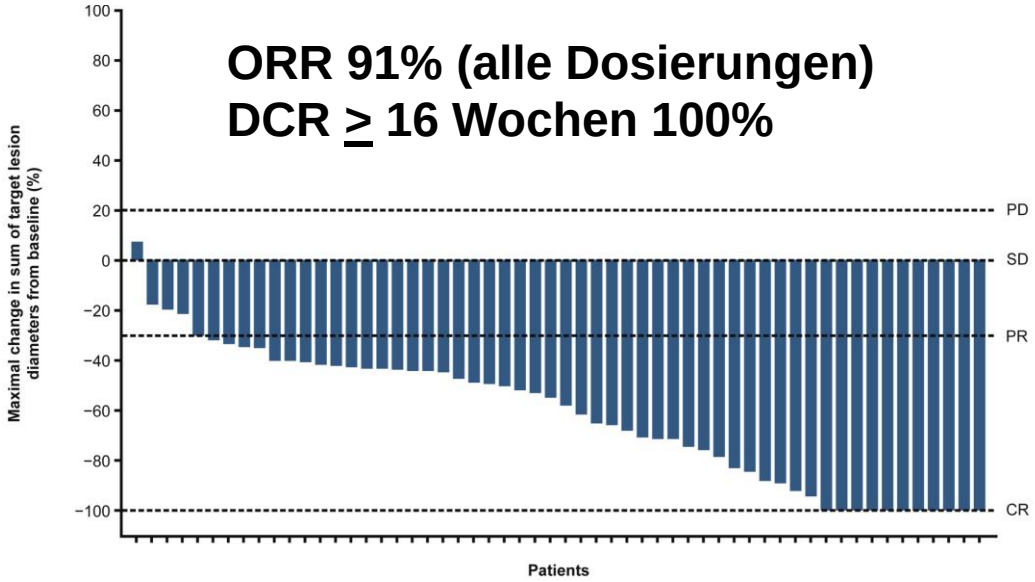
IMATINIB bis zum Progress oder Intoleranz

Blay et al. Lancet Oncol 2024

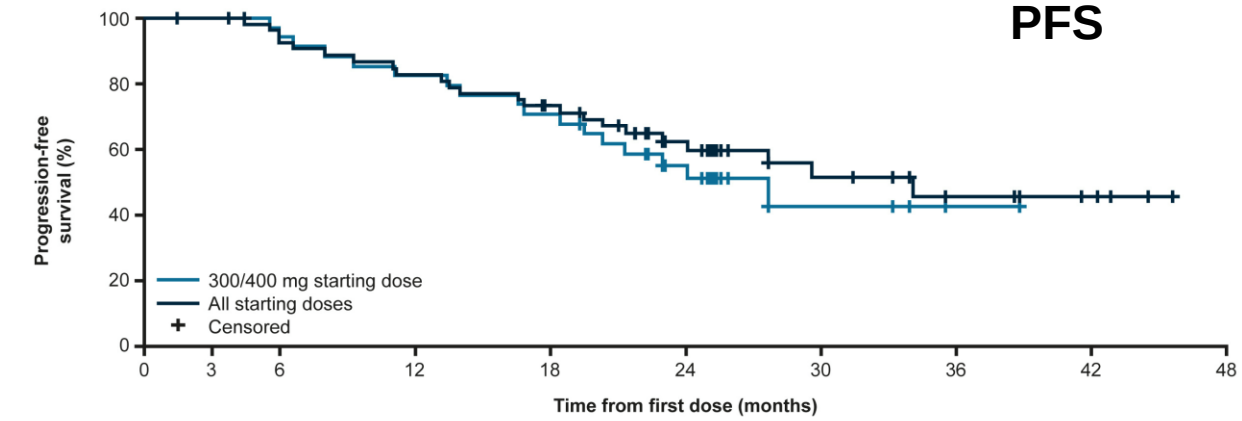
PDGFR D842V-Mutation bei GIST: AVAPRITINIB

PDGFRA D842V mutierte GIST

ORR 91% (alle Dosierungen)
DCR ≥ 16 Wochen 100%



PFS



Number at risk										
300/400 mg starting dose	38	37	32	28	24	14	4	1	0	
All starting doses	56	55	48	43	36	23	12	7	4	0

mDOR 27.6 Monate

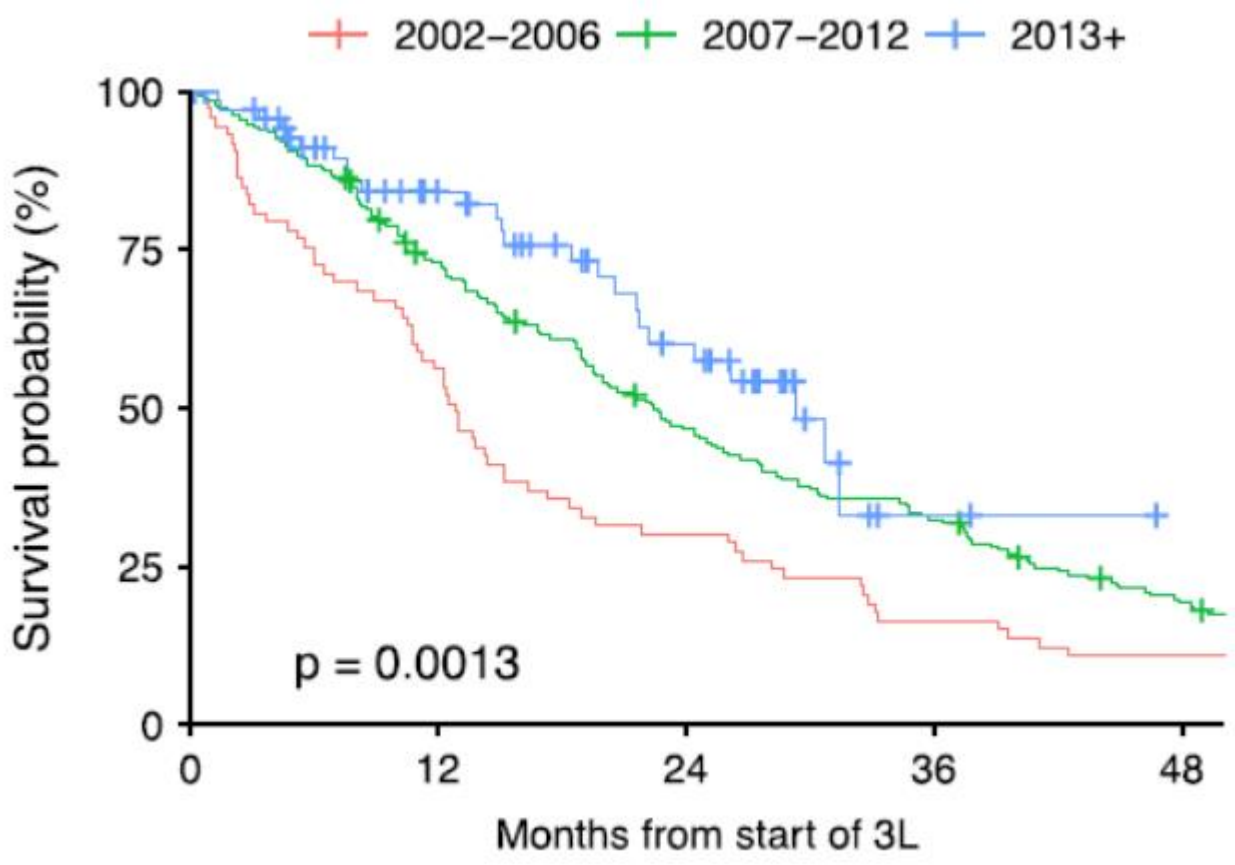
mPFS: (alle Patienten) 34 Monate

Kang et al. JCO 2021, Jones et al. EJC 2021

Zugelassene Therapieoptionen inkl. Folgetherapien

KIT/PDGFRA mutierte GIST

IMATINIB



Signifikante **Verbesserung des OS** durch mehr Therapielinien

RIPRETINIB
mPFS 6.3 mo
ORR 9.4%

PDGFRA D842V mutierte GIST

mPFS 34 mo
ORR 91%

Blanke et al. JCO 2008, Bauer et al. JCO 2022, Kang et al. JCO 2021, Blay et al. Lancet 2020, Jones et al. EJC 2021, Cicala et al. EOID 2024, Call et al. Clin Sarc Res 2019

KIT/PDGFRA mutierte GIST

Änderungen der Therapiesequenz?

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

J Clin Oncol. 2022 Dec 1; 40(34): 3918–3928. PMCID: PMC9746771
Published online 2022 Aug 10. doi: 10.1200/JCO.22.00294 PMID: 35947817

Ripretinib Versus Sunitinib in Patients With Advanced Gastrointestinal Stromal Tumor After Treatment With Imatinib (INTRIGUE): A Randomized, Open-Label, Phase III Trial

Sebastian Bauer, MD,[✉1,2] Robin L. Jones, MD, MBBS,[3] Jean-Yves Blay, MD, PhD,[4] Hans Gelderblom, MD, PhD,[5] Suzanne George, MD,[6] Patrick Schöffski, MD,[7] Margaret von Mehren, MD,[8] John R. Zalcberg, MD, PhD,[9] Yoon-Koo Kang, MD, PhD,[10] Albiruni Abdul Razak, MRCP, MBBCh,[11] Jonathan Trent, MD, PhD,[12] Steven Attia, DO,[13] Axel Le Cesne, MD,[14] Ying Su, MD, PhD,[15] Julie Meade, MD,[15] Tao Wang, PhD,[15] Matthew L. Sherman, MD,[15] Rodrigo Ruiz-Soto, MD,[15] and Michael C. Heinrich, MD[16,17]

original reports

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]; Olivier Mir, MD, PhD, MPH[6]; Shreyaskumar Patel, MD[7]; Yongjian Zhou, MD, PhD[8]; Margaret von Mehren, MD[9]; Peter Hohenberger, MD[10]; Victor Villalobos, MD, PhD[11,12]; Mehdi Brahmi, MD[13]; William D. Tap, MD[14]; Jonathan Trent, MD, PhD[15]; Maria A. Pantaleo, MD, PhD[16]; Patrick Schöffski, MD[17]; Kevin He, PhD[18]; Paggy Hew, MS[18]; Kate Newberry, PhD[18]; Maria Roche, MS[18]; Michael C. Heinrich, MD[19]; and Sebastian Bauer, MD[20]

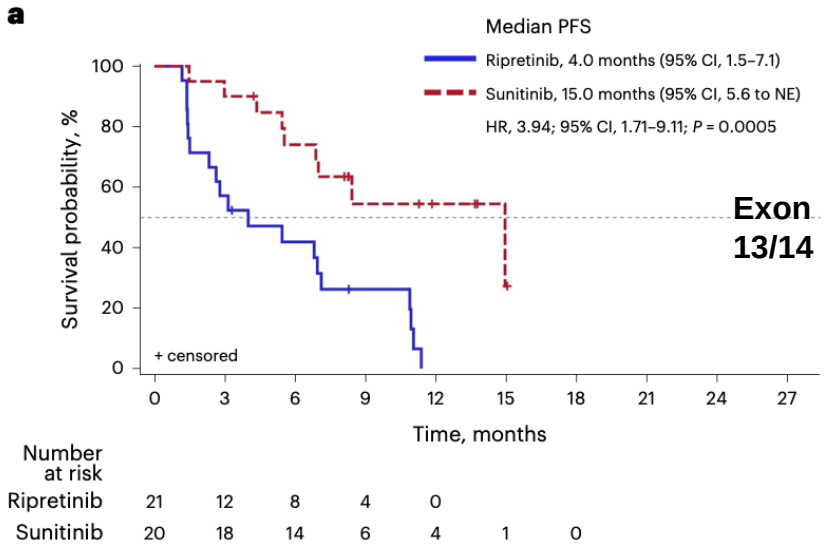
Negative Studien - Kein Vorteil im PFS im Vergleich zu Sunitinib

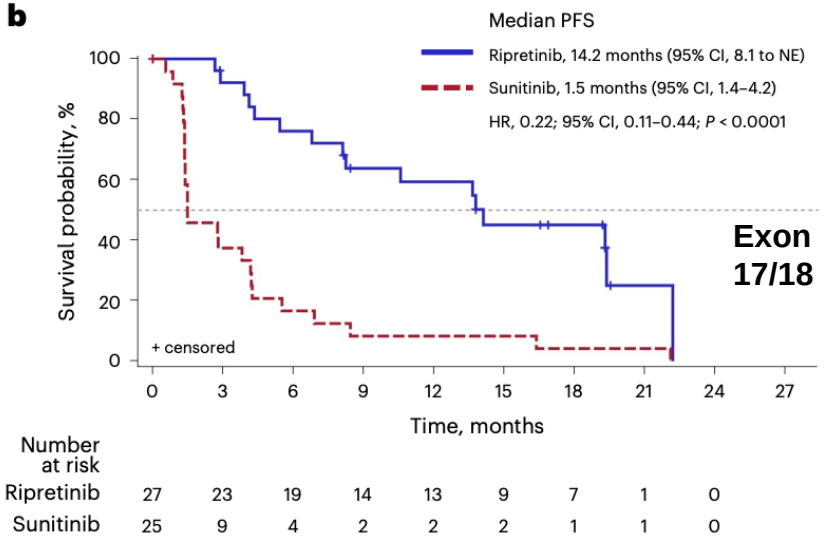
Keine Änderung der Sequenz

Bauer et al. JCO 2022, Kang et al. JCO 2021

KIT/PDGFRA mutierte GIST

Ripretinib in der 2. Linie: Phase III INTRIGUE





Wirksamkeit von **Ripretinib** v.a. bei sekundärer Mutation in **Exon 17/18**

Bauer et al. JCO 2022, Heinrich et al. Nat Med 2024

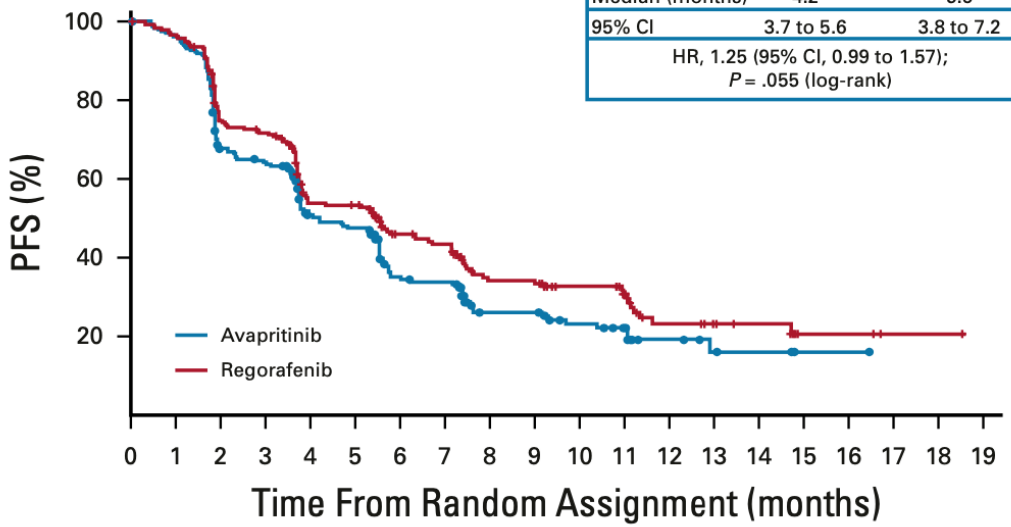
Phase III-Studie VOYAGER – Avapritinib 3. Linie

KIT/PDGFRA mutierte GIST

A

PFS in ITT

	Avapritinib (n = 240)	Regorafenib (n = 236)
Events, No.	154	145
Median (months)	4.2	5.6
95% CI	3.7 to 5.6	3.8 to 7.2
HR, 1.25 (95% CI, 0.99 to 1.57); *P* = .055 (log-rank)		



No. at risk:

Avapritinib	240	221	151	142	94	88	53	50	29	29	22	17	8	5	4	1	1	0
Regorafenib	236	224	169	161	108	106	71	66	46	46	36	31	15	11	9	3	3	1	1	0

	ITT Population	
Best Response	**Avapritinib (n = 240)**	**Regorafenib (n = 236)**
ORR, % (95% CI)	17.1 (12.5 to 22.5)	7.2 (4.3 to 11.3)
CR, No. (%)	0	0
PR, No. (%)	41 (17.1)	17 (7.2)
SD, No. (%)	113 (47.1)	159 (67.4)
PD, No. (%)	67 (27.9)	49 (20.8)
NE, No. (%)	1 (0.4)	0
Unknown, No. (%)	18 (7.5)	11 (4.7)
DCR,[a] % (95% CI)	41.7 (35.4 to 48.2)	46.2 (39.7 to 52.8)

Geringere Wirksamkeit bei KIT Exon 13 und 14 Mutationen

Kang et al. JCO 2021

BARCELONA 2024 ESMO congress

Neue Therapieoptionen im Blick?

AXAGIST: A phase II, single arm study of avelumab in combination with axitinib in patients with unresectable/metastatic gastrointestinal stromal tumor after failure of standard therapy

Piotr Rutkowski[1], Anna Klimczak[1], Paweł Teterycz[1], Tomasz Świtaj[1], Paweł Rogala[1], Maria Pantaleo[2], Katarzyna Kozak[1]

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- Metastatic/advanced unresectable GIST
- Disease progression within 3 months prior to enrolment
- ECOG PS ≤ 2
- Prior therapy with imatinib and sunitinib
- No prior treatment with axitinib and avelumab

n = 58

Axitinib 5 mg po BID*
+
Avelumab 10 mg/kg iv Q2W*

*maximum treatment duration of 2 years

Primary endpoint:
- 3- month progression-free survival rate based on RECIST 1.1 criteria

Secondary endpoints:
- Progression-free survival
- Overall survival
- Objective response rate
- Disease control rate
- Duration of response
- Safety (NCI CTCAE v 4.0)

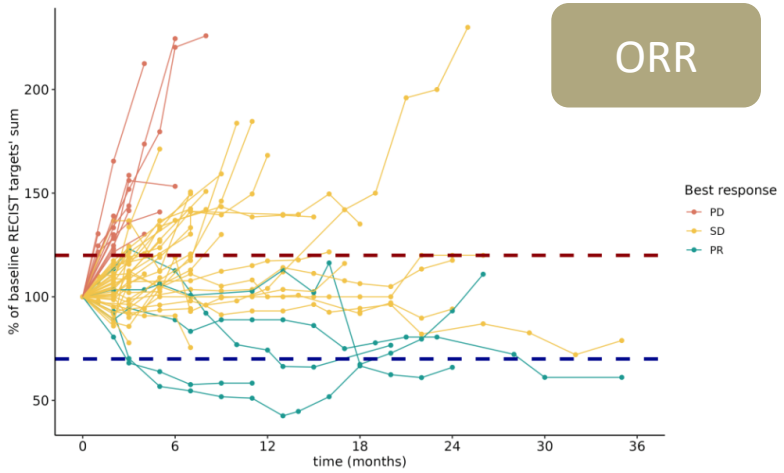
Rutkowski et al. presented at ESMO 2024

BARCELONA 2024 ESMO congress

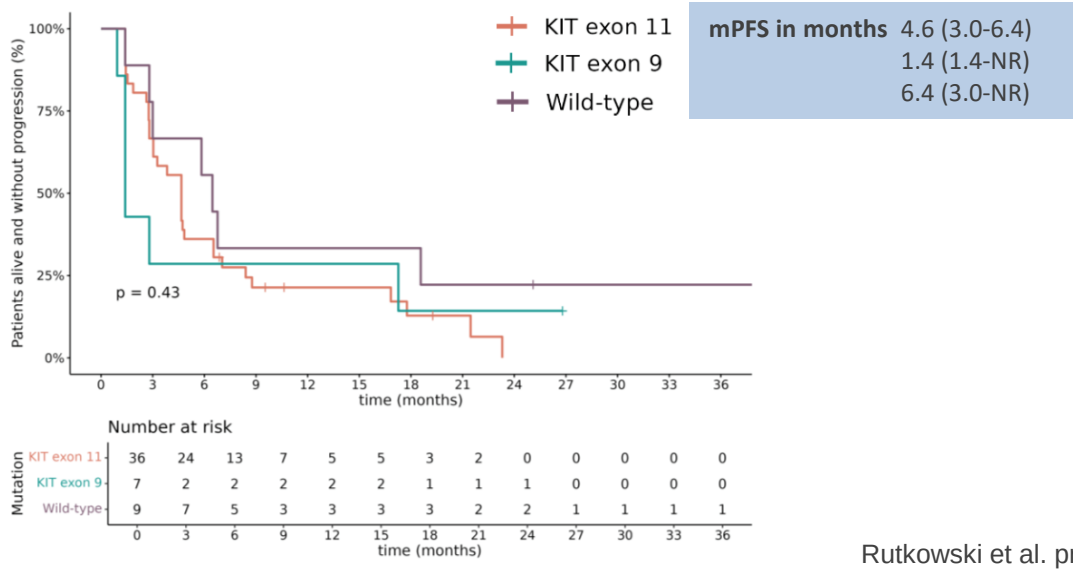
AXAGIST

Outcome	Patients n=56
Partial response, n (%)	5 (8.9)
Stable disease, n (%)	34 (60.7)
Progressive disease, n (%)	17 (30.4)
Disease control rate, n (%)	39 (69.6)
Duration of objective response Median — mo (95% CI)	18.5 (18.3–NR)

ORR



Outcome	Patients n=56
3-month progression free-survival rate, %	57.1
Progression-free survival, median mo (95% CI)	4.6 (2.9-6.4)
Overall survival, median mo (95% CI)	14.2 (9.2-26.3)
Alive at 12 mo — %	59.3



Rutkowski et al. presented at ESMO 2024

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Neue Therapieoptionen im Blick?

LENVAGIST

A multicentre, comparative, placebo-controlled, double-blinded, phase II study of the efficacy of lenvatinib in patients with locally advanced or metastatic GIST after failure of imatinib and sunitinib

Prof. Jean-Yves BLAY, MD, PhD

A Le Cesne, C. Cropet , M. Brahmi, R. Bahleda, E. Bompas, T. Valentin, A. Hervieu, O. Bouche, A. Dufresne, M. Toulmonde, K. Bourcier, F. Duffaud, M. Pracht, F. Bertucci, L. Lebellec, A. Italiano, B. Verret, J. Gautier, D. Perol.

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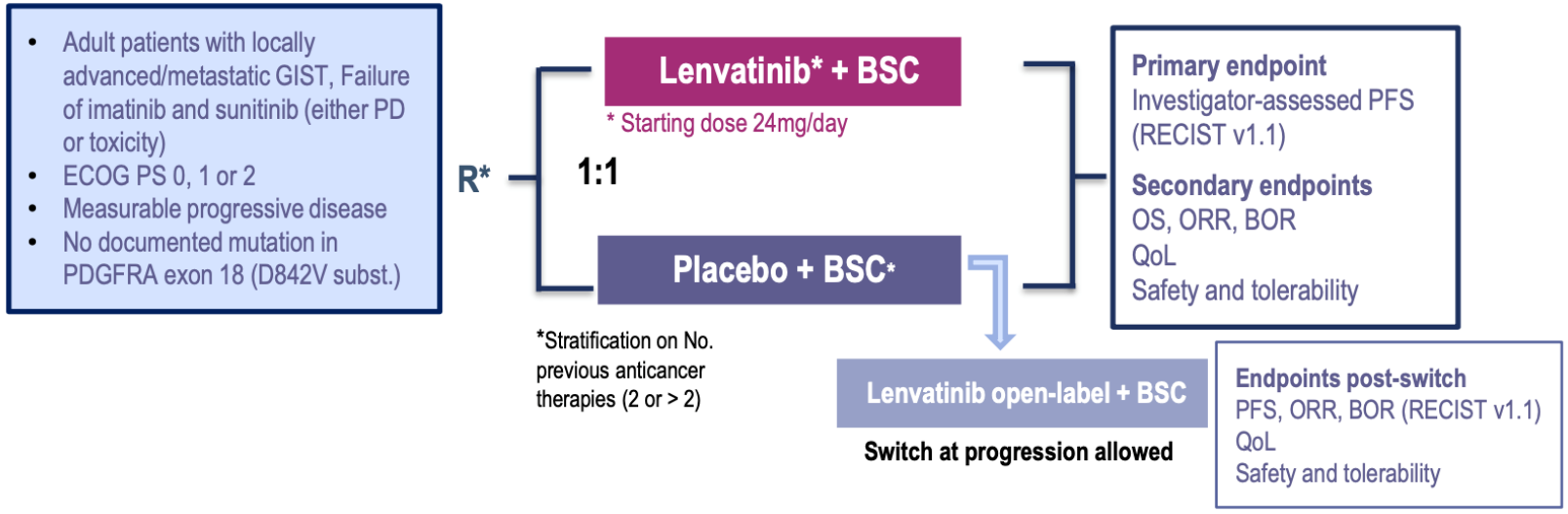


> 50% der Patienten > 3 Vortherapien

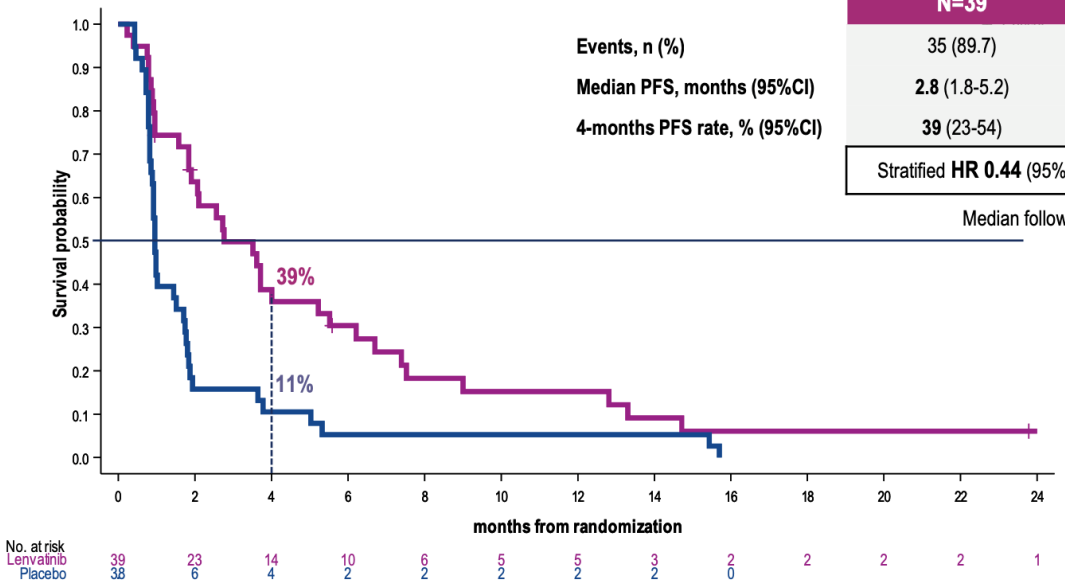
Blay et al. presented at ESMO 2024

LENVAGIST

Primärer Endpunkt PFS (ITT)

	Lenvatinib+BSC N=39	Placebo+BSC N=38
Events, n (%)	35 (89.7)	38 (100)
Median PFS, months (95%CI)	**2.8** (1.8-5.2)	**1.0** (0.9-1.5)
4-months PFS rate, % (95%CI)	**39** (23-54)	**11** (3-23)
Stratified **HR 0.44** (95%CI: 0.27-0.71; p=0.0008)		

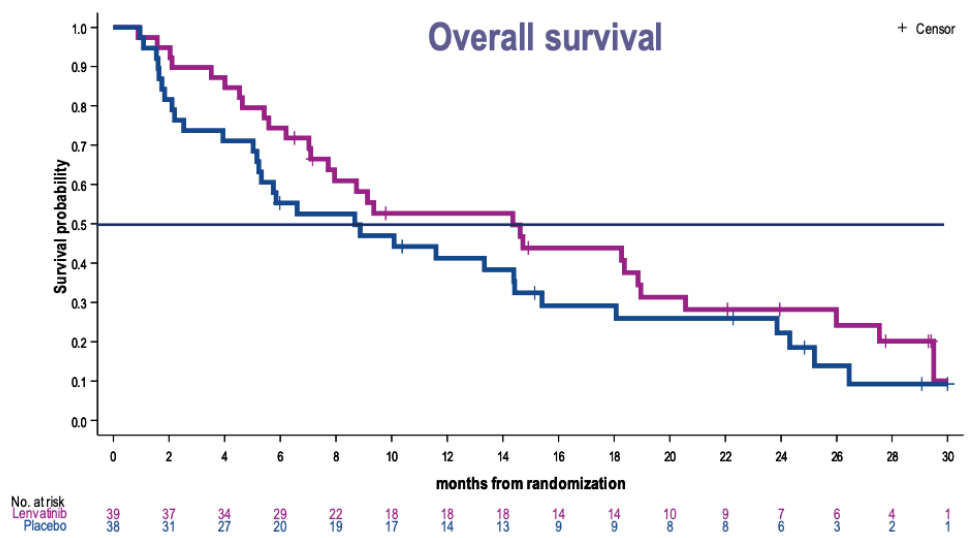
Median follow-up for PFS was 3.7 months



Sekundärer Endpunkt OS (ITT)

	Lenvatinib+BSC N=39	Placebo+BSC N=38
Events (deaths), n (%)	30 (76.9)	31 (81.6)
Median OS, months (95%CI)	14.4 (7.1-18.9)	8.7 (5.2-14.4)
Stratified **HR 0.77** (95%CI: 0.46-1.28; p=0.31)		

Median follow-up for OS was 22.1 months



ORR 5.1% vs. 0%

Klinischer Benefit nach Versagen der Standardtherapien

Blay et al. presented at ESMO 2024

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Neue Theapieoptionen im Blick?

StrateGIST 1: a first-in-human (FIH), phase 1 study of IDRX-42 in patients with metastatic gastrointestinal stromal tumors resistant to prior treatment with tyrosine kinase inhibitors (TKIs)

Patrick Schöffski[1], Michael Heinrich[2], Jonathan Trent[3], César Serrano[4], Sebastian Bauer[5], Margaret von Mehren[6], Neeta Somaiah[7], Peter Reichardt[8], George Demetri[9,10], Nick Lydon[9], Jaap Verweij[9], Vivek Kadambi[9], Jessica Christo[9], Sean Kim[9], Debbie Johnson[9], James Shao[9], Suzanne George[10]

IDRX-42: Hoch selektiver Inhibitor aktivierender und resistenzvermittelnder KIT-Mutationen

Key Eligibility Criteria

- Metastatic and/or unresectable GIST
- Pathogenic mutations in *KIT* or non-exon 18 *PDGFRA*
- Progression on imatinib (phase 1)
- ECOG PS 0-1

Endpoints

- Safety/tolerability
- PK
- Anti-tumor activity (investigator-assessed)†

Phase 1 Dose Escalation (3+3 Design)††

NCT05489237

First patient enrolled: 09 August 2022

- 1200 mg (600 mg BID) capsules, n=6
- 800 mg (400 mg BID) capsules, n=12
- 600 mg QD tablets, n=5
- 600 mg QD capsules, n=12
- 400 mg QD capsules, n=22
- 300 mg QD tablets, n=10
- 240 mg QD capsules, n=3
- 120 mg QD capsules, n=3

tablets provide 1.35× exposure by dose vs capsules

Enrollment beyond 3+3 at doses between 400 mg and 800 mg (backfill and dose confirmation)

Phase 1b Cohorts
at RP1bD(s)‡

- **1st Line** — Treatment naïve
- **2nd Line** — Progression on imatinib
- **≥3rd Line with approved TKIs** — Progression on at least imatinib and sunitinib
- **≥3rd Line with investigational TKIs** — prior bezuclastinib, NB003, or THE-630 (in addition to approved TKIs)

Schöffski et al. presented at ASCO 2024

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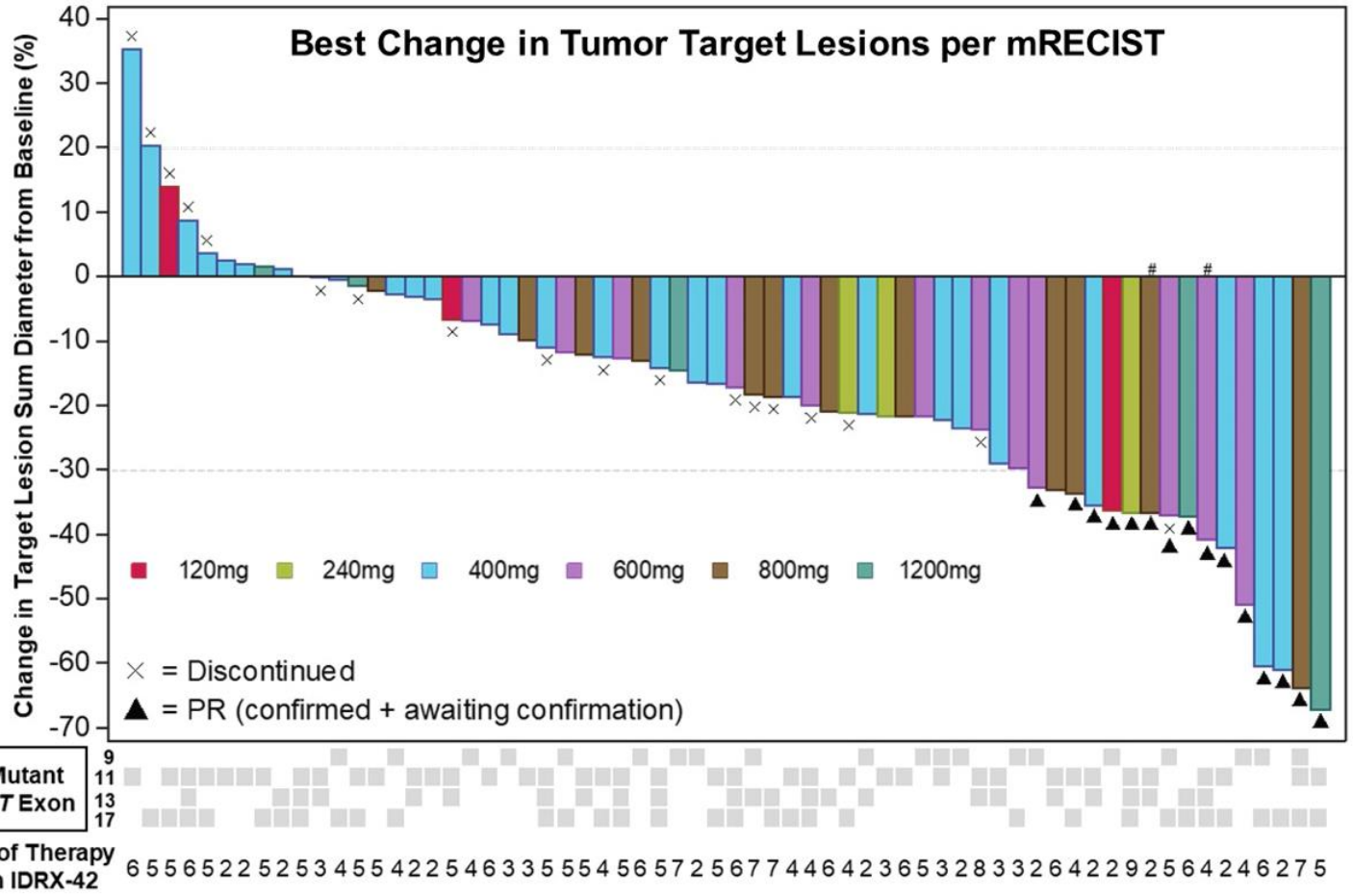
IDRX-42



mRECIST Response Evaluable for Efficacy†

	All Patients N=66	2nd Line Patients N=14
Median follow-up, months	5.6	3.0
Partial Response, n (%) *confirmed + awaiting confirmation*	15 (23) ††	6 (43) ‡
Median time to response, months	2.6	3.7

Vielversprechendes **Ansprechen** bei **multipel vortherapierten GIST** Patienten (Median 4 Linien)
Geringe Rate an Grad 3-4 **Toxizitäten** (je 3-4% Diarrhoe, Anämie, Fatigue, Nausea)

Schöffski et al. presented at ASCO 2024

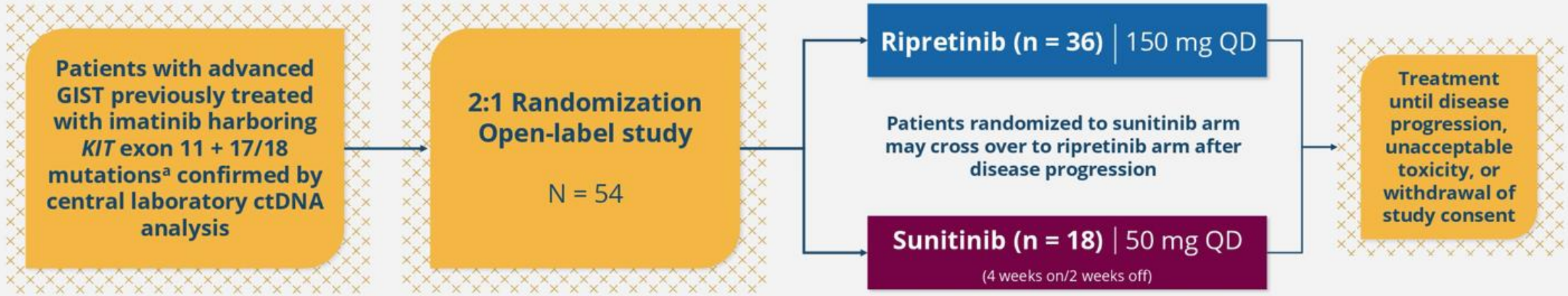
KIT/PDGFRA mutierte GIST

Was können wir von INTRIGUE lernen?

Definition der Ein- und Ausschlusskriterien: Phase III INSIGHT

Study Design

Figure 2. INSIGHT study design

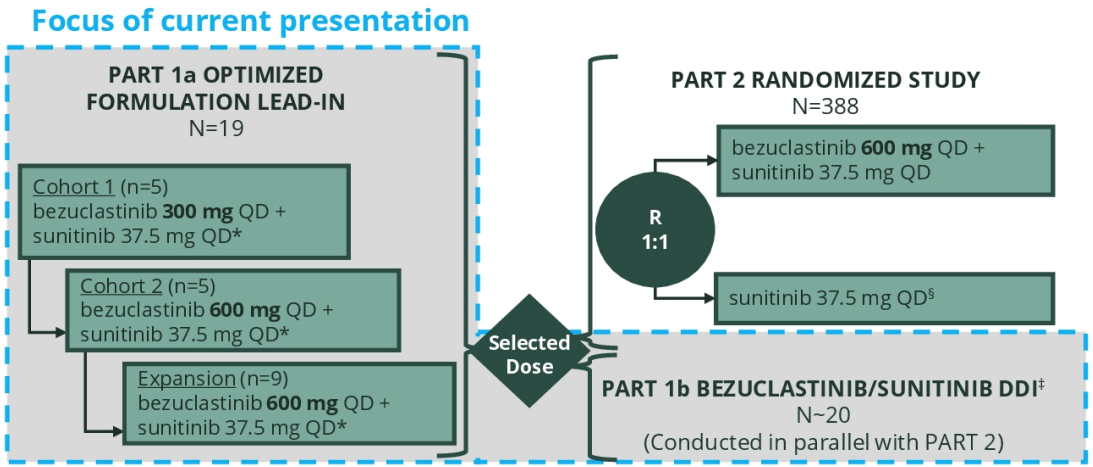


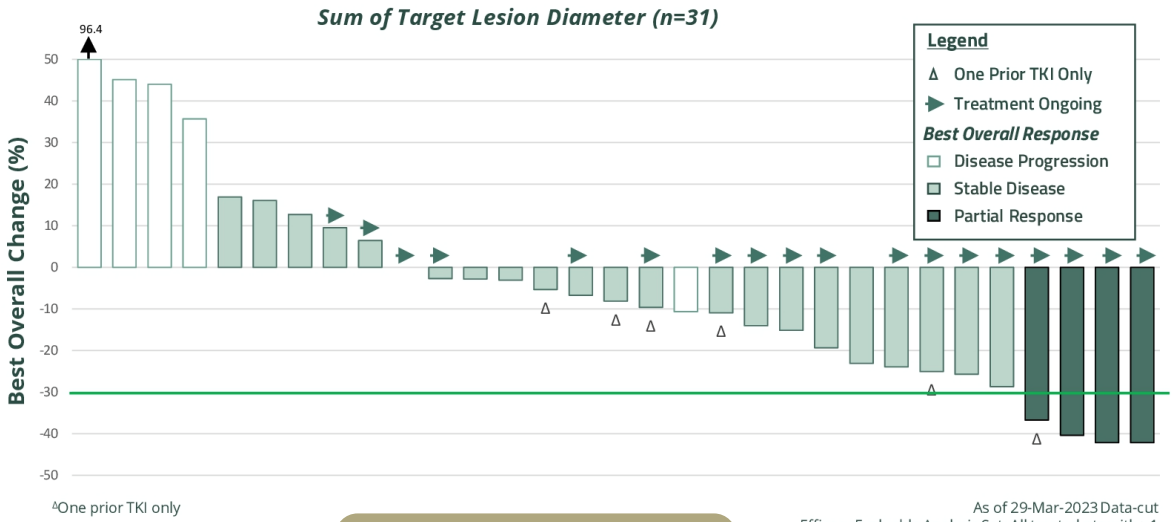
[a]Excludes additional *KIT* primary and secondary mutations in exons 9, 13, or 14.
ctDNA, circulating tumor DNA; GIST, gastrointestinal stromal tumor; QD, once daily.

George et al., presented at ASCO Annual Meeting 2023

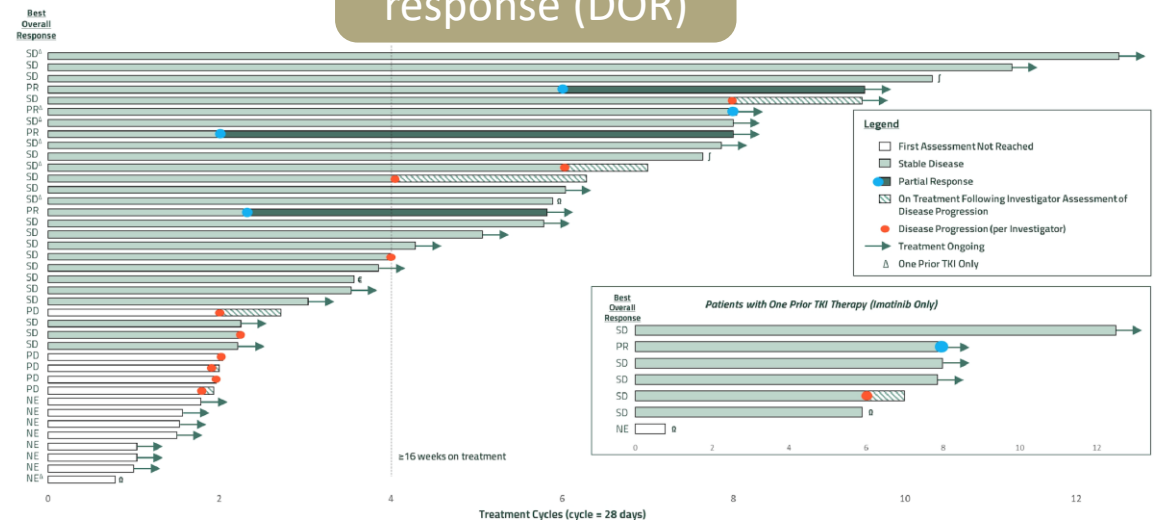
PEAK trial Phase III Part 1

Best overall change (%) in sum of target lesion diameter





Duration of response (DOR)



Inhibition primärer und sekundärer häufiger Mutationen

Bezuclastinib (KIT Exon 9, 11, 17 und 18) + Sunitinib (KIT Exon 9, 11, 13 und 14)

Part 2 läuft, einige Zentren bereits geschlossen

Tap et al., presented at ASCO Annual Meeting 2023

Weitere TKI‘s in der Behandlung von GIST

Drug	Clinical Trial	Setting Treatment Line	ORR (%)	mPFS (mo)	Phase
Avapritinib	Kang (2021)[78]	Third/fourth	17	4.2	III-R
Cabozantinib	Schöffski (2020)[79]	Third	14	5.5	II
Dasatinib	Schuetze (2018)[80]	Second or more	4	2.9	II
Dovitinib	Kang (2013)[81]	Third or more	3	3.6	II
	Joensuu (2017)[82]	Third or more	5	4.6	II
Masitinib	Adenis (2014)[83]	Second	NA	3.7	II
Nilotinib	Montemurro (2009)[84]	Third or more	10	2.8	II
	Sawaki (2011)[85]	Third	3	3.7	II
	Cauchi (2012)[86]	Third or more	0	2.0	II
	Reichardt (2012)[87]	Third	< 1	3.6	III-R
Pazopanib	Ganjoo (2014)[88]	Second or more	0	1.9	II
	Mir (2016)[89]	Second or more	0	3.4	II-R
	Eriksson (2021)[90]	Third/fourth	3	4.5	II
Ponatinib*	George (2022)[91]	Second or more	8	4.3	II
Sorafenib	Kindler (2011)[92]	Second or more	13	5.2	II
	Park (2012)[93]	Third or more	13	4.9	II

Keine offiziellen Zulassungen

Schaefer et al. ASCO Ed Book 2022

Take Home Messages

- **Welches Medikament wann?**
  - Imatinib in der Adjuvanz für 3 Jahre -> eventuell länger? Für alle?
  - 5 zugelassene medikamentöse Therapieoptionen in der metastasierten Erkrankung
  - **KIT/PDGFRA-mutiert:** Imatinib -> Sunitinib -> Regorafinib -> Ripretinib
  - **PDGFRA D824V Mutation:** Avapritinib
  - Sekundäre und tertiäre Mutationen haben einen Einfluss auf die Wirksamkeit in den Folgetherapielinien
    - **Ripretinib bei Exon 17/18 besser als Sunitinib? -> INSIGHT**

Take Home Messages

- **AXAGIST**
  - Axitinib + Avelumab prinzipiell gut verträglich
  - Axitinib der bessere TKI als Sunitinib? Kombination oder Sequenz?

- **LENVAGIST**
  - mPFS nach multiplen Vortherapien 2.8 Monate -> neue Option nach Versagen der zugelassenen 4 Linien?
  - ORR 5.1%

- **IDRX-42**
  - Neuer Player am Horizont?
  - Vielversprechende Wirksamkeit in Phase I mit ORR 23% bei massiv vortherapierten Patienten

- **PEAK**
  - Inhibition aller häufigen Sekundärmutationen durch Kombination 2er TKI

Wir brauchen Studien, um GIST auch in späteren Linien noch besser behandeln zu können!

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