Die lokalisierte GIST-Erkrankung, Rückfall-(Rezidiv)-Risiko und adjuvante (unterstützende) Imatinib-Therapie

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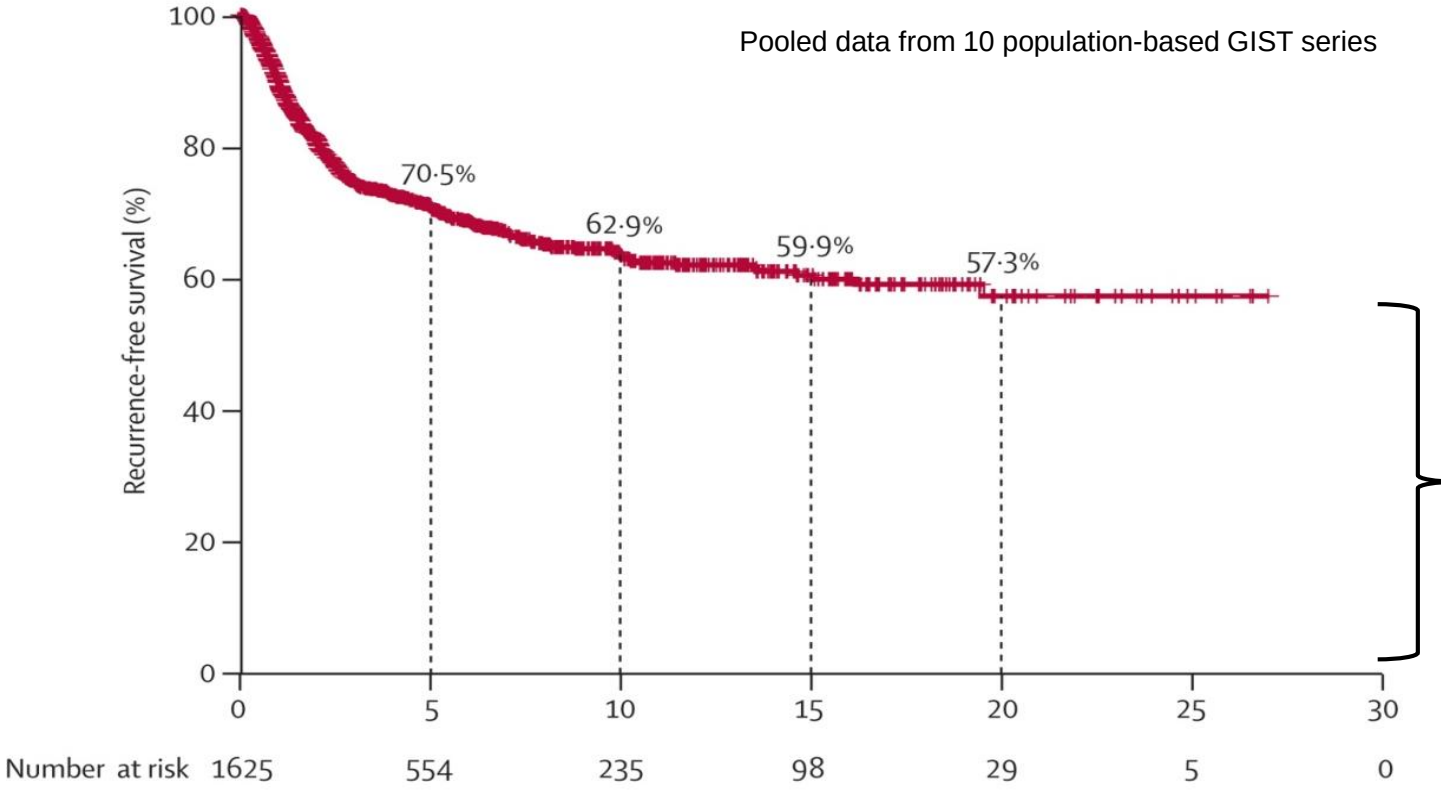
DKG KREBSGESELLSCHAFT | Zertifiziertes Sarkomzentrum

GIST: Lokaltherapie

- Tumoren >2 cm: Biopsie / Excision (Rektum: immer)
- lokalisierte GIST: vollständige chirurgische Entfernung
- präoperative systemische Therapie zur Vermeidung mutilierender Operationen (Mutationsanalyse obligat)

Risk of recurrence after surgey alone

Pooled data from 10 population-based GIST series



~60% likely cured by surgery alone

Joensuu et al. Lancet Oncol 2012; 13:265-74

AFIP Risk Group Classification

Group	Group definition	Patients with progressive disease during long-term follow-up			
		Gastric %	Jejunal %	Duodenal %	Rectal %
1	≤2.0 cm, ≤5/50 HPF	0	0	0	0
2	2.1-5.0 cm, ≤5/50 HPF	1.9	4.3	8.3	8.5
3a	5.1-10.0 cm, ≤5/50 HPF	3.6	24	}	
3b	>10.0 cm, ≤5/50 HPF	12	52	} 34*	57*
4	≤2.0 cm, >5/50 HPF	0*	50*	-	54
5	2.1-5.0 cm, >5/50 HPF	16	73	50	52
6a	5.1-10.0 cm, >5/50 HPF	55	85	}	}
6b	>10.0 cm >5/50 HPF	86	90	} 86*	} 71*

*very low numbers

Miettinen M, Lasota J., Sem Diagn Pathol 2006;23:70-83

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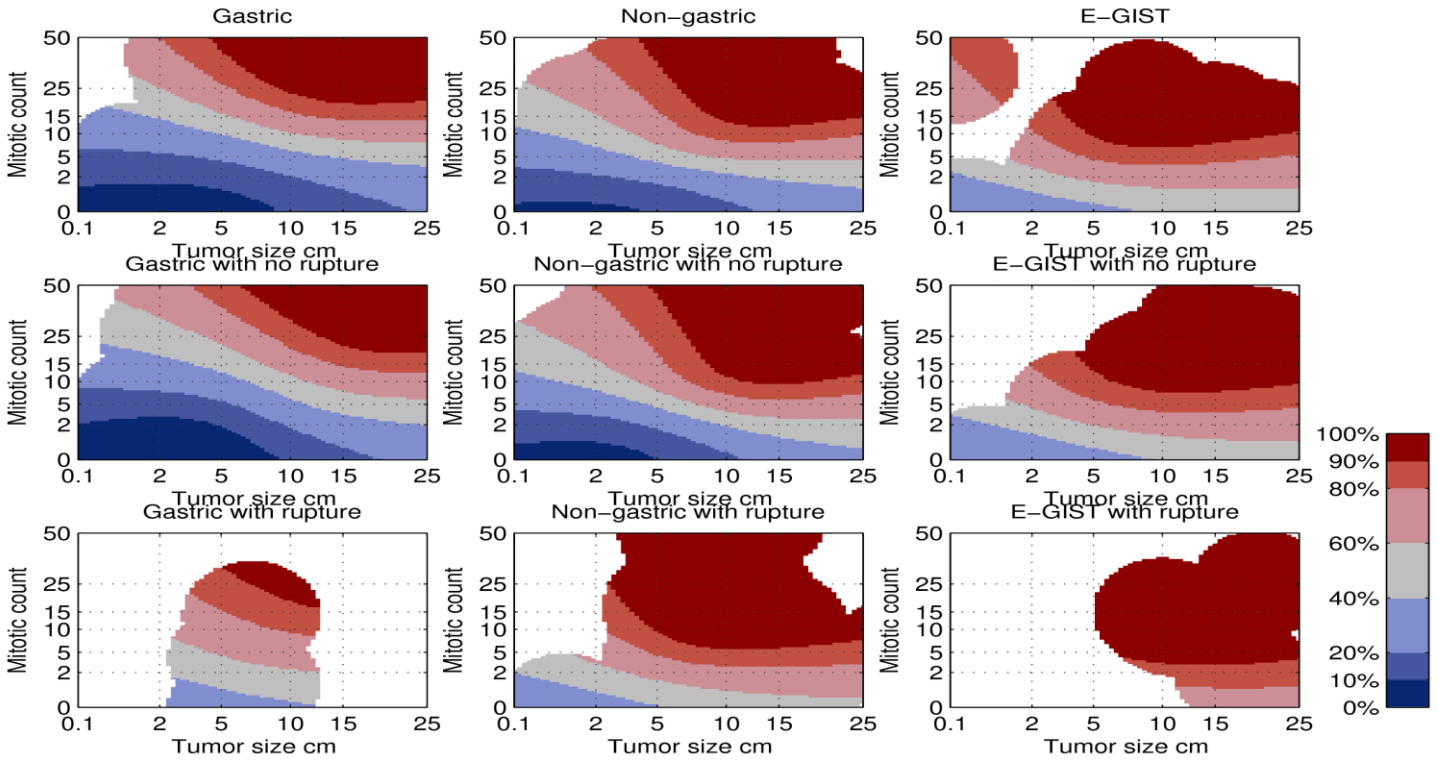
Prognostic contour maps, 10-year RFS

Rupture?

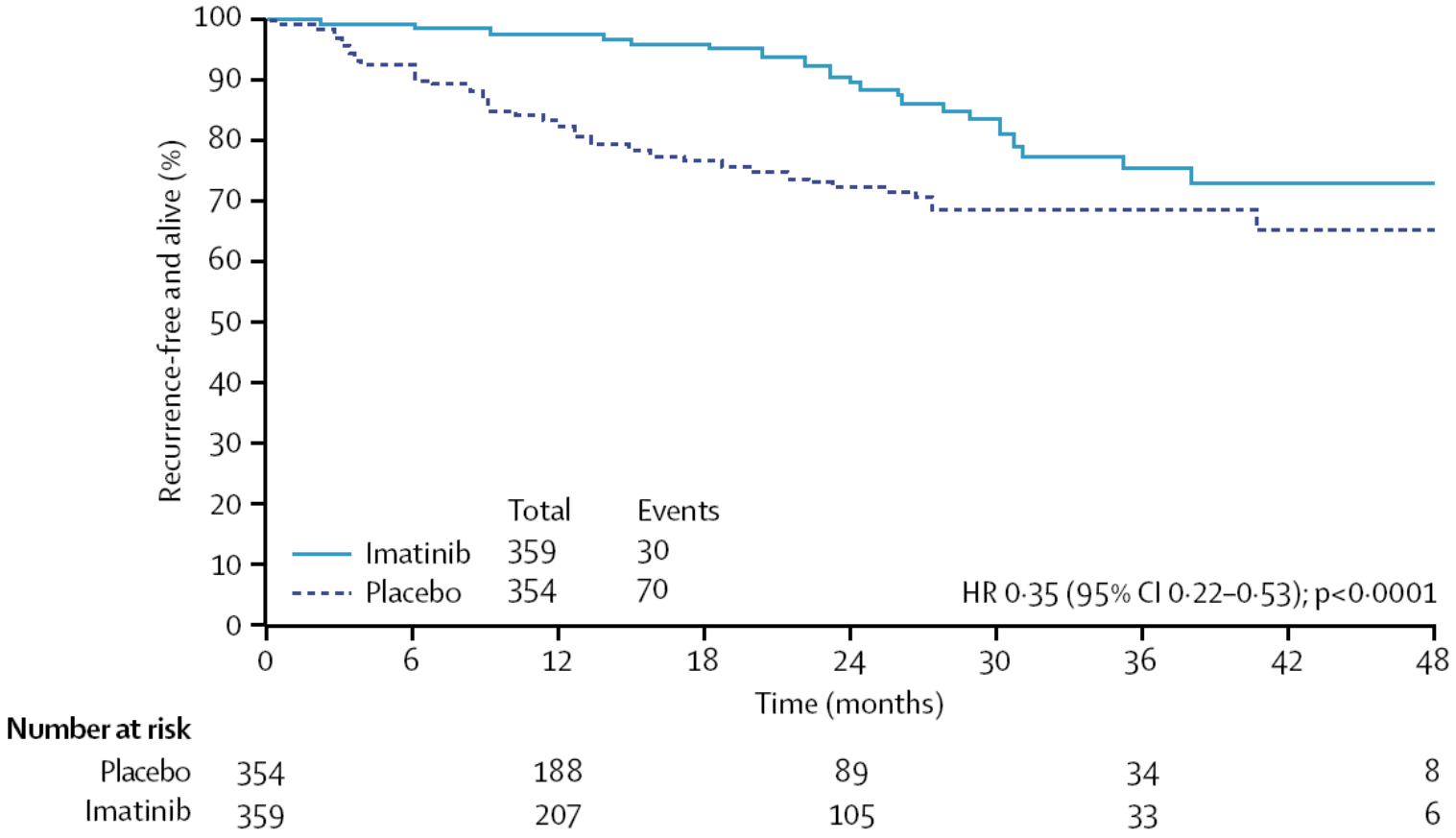
No rupture

Rupture present



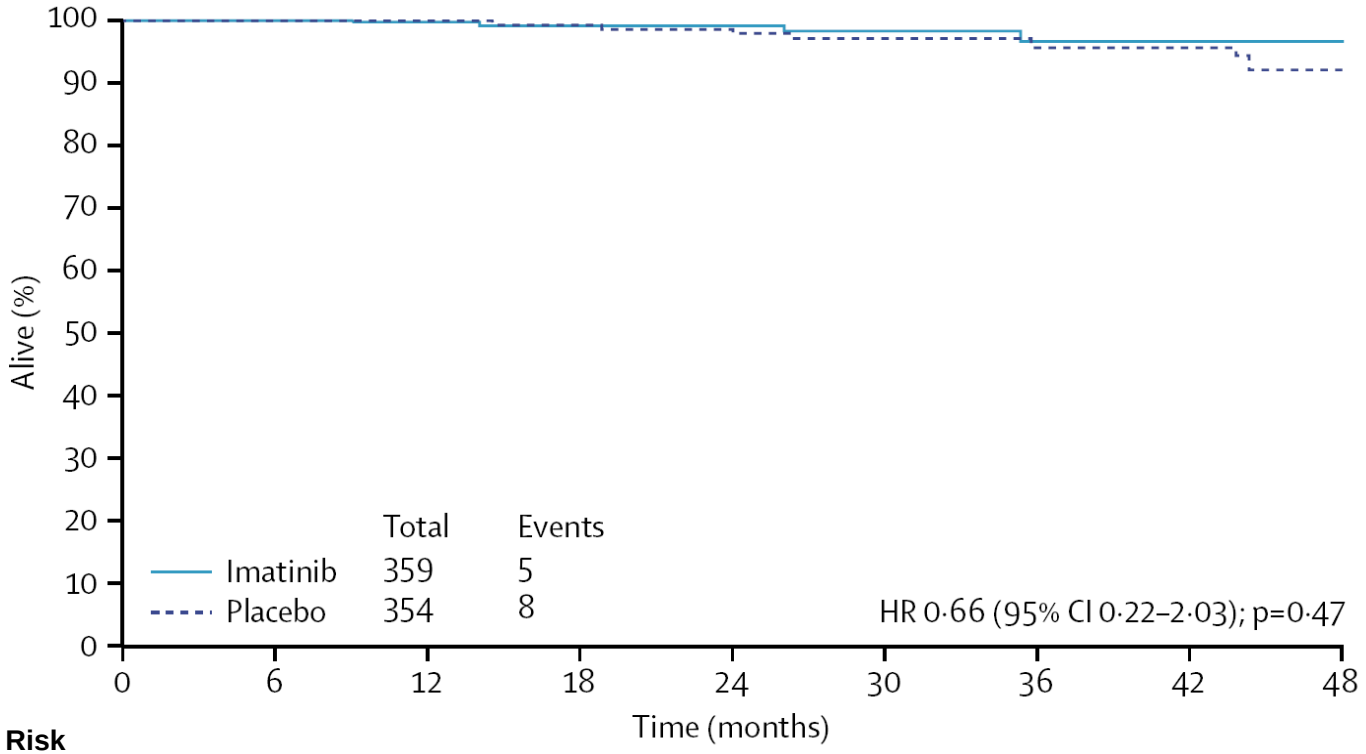
Joensuu et al. Lancet Oncol 2012; 13:265-74

Z9001: Recurrence-Free Survival



DeMatteo et al. Lancet. 2009;373:1097-1104.

Z9001: Overall Survival



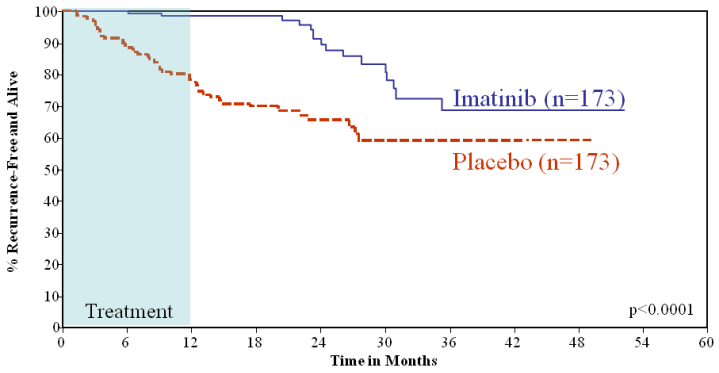
Number at Risk

Placebo	354	241	151	58	15
Imatinib	359	226	137	51	15

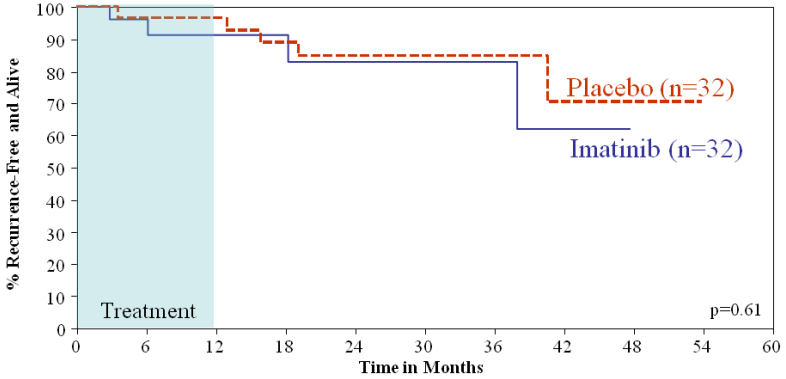
DeMatteo et al. Lancet. 2009;373:1097-1104.

Influence of mutational status on outcome of adjuvant imatinib

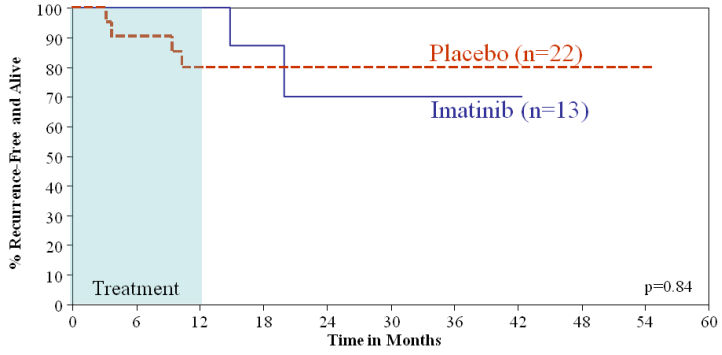
RFS for Exon 11



RFS for Wildtype

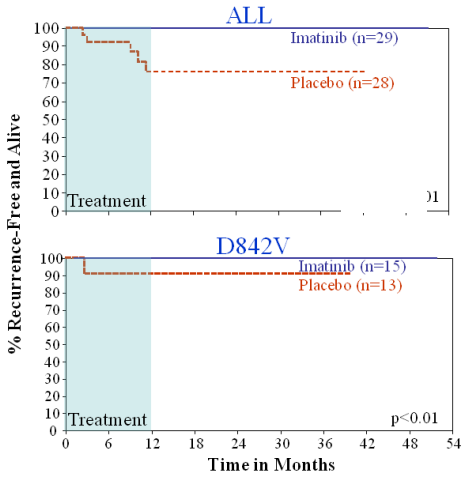


RFS for Exon 9



Corless CL et al. JCO 2010; 28(15s): suppl; abstract 10006.

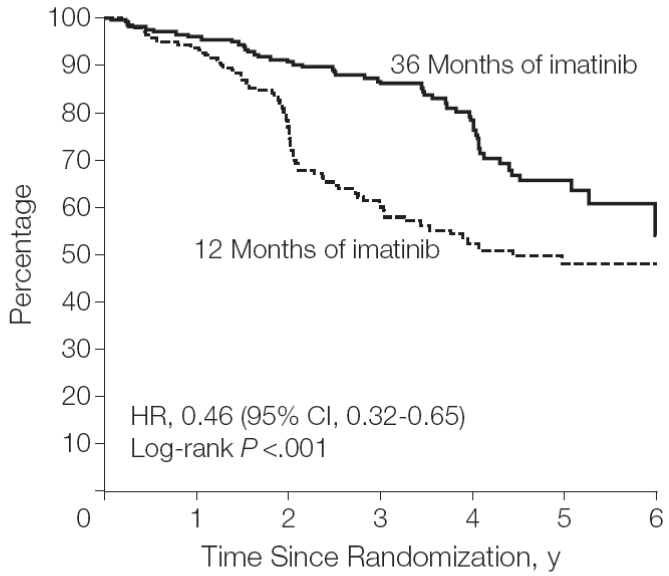
RFS for PDGFRA



Corless CL et al. JCO 2010; 28(15s): suppl; abstract 10006.

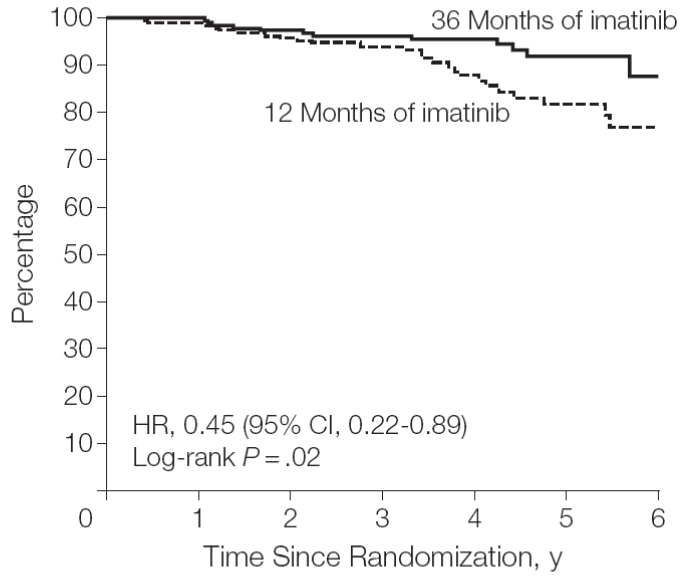
SSGXVIII/AIO: RFS and OS

A Recurrence-free survival: intention-to-treat population



No. of patients							
36 Months of imatinib	198	184	173	133	82	39	8
12 Months of imatinib	199	177	137	88	49	27	10

C Overall survival: intention-to-treat population

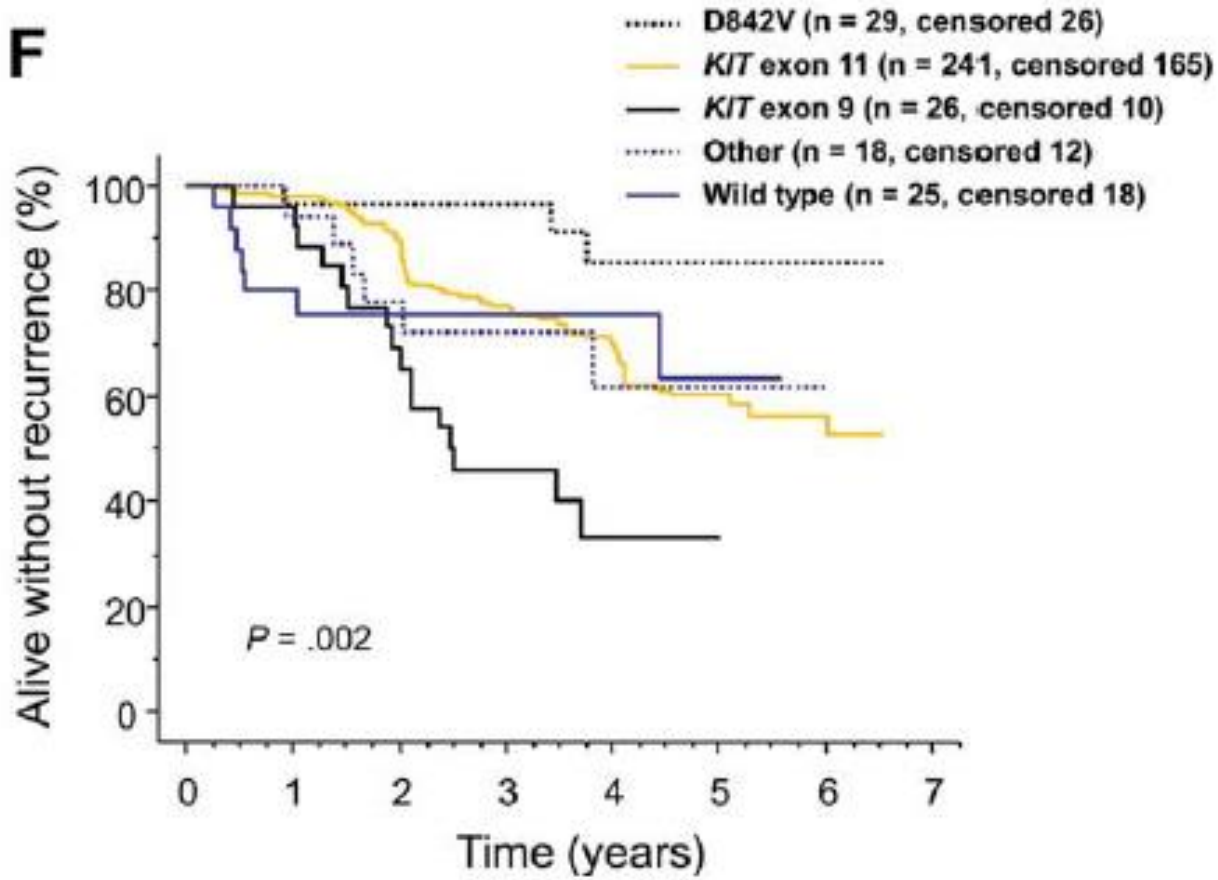


No. of patients							
36 Months of imatinib	198	192	184	152	100	56	13
12 Months of imatinib	199	188	176	140	87	46	20

Joensuu, ..., Reichardt et al., JAMA 307:1265-1272, 2012

Risk Factors for Gastrointestinal Stromal Tumor Recurrence in Patients Treated With Adjuvant Imatinib

Heikki Joensuu, MD[1]; Mikael Eriksson, MD[2]; Kirsten Sundby Hall, MD[3]; Jörg T. Hartmann, MD[4]; Daniel Pink, MD[5]; Jochen Schütte, MD[6]; Giuliano Ramadori, MD[7]; Peter Hohenberger, MD[8]; Justus Duyster, MD[9]; Salah-Eddin Al-Batran, MD[10]; Marcus Schlemmer, MD[11]; Sebastian Bauer, MD[12]; Eva Wardelmann, MD[13]; Maarit Sarlomo-Rikala, MD[14]; Bengt Nilsson, MD[15]; Harri Sihto, PhD[16]; Karla V. Ballman, PhD[17]; Mika Leinonen, MSci[18]; Ronald P. DeMatteo, MD[19]; and Peter Reichardt, MD[5]



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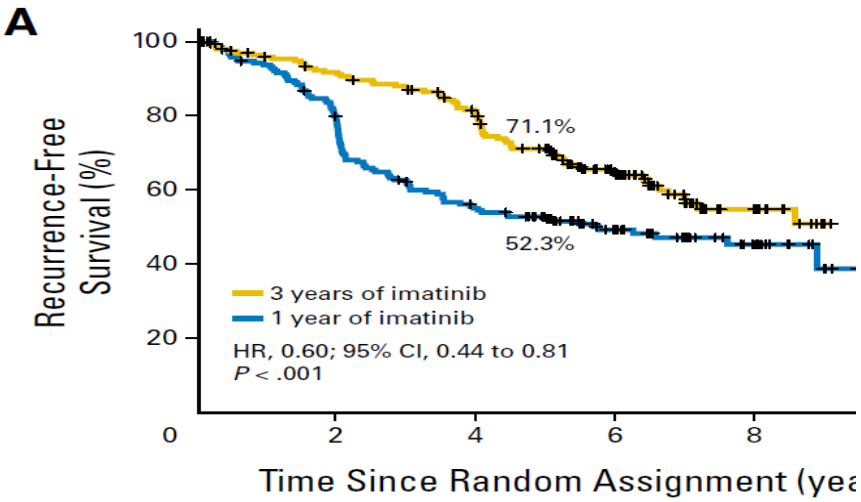
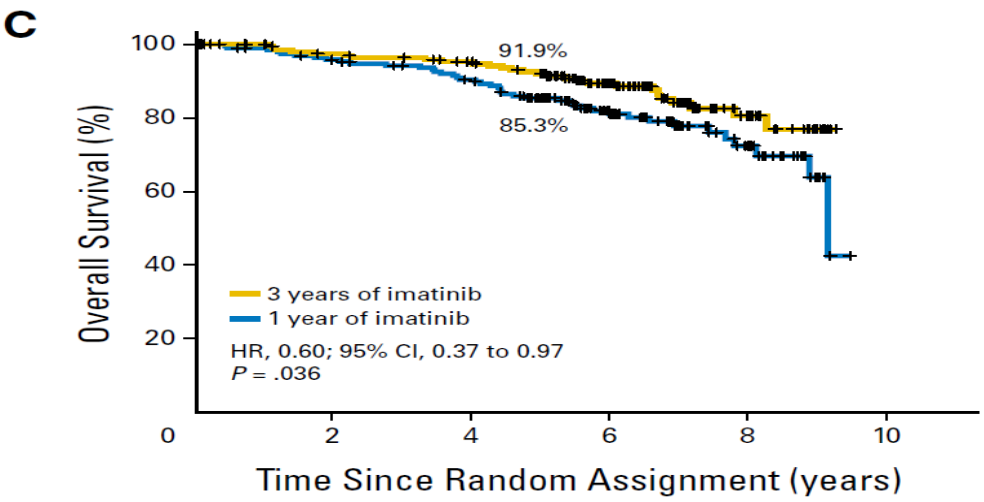
ORIGINAL REPORT

Adjuvant Imatinib for High-Risk GI Stromal Tumor: Analysis of a Randomized Trial

Heikki Joensuu, Mikael Eriksson, Kirsten Sundby Hall, Annette Reichardt, Jörg T. Hartmann, Daniel Pink, Giuliano Ramadori, Peter Hohenberger, Salah-Eddin Al-Batran, Marcus Schlemmer, Sebastian Bauer, Eva Wardelmann, Bengt Nilsson, Harri Sihto, Petri Bono, Raija Kallio, Jouni Junnila, Thor Alvegård, and Peter Reichardt

Recurrence-free Survival



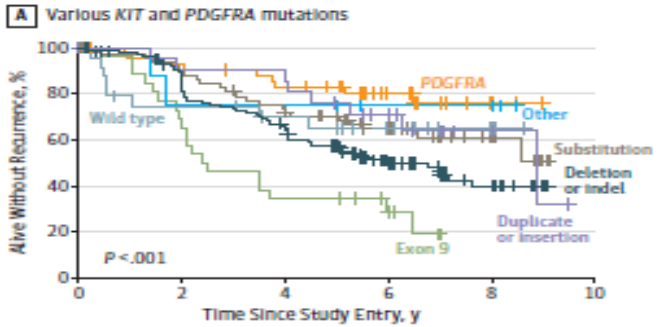


JAMA Oncology | Original Investigation

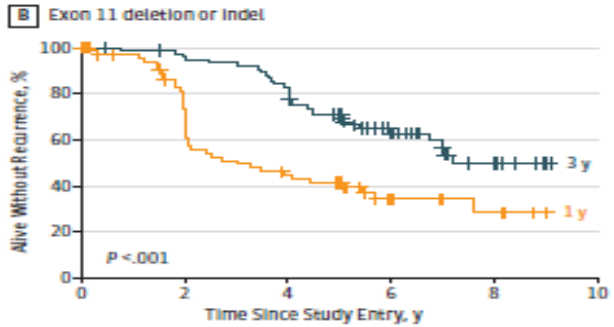
Effect of *KIT* and *PDGFRA* Mutations on Survival in Patients With Gastrointestinal Stromal Tumors Treated With Adjuvant Imatinib

An Exploratory Analysis of a Randomized Clinical Trial

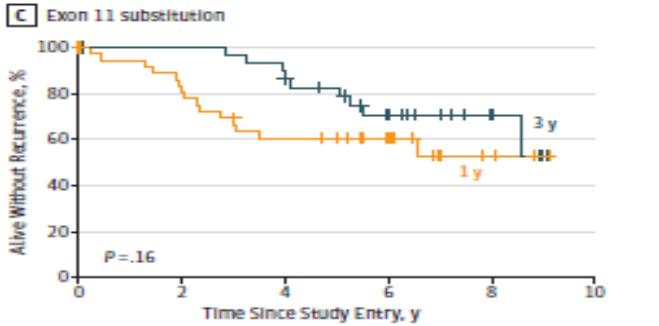
Heikki Joensuu, MD; Eva Wardelmann, MD; Harri Sihto, PhD; Mikael Eriksson, MD; Kirsten Sundby Hall, MD; Annette Reichardt, MD; Jörg T. Hartmann, MD; Daniel Pink, MD; Silke Cameron, MD; Peter Hohenberger, MD; Salah-Eddin Al-Batran, MD; Marcus Schlemmer, MD; Sebastian Bauer, MD; Bengt Nilsson, MD; Raija Kallio, MD; Jouni Junnila, MSc; Aki Vehtari, PhD; Peter Reichardt, MD



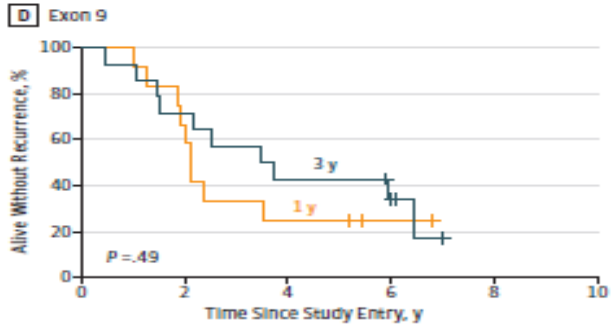
No. at risk						
PDGFRA	43	39	34	21	7	0
Wild type	24	17	14	9	3	0
Other	8	6	6	3	3	0
Substitution	68	58	46	28	8	0
Deletion or Indel	149	116	90	42	16	0
Duplicate or Insertion	22	19	19	11	5	0
Exon 9	26	18	9	5	0	0



No. at risk						
3 y	78	73	63	32	11	0
1 y	71	43	27	10	5	0



No. at risk						
3 y	30	29	25	15	5	0
1 y	38	29	21	13	3	0



No. at risk				
3 y	14	10	6	4
1 y	12	8	3	1

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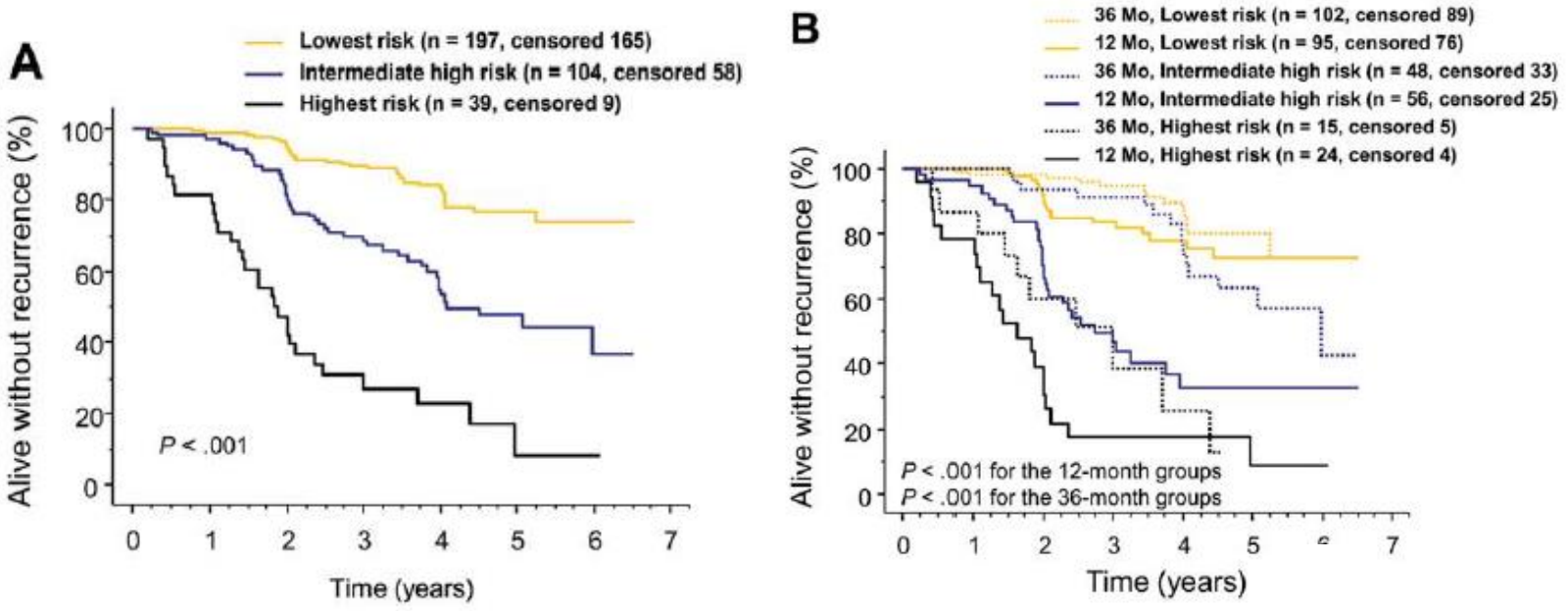
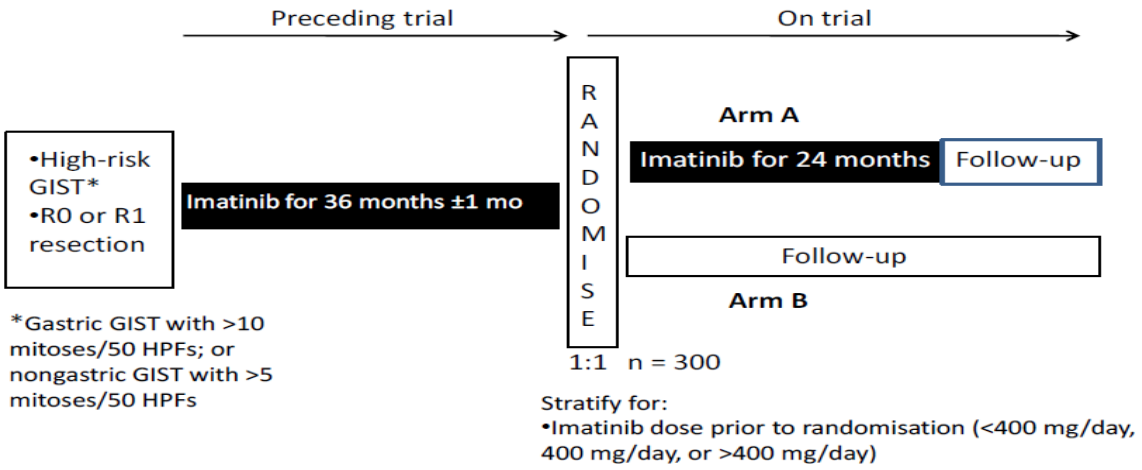


mitoses; highest risk, gastric GIST with > 50 mitoses or non-gastric GIST with > 20 mitoses per 50 high-power fields). (B)

Cancer August 1, 2014

Three versus five years of adjuvant imatinib as treatment of patients with operable GIST with a high risk for recurrence: A randomised phase III study

Trial design



NUMBER OF PATIENTS	300 patients to be randomised in 1:1 ratio, 150 to imatinib for further 24 months and 150 to stop imatinib.
RANDOMISATION	Central randomisation. At randomisation, the patients are stratified by the imatinib dose preceding randomisation (< 400 mg/day, 400 mg/day, or >400 mg/day). The centres will keep a log of patients who received the informed consent.

Standard

- Rückfallrisiko bestimmen
- Mutationsanalyse ist Pflicht
- Imatinib für 3 Jahre bei signifikantem Rezidivrisiko
- Keine adjuvante Therapie bei niedrigem Risiko
- Keine adjuvante Therapie bei PDGFRA Exon 18 D842V
- Keine adjuvante Therapie bei Kit/PDGFRA Wildtyp

Herzlichen Dank für Ihre Aufmerksamkeit!