GIST: Adjuvant Therapy

ESMO Sarcoma and GIST

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GIST Recurrence After Surgery

- Recurrence of GIST following surgery is common\textsuperscript{1-5}
  - Majority of high-risk patients experience recurrence
  - Recurrence frequently involves metastatic sites

- Only 10\% of patients remain disease-free after long follow-up\textsuperscript{4,5}

- DFS 80\% at 1 yr, 67\% at 2 yrs, 45\% at 5-yrs \textsuperscript{2,4,5}

- Several tools are available to assess the risk of recurrent GIST after resection.

Survival Following Surgical Treatment of Primary GIST (N=80)

54% 5-year survival; 35% 5-year survival if tumor is ≥ 10 cm

Risk of Recurrent GIST after Resection

**Size**
- <1.1 cm
- 1.1-2.0 cm
- 2.1-5.0 cm
- 5.1-10.0 cm
- >10.0 cm

**Mitotic Rate**
- <2/50 HPF
- 2-5/50 HPF
- >10/50 HPF
- 6-10/50 HPF

**Site**
- Stomach
- Oesophagus
- Small intestine
- Colon or rectum
- E-GIST

**Rupture**
- No rupture
- Rupture

*p<0.0001*
### GIST: Assessing Malignant Potential

<table>
<thead>
<tr>
<th>Risk</th>
<th>Size</th>
<th>Mitotic rate (HPF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Any Size</td>
<td>&gt;10/50 HPF</td>
</tr>
<tr>
<td></td>
<td>&gt;10 cm</td>
<td>Any rate</td>
</tr>
<tr>
<td></td>
<td>&gt;5 cm</td>
<td>&gt;5/50 HPF</td>
</tr>
<tr>
<td>Intermediate</td>
<td>5-10 cm</td>
<td>&lt;5/50 HPF</td>
</tr>
<tr>
<td></td>
<td>&lt;5 cm</td>
<td>6-10/50 HPF</td>
</tr>
<tr>
<td>Low</td>
<td>2-5 cm</td>
<td>&lt;5/50 HPF</td>
</tr>
<tr>
<td>Very Low</td>
<td>&lt;2 cm</td>
<td>&lt;5/50 HPF</td>
</tr>
</tbody>
</table>

- Even tumors classified as low risk may become metastatic
- No GIST can truly be called benign - recurrences observed 30 yrs or more after primary diagnosis

HPF = high power fields.
### Risk Stratification of Primary GIST by Mitotic Index, Size, and Site

<table>
<thead>
<tr>
<th>Tumor Parameters</th>
<th>Size</th>
<th>Risk of Progressive Disease (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Gastric</td>
</tr>
<tr>
<td>Mitotic Index</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 5 per 50 hpf</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2 cm</td>
<td>None (0%)</td>
<td>None (0%)</td>
</tr>
<tr>
<td>&gt; 2 ≤ 5 cm</td>
<td>Very low (1.9%)</td>
<td>Low (8.3%)</td>
</tr>
<tr>
<td>&gt; 5 ≤ 10 cm</td>
<td>Low (3.6%)</td>
<td>(Insuff. data)</td>
</tr>
<tr>
<td>&gt; 10 cm</td>
<td>Moderate (10%)</td>
<td>High (34%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5 per 50 hpf</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 2 cm</td>
<td>None*</td>
<td>(Insuff. data)</td>
</tr>
<tr>
<td>&gt; 2 ≤ 5 cm</td>
<td>Moderate (16%)</td>
<td>High (50%)</td>
</tr>
<tr>
<td>&gt; 5 ≤ 10 cm</td>
<td>High (55%)</td>
<td>(Insuff. data)</td>
</tr>
<tr>
<td>&gt; 10 cm</td>
<td>High (86%)</td>
<td>High (86%)</td>
</tr>
</tbody>
</table>

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Data based on long-term follow-up of 1055 gastric, 629 small intestinal, 144 duodenal, and 111 rectal GISTs. #Defined as metastasis or tumor-related death. *Denotes small numbers of cases.

Points are assigned for tumor size, mitotic index, and site of origin by drawing a line upward from the corresponding values to the “points” line.

The sum of the 3 points is plotted on the “total points” line and corresponds to RFS predictions.

Risk Assessment Comparison

NIH Consensus

Modified NIH Consensus

AFIP Consensus

Joensuu et al. Volume 13, Issue 3, Pages 265–274
Contour Map Estimating Risk of Recurrence

A. Gastric, rupture unknown
B. Non-gastric, rupture unknown
C. E-GIST, rupture unknown
D. Gastric with no rupture
E. Non-gastric with no rupture
F. E-GIST with no rupture
G. Gastric with rupture
H. Non-gastric with rupture
I. E-GIST with rupture

Joensuu et al. Volume 13, Issue 3, Pages 265–274
GIST Recurrence Risk Assessment

- Identification of high risk patients for closer monitoring and use of adjuvant therapy
  - Very high mitotic rate (>25 m/50hpf) any site
  - Tumor rupture
  - Large, mitotically active (>5 m/50hpf) tumors
  - Rectal GIST, mitotically active
  - Extra-gastrointestinal GIST, mitotically active

- Identification of low risk patients who may need less frequent monitoring and do not need adjuvant therapy
  - GIST < 2cm
  - Gastric GIST ≤ 10cm, mitotically inactive (<5m/50hpf)

- Intermediate risk patients
  - Everything in between
Adjuvant Imatinib Therapy for GIST: Rationale

- High rates of recurrence after resection, especially in patients with high-risk GIST\(^1\)
- Imatinib represents effective oral therapy with low toxicity profile and is safe in the perioperative setting\(^1\)
- Three large randomized trials investigating use of Imatinib in adjuvant setting\(^1\)
  - ACOSOG Z9001 (1 year imatinib 400 mg vs. placebo)
  - EORTC 62024 (2 year imatinib 400 mg vs. placebo)
  - SSG XVIII (3 year imatinib vs. 1 year imatinib, both 400 mg)

ACOSOG Phase III Trial: Adjuvant Imatinib in Patients with High Risk Primary GIST

ACOSOG Z9001: randomized, double-blind study of adjuvant Imatinib vs placebo post resection of primary GIST

**Primary Objective:** Recurrence Free Survival (RFS)

- **Primary Kit + GIST (≥ 3 cm):** Complete Gross Resection 14-70 days prior
- **Placebo x 1 year**
- **Gleevec 400mg x 1 year**
- **Recurrence**
  - **Gleevec 400mg x 2 yrs**
  - **Gleevec 800mg x 2 yrs**

10 years or until death

ACOSOG Z9001: Ph III Trial Summary

- **Objectives**
  - Primary: Recurrence Free Survival (RFS) of patients with resected primary GIST
  - Secondary: OS and safety/efficacy in adjuvant setting

- **Treatment**: 400 mg/day Imatinib for 1 year vs placebo

- **Inclusion criteria**
  - $\geq 3 \text{ cm GIST}$
  - Surgery within 14-70 days prior to registration
  - KIT-positive GIST
  - Imatinib naive
  - No prior adjuvant therapy


ACOSOG Z9001

RFS, N=644

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Imatinib</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>83%</td>
<td>97%</td>
</tr>
<tr>
<td>2 yrs</td>
<td>71%</td>
<td>90%</td>
</tr>
<tr>
<td>$P^*$</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>$HR^*$</td>
<td>0.33 (95% CI = 0.20-0.53)</td>
<td></td>
</tr>
</tbody>
</table>
ACOSOG Phase III Trial: Adjuvant Imatinib in Patients with High Risk Primary GIST

ACOSOG Z9001: randomized, double-blind study of adjuvant Imatinib vs placebo post resection of primary GIST

RFS- Low/Int risk (3-6cm)  
RFS-high risk (>10cm)
Ph III EORTC 62024 Trial of Adjuvant Imatinib in Patients with Primary GIST

Complete resection of GIST

No Treatment

Follow for 5 years

Imatinib (400 mg/d for 2 years)

Discontinued treatment*

*Due to progression or unacceptable toxicity.

Available at: http://clinicaltrials.gov/ct/show/NCT00103168.
Ph III EORTC 62024 Trial of Adjuvant Imatinib in Patients with Primary GIST

- Objectives
  - Primary: overall survival
  - Secondary: relapse-free interval and safety

- Inclusion criteria (NIH Consensus)
  - **High risk** (tumor size 10 cm, mitotic rate 10/50 HPF, or tumor size 5 cm and mitotic rate 5/50 HPF)
  - **Intermediate risk** (tumor size 5 cm and mitotic rate 6-10/50 HPF or tumor size 5-10 cm and mitotic rate >5/50 HPF)
  - Completely resected
  - KIT-positive GIST

*Due to progression or unacceptable toxicity.
Available at: http://clinicaltrials.gov/ct/show/NCT00103168.
Ph III EORTC 62024 Trial of Adjuvant Imatinib in Patients with Primary GIST

RFS-intermediate risk

RFS-high risk
Scandinavian Sarcoma Group (SSG) XVIII
Trial of Adj Imatinib in Patients with GIST

Trial description
- **Short (12 months) versus long (36 months) duration of adjuvant treatment with Gleevec**
- Open-label, randomized, prospective, multi-center

Objectives
- Primary: relapse-free survival
- Secondary: overall survival, GIST-specific survival, and safety

Inclusion criteria
- Resectable GIST, surgically removed
- **High-risk GIST (>10 cm; >10 mit/50 HPF; or >5 cm and >5 mit/50 HPF) or very high risk GIST (metastasis removed)**

Available at: [http://clinicaltrials.gov/ct/show/NCT00116935](http://clinicaltrials.gov/ct/show/NCT00116935)
Survival in the intention-to-treat population.

Heikki Joensuu et al. JCO 2016;34:244-250
Recurrence-Free Survival After Adjuvant Imatinib

Robert S. Benjamin, and Paolo Giovanni Casali JCO
2016;34:215-218
Imatinib in an Adjuvant GIST Setting: Summary

- 400 mg/day Gleevec is safe and well tolerated when administered as adjuvant therapy after primary resection.
- Adjuvant imatinib improves Recurrence Free Survival in high risk tumors.
- Adjuvant imatinib improves survival in high risk tumors treated with imatinib for 3 years.
  - Follow-up period is short.
- Patient should be monitored closely upon completion of adjuvant imatinib.
- Trials currently evaluating longer durations of imatinib.
  - ImadGIST (3 years vs. 6 years)
  - SSG XXII (3 years vs. 5 years)
  - PERSIST (5 years)
Imatinib in an Adjuvant GIST Setting: Discussion

- Is 3 years duration of adjuvant therapy sufficient?
- Are we curing anyone or shifting the curves to the right?
- Should we treat immediately postop or monitor closely and treat at recurrence?
- Can we identify the ~40% of high risk patients who are cured with surgery alone?
- Is there a lower threshold for treating Kit exon 11 557-8?
- Should patients with KIT exon 9 mutation receive 800mg?
- Should patients with PDGFR D842V receive adjuvant imatinib?
- How do we treat Raf, PI3K, Ras, NF1, FGFR/FGF, Gli-1, SDH-deficient GIST?
Sylvester Comprehensive Cancer Center

Sarcoma Team

- **Medical Oncology**
  - Jon Trent
  - Breelyn Wilky
  - Pat Benedetto

- **Pathology**
  - Andrew Rosenberg
  - Darcy Kerr

- **Radiology**
  - Ty Subhawong
  - Jean Jose

- **Mid-Level**
  - Morgan Smith

- **Nursing**
  - Eryka Lacayo
  - Yolanda Roper

- **Social Work**
  - Lisa Merheb

- **Orthopedic Oncology**
  - Sheila Conway
  - Frank Eismont
  - Juan Pretell
  - Mo Al Maaieh

- **Surgical Oncology**
  - Nipun Merchant
  - Alan Livingstone
  - Danny Yakoub

- **Radiation Therapy**
  - Raphael Yechieli
  - Aaron Wolfson

- **Head & Neck Surgery**
  - Zoukaa Sargi
  - Frank Civantos

- **Thoracic Surgery**
  - Dao Nguyen
  - Nestor Villamizar

- **Interventional Radiology**
  - Raj Narayanan
  - Shree Venkat

- **Gynecologic Oncology**
  - Brian Slomovitz
  - Matt Pearson
  - Marilyn Huang

- **Clinical Research**
  - Sandra Epps
  - Tamara Leon
  - Dawn Poller
  - Kristin Englund

- **Lab Research**
  - Ana Paz-Mejia
  - Luyuan Li
  - Karina Galoian
  - Gengzhou Hu
GIST: Adjuvant Therapy

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Mutation Status and Prognosis

- **KIT** and **PDGFRA** mutations are common in GIST and are the best predictors of clinical response to imatinib mesylate\(^1,2\)

- 3 prognostic groups defined by their responses to imatinib\(^3-5\)
  - **KIT** exon 11—favorable response (PR in 61.3%-83.5%)
  - **KIT** exon 9—intermediate response (PR in 29.3%-47.8%)
  - Wild-type or **PDGFRA** D842V—low response (ORR 0%-25%)

- Exon 9 mutations are biologically more aggressive relative to other genotypes\(^6\)

\[\text{ORR= overall response rate} \quad \text{PR= partial response.}\]

<table>
<thead>
<tr>
<th>Trial</th>
<th>Target Enrollment</th>
<th>Ph</th>
<th>Regimen</th>
<th>Primary End Point</th>
<th>Status*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EORTC 62024</td>
<td>750</td>
<td>III</td>
<td>Gleevec 400 mg vs placebo</td>
<td>Overall survival</td>
<td>Recruiting</td>
</tr>
<tr>
<td>SSG XVIII</td>
<td>345</td>
<td>III</td>
<td>Gleevec 400 mg 1 yr vs Gleevec 400 mg x 3 yr</td>
<td>Recurrence-free survival (RFS)</td>
<td>Recruiting</td>
</tr>
</tbody>
</table>

*As of October 24, 2006. †Targeted patient accrual.

EORTC, European Organisation for Research and Treatment of Cancer; SSG, Scandinavian Sarcoma Group.

Ph III SSG XVIII/AIO Trial of Adjuvant Imatinib in Patients with GIST

- 12 months versus 36 months duration of adjuvant treatment with Imatinib for operable GIST with high risk for recurrence
- Observation period: Median 5 years from randomization

Available at: http://clinicaltrials.gov/ct/show/NCT00116935.
Surgery is the Primary Treatment Option for Patients with Resectable GIST

- Goal is a complete resection of the tumor with the pseudocapsule intact
  - Rupture of tumor increases risk of bleeding and disease dissemination
- The abdomen should be examined for metastases since GISTS can adhere to surrounding organs necessitating the removal of adjacent tissue
- Margins should be clear; however, wider resection of uninvolved tissue provides no clear benefit
- Imatinib is first line therapy for malignant unresectable or metastatic GIST

Demetri GD et al J Natl Compr Canc Netw. 2004;21(suppl 1):S1-S26
Patients receiving the full 800 mg/d dose have improved PFS relative to those who required dose reductions during therapy.

### Meta GIST: ↑ PFS in Patients with Exon 9 Mutation Treated with 800 mg/d Gleevec

<table>
<thead>
<tr>
<th></th>
<th>Median PFS (yrs)</th>
<th>3 yrs est (KM)</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>400 mg/d</td>
<td>800 mg/d</td>
<td>400 mg/d</td>
<td>800 mg/d</td>
</tr>
<tr>
<td>All pts (N=1640)</td>
<td>1.58</td>
<td>1.95</td>
<td>30%</td>
<td>34%</td>
</tr>
<tr>
<td>EORTC (N=946)</td>
<td>1.74</td>
<td>2.02</td>
<td>31%</td>
<td>35%</td>
</tr>
<tr>
<td>SWOG 0033 (N=649)</td>
<td>1.46</td>
<td>1.64</td>
<td>29%</td>
<td>33%</td>
</tr>
<tr>
<td>OS (N=1640)</td>
<td>4.08</td>
<td>4.05</td>
<td>60%</td>
<td>61%</td>
</tr>
</tbody>
</table>

### PFS according to KIT exon 9 mutations status

<table>
<thead>
<tr>
<th></th>
<th>400 mg/d</th>
<th>800 mg/d</th>
<th>400 mg/d</th>
<th>800 mg/d</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (N=91)</td>
<td>0.5</td>
<td>1.59</td>
<td>5%</td>
<td>17%</td>
<td>0.58</td>
<td><strong>0.017</strong></td>
</tr>
<tr>
<td>EORTC (N=59)</td>
<td>0.35</td>
<td>1.62</td>
<td>0%</td>
<td>25%</td>
<td>0.43</td>
<td>0.0023</td>
</tr>
<tr>
<td>SWOG 0033 (N=32)</td>
<td>0.78</td>
<td>1.4</td>
<td>14%</td>
<td>6%</td>
<td>0.99</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Van Glabbeke et al, JCO 2007;25:18S, Abst#10004
Primary GIST: Risk Factors for Recurrence After Surgery

Rates of RFS were predicted by mitotic index and tumor size

Mitotic index

- ≤3 mitoses/30 HPF
- >3 to ≤15 mitoses/30 HPF
- >15 mitoses/30 HPF

Tumor size

- <5 cm
- 5-10 cm
- >10 cm

RFS Rates of RFS were predicted by mitotic index and tumor size

HPF, high power fields; RFS, recurrence-free survival.

MetaGIST: Summary of Results from Combined EORTC and SWOG Trials

- Treatment with 800 mg/day Gleevec yields a small but statistically significant advantage in PFS.
- 800 mg/day Gleevec significantly benefits patients with $KIT^+$ exon 9 mutants vs other genotypes.
- Independent predictors for poor PFS include:
  - Male gender
  - Poor performance status (ECOG)
  - Low baseline hemoglobin level
  - High baseline absolute neutrophil count
  - Bowel origin GIST
- NCCN guidelines *updated* to recommends that patients with exon 9 mutations be treated with 800mg/day imatinib.

Van Glabbeke et al JCO 2007;25:18S, Abst#10004
Rate of Recurrence by GIST Tumor Size (N=127)

DeMatteo et al. American Society of Clinical Oncology (ASCO); Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
Rate of GIST Recurrence by Location of Tumor Origin (N=127)

- Stomach (n=74)
- Small Intestine (n=35)
- Colon or rectum (n=14)

Proportion Recurrence Free

Years after Resection

DeMatteo et al. American Society of Clinical Oncology (ASCO); Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
Recurrence-Free Survival Resulting from 1-year Adjuvant Glivec

\[ p < 0.001 \\
HR 0.33 (0.20-0.53) \]

At risk:
- Imatinib: 325, 177, 80, 24
- Placebo: 319, 170, 73, 23

DeMatteo et al. American Society of Clinical Oncology (ASCO), Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
No Change in Overall Survival has been Demonstrated with Adjuvant Glivec

Overall Survival at the 1-year Follow-up

% Alive

At risk:

<table>
<thead>
<tr>
<th></th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>193</td>
</tr>
<tr>
<td>Placebo</td>
<td>196</td>
</tr>
</tbody>
</table>

DeMatteo et al. American Society of Clinical Oncology (ASCO): Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.

p = 0.72
HR 0.76 (0.17-3.4)
Recurrence-Free Survival Resulting from 1-year Adjuvant Glivec

\[ p < 0.001 \]

HR 0.33 (0.20-0.53)

At risk:

<table>
<thead>
<tr>
<th></th>
<th>Imatinib</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>21</td>
<td>62</td>
</tr>
<tr>
<td>0</td>
<td>325</td>
<td>319</td>
</tr>
<tr>
<td>1</td>
<td>177</td>
<td>170</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DeMatteo et al. American Society of Clinical Oncology (ASCO); Chicago, June 1-5, 2007

Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
GIST: Pathogenesis

- Gene mutation key event in malignant transformation in most cases\(^1,2\)
  - *KIT*: 80\%-85\%\(^1\)
  - *PDGFRA*: 5\%-7\%\(^2\)
  - *Wild Type*: 12\%\(^1\)

- Gain-of-function mutations results in gain of function resulting in abnormal, constitutively activated receptor tyrosine kinase activity\(^3\)
  - Ligand independent mitogenic activity
  - Stimulation of downstream signaling pathways

PDGFRA, platelet-derived growth factor receptor alpha.

GIST Overview

- Historically, a lack of well defined pathologic criteria\(^1\)
- GIST is the most common sarcoma and the most common mesenchymal tumor of the GI tract
  - May originate from the same stem cell as ICC (interstitial cells of Cajal) of the myenteric plexus
- Although GISTs are being better characterized, diagnosis remains challenging in some cases
- Clinical presentation is variable
  - Tumors are often asymptomatic
  - Patients may have common, nonspecific symptoms, resulting in underdiagnosis or misdiagnosis

GIST: Epidemiology

- An estimated 10-20 cases per million of GIST are diagnosed in the United States each year\(^1\)
  - 5000-6000 cases per year are diagnosed in the United States\(^2\)
- In certain provinces of the Netherlands\(^3\) and Sweden\(^4\):
  - 14.5 cases per million
  - Prevalence in Sweden: 129 cases per million\(^4\)
- Highest incidence among group aged 50-65 years\(^1\)
  - Similar male/female incidence, although some reports suggest higher incidence in men

GIST: Clinical Presentation

- Often asymptomatic and discovered incidentally
- Signs/symptoms related to location and size of tumor (% of cases at presentation)
  - Palpable abdominal mass (38%), GI hemorrhage (30%), vague GI pain or discomfort (40%)
  - Anemia
  - Anorexia, weight loss, nausea, fatigue, and additional GI complaints
  - Acute intraperitoneal bleeding or perforation
- Risk of malignancy primarily based on tumor size & mitotic index
  - Gender and tumor location also affect risk
  - All GIST have the potential to become malignant

Projected Recurrence-Free Survival
Tumor size 3-6 cm

% Recurrence-Free and Alive

At risk:
Imatinib 128
Placebo 135

Years
0 1 2 3 4

Imatinib (4 events)
Placebo (11 events)

P = 0.15
HR 0.44 (0.14-1.4)

DeMatteo et al. American Society of Clinical Oncology (ASCO); Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
Projected Recurrence-Free Survival
Tumor size 6-10 cm

% Recurrence-Free and Alive

- Imatinib (9 events)
- Placebo (21 events)

p = 0.01
HR 0.37 (0.17-0.81)

At risk:
- Imatinib 112
  - Years:
    - 1: 65
    - 2: 33
    - 3: 13
- Placebo 105
  - Years:
    - 1: 53
    - 2: 27
    - 3: 11

DeMatteo et al. American Society of Clinical Oncology (ASCO); Chicago, June 1-5, 2007
Slides provided courtesy of Dr. Ronald DeMatteo. They are not to be distributed or reproduced without consent.
Randomly assigned after macroscopically complete surgery (N = 400)

Assigned to adjuvant imatinib for 12 months (n = 200)
- Included in the intention-to-treat population (n = 199)
- Excluded (did not provide consent) (n = 1)
- Included in the safety population (n = 195)
- Excluded (did not receive imatinib) (n = 4)
- Included in the efficacy population (n = 181)
  - Excluded (n = 18)
    - Did not have GIST (n = 5)
    - Had metastases at study entry (n = 13)

Assigned to adjuvant imatinib for 36 months (n = 200)
- Included in the intention-to-treat population (n = 198)
- Excluded (did not provide consent) (n = 2)
- Included in the safety population (n = 197)
- Excluded (did not receive imatinib) (n = 1)
- Included in the efficacy population (n = 177)
  - Excluded (n = 21)
    - Did not have GIST (n = 10)
    - Had metastases at study entry (n = 11)