Reflections on GIST
15 Years after Imatinib

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The Connective Tissue Oncology Society
Outline

- GIST
- Treatment before Imatinib
- Imatinib
- Imaging
- Other TKIs
- Adjuvant Therapy
Jeffrey A. Gottlieb, M.D.
1940-1975

SWOG General Secretary
Chairman, Sarcoma Committee
# ADRIAMYCIN-DTIC IN SARCOMAS

## RESPONSE BY SITE OF PRIMARY

<table>
<thead>
<tr>
<th>LOCATION</th>
<th># PTS.</th>
<th>% RESPONSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head &amp; Neck</td>
<td>19</td>
<td>58</td>
</tr>
<tr>
<td>GU &amp; Uterus</td>
<td>17</td>
<td>53</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>26</td>
<td>50</td>
</tr>
<tr>
<td>Unk. Prim. &amp; Misc.</td>
<td>35</td>
<td>49</td>
</tr>
<tr>
<td>Limb</td>
<td>40</td>
<td>39</td>
</tr>
<tr>
<td>Pelvis + Trunk</td>
<td>19</td>
<td>26</td>
</tr>
<tr>
<td>GI Tract</td>
<td>14</td>
<td>21</td>
</tr>
<tr>
<td><strong>All</strong></td>
<td><strong>200</strong></td>
<td><strong>42.5</strong></td>
</tr>
</tbody>
</table>

Gottlieb et al., Cancer Chemotherapy Rep. 1975
GIST

Time to Progression
S0033 Overall Survival by GIST Genotype – 2014 data

Significantly worse OS for KIT exon 9 mutant vs. KIT exon 11 mutant

- KIT exon 9: Median OS = 66 months
- KIT exon 11: Median OS = 40 months
- No Mutation (WT): Median OS = 38 months

\( P = 0.001 \) for KIT exon 9 vs. KIT exon 11
\( P = 0.047 \) vs. No Mutation (WT)
Effects of Imatinib on GIST: CT findings
Effects of Imatinib on GIST: CT findings
Effects of Imatinib on GIST: CT findings
Effects of Imatinib on GIST: CT findings
Effects of Imatinib on GIST: CT findings - Size
Effects of Imatinib on GIST: CT findings - Density

Baseline with Density Measurement

8 weeks with Density Measurement
We Should Desist Using RECIST at Least in GIST
Figure 2  Kaplan-Meier estimates of time to tumour progression  Results represent central radiology assessment of ITT population.

George D Demetri , Allan T van Oosterom , Christopher R Garrett , Martin E Blackstein , Manisha H Shah , Jaap Verw...

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

The Lancet Volume 368, Issue 9544 2006 1329 - 1338

http://dx.doi.org/10.1016/S0140-6736(06)69446-4
Figure 2  Kaplan-Meier survival analysis after treatment with regorafenib or placebo. (A) Progression-free survival, per central review (primary endpoint, final analysis). (B) Overall survival (interim analysis). HR=hazard ratio.

George D Demetri, Peter Reichardt, Yoon-Koo Kang, Jean-Yves Blay, Piotr Rutkowski, Hans Gelderblom, Peter H...

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

The Lancet Volume 381, Issue 9863 2013 295 - 302

http://dx.doi.org/10.1016/S0140-6736(12)61857-1
PFS based on central (A) and local (B) radiological review (intent-to-treat population).

Figure 2  Kaplan-Meier estimates of time to tumour progression  Results represent central radiology assessment of ITT population.

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PFS based on central (A) and local (B) radiological review (intent-to-treat population).

Progression-Free Survival
(Primary endpoint per blinded external review)

<table>
<thead>
<tr>
<th>Arm</th>
<th>Total</th>
<th>Event</th>
<th>Median PFS, months (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>41</td>
<td>30</td>
<td>1.8 (0.9-2.8)</td>
</tr>
<tr>
<td>Placebo</td>
<td>40</td>
<td>34</td>
<td>0.9 (0.8-0.9)</td>
</tr>
</tbody>
</table>

HR: 0.45
(95% CI, 0.27-0.76)

P = 0.00075 (1-sided)

Presented by: Yoon-Koo Kang

Presented at: ASCO Annual Meeting
De Matteo Adjuvant GIST
Comparison of recurrence-free survival in the modified intention-to-treat population (A) and the efficacy population (B). Comparison of overall survival in the modified intention-to-treat population (C) and the efficacy population (D). The 3-year survival rates of patients assigned to 36 months of imatinib and those assigned to 12 months of imatinib are 86.6% vs 60.1% (A), 88.1% vs 62.1% (B), 96.3% vs 94.0% (C), and 97.6% vs 95.8% (D), respectively, and the 5-year survival rates, 65.6% vs 47.9% (A), 67.4% vs 50.3% (B), 92.0% vs 81.7% (C), and 93.9% vs 81.7% (D).
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