Outcome of Advanced Gastrointestinal Stromal Tumor (GIST) Patients Treated With Imatinib Mesylate: Four-Year Follow-Up of a Phase II Randomized Trial

C. D. Blanke, H. Joensuu, G. D. Demetri, M. C. Heinrich, B. Eisenberg, J. Fletcher, C. L. Corless, E. Wehrle, K. B. Sandau, M. von Mehren

Oregon Health and Sciences University, Portland, OR, USA, Helsinki University Central Hospital, Helsinki, Finland, Dana Farber Cancer Institute, Boston, MA, USA, Norris Cotton Cancer Center, Lebanon, NH, USA, Brigham & Women's Hospital, Boston, MA, USA, Novartis Pharma AG, Basel, Switzerland, Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA, Fox Chase Cancer Center, Philadelphia, PA, USA

ABSTRACT

Imatinib mesylate induces an objective response in the majority of pts with advanced, surgically incurable GIST. Late relapses are occasionally seen in patients with initial SD, but secondary resistance and late relapses do occur. A phase II randomized clinical trial was previously performed (NCT00219575, ClinicalTrials.gov: [NCT00219575]), and data from an ongoing long-term evaluation of the study are now available, with median follow-up of 4 years. 149 pts were randomized to treatment with continuous maintenance, 400 mg, or 600 mg imatinib mesylate daily. Time to response was estimated by the Kaplan-Meier method. Survival was analyzed by the log-rank test. As of January 2008, median follow-up was 41 months. At 4 years, 55% (95% CI 46–64%) of pts on 400 mg N=73 remain on study and had an objective response at some time during their treatment. Median time to response was 13 weeks (0–156 weeks). Fifty percent of patients had an objective response at 11 weeks. At 4 years, 40% (95% CI 32–48%) of pts on 600 mg N=74 remain on study and had an objective response at some time during their treatment. Median time to response was 12 weeks (0–156 weeks). Fifty percent of patients had an objective response at 9 weeks. In general, responses lasted longer than with historical controls. No significant differences between the two arms were observed in terms of safety. For 600 mg pts who achieved complete responses, onset of disease control was no later than 2.7 years. Overall survival with imatinib mesylate is significantly longer than with chemotherapy. No deaths occurred in the imatinib mesylate group. The median overall survival of 58 months is considered a clinical benefit. Patients with SD or PR had a similar survival rate suggesting that these responses are of lasting duration.

INTRODUCTION

• Pathologically confirmed, unresectable, or metastatic GIST
• Imatinib mesylate is the current standard of care for GIST
• Imatinib induces an objective response in the majority of pts with advanced, surgically incurable GIST
• Secondary resistance and late relapses do occur

PATIENT SELECTION

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• Secondary resistance and late relapses do occur

STUDY DESIGN

• Primary objectives: time to response, based on conventional bidimensional Southwest Oncology (SWOG) criteria (categories: complete response [CR], partial response [PR], stable disease [SD], or progressive disease [PD])
• Secondary objectives: time to treatment failure, duration of response, and overall survival, safety, and quality of life

RESULTS

• Treatment Wks: 0 48 96
• Duration

Table 1. Best Response

The submitted abstract mistakenly stated that 63% have died of PD. The correct value is 40%. Please correct this in your abstract book.

Table 2. Time to Response

Conclusion: Imatinib mesylate is confirmed as highly effective therapy for patients with advanced metastatic or unresectable GIST.

• Imatinib has an acceptable safety profile in patients with incurable GIST
• No significant differences were seen in the two imatinib dose groups (400 vs 600 mg)
• Although median onset of response is relatively fast with 13 weeks, 25% of patients achieved their response after 23 weeks
• Late responses are often seen in patients with initial SD
• Compared to historical data (Dematteo RP et al. Clinical management of gastrointestinal stromal tumor: before and after STI571. Am Pediatr. 2002;33:466-477), imatinib significantly changed the outcome of GIST patients with a current median overall survival of 248 weeks (58 months) versus approximately 15 months with chemotherapy.

CONCLUSIONS

• Imatinib mesylate is confirmed as highly effective therapy for patients with advanced metastatic or unresectable GIST
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• Patients with SD or PR had a similar survival rate suggesting that these SMSNg response categories may be associated with similar clinical benefit
• Tumor kinase genotype is predictive of clinical response to imatinib. In particular, patients with KIT mutations in exon 11 (the most common exon affected) have very high response rates and superior survival.
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