Age Disparity in the Dissemination of Imatinib Mesylate (Gleevec) for Treating Chronic Myeloid Leukemia

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Funding
• National Cancer Institute
• Leukemia and Lymphoma Society
Chronic Myeloid Leukemia

- Myeloproliferative disorder
- Philadelphia chromosome
- Course of disease:
  - Chronic phase
  - Accelerated phase
  - Blast phase
- Annual number of new cases:
  - United States – 4,830
- Annual number of deaths:
  - United States – 450
1960 – Identification of the Philadelphia Chromosome

Peter Nowell
University of Pennsylvania
School of Medicine

David Hungerford
Fox Chase Cancer Center
1972 – Philadelphia Chromosome results from translocation

t(9,22;q34,q11)

Janet Rowley
University of Chicago
1982 – Abl gene translocated from 9q to 22q
Annelies de Klein and colleagues – Erasmus University
Protein Tyrosine Kinases

- Enzymes – agents of change
- Modulate a number of cellular events:
  - Differentiation
  - Growth
  - Metabolism
  - Apoptosis
The BCR-ABL gene produces an abnormal tyrosine kinase protein that results in the disordered myelopoiesis found in Chronic Myeloid Leukemia.
Imatinib Mesylate  
(Gleevec™, Novartis, Basel, Switzerland)

- Tyrosine Kinase Inhibitor
- FDA approved in May, 2001
- Highly active against Chronic Myeloid Leukemia and Gastro-Intestinal Stromal Tumors (GIST)
Late 1990’s to Mid 2000’s: Clinical Trials for Imatinib

Brian Druker

Figure 1. Kaplan–Meier Estimates of the Cumulative Best Response to Initial Imatinib Therapy.

At 12 months after the initiation of imatinib, the estimated rates of having a response were as follows: complete hematologic response, 96%; major cytogenetic response, 85%; and complete cytogenetic response, 69%. At 60 months, the respective rates were 98%, 92%, and 87%. Data for patients who discontinued imatinib for reasons other than progression and who did not have an adequate response were censored at the last follow-up visit. Data for patients who did not have an adequate response and who stopped imatinib because of progression were censored at maximum follow-up.
Data Sources

1. SEER Program Patterns of Care Study, 2003

2. Survival data from SEER Program, 1990-2004

3. Mortality rates based on death certificates from the National Center for Health Statistics, 1990-2004
Study Objectives

1. Characterize dissemination of imatinib mesylate therapy for chronic myeloid leukemia in the general population

2. Determine if administration of imatinib mesylate therapy influenced survival rates for chronic myeloid leukemia in the general population

3. Determine if administration of imatinib mesylate therapy influenced mortality rates for chronic myeloid leukemia in the general population
SEER Program Patterns of Care Studies

Overview
• Conducted annually since 1987
• Document trends in cancer-related care, with emphasis on diagnosis and treatment
• Targets 3-4 cancer sites/types each year

Methods
• Detailed re-abstract of medical records
• Brief questionnaire sent to physicians
SEER Program Patterns of Care Study - 2003

Target Cancers

- Chronic Myeloid Leukemia
- Multiple Myeloma
- Bladder
- B-Cell Lymphoma

Focus on Chronic Myeloid Leukemia

- Documented use of imatinib mesylate
- $n=403$
Percentage of Chronic Myeloid Leukemia cases treated with imatinib, by race/ethnicity
Percentage of Chronic Myeloid Leukemia cases treated with imatinib, by quartile of median family income
Percentage of Chronic Myeloid Leukemia cases treated with imatinib, by age at diagnosis
Patterns of Care Study Participants: 20-59 years of age at diagnosis
Survival (months) by imatinib status (yes/no)

Wald: p = 0.512
Patterns of Care Study Participants: 60-79 years of age at diagnosis
Survival (months) by imatinib status (yes/no)
Patterns of Care Study Participants: 80+ years of age at diagnosis

Survival (months) by imatinib status (yes/no)
Population-Based Survival

- SEER Program
- Chronic Myeloid Leukemia cases newly diagnosed 1990-2004
  - 1990-1997 Pre-Imatinib
  - 1998-2000 Peri-Imatinib
  - 2001-2004 Post-Imatinib
- Percent surviving by month up to 36 months following CML diagnosis
- Survival function from Cox model
Chronic Myeloid Leukemia: 20-59 years of age at diagnosis
Survival (months) by time period of diagnosis

Wald: p < 0.001
Chronic Myeloid Leukemia: 60-79 years of age at diagnosis

Survival (months) by time period of diagnosis

Wald: p = 0.098
Chronic Myeloid Leukemia: 80+ years of age at diagnosis
Survival (months) by time period of diagnosis
Population-Based Mortality Rates

- National Center for Health Statistics
- Death certificates from all 50 United States
- Chronic Myeloid Leukemia deaths, 1990-2004
- Age-specific mortality rates
Chronic Myeloid Leukemia
Age-specific mortality rates, 1975-2004 by age at death

Mortality Rate per 100,000

Year of Death


80+ years

60-79 years

20-59 years

Annual Percent Change (Final Period)

-7.8

-11.9

-17.6
Summary

• Imatinib mesylate was widely disseminated for the treatment of chronic myeloid leukemia in 2003
• The percentage of patients with chronic myeloid leukemia who received imatinib mesylate decreased with age
• Administration of imatinib mesylate did not vary by sex, race/ethnicity, socioeconomic status, or place of residence (i.e., urban vs. rural residence)
• Widespread dissemination of imatinib mesylate improved survival from chronic myeloid leukemia in the general population; least beneficial for elderly
• Dissemination of imatinib mesylate resulted in an overall decrease in mortality rates for chronic myeloid leukemia; least beneficial for elderly
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