New Horizons 2010

CML Case Studies

Case study #1

- 74 year old man diagnosed with Ph+ CML in the chronic phase (100% Ph+). Intermediate Sokal risk
- COPD (Chronic Obstructive Pulmonary Disease) – former heavy smoker
- Started treatment with imatinib 400mg/day
  - 3 months: CHR, CCyR, FISH 2%
  - 6 months: CCyR, FISH <1%, MMR
  - 12 months: CCyR, FISH <1%, MMR

Case study #1

- However, the patient was experiencing persistent fluid retention, muscle pain and anemia
- Due to these side effects, the patient had frequent therapy suspension for 3-5 days
- With increasing dose interruptions, molecular response and CCyR was lost:
  - 12 months: 0.0003% Bcr-Abl
  - 24 months: 0.013% Bcr-Abl
  - 36 months: 3.15% Bcr-Abl, 40% Ph+

What action would you take?

Case study #1

- Due to consistent AEs, the imatinib dose was reduced to 300 mg/day imatinib.
- Imatinib blood level testing was performed:
  - Imatinib trough level 415 nmol
- Moreover, a G250E Bcr-Abl mutation was detected at this time

What action would you take?

Case study #1

- The patient’s physician recommended a switch to another TKI
- The patient initiated nilotinib 400mg BID. This was well tolerated and resulted in recovery of molecular and cytogenetic responses after 2 months

Any Questions?

Case study #2

- A 34 year-old male was diagnosed with CP-CML (intermediate Sokal risk)
- Imatinib, 400 mg/day, was started
- A complete hematologic response was achieved at 4 weeks
  - 6 months: 25% Ph+ metaphases in bone marrow
  - [illegible]

What action would you take?

Case study #2

- Compliance was adequate (IM plasma levels) and no mutation was found
- Nilotinib, 400 mg BID, was started, with good tolerability
  - 3 months: 10% Ph+ metaphases
  - 6 months: CCyR; 0.32% Bcr-Abl
  - 12 months: CCyR confirmed; 0.28% Bcr-Abl

What action would you take now?

Case study #2

- In the subsequent controls, a fluctuation between 0.24 and 0.14% Bcr-Abl was observed
- The patient was switched to dasatinib 100mg daily

What other options would you consider?

Case study #2

- HLA typing was performed and the patient’s brother was found to be compatible
- The decision on allo-HSCT will be made depending on the response to dasatinib obtained

Any Questions?

Case study #3

- 36 year old male with chronic phase CML
- Sokal score = 1.22, Hasford score = 1158.6
- 9% Bcr-Abl/Abl
- Started imatinib 400 mg/day:
  - 10 months: full hematologic and cytogenetic remission

Would you modify therapy at this stage?

Case study #3

- Insurer switched the patient to copy drug, 400 mg/day:
  - 3 months later (March 2007): anemia, neutropenia, thrombocytopenia
  - loss of cytogenetic response (22% Ph+)
  - loss of molecular response (3% Bcr-Abl/Abl)
  - no mutational analysis performed

What action would you take?

Case study #3

- In May 2007, the patient resumed imatinib therapy at 600 mg/day:
  - 2 months later (July 2007): return to full hematologic and cytogenetic responses
  - 6 months later (Nov 2007): 0.01% Bcr-Abl/Abl

Any Questions?

Case study #4

- A 52 year old male was diagnosed with CML in the chronic phase in 2006 (90% Ph+); no previous medical history, 2 siblings
- Intermediate Sokal risk
- Started imatinib 400 mg/day (well tolerated):
  - CHR in less than one month
  - 3 months: 9% Bcr-Abl
  - 6 months: 4% Bcr-Abl, 40% Ph+
  - 12 months 2.4% Bcr-Abl, 8% Ph+

What treatment would you now prescribe?

Case study #4

- At 12 months:
  - no mutation detected
  - plasma concentration of imatinib was 650 ng/ml
- Imatinib dose was increased, first to 600 mg/day to assess tolerance to increased dose (well tolerated)
- At 18 months:
  - Complete cytogenetic response was achieved
  - 0.6% Bcr-Abl
    - still no evidence of mutation

How would you continue therapy?

Any Questions?

Case study #5

- A 52 year old female was diagnosed with CML in 2008
- High Sokal risk
- Ph+ CML with variant translocation t(1,9,22)

- Upon diagnosis, she was enrolled in a randomised study in Oct 2008 and received imatinib 400 mg daily

Case study #5

- Due to leucopenia, neutropenia and thrombopenia, the imatinib dose was decreased to 100 mg, then increased to 200 mg and 400 mg with interruption due to neutropenia and thrombopenia
- Clinical response:
  - CHR at 3 months
  - At 6 months without cytogenetic response (treatment failure)
- The patient discontinued participation in the clinical trial due to cytogenetic resistance

Case study #5

- In June 2009, she continued on imatinib 400 mg and G-CSF
- Imatinib failure in November 2009
- The patient was switched to nilotinib 400 mg daily (with interruptions due to hematologic toxicity); necessity to use G-CSF, transfusion, resistance to erythropoetin
- Tr

What action would you take now?

Any Questions?