1st Issue
July, 2016

Onco News

Published by : Somex Research and Health Pvt. Ltd.
(A Clinical Research and Academic Organisation)
www.somexresearch.com

From the Desk of Editor

Dear Colleagues,

Greetings !

I am proud and privileged in introducing first issue of Onco News. It is true that in present era all literature and guidelines are available a click away but it is still felt as unmet need in form of comprehensive and informative news bulletin to remain updated in rapidly changing fled of Oncology.

In this introductory issue I am covering Chronic Myeloid Leukemia(CML).I hope this kind of information will be of some use to help our patients in better way.

Your suggestions and advice to make ONCO NEWS a better and more useful resource is a welcome !

With warm regards

Dr Naresh Somani
M.D.,D.M.

INTRODUCTION :

It typically affects middle aged individuals. These diseases are progressive and may result in bone marrow failure or transformation to acute leukemia in terminal phase.

Symptoms are not specific in CML and include weight lost, asthenia, fever, night sweats and malaise. Patients may present in either of the 3 phases: Chronic phase, accelerated phase or blast crisis. The hallmark of diagnosis is spleenomegaly, leukocytosis with basophilia, immature granulocytosis and thrombocytosis.

The confirmation is done by cytogenetics demonstration of translocation t(9;22) (q3.4;q1.1) and by reverse transcriptase polymerase chain reaction showing BCR ABL transcripts.

TREATMENT :

Inteferon alpha was the gold standard before tyrosine kinaseinhibitors (TKIs) were introduced. Response to treatment or moving on to another treatment is determined by the degree of cytogenetic response (CgR) and on detection of BCR ABL Kinase domain point mutations. Response evaluation to treatment is assessed at 3 months, followed by every six months until complete CgR (CCgR) is achieved. Suggestion/Comments from the readers are welcome.

CML: CHANGING LANDSCAPE IN INDIAN SCENARIO :

In India, chronic myeloid leukemia (CML) is the most common adult leukemia, accounting for 30% to 60% of all adult leukemias. CML is characterized by excessive tyrosine kinase activity resulting from a chimeric BCR-ABL fusion protein and balanced reciprocal translocation t(9;22) typically between chromosome 9 and 22.

The male preponderance and median age reported is a decade younger compared with the age presented in European (median age 55years) and American (median age 66 years) literature. The most common signs and symptoms are splenomegaly, hepatomegaly, fatigue, weakness, dragging pain, pallor or sometimes asymptomatic seen in 30% cases.

P.T.O.

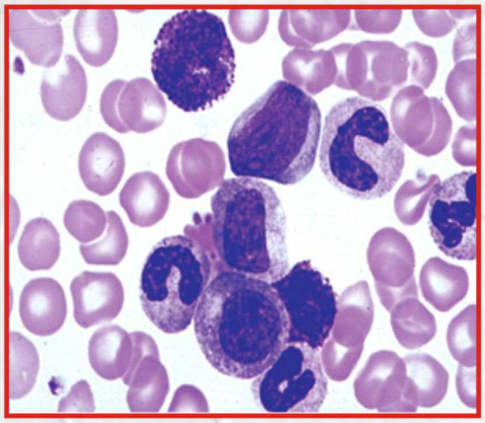

Fig 2.
CML in chronic phase (Peripheral smear)

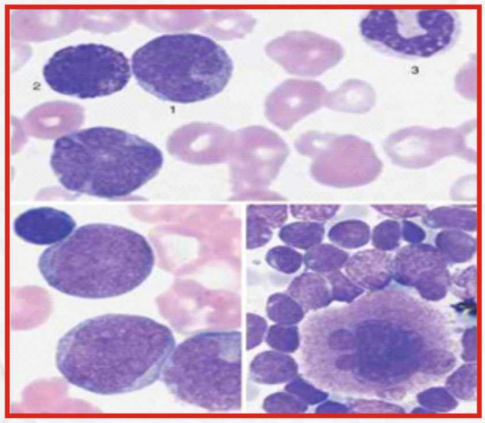

Fig 2.
CML in blast crisis (Peripheral smear)

Response criteria laid down by European leukemia Net (ELN) and World Health Organization (WHO) provide a useful tool in measuring the responses in patient on TKIs.

The majority of patients achieve normal blood counts within 3 months, and more than 90% will have achieved complete hematological response (CHR) after start of treatment.

The natural history of CML has changed in recent years, partly due to earlier diagnosis but mostly as a consequence of the availability of effective therapies that have the potential to eradicate the Ph chromosome positive clone.

Table 1: ELN guidelines 2013 for treatment of CML

	Chronic phase
First line	Imatinib 400 mg, or nilotinib 300 mg x2, or dasatinib 100 mg
Second line	In case of intolerance, switch to another TKI, taking into consideration the side effects of the first TKI, and comorbiditeis
	In case of failure of imatinib, switch to nilotinib, or dasatinib, taking into consideration the presence and the type of BCR-ABL, KD mutation
	In case of failure of nilotinib or dasatinib, switch to dasatinib or nilotinib, taking into consideration the presence and the type of BCR-ABL, KD mutation
	Consider allo HSCT
Third line	In case of failure of two or three TKI, consider allo HSCT
	Accelerated/blastic phase
TKI naïve	Imatinib 600 or 800 mg, or nilotinib 400 mg x 2 or dasatinib 140 mg, and consider allo HSCT
TKI pretreated	Switch to another TKI, consider chemotherapy and allo HSCT

Table2: Response criteria ELN

Time	Optimal	Warning	Failure
Baseline	NA	High risk or CCA/Ph+, major route	NA
3 Months	BCR/ABL 1 <10% or Ph+<35%	BCR-ABL 1>10% or Ph + 36-95%	Non CHR or Ph+ >95 %
6 Months	BCR-ABL1 <1 % or Ph +0 (CCyR)	BCR-ABL 1 1-10% or Ph 1-35 % (PCyR)	BCR-ABL 1 >10 % or Ph+ >35 %
12 Months	BCR-ABL 1 <0.1 % (MMR)	BCR-ABL1 0.1-1%	BCR-ABL >1% or Ph+ > 1%

In treatment of CML, the primary goal is to reach a major molecular response (3 log reduction <0.1 %) but the CMR (4-5 log reduction <0.01% - 0.001%) is prerequisite for drug interruption trial.

The next goal is to achieve a condition of treatment free remission (TFR).The early surrogate markers of TFR will be a rapid decline of BCR-ABL1 transcripts, a BCR-ABL 1 trasncripts level d"1 % within 3 months, d"0.1 % within 1 year and d"0.01% late on. It is likely that an extended use of second-generation TKIs that are more potent and induce faster and deeper molecular remissions, will bring more patients into TFR. It is likely that the earlier and deeper the early molecular response, the higher will be the number of patients in TFR .

My experience of CML with second generation drugs:

CHRONIC MYLOID LEUKEMIA

Front line Nilotinib my experience

- No. of patient - 16
- Analyzed based upon the BCR-ABL(IS scale) (from Jan 2013 to Jan 2016)

BCR-ABL Data Analysis

Patient No (Age/Sex)	At Baseline	At 3 Month follow-up	At 6 Month follow-up	At 12 months follow-up
001 (30Yrs/M)	5.03%	0.26%	0.185%	0.12%
002 (40Yrs/M)	64.97%	23%	9.89%	2%
003 (26Yrs/M)	70.79%	4.53%	1.25%	0.42%
004 (28Yrs/M)	>100%	68.45%	4.26%	0.10%
005 (25Yrs/F)	69%	12%	0.48%	0%
006 (33Yrs/M)	80.46%	22.94%	-------	0%
007 (31Yrs/M)	42.71%	-------	-------	Continued follow-up
008 (38Yrs/F)	50.89%	-------	-------	5%
009 (42Yrs/F)	62.45%	15.87%	1.48%	0%
010 (35Yrs/M)	85.46%	5.69%	1.27%	0%
011 (28Yrs/M)	75.25%	6.895%	0.48%	0%
012 (32Yrs/F)	85.48%	25.89%	2.96%	Continued follow-up
013 (25Yrs/M)	42.26%	1.56%	0%	0%
014 (35Yrs/M)	60.47%	10%	Continued follow-up	0%
015 (30Yrs/M)	72.85%	0%	0%	0%
016 (27Yrs/M)	28.48	4%	1%	Discontinued

High Lights :

- No mortality
- One patient discontinued treatment due to increase LFT
- Two patients presently off Rx ("Functional Cure") and continued to be in CMR

P.T.O.

ONCO FACTS :

1. EGFR positive Non small Lung cancers should be treated with oral drugs like Gefitinib/ Erlotinib or Afatinib and ALK positive withCrizotinib, instead of chemotherapy.
2. BRCA 1/2 tests can predict the risk of hereditary breast cancer .
3. Ibrutinb is new breakthrough molecule for CLL.
4. Hormone therapy (Combined androgen blockade with orchiedectomy and bicalutamide)and chemotherapy with docetaxel is standard of care forupfront treatment of high risk ,fit metastatic prostate cancer.

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- ❖ It is a clinical research and academic orgazation for promotion of same in Rajasthan.
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- ❖ Somex also designes and conducts Seminars, CMEs & Medical Conferences. It has conducted more than 25 CMEs in various medical fields.
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SoMex Research & Health Ethics Committee

- ❖ This committee is registered with DCGI as independent Ethics Committee and works accordingly and so far monitored 18 trials. For details of Ethics committee and its SOP, please login www.somexresearch.com OR contact - e-mail : ec@somexresearch.com

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