

So, finally she is a case of CML-CP

Low risk by ELTS

25yr old unmarried



Treatment to be started

tyrosine kinase inhibitor



our primary goals in treating her

1) prolonging her survival (OS, EFS)

2) Not let her progress into AP or BC
(~~BC~~ TFS)

3) Treatment Free remission

Quality of life

4) QOL (not a major problem for her because she will tolerate all TKIs)

} by attaining
MMR
and deeper
molecular
remissions

1) preferable first line TKI



2nd generation TKIs attain faster and deeper remissions than 1st generation TKI



but on terms of OS all are equal

Being ELTS low risk here chance of transformation to advanced phases also low



so on terms OS, TFS all may be equal

but being very young with the goal of TFR



we need to start a potent TKI to attain a deeper and faster remission



It also helps in planning pregnancy earlier after marriage

DASATINIB, NILOTINIB, BOSUTINIB

No head to head comparison b/n 2nd gen TKI



among them to be chosen based on toxicity profile, affordability and ease of administration after discussing with the patient

Nilotinib, Dasatinib and Bosutinib all are decent options for her

2) Any other base line work up before starting treatment



For all visual markers, LFT, RFT before starting treatment

| | |
|---------------------------------|-----------------------------------------------------|
| Before Dasatinib | CXR P/A view, 2DECHO |
| [specifically before] Nilotinib | Base line RBS, lipid profile ECG, amylase/lipase |

3) Next follow up disease evaluation:

↓
CBC once weekly till CHR

↓
Complete Hematologic response

2nd gen TKIs especially cause cytopenias
in few patients in initial days
(to be careful)

bcr abl quantitative analysis

↓
@ 3rd months, 6th months and 12th months
is fine in 1st year

↓
once MMR attained bcr abl every
6 months → less stringent
(once in a year is also fine in
indian set up)

NO much role of assessing cytogenetic response
now a days
↓

wide spread availability of PCR based
monitoring and also well defined
time points to define optimal response

cytogenetics to be done → when patients loose molecular response or resistant to TKI

No routine cytogenetic response assessment needed in 2021
to look for ACA } of present upgraded to AP

in era of molecular monitoring

in fact ELN removed cytogenetic response from response criteria

4) Need for HLA matching studies now



not needed as of now

There is no much role of allotransplant
in CMU-Cp in the era of tyrosine
kinase inhibitors

CMU-Cp low risk ELTS }
↓

In this case resistance to TKI,
progression to advanced phase is
low (especially when considering 2nd
gen TKI)



So need of allo transplant at any
point of time is extremely low
for her



So HLA studies not needed now

Indications of
allotransplant
in CMU-Cp

} Resistant to two tyrosine kinase
inhibitors
} accelerated phase or blastic
transformation

5) Strategy of she gets married and wants to get pregnant

In era of TKI cml-cp patients getting onto remission and planning pregnancy and delivering healthy babies is common



Basic criteria
for planning
pregnancy

at least 2 yrs of Deep
molecular response
(MR4)



once she completes 4-5 yrs of TKI and
2 yrs of DMR (at least MR4) she
can plan pregnancy



1) if stopping TKI and planning →
monthly bcx and for 1st yr
at least

2) some physicians practice → stop TKI as
soon as there is missed period and
monitor in pregnancy

6) Expected drug related toxicities and how to monitor her

Each TKI has its specific toxicities



Common to all myelosuppression

(bit more common with
2nd gen TKIs)

Dasatinib
Nilotinib
Bosutinib

myelosuppression



weekly CBC till CHR

once in 2 wks for first 3 months

less frequently thereafter

Dasatinib

CXR P/A view @ base line

once after 1-2 months of
starting

2DEcho @
baseline

thereafter when symptomatic
(pleurisy / SOB)

and when
symptomatic

ECG ✓ (less frequent
very frequent
QTc prolongation)

Nilotinib

lipid profile, RBS, amylase / lipase

ECG

on first several months

(at least once in 2 months)

more QTc
prolongation
than
Dasatinib



less frequent thereafter

with all TKIs

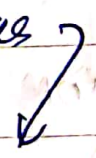
RFT, LFT every 2 wky in 1st 2 months

Imatinib

lesser myelosuppression

(hypophosphatemia)

myalgias



may decrease with
calcium

supplementation

Bosutinib

myelosuppression

LFTs - can cause jaundice
to be monitored



no QTc prolongation

no PE/PAH

7) if fails to respond



check milestones @

3rd months, 6th months and 12th months

≤ 10%

≤ 1%

≤ 0.1%

EMR has impact on survival

(≤ 10%
@ 3 months)

and attaining MMR later



but some patients respond slower



not ideal to jump into conclusion @
3rd months



if 3rd months mile stone not met



can wait till 6th months (still fine)

Not much
problematic
with 2nd
gen TKI

more pts get
EMR compared
to smaximib

At any failure

Double check compliance (most most and most important)

Recheck all medications patient using →
check interactions b/w those drugs
and TKI

if compliant and no concomitant
medications

Kinase domain mutation testing
and choosing TKI based on that

on imatinib failure chance of attaining a
response to 2nd gen TKI 50-60%.

2nd gen TKI chose TKI based on sensitivity
pattern (IC₅₀ values)

of failure on 2nd
gen TKI

ponatinib may give
better responses than
alternate 2nd gen TKI

most potent
3rd gen TKI

problem :
non availability
in india

So finally after checking compliance and
concomitant medications

↓
mutation testing

↓ ↓
choosing TKI based on
that

So finally

2nd gen TKI is preferable for her
(helps in attaining TFR and planning pregnancy)

No need of
HCA studies @ presentation

Base line work based on toxicity profile to
be done

CBC once weekly till CHR
and less frequently thereafter
bcx asl @ 3rd, 6th and 12th months and
then once in 6-12 months

can plan pregnancy with 4-5 yrs
of TKI and 2 yrs of DMR

check for toxicities specific to TKI
in 1st few months and later
when symptomatic

@ failure check compliance and then
mutation testing and choosing TKI based on
that