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 on treating her

1) prolonging her survival (OS, EFS) } by attaining MMR and deeper molecular remissions

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

3) Treatment Free remission

Quality of life

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

1) Preferable first line TKI

↓

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

↓

but in terms of OS all are Equal

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

↓

so in 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 comparision 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 patients — Viral 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 as 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 bcr abl monitoring and also well defined time points to define optimal response

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

↓

to look for ACA

↓

of present upgraded to AP

No routine cytogenetic response assessment needed in 2021 in era of molecular monitoring

↓

infact 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 CML cp in the era of tyrosine kinase inhibitors

CML-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 CML-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 into remission and planning pregnancy and delivering healthy babies is common

↓

Basic criteria for planning pregnancy → atleast 2 yrs of Deep molecular response (MR4)

↓

Once she completes 4-5 yrs of TKI and 2 yrs of DMR (atleast MR4) she can plan pregnancy

↓

1) of stopping TKI and planning → monthly bcr abl for 1st yr atleast

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 @ baseline, once after 1–2 months of starting, thereafter when symptomatic (pleurisy / SOB)
- 2DEcho @ baseline and when symptomatic
- ECG ✓ (very less frequent QTc prolongation)

Nilotinib — Lipid profile, RBS, amylase / lipase on first several months (atleast once in 2 months) → less frequent thereafter

ECG → more QTc prolongation than Dasatinib

With all TKIs — RFT, LFT every 2 wkly 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% @ 3months) 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 (pts fine)

Not much problematic with 2nd gen TKI

more pts get EMR compared to imatinib

At any failure →

Double check compliance (most most and most imp thing)

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

↓

If compliant and no concomitant medications

↓

Kinase domain mutation testing and chosing TKI based on that

↓

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

& 2nd gen TKI chose TKI based on sensitivity pattern (IC_{50} 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

↓

Chosing TKI based on that

↓

So finally

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

No need of HLA studies @ presentation

↓

Baseline work up to be done based on toxicity profile

↓

CBC once weekly till CHR and less frequently thereafter bcr abl @ 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 chosing TKI based on that