

# GUIDELINES AND REALITY

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# INTRODUCTION

- Guidelines can be defined as general rules, principles or pieces of advice.
- Others define it as information intended to advise people on how something should be done or how something should be done
- It is thus a recommendation to everyone to do things in a particular way to achieve a particular outcome.

- Guidelines are usually made with optimum conditions in mind; early detection of disease, quick diagnosis, availability of drugs and compliance by patients to treatment
- The reality however is that one might not have all these conditions readily available
- This does not mean guidelines are not necessary; it only means it should be able to cater for different situations without compromising on standards

- There are various guidelines for the management of CML
- These include the World Health Organization Guidelines, National Comprehensive Cancer Network (NCCN), ESMO guidelines and European Leukaemia Net (ELN) guidelines
- Most people use the ELN guidelines
- These guidelines address important signposts needed to obtain a successful treatment outcome

# How to monitor patients on TKI- by ELN

**Response definitions for any TKI **first line**,  
and 2nd line in case of intolerance, all patients (CP, AP, and BC)**

Time	Optimal response	Warning	Failure
<b>Baseline</b>		High risk Major route CCA/Ph+	
<b>3 mos.</b>	BCR-ABL <sup>IS</sup> ≤10%* Ph+ ≤35% (PCyR)	BCR-ABL <sup>IS</sup> >10%* Ph+ 36-95%	No CHR* Ph+ >95%
<b>6 mos.</b>	BCR-ABL <sup>IS</sup> <1%* Ph+ 0% (CCyR)	BCR-ABL <sup>IS</sup> 1-10%* Ph+ 1-35%	BCR-ABL <sup>IS</sup> >10%* Ph+ >35%
<b>12 mos.</b>	BCR-ABL <sup>IS</sup> ≤0.1%* (MMR)	BCR-ABL <sup>IS</sup> 0.1-1%*	BCR-ABL <sup>IS</sup> >1%* Ph+ >0%
<b>Then, and at any time</b>	MMR or better	CCA/Ph- (-7, or 7q-)	Loss of CHR Loss of CCyR Loss of MMR, confirmed** Mutations CCA/Ph+

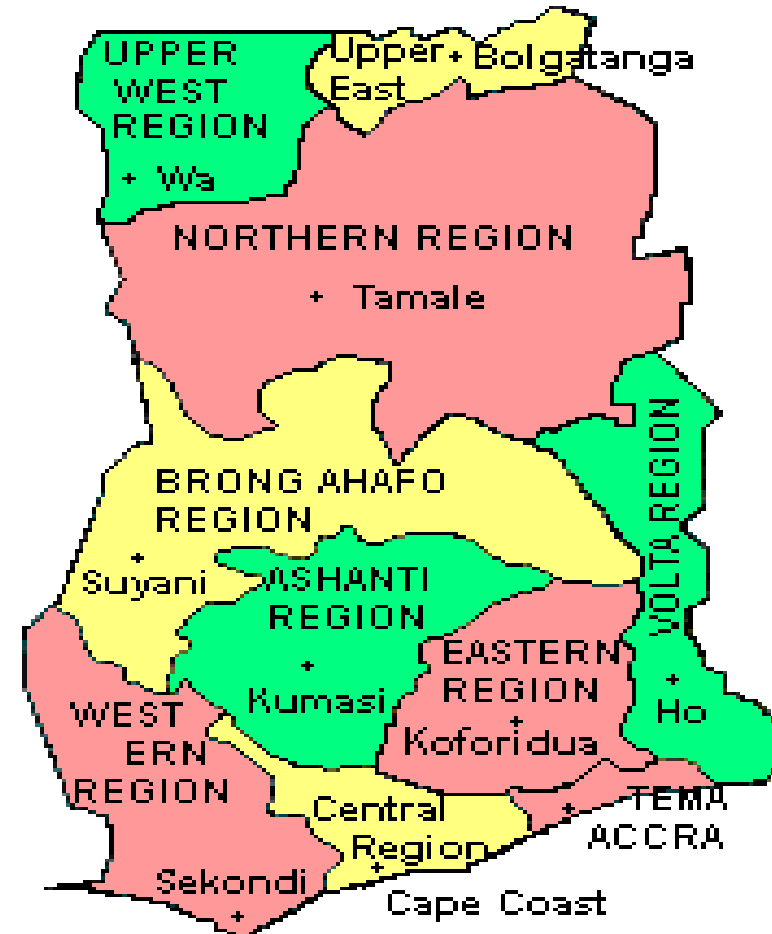
\*and/or \*\*in 2 consecutive tests, of which one ≥1%

IS: BCR-ABL on International Scale

# PHYSICIAN BARRIERS TO FOLLOWING ESTABLISHED GUIDELINES

- Awareness of the disease in the general populace
- Presentation of the disease in advanced stages
- Diagnostic and monitoring capabilities
- Affordability of Health

Using Ghana as a template.....



- In Ghana, like most low and middle income countries (LMIC), patients usually present late with complications such as hearing loss whereas in more advanced countries 50% of patients with CML are diagnosed when they are asymptomatic
- Usually guidelines do not take into consideration advanced stages of presentation of the disease at diagnosis
- For example if at diagnosis BCR-ABL is 160% ( IS) after 3 months if its 15% would one consider it to be a warning sign as per ELN?



- Diagnostic capabilities differ from place to place making the implementation of guidelines challenging
- It is more so in LMIC regions where early confirmation of diagnosis, early initiation of therapy and enhanced treatment outcomes is sometimes not possible
- Affordability and availability of drugs in real life situations can also be a hinderance to treatment

- In certain centres, one would be spoilt for choice whereas in others the situation is different
- Adhering to recommended monitoring periods in reality is therefore always not possible
- Reasons could be affordability, access to a laboratory that can perform the test, turnaround time to get results and compliance of the patient to review dates and therapy

- The definition of various stages of CML can be difficult especially that of accelerated phase
- The early recognition of this stage indicates disease progression and has an impact on prognosis and treatment
- The boundaries between the stages depicted by clinical and morphological features are sometimes not specific and differ from one guideline to another

- Guidelines usually give advice on side effects that affect major organs but briefly mention side effects that affect quality of life
- Side effects that affect the patients day to day activities can lead to non-compliance and this can derail milestones set out by the guidelines to obtain desired treatment outcomes

# CASE 1

28 -year male presented to the hospital with upper back pain. Investigations which included a Full Blood Count revealed an increased WBC ( $766 \times 10^9/L$ ). BCR-ABL transcript level at diagnosis was 120%. He was started on Glivec 400mg daily.

Six months later BCR- ABL was 1.1%

However a year later his PCR was 0.012%

Despite delay in achieving optimum milestones at six months, he made it in a year at the same dose.

Could a very high PCR at diagnosis have contributed to the delay?

## Case 2

43- year old female presented with intermittent fever and fatigue of 2 months duration. White cell count (WBC) was  $22.1 \times 10^9/L$  and platelet count was  $900 \times 10^9/L$  at presentation. BCR-ABL transcript level was 44%. She was able to repeat in 18 months and her transcript level was 0.0007%.

BCR-ABL has become more affordable for her now because it can be done “in house”. She now does it every three months and is in complete molecular response

# Sub-optimal response: possible reasons

- Compliance
  - Side effects
  - Complacency
- Resistance to treatment
  - New mutations could have occurred

# Sub-optimal response: When/ why should there be a concern?

- If patient compliance to treatment
- If there was an initial response to treatment
- No change in BCR-ABL transcript levels after delay in achieving treatment milestones
- Occurrence of new mutations during treatment



# Conclusion

- Guidelines are good. It suggests a blue print for everyone to follow in order to achieve an expected outcome.
- However circumstances and situations are different and this has an impact on its implementation.

- These should be taken into account so that as much as possible it caters for all circumstances without compromising on standards. Better still local guidelines can be used to augment international ones.
- The onus however lies with both the physician and the patient to achieve the goal of guidelines which is to optimize treatment outcomes.

# Acknowledgements

- iCMLf for training and funds for diagnosis, and for providing the GeneXpert instrument together with Cepheid and the Max foundation
- Norvatis and Max Foundation who through Glivec International Patient Assistance Programme (GIPAP; Max Solutions) provide Glivec free of charge to our patients

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THANK YOU