INFORMING PATIENTS ABOUT TFR

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CML Horizons 2018
Warsaw
TFR PHASES

Consideration, discussion and decision phase

Stopping Phase: Probation period

- Therapy-free remission failure phase
- Stopping phase: Long-term therapy-free remission
CML Patient Environment- 2017

- Lack of “patient-friendly” TFR information- you can’t decide stopping if you do not have the data
- Different standards at different TFR trials
- TFR done in and out of clinical trials
- Companies are pushing second-generation TKIs as better option for future TFR – not really proven in real life yet
- Bottom line: TFR not well understood, much confusion as well as hope, excitement
WHAT HAS CHANGED IN THE LAST YEAR

• Lack of “patient-friendly” TFR information - you can't decide stopping if you do not have the data

Changes:
• TFR leaflet by the “What If What Now” Team
• TFR Video Interview of Prof Saglio by Giora
• TFR Position Paper to be published soon in the journal *Clinical Lymphoma, Myeloma and Leukemia*
WHAT IS “WHAT IF WHAT NOW”?

- Working group consisting from 7 CML Advocates: Mina Daban, Jan De Jong, Nigel Deekes, Felice Bombaci, Jelena Cugurovic, Sarunas Narbutas and Giora Sharf
- 5 CML experts- Prof Saglio, Dr Andrija Bogdanovic, Dr Antonio Medina Almeida, Dr Valentine Garcia Gutierrez and Dr Daniela Zackova.
- Organized and sponsored by Novartis region Europe
WHAT IS “WHAT IF WHAT NOW”? 

Team Work parallely on 6 CML educational topics:

- Treatment-free remission
- Generic tyrosine kinase inhibitors
- CML: understanding your diagnosis
- TKIs: managing side effects
- CML, fertility and the young adult
- Information for caregivers

There is a video on each of these topics done by one of the advocates and one of the experts.
WHAT IS “WHAT IF WHAT NOW”? 

• All Materials are now available without any branding
• It will be soon available in 7 languages and we can add more if needed
• We are now exploring taking over the responsibility to continue to develop educational material for CML patients that all our members will be able to use freely.
WHAT IS “WHAT IF WHAT NOW”? 

Treatment Free Remission:

• Video Interview of Prof Saglio by Giora
• Available on CML Advocates Website
WHAT IS “WHAT IF WHAT NOW”?

TFR Leaflet

WILL MONITORING CONTINUE INTO LONG-TERM TFR?
It is very important that PCR monitoring continues long after you have stopped taking medication, even though the risk of relapse is highest during the first few months after stopping. Late remissions, even if rare, are possible and it is important to detect them as soon as possible so that TKI treatment can be restored.

HOW CONCERNED SHOULD I BE ABOUT MY PCR RESULTS?
A system to standardize PCR results has been established to make monitoring as accurate as possible and to measure a complete molecular response. As long as your PCR is below a certain level, there is no need to worry. Results show improvements in a little while but you only need to contact treatment if there is a rise of PCR level.

Many patients feel comfortable that PCR results can be monitored. It can be faster if you have a group of patients with similar treatments that you would recommend that you would like them to discuss together.

IS THERE ANY RISK IN DISCONTINUING TREATMENT?
As long as TKI treatment is discontinued properly, there are no risks from attempting TFR.

Even if the BCR-ABL level is rising above the MR4 threshold, studies have shown that most patients are able to achieve a deep molecular response after restaging using TKI. According to current knowledge, there are no side effects of proceeding to TKI therapy while still on treatment.

ARE THERE ANY SIDE EFFECTS TO STOPPING TREATMENT?
After discontinuation, some patients may experience a withdrawal syndrome, characterized by pain in the upper chest, joint pain, and diarrhea. It is most common to occur in the first 3 months and can be treated with symptomatics. Symptoms can be treated with anti-emetics, antacids, and corticosteroids, and generally get better on their own.

IS THERE ANYTHING I CAN DO IF I FEEL WORRIED ABOUT STOPPING TREATMENT?
Stopping treatment can undermine your treatment regimen. If you feel worried, you may find it helpful to talk to other patients going through TKI therapy. They can provide you with support and tell you what it is like to be in your situation. You should discuss this with your doctor or another healthcare provider.

MAY I FAIL IF I AM NOT ELIGIBLE FOR TFR OR NEED TO START AGAIN?
You should never feel like you have failed if TFR does not work for you. It does not mean you are unable to stop taking medication, or if you need to stop taking it again. Regardless of the decision you and your doctor make about your future course of treatment, all patients are always to patient disease progression, achieve a deep molecular response, and improve your quality of life.

COULD I STILL BE OFFERED THE CHANCE TO STOP TREATMENT EVEN IF I DON'T MEET ALL THE CRITERIA?
It can be risky to attempt TFR if you do not meet criteria. Unfortunately, not all patients will be eligible for TFR. If you are not suitable for TFR, talk to your doctor who will discuss other treatment options.

GLOSSARY
- TKI: Tyrosine Kinase Inhibitor
- PCR: Polymerase Chain Reaction
- MR: Major Molecular Response
- MR4: At least a 4-log reduction in BCR-ABL
- MR4.5: At least a 4.5-log reduction in BCR-ABL
- MR5.0: At least a 5-log reduction in BCR-ABL
- MR5.5: At least a 5.5-log reduction in BCR-ABL
- PCR: Polymerase Chain Reaction
- BCR-ABL: Breakpoint Cluster Region and Abelson Tyrosine Kinase
- MR4: Major Molecular Response
- MR4.5: Major Molecular Response 4.5
- MR5.0: Major Molecular Response 5.0
- PCR: Polymerase Chain Reaction
- BCR-ABL: Breakpoint Cluster Region and Abelson Tyrosine Kinase
WHAT HAS CHANGED IN THE LAST YEAR

TFR done in and out of clinical trials

Change-
• Very few open trials for stopping. Only 2 trials are currently recruiting: One in Malaysia and one in Germany for a 2 ed stop.
• Most stopping occur in clinical practice.
WHAT HAS CHANGED IN THE LAST YEAR

Companies are pushing second-generation TKIs as better option for future TFR – not really proven in real life yet

Change
• Nilotinib received an EHA and FDA label for TFR drug.
• Similar label is being requested for Dasatinib (Probably)

Has this changed the perspective of Drs and patients in regards to using 2 ed generation out-front for possible future TFR???
What Has changed in the last year

TFR not well understood, much confusion as well as hope, excitement

Change-
No Change Yet. Hopefully the data from our global TFR study will give some answers to clarify the topic, in addition to the planned HCP and Patients educational TFR material
GLOBAL TFR SURVEY

Organized by CML Advocates network

- TFR Workgroup of 10 CML patients on TFR
- Team work Led by Giora and Celia
Giora Sharf
Jan Geissler
Pat Elliot
Rita O. Christensen
Bernhard Schwarzer
Felice Bombaci
Nigel Deekes
Bahija Gouimi
Mina daban
Tamie Kimmelmann
Sriram Ranganathan
TREATMENT-FREE REMISSION FOR CML PATIENTS

-Interim results from the global online survey of TFR patients -

#TFR4CML
55 countries
+500 responses
6 weeks...

Have you already taken the #TFR4CML survey?

CML Advocates Network  bit.ly/tfr4cml
Introduction

• The “TFR 4 CML PATIENTS” project consists of a global online survey of TFR patients to collect the viewpoints, needs and experiences of CML patients that are considering or have already started Treatment Free Remission (TFR)

• The aim is to provide CML patients and healthcare providers with more evidence when considering or managing TFR

• Fieldwork is underway at: www.cmladvocates.net/tfr-cml-patients
Questionnaire Design

• The questionnaire was developed and designed over a number of months in 2017/18, following detailed discussion between CML Advocates and the survey provider, Quality Health.

• The questionnaire has been tested by patient volunteers and reviewed by a number of stakeholders. This exercise contributed towards refining the questionnaire into a finished version.

• The survey was originally available in seven languages: English, Spanish, German, Italian, French, Finnish and Hebrew. Additional languages, including Danish and Arabic, are currently available online.
Response Rates

- The number of respondents at the time the interim results were analysed was 546

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Response Rates
TFR for CML Patients Survey Impact
14th March- 30 April 2018

+12.200 on TFR website:
http://www.cmladvocates.net/tfr-cml-patients
+35.000 impressions in Twitter with #TFR4CML and @cmlnet
+1100 views TFR video Youtube
+20.000 organic reach of #TFR4CML publications in Facebook, Instagram, Google+, LinkedIn, other channels

#TFR4CML
Topic One: Reasons to consider TFR (Phase I)

• Respondents could tick all the reasons that made them consider stopping treatment:

16. What are the main reasons that made you consider stopping treatment?

   Please tick all that apply

   - To get rid of current treatment side effects
   - The fear of side effects caused by long-term treatment
   - Not needing to take medication everyday
   - To see if I can be free of CML without therapy
   - My doctor proposed I join a ‘stopping treatment’ clinical trial
   - Financial reasons - reduction of costs
   - Planned or unplanned pregnancy
   - Other, please specify below
Topic Two: Time living with CML (Phase II)

Q25. How many years were you on medication for CML before stopping?
Topic Two:
Time living with CML (Phase II)

Q26. How long were you in deep molecular response (at least MR4, or BCR-ABL below 0.01%) before you stopped CML treatment?
Topic Three: Which medication were you on before stopping treatment (Phase I)

Q10. What CML medication were you taking just before you stopped?

![Bar chart showing medication usage]

- Imatinib
- Nilotinib
- Dasatinib
- Bosutinib
- Ponatinib
- Interferon
- ABL001/Asciminib
- Other
**Topic Four:**
**Reasons to worry about stopping (Phase I)**

- Respondents could tick all the reasons that made them worry about stopping treatment

17. **What are the main reasons that made you worry about stopping treatment?**
   Please tick all that apply

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<tr>
<td>I wouldn’t feel safe going off treatment</td>
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<tr>
<td>There is a lack of proper quality PCR monitoring</td>
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<tr>
<td>The fear of withdrawal symptoms</td>
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<tr>
<td>Recurrence of disease (stopping treatment unsuccessful)</td>
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<tr>
<td>I wasn’t worried about stopping treatment</td>
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<td>Other please specify below</td>
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Topic Five: Withdrawal symptoms (Phase II)

- Respondents could tick all the withdrawal effects they experienced when treatment stopped *

31. What withdrawal effects did you experience when treatment was stopped?
   Please tick all that apply

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<td></td>
<td>Sweating or skin problems</td>
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<td></td>
<td>Depressive episodes or fear or bad mood</td>
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<td>Tiredness</td>
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<td>Weight loss</td>
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</table>
Q35. Did you receive psychological and/or emotional support during the stopping of treatment?

Answers

- Yes
- No, but I would have liked this
- No but this wasn't necessary
Topic Seven: Monitoring (Phase II)

• The chart below compares the frequency of monitoring of respondents in the 6 month probationary period (Q38) to those in long term remission (Q60)
Conclusions

• Looking at the participating countries it is clear that TFR is currently implemented mainly in developed western countries.
• We need better monitoring in other countries to let patients stop safely.
• We need clear and agreed guideline for stopping treatment, so patients can do it safely.
• More information is needed for both patients and Healthcare providers.