Standard Operating Protocol
Data entry to CML registry

1. Purpose

1.1 To create a uniform system and define a policy in entering data into the various fields in the CML database

2. Scope and Responsibilities

2.1 HCC
2.2 HCC CML Committee
2.3 CDMC
2.4 Data operators

3. **Definitions**

3.1 Null values: Null is the absence of a recorded value for a field. A null value differs from a value of zero in that zero may represent the measure of an attribute, while a null value indicates that no measurement has been taken.

3.1.1 In the HCC registry- unless otherwise indicated ; 99999 will represent null values

3.2 Date: Format dd-mm-yyyy

3.3 Date of birth : Format dd-mm-yyyy

3.3.1 If the exact birth date is not available then the year should be entered as 01-01-yyyy where yyyy is the year of birth

3.4 **Febrile Neutropenia : This** is **defined** as an oral temperature >38.5°C or two consecutive readings of >38.0°C for 2 h and an absolute neutrophil count $<0.5 \times 10^9$/l, or expected to fall below 0.5×10^9/l.

3.5 Invasive fungal infection to be defined as per the EORTC criteria.

3.6 **Intensity of conditioning regimen**: Reduced intensity, myeloablative and non myeloablative conditioning will be defined as per the Reduced-Intensity Conditioning Regimen Workshop, convened by the Center for International Blood and Marrow Transplant Research (CIBMTR) during the Bone Marrow Transplantation Tandem Meeting in 2006 or https://www.cibmtr.org/manuals/fim/1/en/topic/q155-315-pre-hct-preparative-regimen-conditioning

3.7 **Donor type** : This will be defined as per the Donor category as mentioned in the forms instruction manual of CIBMTR.org available at https://www.cibmtr.org/manuals/fim/1/en/topic/donor-information

3.8 Complete remission will be defined as per standard CML response criteria. Available at https://www.cibmtr.org/manuals/fim/1/en/topic/CML-response-criteria

4 **Policy and data rules**

A. PATIENT INFRORMATION

4.1 Name/Initials :Either full name or initials to be filled

4.2 Hospital Number : This is an alphanumeric filed and signifies original medical record number/HID number

4.3 Patient Number: Auto generated followed by Centre code.

4.4 Village/Town/City: Residence of patient, whether from Village/Town/City

4.5 District: Name of the district to which patient belongs.

4.6 Pin Code: 06 digit numeric. In case patient is a foreign national, to enter 999999.

4.7 State :Name of the state from drop down menu

4.8 Country: Name of the country. Default is India

B. Baseline Data

4.9 Date of Birth :Dd-mm-yyyy format which has to be entered using date-picker. If the exact birth date is not available then the year should be entered as 01-01-yyyy where yyyy is the year of birth

4.10 Sex : To enter male or female

4.11 Comorbidities: Diabetes, Hypertension, IHD, Known other diseases at the time of diagnosis. Tick whichever is applicable out of these

4.12 Height :At time of diagnosis in cm

4.13 Weight: at time of diagnosis in kg

4.14 ECOG Performance status Mandatory field. One of the options to be selected

4.14.1 Fully active, able to carry on all pre-disease performance without restriction

4.14.2 Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work

4.14.3 Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours

4.14.4 Capable of only limited self-care, confined to bed or chair more than 50% of waking hours

4.14.5 Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair

4.14.6 Not Available

4.15 Date of registration : Registered for CML diagnosis

4.16 Date of diagnosis: Date when diagnosis was made at your centre (Date of the initial FISH test/RTPCR test/bone marrow which was done to diagnose CML).

4.17 Duration of Symptoms prior to diagnosis (in days):Approximate duration of main symptoms prior to date of diagnosis at your centre

C. Baseline Parameters

4.18 Spleen size : (Below coastal margin in cm) (to see from phyisican notes)

4.19 Liver size: (Below coastal margin in cm) (to see from phyisican notes)

4.20 Lymph nodes. ☐ Yes ☐ No (to see from phyisican notes)

4.21 Hb: Numeric field in gm/dl (at diagnosis)

4.22 TLC at diagnosis in/mm3: These parameters recorded at date of diagnosis (as recorded above) or any higher TLC recorded prior to registration (in mm3)

4.23 Platelet: Platelet counts in /mm3 at time of diagnosis at your centre

4.24 Peripheral Blood blasts %: percentage of blasts in peripheral blood at time of diagnosis

4.25 N (Neutrophils)%: percentage of **Ne** in peripheral blood at time of diagnosis

4.26 E(Eosinophils)*%: percentage of **Eo** in peripheral blood at time of diagnosis

4.27 B(Basophils)*%: percentage of **Ba** in peripheral blood at time of diagnosis

4.28 Blasts *%: percentage of **BL** in peripheral blood at time of diagnosis

4.29 Nucleated RBC %: percentage of **NRBC** in peripheral blood at time of diagnosis

4.30 M (Monocytes)%: percentage of **Mo** in peripheral blood at time of diagnosis

4.31 My(Myelocytes): percentage of b **My** in peripheral blood at time of diagnosis

4.32 MM(Metamyelocytes): percentage of **MM** in peripheral blood at time of diagnosis

4.33 PM (Promyelocytes): percentage of **PM** in peripheral blood at time of diagnosis

4.34 LDH: Value at the time of diagnosis

4.35 Upper limit of normal for LDH for the lab

4.36 AST (IU/L): At the time of diagnosis at your center

4.37 ALT(IU/L): At the time of diagnosis at your center

4.38 Creatinine (mg/dL) : At the time of diagnosis at your center

4.39 Albumin (g/dl): At the time of diagnosis at your center

4.40 Alkaline Phosphatase (IU/L): At the time of diagnosis at your center

4.41 Bilirubin Total (mg/dL): At the time of diagnosis at your center

4.42 Direct (mg%): At the time of diagnosis at your center

4.43 Protien Total (g/dl): At the time of diagnosis at your center

4.44 Bone Marrow: At the time of diagnosis at your center

4.44.1 **Fibrosis** ☐ Yes ☐ No ☐ Not assessed (from the detailed bone marrow trephine biopsy report – to check with physician)

4.44.2 **If yes, Grade of fibrosis** ☐ I ☐ II ☐III

4.45 CNS disease to be assessed and cross – checked by clinician verifying the data entry

4.45.1 Yes Definition of CNS in CML is as per the protocol being use by participating centers

4.45.2 Not present clinically (to see clinical notes)

4.46 Conventional karyotyping (CK): (Conventional Karyotype (CK) results from BM aspirate samples at the time of initial diagnosis. To be assessed and cross - checked by clinician verifying the data entry. One of the options to be selected, abnormal , Not done , No metaphases/failure

4.46.1 If done, Metaphase with t(9:22) ___ / 20

4.46.2 If yes t(9;22)%_____

4.47 FISH: (Abnormal results of FISH to be depicted. To be assessed and cross checked by clinician verifying the data entry)

If yes t(9;22)_____%

If abnormal, please specify either: In case of abnormal results for cytogenetic testing (see above), from drop down menu pick up the option. More than 01 option can be ticked

4.48 ACA (Additional cytogenetic abnormalities) (By Karyotype or FISH)

4.48.1 ☐ Yes ☐ No

4.48.2 if yes, _____ (write the abnormality noted in the report)

4.49 PCR ☐ Yes ☐ No

4.49.1 If yes: ☐ Qualitative ☐ Quantitative

4.49.2 If quantitative BCR ABL % _____

4.49.3 Type of transcript: ☐ p210 ☐ p190 ☐ p230 ☐ Not known ☐ Other types of transcripts

4.50 (It is mandatory to have one of these tests to be positive to proceed further)

Risk stratification (would be auto calculated based on inputs)

Sokal _____ **Hasford _____**

Eutos _____ **ELTS_____**

4.51 DISEASE PHASE: (only one to be selected)(At diagnosis Mandatory for new patients <2 weeks and non mandatory for > 2 weeks treatment)

4.51.1 Chronic

4.51.2 Accelerated

4.51.3 Blast

4.52 Treatment Received: To indicate in Yes/No where any form of treatment for CML was initiated at your centre

4.53 If No, reason: If no treatment was offered, one of the reasons to be selected

4.50.1 Financial inability (Inability to meet the costs of therapy represent-Economic)

4.50.2 Socio-cultural barrier (Inability to arrange support during stay or language barrier represent)

4.50.3 Unawareness and apathy (Denial of disease or utility of conventional therapy represent)

4.50.4 Opted to take treatment at another center

4.50.5 Age Factor

4.50.6 Poor performance status

4.50.7 Other: To specify in text format

5 **INITIAL THERAPY** (Entry within 4 weeks of start of TKI)

5.1 ***Date of starting TKI :** At the time of Diagnosis
*TKI (one of these to be selected)
5.1.1 Imatinib: Daily Dose: 100/200/300/400/600/800.
5.1.2 Dasatinib: Daily dose: 50/100/140/other dose (to be specified)
5.1.3 Nilotinib: Daily dose: 600/800/other dose (to be specified)
5.1.4 Bosutinib: Daily dose: _____
5.1.5 Others: (Name of TKI/ other drug and dose to be specified)

5.2 Generic Innovator_____
If selected to select one of the brand names (list to be populated)

5.3 Any other drugs (For CML) ☐ Yes ☐ No
5.3.1 To be specified if Yes

Note:
1. To fill up 03 months follow-up after this. In case patient is lost to follow-up/dead separate follow-up form to be filled.
2. In case of blast transformation at any stage, 'Blast phase' form to be filled.

Assessment to be done from 2.5 months to maximum of 4 months from start of treatment

6 **Response assessment** (Only for first line therapy without progression)

If Done (Date of follow-up_____

Response assessment (A)

6.1 CHR*:

Yes -Complete: Platelet count < 450 × 10^9/L; WBC count < 10 × 10^9/L; differential without immature granulocytes and with less than 5% basophils; nonpalpable spleen

6.2 Cytogenetic response:

6.2.1 Complete (Ph + 0)
6.2.2 Partial/Major (Ph + 1%-35%)
6.2.3 Minor (ph+36%-65%)
6.2.4 Minimal (ph+66%-95%)
6.2.5 None (ph+>95%)
6.2.6 Not assessed

6.3 FISH

6.3.1 Complete
6.3.2 Partial
6.3.3 None
6.3.4 Not assessed

6.4 Molecular response (whether RQ PCR test done?)

6.4.1 Done -If done, RQ PCR BCR ABL (IS)%____

(Type of molecular response will be auto calculated based on PCR values)

(All previous BCR ABL done with dates will be shown for comparison, log reduction will be auto calculated)

6.5 Toxicity (B) (to check with physician)

6.5.1 Any interruption in drug therapy: yes / no
6.5.2 Hematological toxicity requiring interruption yes / No
6.5.3 Bleeding tendencies Yes /No
6.5.4 Liver dysfunction requiring interruption Yes / No
6.5.5 Diarrhea - yes / no (Put comment: Grade III diarrhea)
6.5.6 Vomiting yes /no
6.5.7 Myalgias – yes /no
6.5.8 Pleural effusion- yes / no
6.5.9 Pulmonary hypertension-- yes / no /not evaluated
6.5.10 Dyslipedemia - yes /no / not evaluated
6.5.11 Hyperglycemia -- yes /no / not evaluated
6.5.12 Peripheral vascular disease - yes / no / not evaluated
6.5.13 C**hemical Pancreatitis** -- ☐yes ☐no ☐not evaluated

6.6 Any change in therapy (C) (Any change in therapy subsequently all entries will be in the "follow up " form)

6.6.1 If Yes: a) Approximate number of doses missed _____(in figures)

6.6.2 b) Reasons for drug interruption / Unintentional / Non availability / Concur-rent illness / Adverse events (patient perceived) / Others _____

6.6.3 C) Any change in therapy - yes /no (previous drug treatment to be shown along with start date of treatment, if no selected at this stage no further entries required)

6.7 Any change in dose: Yes / No

6.7.1 If Yes: – dose increase / dose reduced

6.8 Any Change in drug: To select new drug

6.8.1 Imatinib

6.8.2 Dasatinib

6.8.3 Nilotinib

6.8.4 Bosutinib/

6.8.5 Others specify_____(Dose of new drug to be entered manually)

6.9 Date of change _____

6.10 Reason – Enter for both drug change as well as for dose change.

6.10.1 No response

6.10.2 loss of CHR

6.10.3 loss of molR

6.10.4 loss CyR

6.10.5 toxicity

6.10.6 cost

6.10.7 others

6.11 IRMA (if loss of response or others are selected)– yes /no /not done (Tyrosine kinase domain mutation testing)

6.11.1 if yes enter the mutation_____

6.12 Progression: Yes / No (If selected further entry in progression)

6.12.1 Accelerated phase

6.12.2 Blast crisis (If selected further entry in "Blast crisis" page)

6.12.3 Loss of Mol R / Loss of CCR / loss of CHR

2nd assessment time point (5-7 months)

Repeat as in First assessment point

3rd assessment time point (8 to 15 months)

Repeat as in First assessment point

4th assessment time point (16 to 20 months)

Repeat as in First assessment point

5th assessment time point (21 to 26 months)

Repeat as in First assessment point

progressive disease form

7. Response assessment done ☐Yes ☐No

7.1 Date of progression _____

7.2 Type of progression:

7.2.1 AP
7.2.2 BC
7.2.3 loss of CHR
7.2.4 loss of CyR
7.2.5 loss of molR ☐Others

7.3 Any change in therapy - Yes / No
(previous drug treatment to be shown along with start date of treatment, if no selected at this stage no further entries required)

7.3.1 if yes, change in dose: Yes /No
7.3.2 If Yes: –
7.3.2.1 dose increase
7.3.2.2 dose reduced
7.3.3 If No Change in drug: To select new drug
7.3.3.1 Imatinib
7.3.3.2 Dasatinib
7.3.3.3 Nilotinib
7.3.3.4 Bosutinib
7.3.3.5 Others
7.3.3.6 If others**, specify**_____(Dose of new drug to be entered manually)
7.3.4 Date of change _____
7.3.4.1 Reason – ☐No response (Enter for both dur change as well as for dose change)
7.3.4.2 ☐loss of CHR
7.3.4.3 ☐loss of molR
7.3.4.4 ☐loss CyR
7.3.4.5 ☐toxicity (POPUP-If toxicity is picked here, then there must be some toxicity yes entry, if not block progress further)
7.3.4.6 ☐cost
7.3.4.7 ☐others

7.4 IRMA (if loss of response or others are selected) – ☐yes ☐no ☐not done
7.4.1 if yes enter the mutation_____

7.5 <u>TREATMENT</u>

7.5.1 TKI (one of these to be selected)
7.5.1.1 Imatinib: Dose: 100/200/300/400/600/800.
7.5.1.2 Dasatinib: Daily dose: 50/100/140/other dose (to be specified)
7.5.1.3 Nilotinib: Daily dose: 300/400 /other dose (to be specified)
7.5.1.4 Others: (Name of TKI and dose to be specified)
7.5.1.5 Any other drugs (For CML) ☐Yes ☐No

7.5.2 AlloSCT* ☐Yes ☐ No

8. **BLAST CRISIS**

(To be filled in case of progression to documented blast crisis at any stage of disease including upfront Blast crisis)

8.1 **Date of diagnosis of Blast crisis**_____
8.2 **Site of BC**: Medullary, Extramedullary, Both
8.3 **Type of BC**:
- 8.3.1 Myeloid
- 8.3.2 Lymphoid
- 8.3.3 Mixed phenotype
- 8.3.4 Others
- 8.3.5 Not known

8.4 CNS positive ☐Yes ☐No (document if CNS was involved at the time of blast crisis)

TREATMENT :

8.5 TKI (one of these to be selected)
- 8.5.1 **Imatinib** **Dose:** 100/200/300/400/600/800.
- 8.5.2 **Dasatinib:** **Daily dose**: 50/100/140/other dose (to be specified)
- **8.5.3 Nilotinib: Daily dose: 600/800 /other dose (to be specified)**
- 8.5.4 **Others: (Name of TKI and dose to be specified)**

8.6 **Any other drugs (For CML)** ☐ Yes ☐No
- **8.6.1 To be specified if Yes**

8.7 **chemotherapy with curative intent*** ☐Yes ☐ No
8.8 **AlloSCT*** ☐Yes ☐ No

(Outcome to be filled up in follow-up form)

9 Transplantation

9.1 **Transplant (as front line therapy)**: This refers to stem cell transplantation (Either allogeneic or autologous) done on a newly diagnosed patient either as post remission therapy or as part of remission induction treatment. It does not include stem cell transplantation done in a relapsed setting or in CR2 or above.

9.1.1 **Yes** – Patient has received stem cell transplantation

9.1.2 **No** – Patient did not receive stem cell transplantation

9.2 **Indication for doing transplant:**

9.2.1 TKI Failure

9.2.2 TKI intolerance

9.2.3 Accelerated phase

9.2.4 Blast phase

9.3 **Date of transplant (HSCT):** This refers to the date of infusion of the stem cells. In case of more than one day of infusing stem cells; the last day of infusion will be considered as the date of transplant**.**

9.4 **Donor**

9.4.1 The donor could be **either** Matched Related , Matched Unrelated ,Haploidentical or an Autologous donor

9.5 Pre transplant disease status CR : CR refers to the CML disease status immediately prior to taking up the patient for transplant

9.5.1 **Yes :** When patient is in complete remission

9.5.2 **No :** When patient is not in complete remission

9.6 Pre transplant BCR ABL_____

9.7 **Acute GVHD**

9.7.1 **Yes** – Patient has Acute GvHD

9.7.2 **No** – Patient has no Acute GvHD

https://www.cibmtr.org/manuals/fim/1/en/topic/f2100-q131-233

9.8 **Chronic GVHD**

9.8.1 **Yes** – Patient has Chronic GvHD

9.8.2 **No** – Patient has no Chronic GvHD

10 **Pregnancy page** (This page to be filled only if pregnancy detected while on TKI for CML)

10.1 **Date of detection of pregnancy** _____(Date Picker)

10.2 **Interruption in TKI** ☐ Yes ☐ No

10.3 **Date of stoppage of TKI, if interrupted/stopped during pregnancy** _____

10.4 **Date of restart of TKI, if interrupted/stopped during pregnancy** _____

10.5 **Last BCR ABL prior to detection of pregnancy** _____%

10.6 **Outcome**

- 10.6.1 Term pregnancy
- 10.6.2 Preterm delivery
- 10.6.3 MTP
- 10.6.4 Abortion

10.7 **CML status post pregnancy**

- 10.7.1 CP
- 10.7.2 Accelerated
- 10.7.3 Blast crisis

10.8 **Fetal anomaly/ Teratogenic effects** ☐ Yes ☐ No

11 Follow-up

11.1 **Lost from follow up**: Occasionally, centers may lose contact with patient for a variety of reasons, including the patients' moving, changing physicians, or death. If contact with a patient appears lost, please consider calling the patient at home or work, sending a letter. If the center receives documented information that a patient is alive or dead, the form should be filled out with the patient survival status. If no documentation exists and several unsuccessful attempts have been made to contact the patient, they are considered lost to follow-up and the form may be marked as such. It will be one of the following

11.1.1 **Yes** – Patient lost to follow up

11.1.2 **No** – Patient in contact with the centre

11.2 **Relapse/Progression date**: This refers to the date of the bone marrow examination/ biopsy or the peripheral blood report which document the first evidence of increase in the number of blasts.

11.2.1 Format dd-mm-yyyy

11.3 **Site of relapse:** This refers to the site in 4.2 where the increase in blasts has been documented. This could be either /and Medullary , Extramedullary

11.3.1 **Medullary** : This refers to the increase in blasts documented only in the peripheral blood or the bone marrow

11.3.2 **Extramedullary**: This includes a documented increase/presence of blasts which is not in the peripheral blood or bone marrow. These include **but are not limited to** CSF and other organ/area biopsy sites.

11.3.3 **Both:** This option will be marked if blasts are documented in both marrow/peripheral blood and other organ/area biopsy sites including but not limited to the CSF.

11.4 **Treatment at relapse:** This refers to treatment received by patient on documentation of 4.2

11.4.1 **Salvage chemotherapy with curative intent:** This refers to intensive chemotherapy received by patient where the intent is to induce remission of disease. It could be either of

11.4.1.1 Yes : When patient has received /started on salvage chemotherapy

11.4.1.2 No : When patient has not received /started on salvage chemotherapy

If No salvage chemotherapy then either of

Palliation : Supportive care or chemotherapy where the intent is not to induce remission but improve quality of life

DAMA : Patient does not receive any treatment and takes discharge against medical advice

11.4.2 **Salvage AlloSCT:** This refers to allogeneic transplant performed for the patient after relapse with the intent to cure.

11.4.2.1 Yes : When patient has received /started on salvage transplant

11.4.2.2 **No :** When patient has not received /started on salvage transplant

11.5 **Death :** This refers to patient mortality. This could be either Yes or No.

11.5.1.1 **Phase of therapy when death happened:** Indicate in which phase of therapy patient mortality occurred. It could be either of. Chronic phase, AP, BP, post-transplant

11.5.1.2 **In CR at time of death:** Indicate if the patient is in remission of his disease as defined as per x.x.

11.5.1.2.1 Report "Yes" if in remission.

11.5.1.2.2 Report "No" if not in remission.

11.5.1.2.3 Report "Unknown" if no information is available to determine whether in remission or not

11.5.1.3 **Cause of death**:

Unrelated to CML, or CML progression Write the cause of death (d/w physician)

11.6 **Date of last follow-up :** This is the date of last contact with the patient which could be either established as date of last visit or the date of telephonic conversation or messaging or over mail

11.6.1 Format dd-mm-yyyy

11.7 **Disease Status at last follow up:** This refers to the status of disease control in the patient at the time of last contact. It could be either / and of CR ;Not in CR; Not Available; Palliation or DAMA

11.8 **Long term complications:** This refers to presence or absence of late complications potentially due to the chemotherapy or treatment received by patient for his disease

11.8.1 It could be reported as either Yes, No or unknown based on the availability of documentation/information

11.8.2 If reported 4.8 is reported yes, then it could be either/ and of Infertility; Cardiac toxicity; viral reactivation/ hepatitis; second malignancy

11.8.3 Report Others if effect not reported as in 4.8.2

11.9 For patients who discontinue intensive therapy: This section refers to the reason as to why patient chose not to proceed or discontinue intensive therapy. It could be reported as either/and of

11.9.1 Financial inability (Inability to meet the costs of therapy represent-Economic)

11.9.2 Socio-cultural barrier (Inability to arrange support during stay or language barrier represent)

11.9.3 Unawareness and apathy (Denial of disease or utility of conventional therapy represent)

11.9.4 Opted to take treatment at another center

11.9.5 Age Factor

11.9.6 Poor performance status

11.9.7 Other: If not any of above reason (4.9.1-4.9.6): To specify in text format

12 Procedural limitations/reservations

12.1The data entry operator should confirm with the centre PI any ambiguity

12.2The data authenticity is the responsibility of the individual centre represented by their PI

12.3After treating clinician verifies all filled details at end of induction, page can be finalized.

12.4To note, if no further intensive therapy planned or not given due to whatever reasons, to go directly to follow-up page and complete

13 **References :** https://www.cibmtr.org/manuals/fim?v=1&l=en