Instruction: Pre-screening, screening and randomisation

GENERAL INFORMATION

Informed Consents

There are two Informed Consents in the trial, one for the pre-screening and one for the trial.

At the pre-screening visit the patients will receive both oral and written information of the pre-screening part of the protocol, and the first Informed Consent (pre-screening) will be used, to get the patients permission to pre-screen. In Pre-screening it will be assessed whether the patient is at high risk for infections and/or early treatment.

If it is confirmed that the patient is at high risk a new visit where both oral and written information of the trial will be given. At this visit – the second Informed Consent will be used to ask if patients at will participate in the trial.

The patients who after the pre-screening are not at high risk will not be offered participation in the trial and will not receive the second Informed consent.

Patient ID/Record ID

When the patient is assigned a Patient ID (Called Record ID in REDCap), during pre-screening this number will follow the patient throughout the study no matter if the patient ends up in the Low risk category for follow-up, or in the high risk category and might be randomized for treatment or observation.

PRE-SCREENING

All patients with CLL at site who are possible candidates to be pre-screened will be asked if they want to participate. All patients that has been given the possibility of participation in pre-screening should be listed in the PreVent-ACaLL Pre-screening Log.

Patients must sign the pre-screening Informed Consent before undergoing any pre-screening study procedures that are beyond standard of care.

Every patient who signs the pre-screenings Informed Consent, will be assigned a Record ID/Patient ID in REDCap (Please see **How to create a subject** in the Instruction: REDCap guide). This Patient ID follows the patient throughout the study.

When the patient has signed the Pre-screening Informed Consent, the patient has to be listed in the PreVent-ACaLL Patient Identification Log.

Assessment of Risk of infection, CLL-TIM

All the data you have entered in the forms in the pre-screening project is used in an algorithm called CLL-TIM to calculate the risk of treatment/infection within 2 years. The algorithm needs as much data as possible to make a valid assessment, which means **high confidence**. The Algorithm is run through REDCap and will come up with a result for **Risk** as High or Low and a result for **Confidence** as High or low. If the confidence is low, the assessment is not valid and the patient cannot be enrolled in the study.

Please enter all the data asked for in the pre-screening e-CRFs in REDCap. **Do not make any assumption that some data are more important that other.**

For the e-CRF **Infection (blood culture) and inflammation**, it is important to enter all available information 7 year back. If there are more results from the same date, do not chose one over the other. All results must be entered,

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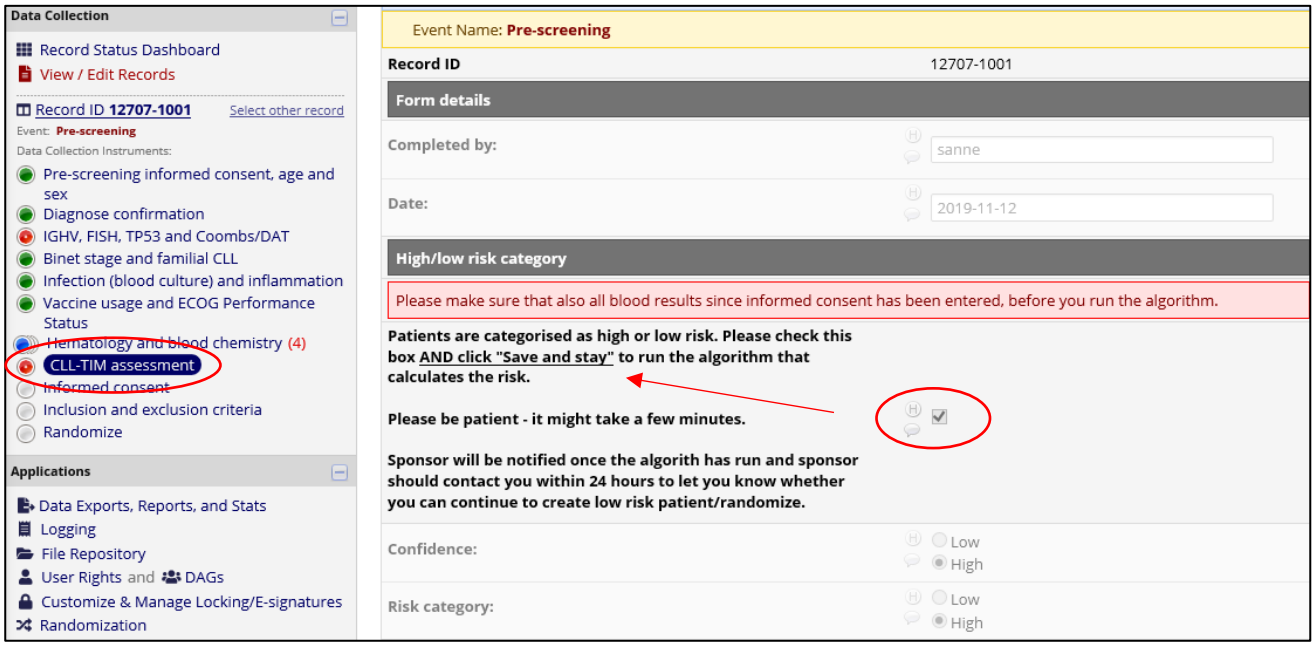
no matter if they are positive or negative. If the results are from the same date, make a new entry with the same date.

For the e-CRF **Hematology and blood chemistry** it might be enough to enter one year back. If there are more results are from the same date, make a new entry with the same date. Do not choose one result over the other.

When all data is entered go into the CLL-TIM assessment form, choose the box shown below, and click “save and stay” to run the algoritm.



To minimize the risk of typos for values and/or units in the hematology/blood chemistry, a script is developed to assess for outliers and other abnormalities, which means that sponsor will check the data before you can continue.

Sponsor will automatically be notified once the algorithm has run and sponsor should contact you as soon as possible and within 24 hours to let you know whether you need to validate any values or you can continue to create low risk patient/randomize.

You will not be able to create low risk patient/randomize before you have had feedback from sponsor.

If the result after running the algorithm is low confidence it is possible to enter more data in the pre-screening section and run the algorithm again. It is not allowed to change data already entered. Every time you run the algorithm, sponsor will check the data and contact you again.

If the result of the algorithm is still low confidence the patient cannot be enrolled in the study

Low risk
If the result of the algorithm is “low risk”, then a link is displayed which lets you create the patient in the low risk arm in the “PreVent-ACaLL – low risk/observation/treatment” project

High risk
If the patient is high risk, the randomization section is displayed, and the patient can be randomized. Once randomized a link is displayed which lets you create the patient in the observation/treatment in the “PreVent-ACaLL – low risk/observation/treatment” project.

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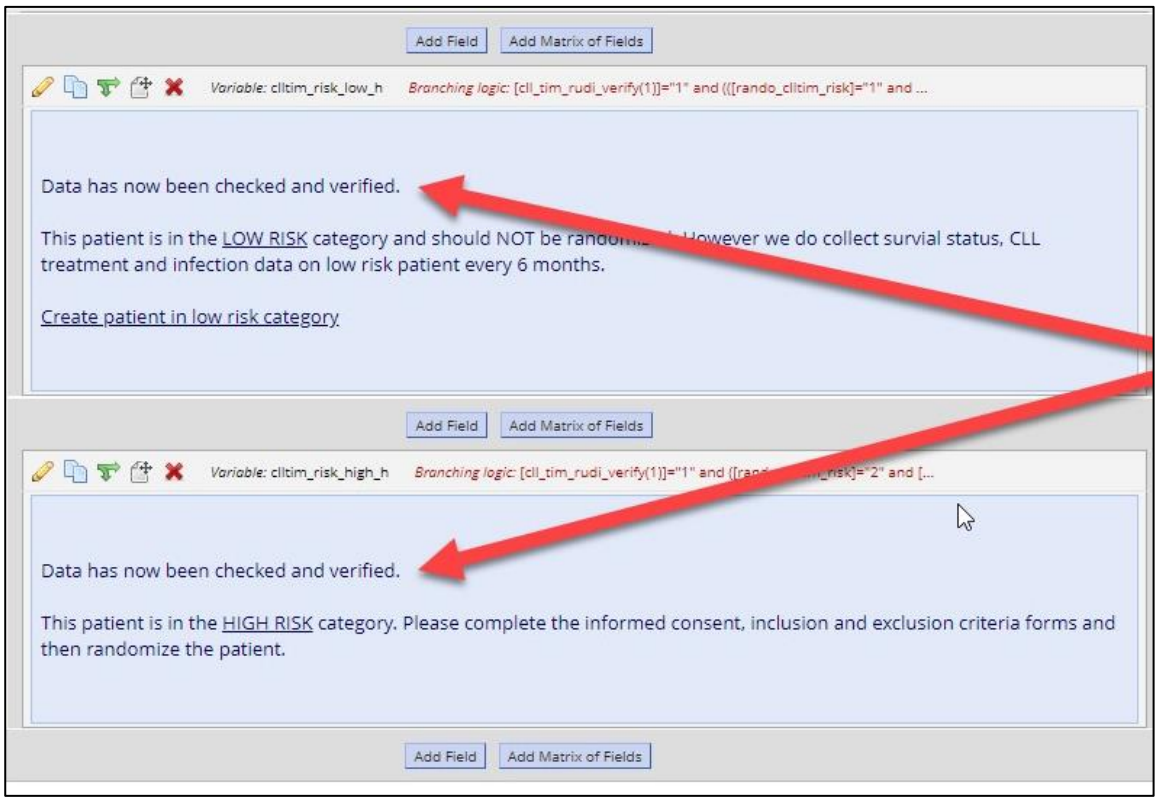
Make sure to go through the screening process before randomizing the patient.

When sponsor has reviewed data you will for data that is high confidence see one of the following in REDCap.



SCREENING

All patients that are assessed as high risk of infection/CLL treatment at pre-screening will be asked to participate in the PreVent-ACaLL study.

Patients must sign the second Informed Consent (for the actual trial) before undergoing any study procedures that are beyond standard of care.

When the patient has signed the Informed Consent, the patient has to be listed in the PreVent-ACaLL Screening and Enrolment Log. The patient is already on the Patient Identification Log (listed during Pre-screening).

To qualify for randomization, a patient must meet all in-and exclusion criteria for the study. There is no exemption to the PreVent-ACaLL eligibility. All eligibility criteria must be verifiable in the source document. The PreVent-ACaLL Eligibility checklist can be used as source documentation. The checklist then must contain the appropriate patient identifiers (e.g. patient name) and be signed and dated by an investigator.

Make sure that the CT scan and bonemarrow biopsy is ordered and performed after the Informed Consent is signed (if not done as standard of care) and before the patient is randomized.

RANDOMIZATION

When all data for the screening visit has been taken/collected the patient can be randomized in the e-CRF as described above.

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When the patient is randomized to either the observation or treatment arm, the e-CRFs are available in the project **low risk/observation/treatment**. The patient will be available as a existing patient as the Patient ID is the same as in the Pre-screening project (Please see **How to enter an existing patient/select an existing e-CRF** in the Instruction: REDCap guide). NEVER add a new patient in the **low risk/observation/treatment project.**

Make sure to document in the patient record that the patient in participating in the PreVent-ACaLL study, that the patient is informed verbally and written, has signed the Informed Consent and what date it was signed, what arm the patient is randomized to and what study drug the patient is ordered as part of the study.

After the patient has been randomized the patient has to start the treatment/observation within two weeks of randomization.