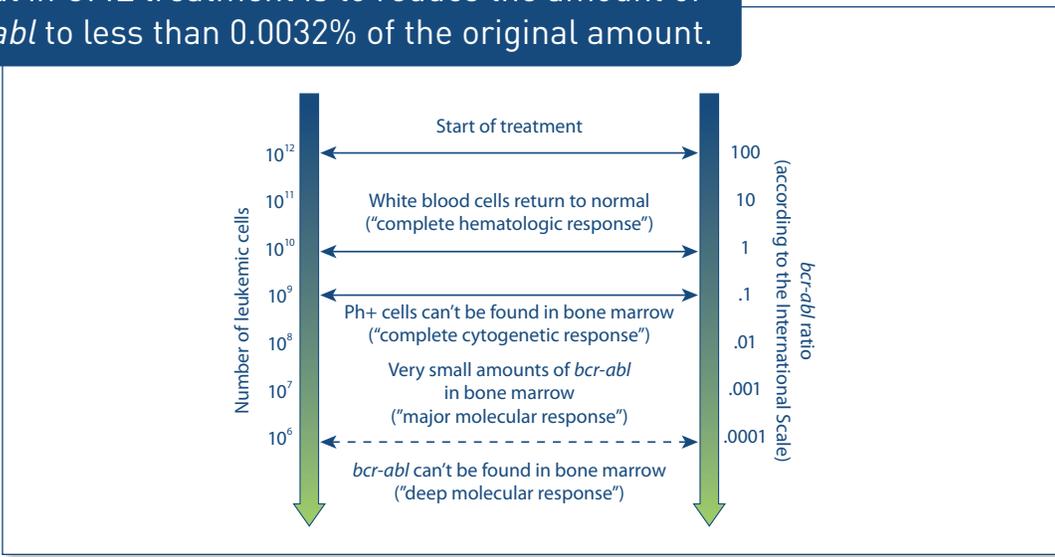


# Molecular response:

a measure of treatment success in Philadelphia chromosome-positive Chronic Myeloid Leukemia (Ph+ CML)

- Each CML cancer cell makes a genetic material called *bcr-abl* and releases it into the blood. *Bcr-abl* is the definitive genetic marker for Ph+ CML
- Doctors use a special kind of test for *bcr-abl* to tell if your cancer is still active, even if the cancer cells cannot be found using other types of tests
- By testing the amount of *bcr-abl* in your blood before treatment and then testing how much it has been reduced, doctors can tell how well treatment is working

A goal in CML treatment is to reduce the amount of *bcr-abl* to less than 0.0032% of the original amount.



- This is sometimes called “deep molecular response”
- Achieving a deep molecular response is a sign of disease remission
- Doctors may also refer to this as “molecular response 4.5,” or “MR4.5.” This means levels of *bcr-abl* in your blood are 4.5 logs, or 10,500 times, lower than they were before treatment started

Patients who are treated and achieve deep molecular response (MR4.5) are considered to be in remission, and after a period of time may have the option of living free of drug therapy.

# How molecular response will be monitored during the **ENESTop** study

- Your doctor will take a sample of your blood every 4 to 12 weeks. The sample will be sent to a Novartis designated central laboratory to be tested
- The laboratory will use a test called “polymerase chain reaction,” or “PCR,” to measure the amount of *bcr-abl* in your blood sample

PCR testing is a way to take very small amounts of genetic material — sometimes even a single strand of RNA — and make thousands of exact copies so that there is enough for doctors to measure. Doctors can then calculate how much of the genetic material is in the original test sample.



- If during the first year of the study the amount of *bcr-abl* in your blood is maintained at 0.0032% or lower (no 2 consecutive results above 0.0032%), you are considered to have a deep molecular response (MR4.5). You may be eligible to enter the treatment-free phase of the study
- During the treatment-free phase, if the amount of *bcr-abl* in your blood increases to >0.01% on 2 consecutive tests, you will no longer be considered to have a deep molecular response. You will need to restart study treatment immediately. Retesting is not necessary to confirm this result