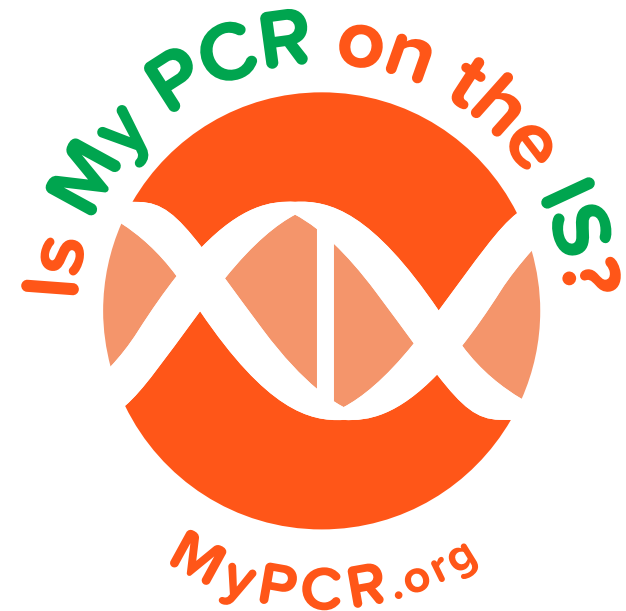


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My PCR

International Scale (IS) PCR

Frequently Asked Questions

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Q.1 What is the IS?

The 'IS' stands for 'International Scale'. International Scale is a means for standardizing and validating a patient's PCR test results. It refers to a reference range developed for reporting of quantitative PCR results for Bcr-Abl for patients with Ph+ (Bcr-Abl+) leukemias.

The International Scale (IS) was developed as a result of the landmark IRIS trial. In this trial, untreated blood samples of 30 patients were shared between three precise and experienced PCR laboratories (Seattle, London, Adelaide), using the same control gene (BCR) to establish a typical starting point (untreated level) as well as a point which represented a 1000-fold reduction (3-log reduction) from the starting point. The mean untreated level was defined as 100% and a 'major molecular response', or MMR, was defined at 0.1% in these labs. MMR, a further improvement over complete cytogenetic response (CCyR), is an important landmark for patients.

From this starting point, other labs using different systems could normalize their results so the scale used around the world would be the same: at diagnosis a CML patient's PCR value would be in the range of 100% (+/-) and a major molecular response would come in at 0.1%.

Q.2 Why is it important to standardize PCR labs?

It is important to standardize PCR labs so that physicians in different medical centers or offices can all 'speak the same language' and 'use the same tool to measure'. Results can be compared between labs and centers and response milestones understood and confirmed. Without standardization of PCR for Bcr-Abl it is hard to know how to interpret changes in Bcr-Abl levels- for example, does the change represent loss of a treatment milestone? Is the change the result of variations in the instrument used to run the PCR test?

PCR monitoring of Bcr-Abl is a crucial part of monitoring response to treatment for Chronic Myeloid Leukemia (CML). Guidelines describing the best way to navigate treatment options, especially early in treatment, are based on PCR results reported on the International Scale. For example, the first milestone in updated guidelines for management of CML treatment suggest PCR testing at three months of treatment looking for a reduction in Bcr-Abl to less than 10% in the 'IS'. Without IS standardization, deciding if milestones are met or not, or lost, are challenging if not impossible!

Q.3 What happens if my PCR is not standardized?

Indeed many quality medical centers and CML experts do not have access yet to 'IS PCR'. In the absence of results reported using this scale, treating physicians can inquire for key details about the way the test was run and the parameters of the assay to accurately quantify response and potentially estimate depth of response as is done with IS reporting. It is somewhat unreliable and challenging, however, to make such estimations and this can often lead to under- or over-estimation of response; thus caution is recommended for any extrapolation.

At the very least, in the absence of IS reporting it is recommended that a patient's PCR is always done in the same lab to minimize variations and to improve the ability to interpret changes over time.

Q.4 What should I ask of my doctor with regards to IS PCR?

ASK WHAT YOUR PCR RESULTS ARE ON THE IS SCALE!

Physicians caring for those with CML should know the important role PCR testing has in making the diagnosis and more importantly in following someone's response to treatment. If results are reported on the IS it is much easier to convey how someone is doing relative to well-established 'milestones' of treatment response.

Patients should ask their physicians if there is an IS standardized lab available to run their PCR, and to use it preferentially and consistently. In some countries there are resources available to help patients access IS PCR. For country specific inquiries write to info@themaxfoundation.org.

If you are a provider caring for a person living with CML: Our goal should be to provide IS PCR for our patients as best practice; if you are a patient with CML: It is YOUR CML and YOUR RESPONSE, so you ALWAYS DESERVE TO KNOW!