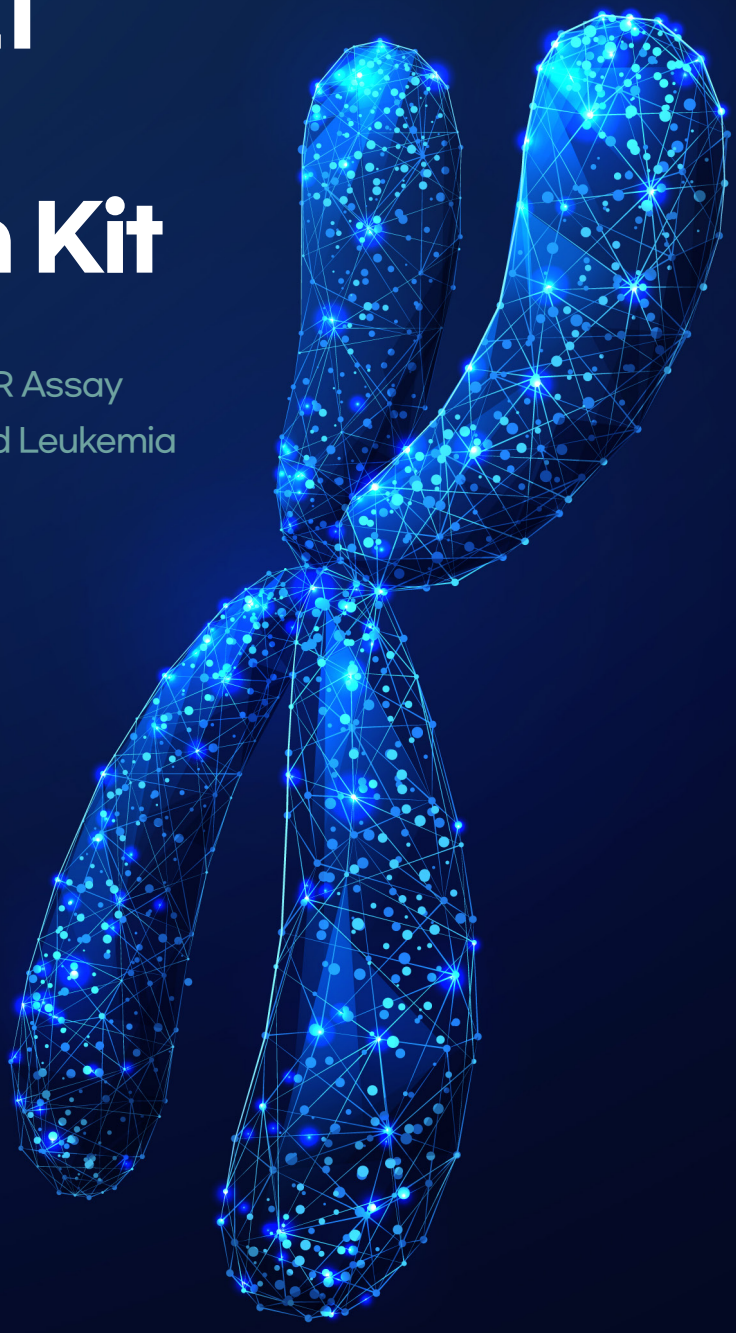
Dr. PCR™ BCR-ABL1 Major IS Detection Kit

Highly Sensitive Digital PCR Assay
Monitoring Chronic Myeloid Leukemia

CE IVD



OPTOLANE
Digital Diagnostics

Contents

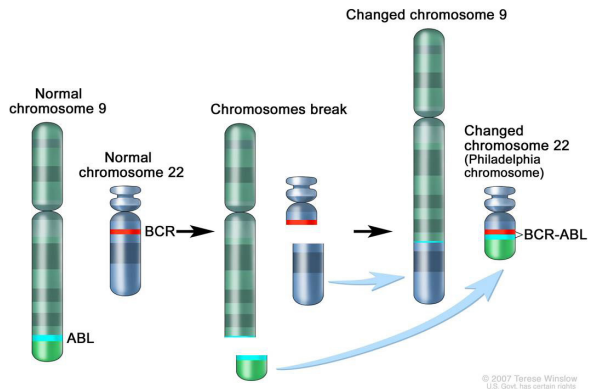
TECHNOLOGIES

Semiconductor-based
Real-Time Digital PCR (Dr. PCR™)

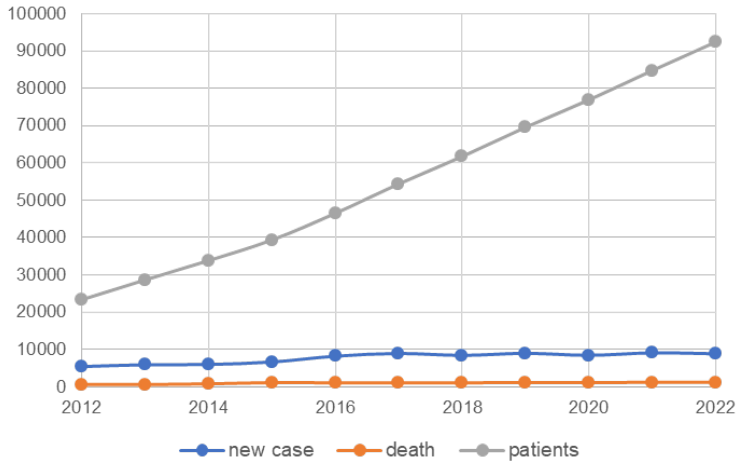
The Need

Molecular diagnosis of CML and patient monitoring is based on quantification of BCR-ABL1 transcript levels

Philadelphia Chromosome, biomarker of CML[1]



CML statistics in the USA[4]



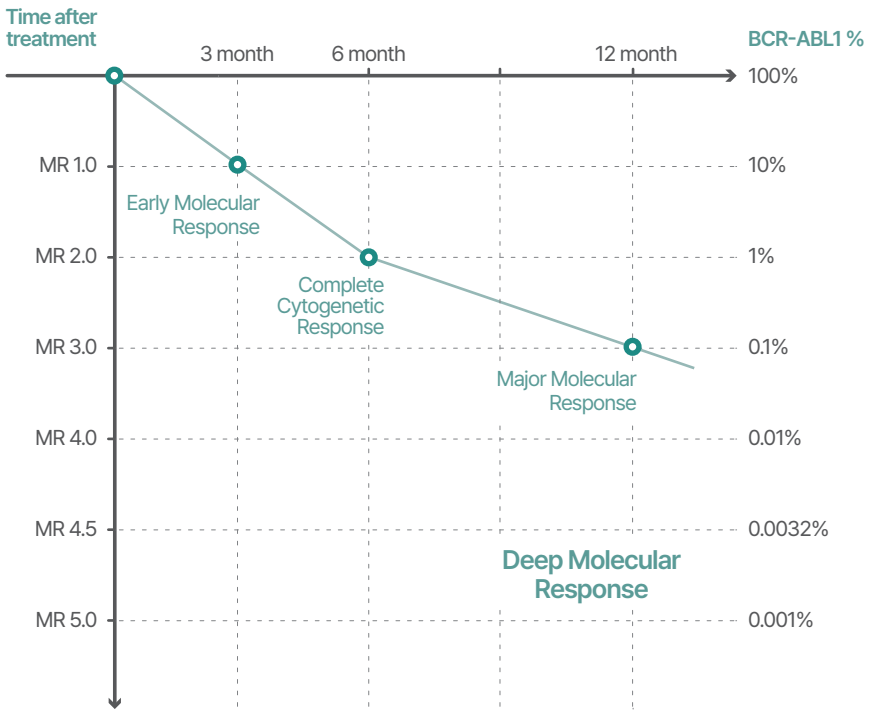
Chronic myeloid leukemia (CML) is caused by the production of BCR-ABL1 fusion protein due to chromosomal translocation and accounts for 15% of adult leukemias.[2]

CML often has no clinically evident symptoms. Therefore, some patients are diagnosed incidentally through medical examination. In the early stages of the disease, fatigue or abdominal pain occur, and infection and haemorrhage cause death. With affects on medical improvement and an aging population, the number of patients is increasing every year.[3]

[1] Terese Winslow, 2007 [2] Michael W. Deininger, 2021 [3] http://seer.cancer.gov, 2021 [4] Rebecca L Siegel, 2012~2022

Clinical practice to guide therapeutic decisions

Why is it critical to achieve a deep molecular response in chronic myeloid leukemia?



BCR-ABL1 transcript levels on the International Scale

[From Criteria for TKI Discontinuation by NCCN guideline v2021.02]

1. Stable molecular response (MR4; BCR-ABL1 ≤0.01% IS) for ≥2 years.
2. Access to a reliable qPCR test with a sensitivity of detection of at least MR4.5 (BCR-ABL1 ≤0.0032% IS).

IS (International Scale) is the ratio of the BCR-ABL1 gene to the normal ABL1 gene in the blood as a percentage. IS is an important criterion for judging the cancer condition and medicine in the treatment of CML patients. NCCN* recommends confirming IS by qPCR once every 3 months after TKI** treatment.

TKI treatment can be stopped when a patient shows a sufficiently low IS. NCCN defines this as when the IS is maintained at 0.01% for more than 2 years. However, a recurrence rate was 28% when the treatment was discontinued at the 0.01% IS stage.[5] Thus, detection techniques with a high sensitivity more than MR 4.5 have a strong medical value in BCR-ABL1 monitoring.

*NCCN, National Comprehensive Cancer Network **TKI, Tyrosine kinase inhibitor

[5] Stuckey, Ruth, Juan Francisco López Rodríguez, and María Teresa Gómez-Casares, 2022

Dr. PCR™

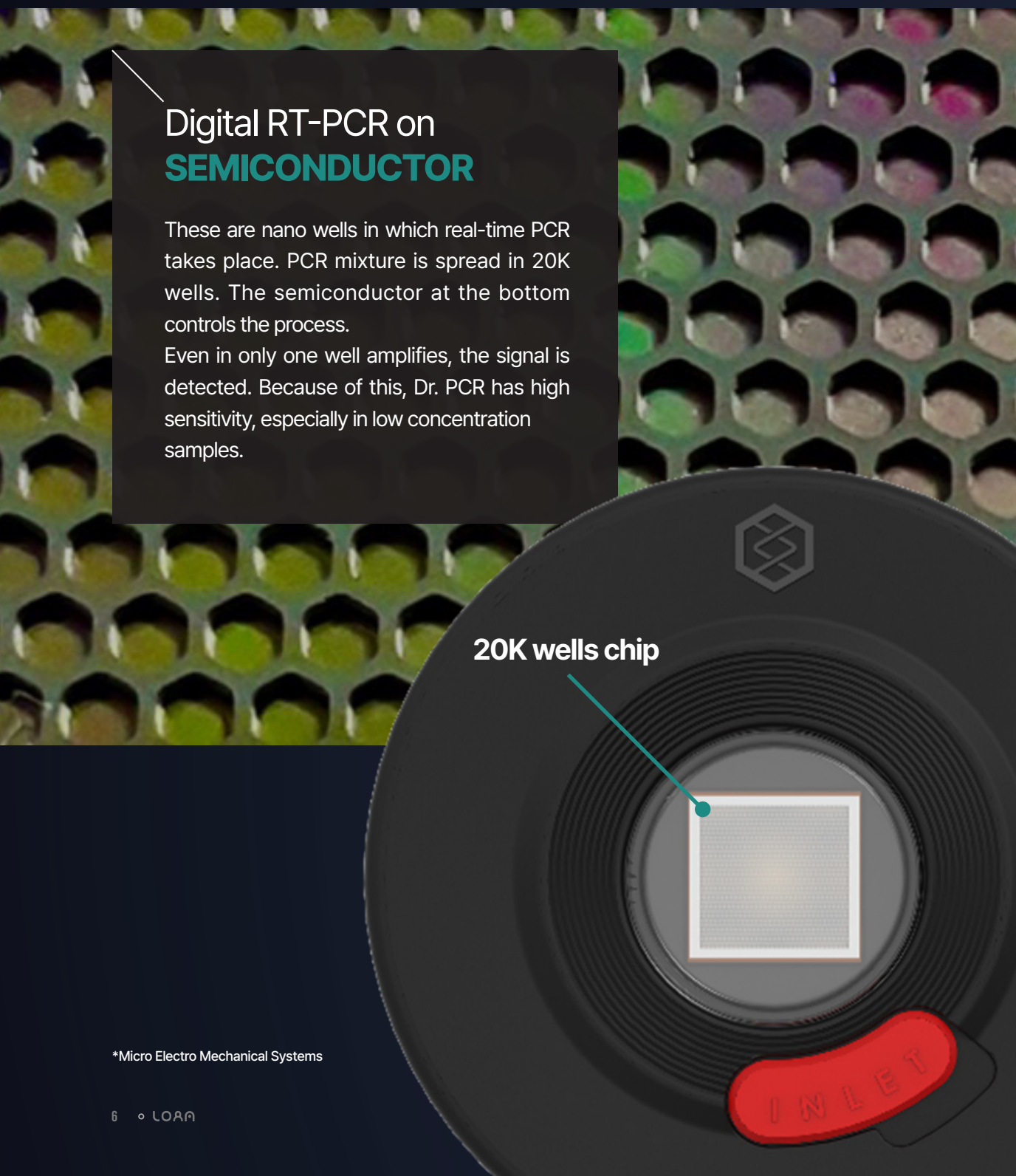
20K wells Chip Inside

Silicon MEMS* and microfluidics technology

Digital RT-PCR on SEMICONDUCTOR

These are nano wells in which real-time PCR takes place. PCR mixture is spread in 20K wells. The semiconductor at the bottom controls the process.

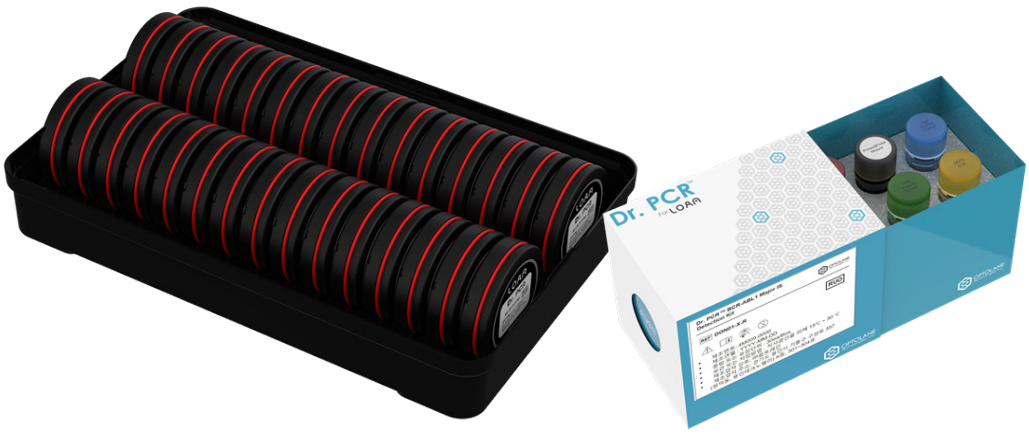
Even in only one well amplifies, the signal is detected. Because of this, Dr. PCR has high sensitivity, especially in low concentration samples.



*Micro Electro Mechanical Systems

The Solution

Dr. PCR™ BCR-ABL1 Major IS Detection Kit



High precision and accuracy

Minimal variability across dynamic range of IS and MR values

Absolute quantification

Digital Real-time PCR based platform which leads to no need of the standard curves necessary for RT-PCR.

1 2
3 4

Fast & simplified workflow

1.5 hr for PCR running time except RNA extraction. Easy to prepare the samples.

Walkaway automation

Onestep real-time digital PCR from cDNA synthesis to result output.

	OPTOLANE (Dr. PCR™ BCR-ABL1 Major IS Detection Kit)	B company	C company
PCR principle	**Digital PCR**	Digital PCR	qPCR
Detection mode	**Real-time**	End point	Real-time
Absolute quantification	**Capable**	Capable	Incapable
Running time	**1.5 hrs**	6 hrs	2.5 hrs
Detection capability	**MR 4.6 (0.0025% IS)**	MR 4.7 (0.002% IS) *Two wells	MR 4.5 (0.003% IS)
Target region	**e13a2, e14a2**	e13a2, e14a2	e13a2, e14a2

Result Analysis

Display in LOAA - Data exporting in PDF and HL7 support

Distribution per channels & IS value

Ch01 : BCR-ABL1 Ch02 : ABL1

Scatter chart change by cycle

Amplification curves for each wells

Scatter chart

Performance

Analytical performance

· Accuracy data

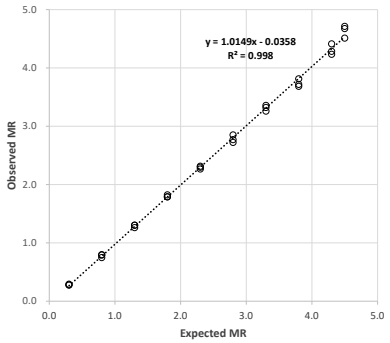
LOT No.	Samples	Slope	Intercept	R^2 Value
1	1st WHO International Genetic Reference Panel for the quantitation of BCR-ABL1 translocation (NIBSC code: 09/138)	0.9862	0.0339	0.9946
2		1.0126	0.0017	0.9985
3		0.9751	0.0317	0.9973

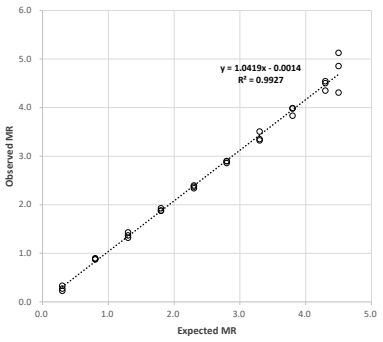
· Sensitivity and specificity

	Dr. PCR™ BCR-ABL1 Major IS Detection Kit
Limit of blank (LOB)	0
Limit of detection (LOD)	0.0025%IS (MR 4.6)
Limit of quantification (LOQ)	0.0025%IS (MR 4.6)
Measurement range (e13a2, e14a2)	50 - 0.0025%IS (MR 0.3 - MR 4.6) *below graph

· Precision data

Sample	Target conc.	n	%IS			MR level		
			Mean	SD	%CV	Mean	SD	%CV
MR2	1.000 %IS (MR 2.000)	90	1.189	0.1018	8.56	1.926	0.0371	1.92
MR3	0.100 %IS (MR 3.000)	90	0.119	0.0178	14.99	2.930	0.0650	2.22
MR4	0.010 %IS (MR 4.000)	90	0.012	0.0040	33.65	3.951	0.1639	4.15

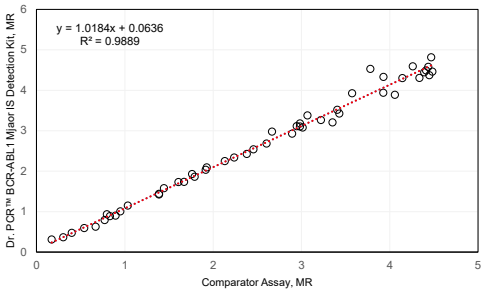




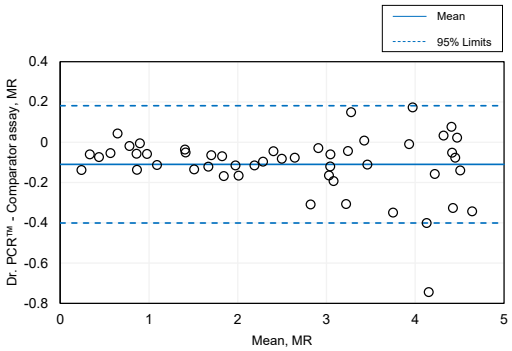
Performance

Clinical performance

The Clinical performance of Dr. PCR™ BCR-ABL1 Major IS Detection Kit was evaluated by comparison to an MFDS*-cleared molecular assay, which detects and quantifies the mRNA transcripts for the p210 translocation types and uses the ABL1 gene as an endogenous control mRNA transcript.
Frozen RNA specimens extracted from EDTA whole blood samples collected from patients diagnosed with Chronic Myeloid Leukemia (CML) at any stage of the disease were used. These samples were obtained after the initial diagnosis, whether the patients had received Tyrosine Kinase Inhibitor therapy or other treatments for CML or not.



Correlation between Dr. PCR™ BCR-ABL1 Major IS Detection Kit and conventional RT-PCR kit on 80 patient samples (solid white circles).
$y = 1.1084x + 0.0636$, $R^2 = 0.9889$.



Bland-Altman Plot. Bias between the two assays appears low and uniform by visual inspection and mean, 95% limits values.

		Comparator (RT-PCR)		Total
		Positive	Negative	
Dr. PCR™ BCR-ABL1 Major IS Detection Kit	Positive	50	0	50
	Negative	0	30	30
Total		50	30	80

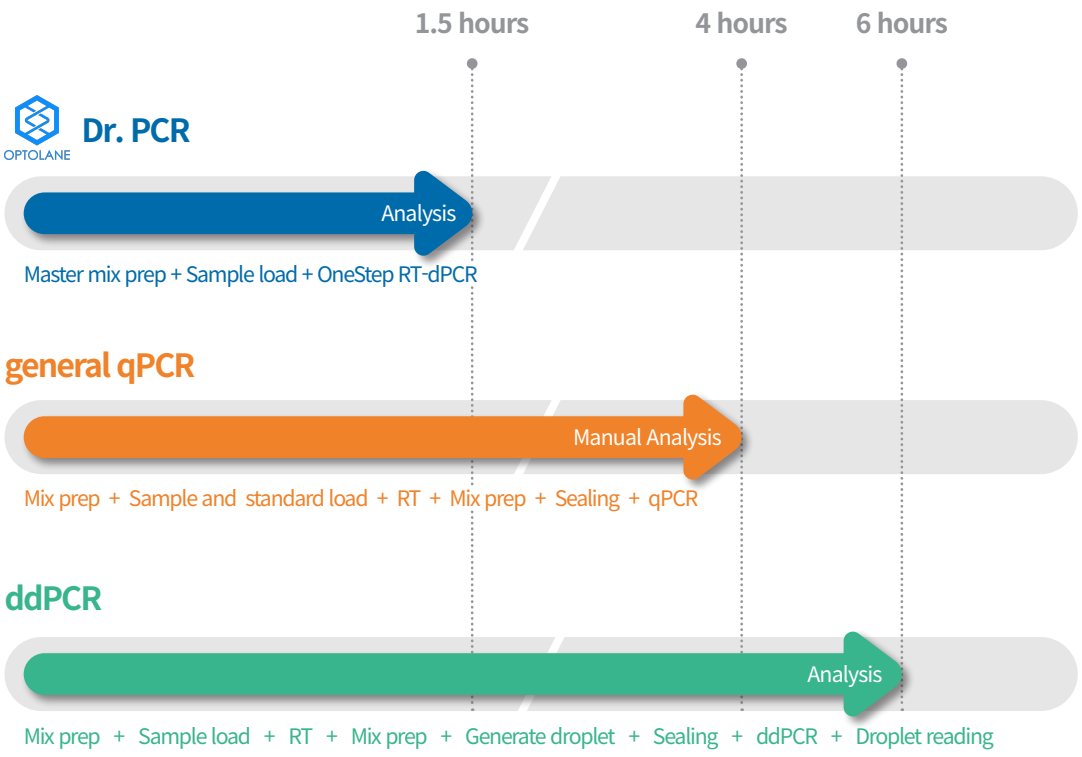
Clinical sensitivity and specificity are 100%.

*Ministry of Food and Drug Safety, Republic of Korea

Simplifed workflow by LOAA platform

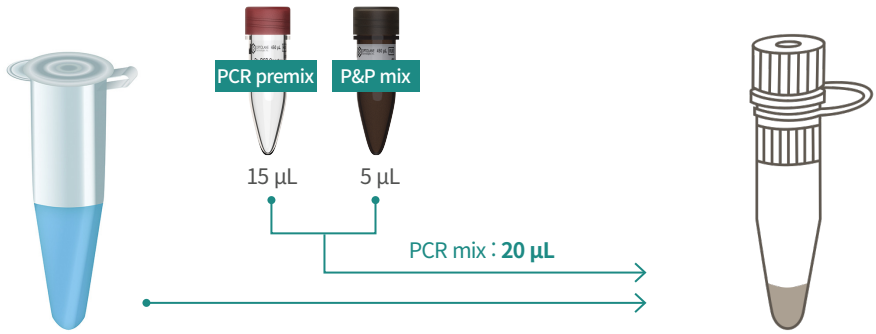
Improved efficiency & No calibration required

JUST 3 STEPS TO GET RESULT, NO MORE COMPLICATION



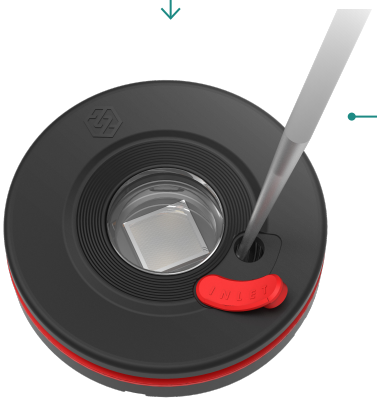
Workflow

One-day report system for BCR-ABL1 molecular diagnostic testing



1 **10 µL**
RNA sample

2 **30 µL**
Final loading volume



Small footprint saves you bench space

3 Inject to cartridge

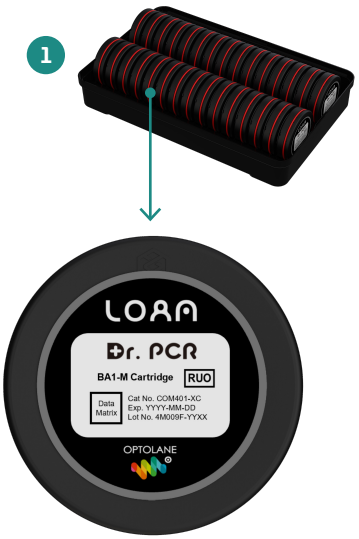
4 Loading the cartridge on the tray

YouTube
QR link to
BCR-ABL1 major IS Detection Kit
workflow Video

Dr. PCR™ BCR-ABL1 Major IS Detection Kit

LOAA Analyzer (On-Point)

Dr. PCR™ Cartridge



No.	Reagents	Unit	Quantity
1	Dr. PCR™ BA1-M cartridge	30 EA	1 Box
2	Dr. PCR™ Onestep dRT-PCR Mixture (2X)	450 µL/ tube	1 tube (red cap)
3	BCR-ABL1/ABL1 Primer & Probe Mixture	150 µL/ tube	1 tube (amber tube)
4	High Positive Control	100 µL/ tube	1 tube (blue cap)
5	Low Positive Control	100 µL/ tube	1 tube (green cap)
6	DEPC treated D.W.	200 µL/ tube	1 tube (yellow cap)

Ordering Information

LOAA instruments, cartridges and reagents

· Instruments

Catalogue Number	Products	Quantity
LAM301-01	LOAA Analyzer (On-Point)	1 EA

· Cartridges & Reagents

Catalogue Number	Products	Quantity
DON01-X	Dr. PCR™ BCR-ABL1 Major IS Detection Kit *Reagents included	1 Kit (30 Tests)

Reference

[1] Terese Winslow LLC, Medical and Scientific Illustration, Philadelphia Chromosome, 2007 [2] Michael W. Deininger, MD, PhD, Chronic Myeloid Leukemia,Version 2.2021 [3] http://seer.cancer.gov, 2022 [4] Rebecca L Siegel, Cancer Statistics, 2012~2022 [5] Stuckey, Ruth, Juan Francisco López Rodríguez, and María Teresa Gómez-Casares. "Discontinuation of Tyrosine Kinase Inhibitors in Patients with Chronic Myeloid Leukemia: a Review of the Biological Factors Associated with Treatment-Free Remission." Current Oncology Reports (2022): 1-12.

PCR Analyzer

LOAA Analyzer On-Point

· Specifications

Purpose	Real-time digital PCR amplification and analysis
Capacity	1 sample / run
Turnaround time	1.5 hrs
No. of channels	2
Display	15.6” FHD LCD (IPS)
Touch	Multi-touch type
Barcode scanner	Aztec, Codabar
Storage capacity	690 – 1,500 tests
Language	English, Spanish
Weight	3 kg
Dimension (WxDxH)	21 cm x 25 cm x 24 cm
Result export	USB memory export LIS connection Closed network system

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