

# BCR-ABL1 t (9;22) ONE-STEP RT-PCR QUALITATIVE DETECTION (p210, p190, p230)

## ORDERING INFORMATIONS

REF: *ONC-010-25*  
CND Code: *W01060208-T(9;22)*  
RDM Code: *2079229/R*  
Tests: *25*  
Reactions: *31 x 3*  
Manufacturer: *BioMol Laboratories s.r.l.*

## CONTENTS OF THE KIT

The kit consists of reagents for reverse transcription and Real-Time PCR amplification  
*\*the reagents for RNA extraction are not supplied in the kit.*

For in vitro diagnostic use



## PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-SOMATIC MUTATIONS**. Qualitative detection of the t(9;22) BCR-ABL1 translocation by RT-PCR technique (Reverse transcriptase-polymerase chain reaction) and subsequent detection in Real-time-PCR.

**The device has been developed in accordance with Europe Against Cancer (EAC) guidelines** and optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris bCUBE and Hyris bCUBE3 with Hyris bAPP.

## SCIENTIFIC BACKGROUND

Myeloproliferative neoplasms (MPNs) are hematologic malignancies characterized by the proliferation of one or more myeloid lineages: granulocytic, erythroid, megakaryocytic, and/or mast cell. According to the 2016 World Health Organization criteria, the MPN classification includes seven subcategories: chronic myeloid leukemia (CML), chronic neutrophilic leukemia, polycythemia vera (PV), primary myelofibrosis (PMF), essential thrombocythemia (ET), eosinophilic leukemia chronic - not otherwise specified and MPN, unclassifiable (MPN-U).

The Philadelphia chromosome (Ph) derived from the translocation between chromosomes 9 and 22 with subsequent BCR-ABL1 fusion, is present in about 95% of cases of chronic myeloid leukemia (CML), in 25-30% of cases of acute lymphoblastic leukemia (ALL) of adults and in 2-4% of ALL of children.

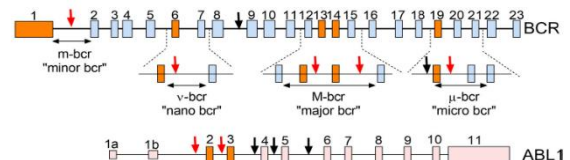
- § Am J Hematol. 2024 Aug 2;doi: 10.1002/ajh.27443. Online ahead of print. Chronic myeloid leukemia: 2025 update on diagnosis, therapy, and monitoring
- § Genetic basis and molecular pathophysiology of classical myeloproliferative neoplasms. Blood. 2017 Feb 9; 129(6):667-679. Review.
- § The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19; 127(20): 2391-405.
- § Leukemia. 2015 May;29(5):999-1003. doi: 10.1038/leu.2015.29. Laboratory recommendations for scoring deep molecular responses following treatment for chronic myeloid leukemia
- § Guidelines for the measurement of BCR-ABL1 transcripts in chronic myeloid leukaemia. Br J Haematol. 2011 Apr; 153(2):179-90.
- § J Clin Oncol. 2009 Dec 10;27(35):6041-51. doi: 10.1200/JCO.2009.25.0779. Epub 2009 Nov 2. Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet
- § Leukemia. 2009 Nov;23(11):1957-63. doi: 10.1038/leu.2009.168. Epub 2009 Aug 27. Harmonization of molecular monitoring of CML therapy in Europe
- § European LeukemiaNet (2009). Chronic myeloid leukemia: an update of concepts and management recommendations of European LeukemiaNet. Journal of Clinical Oncology, 27, 6041-6051.
- § Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms. Leukemia. 2008 Jan; 22(1):14-22. Review.
- § Leukemia. 2003 Dec;17(12):2318-57. doi: 10.1038/sj.leu.2403135. Standardization and quality control studies of 'real-time' quantitative reverse transcriptase polymerase chain reaction of fusion gene transcripts for residual disease detection in leukemia - a Europe Against Cancer program.

## CLINICAL SIGNIFICANCE

The BCR-ABL1 rearrangement results in the generation of fusion proteins with constitutive tyrosine kinase activity. Based on the specific breakpoints of the rearrangement, different isoforms of the BCR-ABL1 fusion protein are generated, which correlate with different leukemic phenotypes.

Three breakpoint regions in the BCR gene have been described: major (M-BCR), minor (m-BCR), and micro ( $\mu$ BCR). More than 95% of Ph+ CML patients have the rearrangement in the M-BCR region (p210 BCR-ABL1), with the e13a2 and e14a2 transcripts most represented. The breakpoint in the m-BCR region generates the p190 BCR-ABL1 protein with the e1a2 transcript mostly represented. A third BCR-ABL1 protein, p230BCR-ABL1, can also be observed.

The ONC-010 medical device allows the qualitative detection of the t(9; 22) BCR-ABL1 translocation and the M-bcr (e14a2, e13a2, e13a3 and 14a3), m-bcr (e1a3 and e1a2), and  $\mu$ -bcr (e18a2, e18a3, e19a2 and e19a3) transcripts by RT-PCR (Reverse transcriptase-polymerase chain reaction) technique and subsequent detection in Real-time PCR.



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DESCRIPTION	LABEL	VOLUME	STORAGE
		<b>ONC-010-25</b>	
Mix oligonucleotides and probes	Mix PCR p210 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR p190 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix oligonucleotides and probes	Mix PCR p230 BCR-ABL1 4X	1 X 155 µl	- 20 °C
Mix buffer and RT enzyme and Taq-polymerase	Mix RT-PCR 4X	1 X 465 µl	- 20 °C
Deionized H <sub>2</sub> O	Deionized H <sub>2</sub> O	1 x 1 ml	- 20 °C
Recombinant RNA	<b>Positive control</b> p190/p210/p230-abl	1 X 90 µl	- 20 °C
Recombinant RNA	<b>Negative control</b>	1 X 90 µl	- 20 °C

## TECHNICAL CHARACTERISTICS

### COD. ONC-010-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Total RNA extracted from white blood cells from whole blood or bone marrow aspirate.
CONTROLS	Recombinant RNA for at least 3 analytical sessions (ONC-010-25); positive control for p190/p210/p230 and abl; negative control for abl.
TECHNOLOGY	RT-PCR ONE STEP in Real-time; oligonucleotides and specific probes for the translocation and for the abl gene; 2 FAM/HEX fluorescence channels
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx, Agilent AriaDx, Hyris b-CUBE and Hyris b-CUBE3 with Hyris bAPP.
RUNNING TIME	100 min
THERMAL CYCLING PROFILE	1 cycle at 50 °C (25 min); 1 cycle at 95 °C (2 min); 45 cycles 95 °C (5 sec) + 60 °C (45 sec).
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 10,8 copies; ≥ 0,0032%
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%