OTH06

Measurable Residual Disease Detection in Mantle Cell Lymphoma (MCL) Subjects Using NGS B-Cell MRD Assay

Presha Shah[1], Austin Jacobsen[1], Oscar Diaz II[1], Natalie Hill[1], Alyssa Zlotnicki[1], Alejandro Medina[2] and Ying Huang[1]
[1]Invivoscribe, Inc.; San Diego, United States and [2]Hospital Universitario de Salamanca; Salamanca, Spain

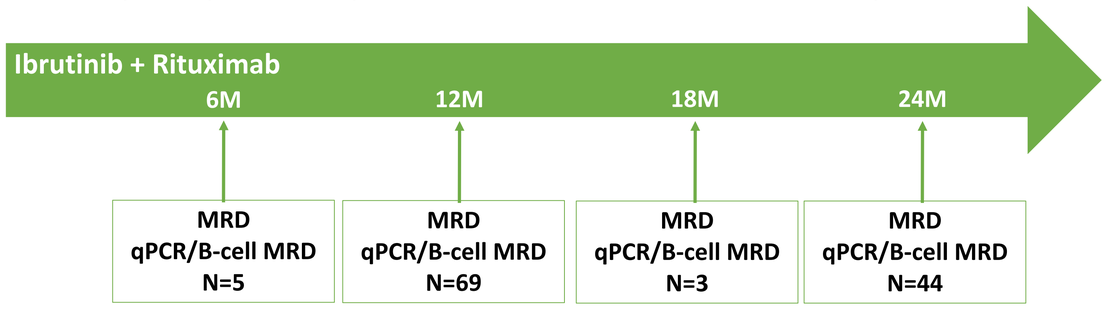
Background

Mantle Cell Lymphoma (MCL) is an aggressive, rare form of non-Hodgkin B-cell lymphoma. Measurable Residual Disease (MRD) assessment can provide useful information when assessing and tracking response to therapy, refining treatment and predicting clinical outcome for subjects with B-cell lymphoproliferative diseases.

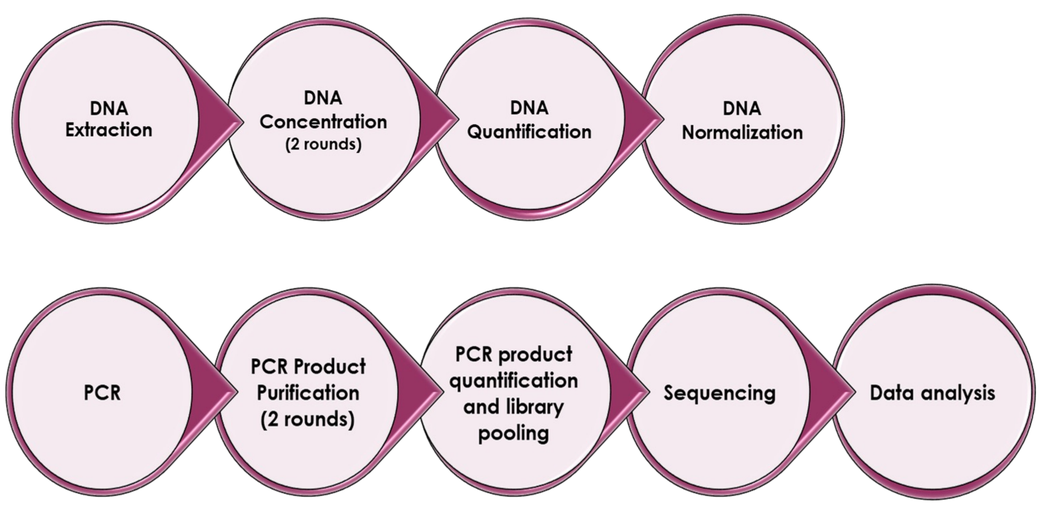
One method of MRD detection is to identify and track specific clonal immunoglobulin heavy chain (*IGH*) gene rearrangement sequences on a next-generation sequencing (NGS) platform. Here, we present the NGS-based B-cell MRD Assay with 10^{-6} sensitivity for detecting MRD in malignancies in mantle cell lymphoma (MCL).

Materials and Methods

Residual DNA samples from different specimen types (44 BM and 77 PB) at different post-treatment time points (6, 12, 18 and 24 months) were obtained from anonymized 47 MCL subjects that had been enrolled in a study approved by the Spanish Group of Lymphoma and Autologous Stem Cell Transplantation (clinical trial: NCT02682641, publication reference: 10.1200/JCO.21.02321). 121 of these follow up samples were tested by the B-cell MRD Assay (Invivoscribe) by tracking the clonal sequences detected in corresponding baseline samples. Among them, 90 follow up samples were paired PB (n=45) and BM (n=45) samples.



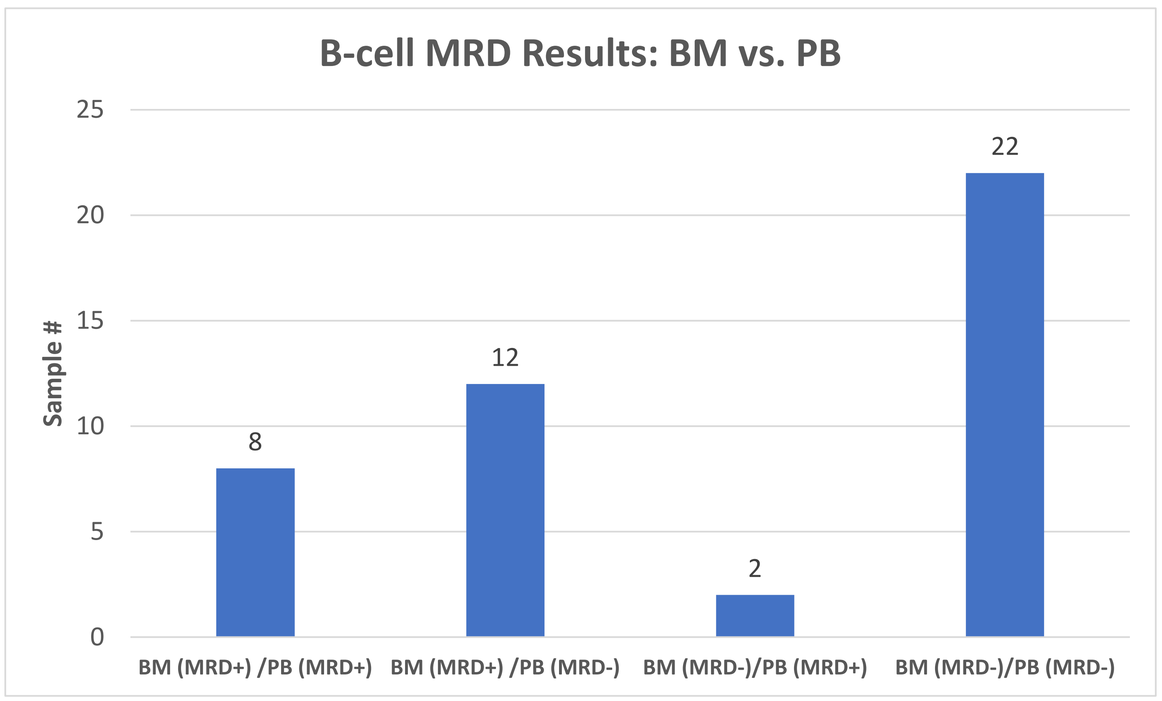
The B-cell MRD Assay workflow consists of DNA extraction and PCR based library preparation with proprietary multiplex master mixes targeting either *IGH* Framework 1 (FR1) or 3 (FR3) regions, which both track the subject- and tumor-specific CDR3 sequence. Purified libraries are then equimolar pooled and sequenced on Illumina's NextSeqDx platform. The FASTQ output files from sequencing are analyzed using Invivoscribe's B-Cell MRD Software-NextSeqDx. Results from Invivoscribe were compared to the results from Salamanca lab that were generated by qPCR.



Results: B-cell MRD Detection Rates at Different Time points

B-cell MRD Results	Time point at Different Post Treatment				
	6M (%) N=5	12M (%) N=69	18M (%) N=3	24M (%) N=44	Overall (%) N=121
MRD Detected	2 (40%)	25 (36%)	2 (67%)	13 (30%)	42 (35%)
MRD Not Detected	2 (40%)	41 (59%)	1 (33%)	29 (66%)	73 (60%)
Invalid	1 (20%)	3 (4%)	0 (0%)	2 (3%)	6 (5%)

Results: B-cell MRD Detection for BM/PB Paired Samples



Results: B-cell MRD vs qPCR

MRD Detection Results (*n=84)		qPCR Reference Method (Salamanca)	
B-cell MRD NGS Method (Invivoscribe)	N=84	MRD Detected	MRD Not Detected
	MRD Detected	19	12
	MRD Not Detected	5	48
* Consists of all samples (BM and PB) with MRD results available by both methods	Concordance	80%	
	PPA	79%	
	NPA	80%	

Conclusions

- Good concordance was observed for MRD detection in post treatment MCL samples between B-cell MRD NGS method and qPCR reference method.
- It was observed that MRD BM specimens type was more sensitive in detecting MRD compared to PB specimens based on paired PB and BM results.
- The B-cell MRD Assay can be utilized for MRD detection in follow-up sample types for MCL subjects.

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