Supplementary material

Methods - Sequencing

Library preparation, sequencing and raw data processing were performed by FIMM Genomics NGS Sequencing unit at University of Helsinki supported by HiLIFE and Biocenter Finland. Up to 50 nanograms of available residual gDNA from Euro-MRD probe design derived from affected MCL lymph nodes (LN), bone marrow (BM) and peripheral blood (PB) was processed according to Twist Library Preparation EF 2.0 with Enzymatic Fragmentation DOC-001239 REV 1.0 and Twist Target Enrichment Protocol DOC-001085 REV 2.0 manual (Twist Bioscience, San Francisco, CA, USA) with following modifications. Following adapters were used for ligation: IDT xGEN unique dual index (UDI) with unique molecular identifier (UMI), lengths 8 bp or 10 bp, 4 µl of 15 µM (Integrated DNA Technologies, Coralville, IA, USA). Library quantification and quality check was performed using LabChip GX Touch HT High Sensitivity assay (PerkinElmer, Waltham, MA, USA) and Qubit Broad Range DNA Assay (Thermo Fisher Scientific, Waltham, MA, USA). Libraries were pooled up to 16-plex reactions according to concentration (Qubit BR assay). The target enrichment was performed using Twist custom panel probes targeting lymphoma-relevant targets including *TP53* coding exons identical to previously reported (PMID: 34932792). The captured library pools were quantified for sequencing using QuantStudio 5 Collibri Library Quantification kit (Thermo Fisher Scientific, Waltham, MA, USA) and LabChip GX Touch HT High Sensitivity assay (PerkinElmer, Waltham, MA, USA). Sequencing was performed with Illumina NovaSeq 6000 (Illumina, San Diego, CA, USA) system using S4 flow cell with lane divider and v1.5 chemistry. Read length for the paired-end run was 101+19+10+101 bp and demultiplexing of samples was performed 101+i8y9+i8+101 bp and 101+i10y9+i10+101 depending the used Dual Index set. The analysis was performed using the Illumina DRAGEN pipeline (version 07.021.645.4.0.3) with UMI and reference genome GRCh38. Tumors with available BM/PB gDNA with no MCL detected by flow cytometry were analyzed with tumor+normal pipeline and those without with tumor-only pipeline. The resulting hard-filtered variant lists were annotated with Annovar (PMID: 20601685), filtered for somatic quality (SQ ≥ 6.5 or ≥17.5, for tumor-only or tumor-normal pipelines, respectively) and known polymorphisms were dropped using ExaC database (unreported or adjusted allele frequency < 0.0001). For LN samples, only variants with variant allele fraction (VAF) ≥ 10% were kept. For BM and PB samples used in genotyping, only variants with VAF falling between range of 0.25–1.10 times the fraction of MCL involvement in the genotyping tissues as measured by flow cytometry were kept. Coding variant types including stopgain/stoploss, nonsynonymous single nucleotide variant, nonframeshift/frameshift insertion/deletion and splicing variants within targeted regions padded with 10 base-pairs were considered.

Table 1S

Treatment emergent adverse events (maximal grade)

	Grade 1-2	Grade 3	Grade 4
Haematological adverse events			
Thrombocytopenia	Not reported	13 (22%)	8 (14%)
Anaemia	Not reported	7 (12%)	1 (2%)
Neutropenia	Not reported	28 (47%)	24 (41%)
Non-haematological adverse events			
Gastrointestinal	32 (54%)	3 (5%)	0
Infections	15 (25%)	6 (10%)	2 (3%)
Cutaneous	24 (41%)	6 (10%)	0
Respiratory	15 (25%)	1 (2%)	1 (2%)
Neurological	19 (38%)	1 (2%)	1 (2%)
Muscular	14 (32%)	0	0
CNS	8 (14%)	1 (2%)	0
Cardiovascular	8 (14%)	3 (5%)	1 (2%)
Renal	6 (10%)	1 (2%)	0
Hepatic	5 (8%)	2 (3%)	1 (2%)

Data are n (%). For grade 1-2 events, only the ones occurring in ≥10% of patients are reported. Haematological adverse events less than grade 3 were not reported.

Figure 1S

Overview of patients included in the MCL7-Valeria trial