

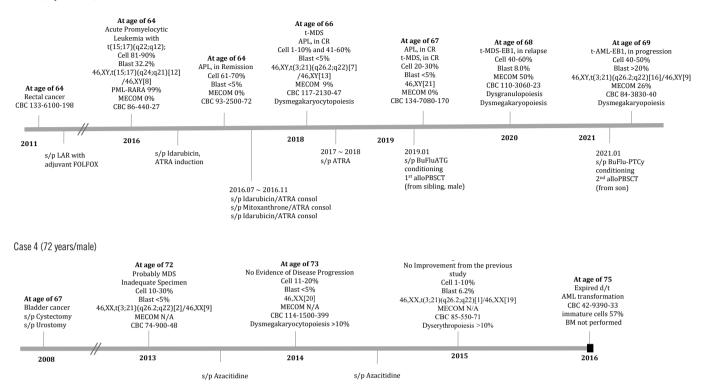
**Supplemental Data Figure S1.** Progression timelines with patient information from BM, CBC, and cytogenetic analyses. Disease progression and treatments are presented in the timeline by year. CBC, hematologic diagnosis, and bone marrow blast counts are shown. The chromosome and FISH results are described. The black rectangle indicates a patient's death.

Abbreviations: M, male; F, female; BM, bone marrow; Cell, cellularity; CBC, complete blood count; APL, acute promyelocytic leukemia; AlloPBSCT, allogeneic peripheral blood stem cell transplantation; MCR, marrow complete remission; DLI, donor leukocyte infusion; GVHD, graft-versus-host disease; d/t, due to; CR, continuous remission; THRA, total hip replacement arthroplasty; VATS, video-assisted thoracic surgery; LAR, low anterior resection; Bu, busulfan; Flu, fludarabine; Cy, cyclophosphamide; ATG, antithymocyteglobulin; PTCy, transplantation cyclophosphamide; ICE, ifosfamide, carboplatin, and etoposide; Highdose araC, high-dose cytarabine; FOLFOX, folinic acid, fluorouracil, and oxaliplatin; ATRA, all-trans-retinoic acid.

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## Case 3 (64 years/male)



Supplemental Data Figure S1. Continued.



1. Bioinformatic analyses

• Sequencing data (FASTQ)

→ Aligning (hg 19 reference genome)

→ Sorting and indexing BAM files (SAMtools)

→ Removing duplicated reads (Picard MarkDuplicates)

→ Detect errors (GATK BaseRecalibrator)

→ Variant calling (GATK HaplotypeCaller)

→ Annotate mutations (Annovar)

2. Variant filtering

• Population frequency < 0.01 (gnomAD, ExAC, KOVA, 1000genome, cg46, abraom, GME, Kaviar)

→ GATK hardfilter (QD: qual by depth values > 2; FS: FisherStrand values < 60, InDel < 200;)

→ MQ:RMSMappingQuality, SNPs-over 40; MQRankSum:MappingQualityRankSumTest, SNPs-over -12.5;

→ ReadPosRankSum:ReadPosRankSumTest, SNPs-over -8, InDels- over -20;

→ SOR:StrandOddsRatio, SNPs-under 3, InDels- under 10)

→ Revmoved benign and likely benign (ACMG classification)

3. Germline predisposition/Somatic variants

• Predisposition genes

→ Previously reported or known disease-associated variant

→ Systemic review of patient's disease and treatment history (e.g. PBSCT)

→ Reported pathogenicity (HGMD, ClinVar)

• Somatic variants → Reported pathogenicity (ClinVar, Cosmic, cbioportal)

→ Review of NCCN guidelines and WHO classification

→ Prediction: SIFT, Polyphen2, and CADD score

→ Sorting: Tier groups (I, II, III, IV)

**Supplemental Data Figure S2.** Variant-calling strategy for somatic and germline variants. Evaluation of the multigene target sequencing results for somatic and germline variants from bioinformatics analyses to the interpretation of the variants.

Abbreviations: PBSCT, peripheral blood stem cell transplantation; ACMG, American College of Medical Genetics; HGMD, Human Gene Mutation Database; NCCN, National Comprehensive Cancer Network; SIFT, sorting intolerant from tolerant; CADD, combined annotation-dependent depletion.