Supplement Materials:

Methods of *CSF3R* and *CALR* mutation studies

For *CSF3R* mutations: primer set used at MDACC: exon 14 forward 5′-CCACGGAGGCAGCTTTAC-3′ and reverse 5′-AAATCAGCATCCTTTGGGTG-3′; exon 17 forward 5′-CTGTCACTTCCGGCAACAT-3′ and reverse: 5′-TGGCCCAAAGACACAGTCGT-3′. Primer set used at CCF: exons 13-14 forward 5’-AGAAGTCCAACCGGGCTC-3′ and reverse: 5′-AAATCAGCATCCTTTGGGTG-3′; exon 17 forward 5’-CCAGACAGGGACAGTGGC and reverse 5’-ACCCTCCCCTCTTCTCCAG-3′. Primer set used at UNM: exon 14 forward 5'-TGTATCACATCCACCTCATGG-3′ and reverse 5'-CTCAAAATCAGCATCCTTTGG-3′. At CCF, for eventual germ-line confirmation, Genomic DNA was extracted from CD3 positive cells isolated using CD3 micro beads (Miltenyi Biotech, Biotech, CA, USA) and subjected to PCR amplification. Following amplification, the PCR products were sequenced via standard capillary electrophoresis by Applied Biosystems 3130, 3500, or 3730xl series DNA Analyzers (Carlsbad, CA, USA), and results were analyzed using Applied Biosystems SeqScape 2.7 software. Pyrosequencing for *CSF3R T618I* and *T615A* point mutations was also performed at MDACC. PCR was performed using PCR primer set forward 5’-CCG CCA GTC TGT ATC ACA TCC-3′ and reverse 5’-TCC CCT TAC CTG GGG TCA A-3′. Pyrosequencing was performed using PSQ96 HS System (Biotage AB, Uppsala, Sweden) per manufacturer’s instructions using sequencing primer CACCAACAGTACAGTCCT.

For *CALR* mutation screening, genomic DNA was isolated from bone marrow at MDACC following standard protocol. Fluorescent tagged oligonucleotide primers of exon 9 of *CALR* were used to amplify a 207 bp product: (*CALR Forward* 5′-AAGGCCCTGAGGTGTGTG-3′ (*CALR Reverse* 5′- GGGACATCTTCCTCCTCAT-3′). PCR products were subjected to standard capillary electrophoeresis by Applied Biosystems 3130xl series DNA Analyzers (Carlsbad, CA, USA). Mutations (deletion and insertions) were identified using Applied Biosystems Gene Mapper Software v4.1 (Applied Biosystems, Carlsbad, CA,, USA).

Supplement Table 1. Univariate Cox Regression Analysis of Patients with Atypical Chronic Myeloid Leukemia (aCML) and Myelodysplastic/Myeloproliferative Neoplasm-Unclassifiable (MDS/MPN-U)

	aCML		MDS/MPN-U	
	OS (p-value)	**AMLFS (p-value)**	**OS (p-value)**	**AMLFS (p-value)**
Age (years)	0.0913	0.8923	0.7453	0.6057
• ≥70 years	0.1908	0.8428	0.5217	0.5081
Sex (Female)	0.2425	0.5717	0.4927	0.2484
Increased LDH	0.1794	0.0744	0.0185	0.0224
Organomegaly	0.8047	0.4483	0.6337	0.9857
White blood cells (WBC)	0.0002	0.0003	0.0106	0.0174
• ≥50($x10^9$/dL)	0.0138	0.0636	NA	NA
• ≥40($x10^9$/dL)	NA	NA	0.0113	0.0077
Hemoglobin(g/dL)	0.9363	0.8161	0.9956	0.9954
• ≥10 g/dL	0.7426	0.8902	0.5609	0.8783
Platelets(g/dL)	0.1844	0.3604	0.0299	0.1103
• ≥450 ($x10^9$/dL) (ref)	---	---	---	---
• 100-450($x10^9$/dL)	0.1965	0.4679	0.0869	0.1718
• <100($x10^9$/dL)	0.1252	0.3316	0.0125	0.0550
Blood myeloid precursors	0.0003	0.0044	0.0008	0.0004
• ≥10%	NA	NA	0.0152	0.0145
Peripheral blood blasts	0.7246	0.4449	0.0608	0.0504
• ≥5%	0.4787	0.2055	0.3889	0.2981
Bone Marrow blasts	0.0601	0.0015	0.0188	0.0028
• <5% (ref)	---	---	---	---
• 5-9%	0.1398	0.2847	0.0565	0.0292
• >10%	0.1906	0.0140	0.0977	0.0281
Myelofibrosis (MF 2 or 3)	0.6762	0.9635	0.6891	0.7534
Dysgranulopoiesis	NA	NA	0.7863	0.6028
***Cytogenetics (**Category1)	---	---	---	---
• Category 2	0.5323	0.4863	0.3464	0.3204
• Category 3	0.9086	0.2485	0.0001	0.000
• Category 3 vs 2	0.7680	0.1306	0.0008	<.0001

*Category 1(normal or –Y), cytogenetic category 3 (complex and -7/-7q), and category 2 (all other abnormalities)

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