

Clonal dynamics using droplet digital polymerase chain reaction in peripheral blood predicts treatment responses in myelodysplastic syndrome

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Supplementary Table S1.

Pre-treatment samples were screened with an in-house NGS panel of 44 myeloid genes and the Ion Torrent sequencing platform.

ASXL1	GATA2 2-6	RAD21
BCOR	IDH1 4	RUNX1
BRAF 15	IDH2 4	SETBP1 4
CALR 9	JAK2 14	SETD2
CBL 8-9	KDM6A	SF3B1 13-16
CDKN2A	KIT 8,11,17	SMC1A 2,11,16-17
CEBPA	KRAS 2-4	SMC3 10,13,19,23,25,28
CREBBP	MPL 10	SRSF2 1
CSF3R 14-17	NF1	STAG2
CUX1	NPM1 12	TET2
DNMT3A	NRAS 2-4	TP53
ETV6	PDGFRA 12,14,18	U2AF1 2,6
EZH2	PHF6	WT1 2,7,9
FLT3 14,15,16,20	PTPN11 3,13	ZRSR2
GATA1 2	EP300	

Supplementary Table S2.

Pre-treatment NGS annotations of the found pathogenic variants. In red SRSF2 without primer for ddPCR. DNA extraction was performed on mononuclear cell pellets using Blood DNA kit on Maxwell® RSC system (Promega, Madison, WI, USA) according to the manufacturer's protocol.

Patient	Gene Symbol	Position	Transcript ID	Variant	Protein variant
1	DNMT3A	chr2:25457243	NM_175629.2	c.2644C>T	p.Arg882Cys
	EZH2	chr7:148512045	NM_004456.4	c.1633C>T	p.Gln545Ter
2	IDH2	chr15:90631934	NM_002168.2	c.419G>A	p.Arg140Gln
	DNMT3A	chr2:25457243	NM_175629.2	c.2644C>T	p.Arg882Cys
3	SF3B1	chr2:198267360	NM_012433.2	c.1997A>G	p.Lys666Arg
4	TP53	chr17:7578211	NM_000546.5	c.638G>A	p.Arg213Gln
5	SF3B1	chr2:198266834	NM_012433.2	c.2098A>G	p.Lys700Glu
6	TP53	chr17:7578413	NM_000546.5	c.517G>A	p.Val173Met
7	SF3B1	chr2:198266834	NM_012433.2	c.2098A>G	p.Lys700Glu
8	U2AF1	chr21:44524456	NM_006758.2	c.101C>T	p.Ser34Phe
	SRSF2	chr17:74732959	NM_003016.4	c.284C>A	p.Pro95His
9	RUNX1	chr21:36252940	NM_001754.4	c.422C>A	p.(Ser141Ter)
10	SF3B1	chr2:198266834	NM_012433.2	c.2098A>G	p.Lys700Glu
	EZH2	chr7:148504797	NM_004456.4	c.2197T>G	p.(Tyr733Asp)
11	NRAS	chr1:115258747	NM_002524.4	c.35G>A	p.Gly12Asp
	U2AF1	chr21:44524456	NM_006758.2	c.101C>T	p.Ser34Phe
12	NRAS	chr1:115258747	NM_002524.4	c.35G>T	p.Gly12Val
	IDH2	chr15:90631934	NM_002168.2	c.419G>A	p.Arg140Gln
	SRSF2	chr17:74732959	NM_003016.4	c.284C>G	p.Pro95Arg
13	SRSF2	chr17:74732959	NM_003016.4	c.284C>G	p.Pro95Arg
	TET2	chr4:106157971	NM_001127208.2	c.2872C>T	p.Gln958Ter

	TET2	chr4:106164778	NM_001127208.2	c.3646C>T	p.Arg1216Ter
14	TET2	chr4:106155620	NM_001127208.2	c.521C>A	p.Pro174His
15	TET2	chr4:106157845	NM_001127208.2	c.2746C>T	p.Gln916Ter
16	WT1	chr11:32417914	NM_024426.4	c.1138delinsGG	p.Arg380Glyfs*5
	NRAS	chr1:115258747	NM_002524.4	c.35G>A	p.(Gly12Asp)
	IDH1	chr2:209113113	NM_005896.3	c.394C>T	p.(Arg132Cys)
17	TP53	chr17:7577555	NM_000546.5	c.726C>A	p.Cys242Ter
18	TP53	chr17:7578535	NM_000546.5	c.395A>T	p.(Lys132Met)
19	DNMT3A	chr2:25463235	NM_175629.2	c.2255_2257del	p.Phe752del
	TP53	chr17:7578459	NM_000546.5	c.469_471delinsTTT	p.Val157Phe

Supplementary Table S3

Peripheral blood ddPCR variant allele frequencies (VAFs, %), before start of treatment (Bsot) and days from start of treatment. IWG-2006 response days from start of treatment. BM: VAFs from bone marrow samples.

Pt 1

Days	EZH2 Gln545Ter	DNMT3A Arg882Cys	Response
Bsot	1,6	7,2	
24	2,8	6	
59	0,4	1,1	
87			mCR
114	0,1	0,4	

Pt 2

Days	DNMT3A Arg882Cys	IDH2 Arg140Gln	Response
Bsot	BM: 35	BM: 24	
38	25	1,5	
78	28	4,2	mCR
127	28	5,3	
176	26	7,3	

Pt 3

Days	SF3B1 Lys666Arg	Response
Bsot	14	
135	20	
202	18	SD
282	15	
371	22	
449	10	
542	27	
597	19	
647		PD
659	34	
758	19	
814	23	
897	24	
989	31	

Pt 4

Days	TP53 Arg213Gln	Response
Bsot	48	
52	31	
59		HI-P
98		HI-E
137	5,7	
199	20	
254	25	

Pt 5

Days	SF3B1 Lys700Glu	Response
Bsot	11	
82	3,7	
166	1,7	
250	0,4	
333	0,1	
442	2,9	
490		CR
518	25	
567		Relapse
614	30	
699	30	
784	31	

Pt 6

Days	TP53 Val173Met	Response
Bsot	21	
26	5,2	
53	4,2	
87	1,4	
117	0,7	CR
145	0,8	
178	1,7	
208	0,6	
236	0,8	
270	2,6	
301	1,4	
356	4,9	AML

Pt 7

Days	SF3B1 Lys700Glu	Response
Bsot	24	
93	14	
143		SD
149	11	
247	12	

Pt 8

Days	U2AF1 Ser34Phe	Response
Bsot	BM: 43	
56	16	
69	6,4	
133	4,9	
165		SD
200	5,3	
292	12	

Pt 9

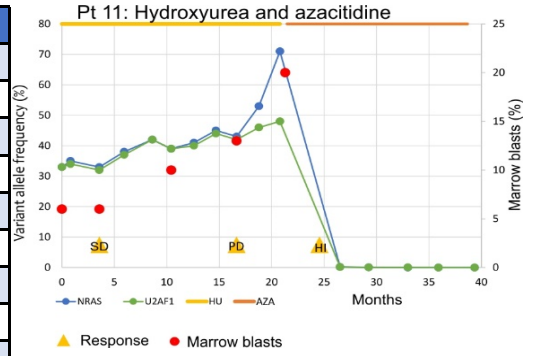
Days	RUNX1 Ser141Ter	Response
0	BM: 48	
22	37	
56	25	
86	24	mCR
162	34	
178		AML

Pt 10

Days	SF3B1 Lys700Glu	EZH2 Tyr733Asp	Response
Bsot	3,4	1,4	
64	0,2	0,1	
94			HI
120	0,1	0,1	
175	0	0	
233	0,1	0	
288	0,1	0	

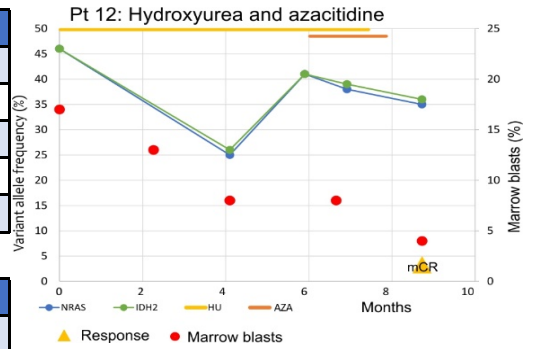
Pt 11

Days	NRAS Gly12Asp	U2AF1 Ser34Phe	Response
Bsot	33	33	
25	35	34	
109	33	32	SD
181	38	37	
263	42	42	
318	39	39	
384	41	40	
448	45	44	
508	43	42	PD
573	53	46	
634	71	48	
749			HI
809	0,2	0,1	
892	0,1	0,1	
1006	0	0,1	
1095	0	0	
1200	0	0	



Pt 12

Days	NRAS Gly12Val	IDH2 Arg140Gln	Response
Bsot	46	46	
125	25	26	
180	41	41	
211	38	39	
266	35	36	mCR



Pt 13

Days	TET2 Gln958Ter	TET2 Arg1216Ter	Response
Bsot	BM: 13	BM: 5	
27	1,7	6,9	
61	4,5	3,5	
83	3,4	2,8	SD
112	2,2	3,8	
138	2,4	6,1	

Pt 14

Days	TET2 Pro174His	Response
Bsot	BM NGS: 51	
24	50	
51	50	
105	51	SD
204	50	
324	50	
442	50	

Pt 15

Days	TET2 Gln916Ter	Response
Bsot	23	
60	36	
127	42	SD
156	44	
196	45	PD

Pt 16

Days	WT1 Arg380Gly	NRAS Gly12Asp	IDH1 Arg132Cys	Response
Bsot	0,8			
53	2			
89	2,4			mCR
118	1,6			
160	5,7	4,3	6,1	
186	6,4			AML
245	4,3	7,7	15	
319	0,1	15	0	
378	0,1	36	0,5	
439	0,2	46	0	

Pt 17

Days	TP53 Cys242Ter	Response
Bsot	71	
53		mCR
105		CR
112	1,2	
163	1,5	
273	1,9	
396	2,3	
435		Relapse
449	7	
487	80	

Pt 18

Days	TP53 Lys132Met	Response
Bsot	47	
26	3,4	
53	4	
158	6,1	
209		mCR
252	3,4	
362	5,4	

Pt 19

Days	DNMT3A Phe752del	TP53 Val157Phe	Response
Bsot	BM: 37	BM: 17	
99	34	10	
148	34	11	mCR
178	33	6,8	
189	33	9,4	