

Supplementary Table S1. Sequences of primers used for NGS

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Primer	Sequence
BRAF_exo n_15_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGCTGTTTCCTTACTTACTACACCTCA
BRAF_exo n_15_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTAATCAGTGGAAAAATAGCCTCAAT
NRAS_exo n_1_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGCTCGCCAATTAACCCCTGAT
NRAS_exo n_1_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGGGATCATATTCATCTACAAAGTGGTCTG
NRAS_exo n_2_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGAAAACAAGTGGTTATAGATGGTGAAA
NRAS_exo n_2_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTGATGGCAAATACACAGAGGAAG
KRAS_exo n_1_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGTAAGGCCTGCTGAAAATGACTGAATA
KRAS_exo n_1_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGGCACCAGTAATATGCATATTAACAAGA
KRAS_exo n_2_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGAAACCTGTCTCTTGGATATTCTCG
KRAS_exo n_2_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGGCTTATTATATTCAATTTAAACCCACCTA
HRAS_exo n_1_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGCCCCTGAGGAGCGATGACG
HRAS_exo n_1_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGCGCCAGGCTCACCTCTATA
HRAS_exo n_2_F	TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGATGGGGAGACGTGCCTGTTGG
HRAS_exo n_2_R	GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTGTACTGGTGGATGTCCTCAAAAG

Supplementary Table S2. Demographic and clinical profile of study subjects.

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Parameters	Total	Percent
Female	27	52,94 %
Male	24	47,05 %
Age in years, median	61 y	-
IgG kappa	14	27,45 %
IgG lambda	10	19,60 %
IgA kappa	4	7,84 %
IgA lambda	7	13,72 %
IgD lambda	1	1,96 %
Free kappa	9	17,64 %
Free lambda	4	7,84 %
Cytogenetics (90,19 %)		
t(14;16)	4	7,84 %
del17p13	18	35,29 %
del13q14	2	3,92 %
Gain 1q21	11	21,56 %
t(4;14)	9	17,64 %
t(11;14)	1	1,96 %
del11q	1	1,96 %
Risk stratification		
Standard-risk	21	41,17%
Intermediate-risk	8	15,68%
High-risk	22	43,13%
ISS Classification		
ISS-I	8	15,68 %

ISS-II	10	19,60 %
ISS-III	26	50,98 %
Induction therapy		
VRd	4	7,84 %
KRd	4	7,84 %
DaraVTd	2	3,92 %
PAD	13	25,49 %
VelDex	1	1,96 %
CyBorD	15	29,41 %
Dara-CyBorD	13	11,76 %
No treatment	6	25,49 %
Maintenance therapy		
Lenalidomide	10	19,60 %
KRd	3	5,88 %
LenDex	3	5,88 %
Bortezomib	2	3,92 %
Melphalan	2	3,92 %
VTd	1	1,96 %
Refractory to the last treatment line	11	21,56 %

Supplementary Table S3. Mutations and cytogenetic abnormalities identified in the refractory patient subgroup.

Refractory patient	Mutation	Cytogenetics	Refractory to induction therapy	Refractory to maintenance therapy
1	NRAS p.Q61K	t(4;14)		yes
2	BRAF p.V640G	del17p, gain 1q	yes	yes
3	KRAS p.G12A	del17p, t(4;14)	yes	
4	N/A	del17p		yes
5	BRAF p.D634N	gain 1q		yes
6	N/A	N/A	yes	yes
7	N/A	N/A	yes	
8	N/A	N/A		yes
9	N/A	N/A	yes	yes
10	N/A	N/A	yes	
11	N/A	N/A	yes	