Supplementary Note 1

(Casewise clonal evolution)

{V= Bortezomib, C= Cyclophosphamide, T= Thalidomide, R= Lenalidomide, D=Dexamethasone, M= Melphalan, P=Pomalidomide}

Branching Clonal Evolution

SM0018 (Female / 54 years old / MM R-ISS2 with OS of 182.43, PFS of 106.14 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (3, 1); Rising clones (cellular prevalence at TP1 to TP2) = 3 (15.67 to 30.43), 1 (0.00 to 42.74);
- TMB at TP1 is 0.59; TMB at TP2 became 1.44
- Therapy: VCD
- Two founder clones (1,3) were detected at diagnosis that diversified into 4 clones by the time of progression (Figure S1.01). The founder clone 3 possessed mutations in 5 genes including *MUC6* (p.(Ala2054Val) that reduced in cellular prevalence from 0.31 at TP1 to 0.26 at TP2), rising mutations in *NBPF1*(c.3444G>A(p.(LysTer1148=)), *NPIPB15* (p.(Ala238Thr)), *GSTA2* (p.(Pro110Ser)), and *MUC17* (p.(Thr959Ala)). Similarly, founder clone 1 had multiple mutations that increased with progression. These comprised of driver mutations in *RNF213* (p.(Val1195Met)), *KMT2C* (p.(Tyr987His)) a tumor suppressor gene and others.

SM0022 (Male / 62 years old / MM R-ISS2 with OS of 304.86, PFS of 74.71 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (2, 4); Rising clones (cellular prevalence at TP1 to TP2) = 4 (0.00 to 45.15); Falling clones (cellular prevalence at TP1 to TP2) = 2 (31.76 to 23.14);
- TMB at TP1 is 1.75; TMB at TP2 became 1.43
- Therapy: VCD
- This patient had 4 clones of which clones 2 and 4 were founders at diagnosis (Figure S1.02). Clone 2 had several falling mutations such as in CHI3L1 (5'UTR), ATP8B1(p.(Gln461Lys)), UNC80 (p.(Arg1030His)) and mutations with rising cellular prevalence such as termination in PABPC1 (p.(Glu345Ter)), LIMS1 (p.(Arg74His)) and others. Founder clone 4 had predominantly rising mutations in MYC (3'UTR), MTA1(splice variant), BAGE2 (5'UTR), AHNAK2 (p.(Met2187Val)), CARMIL3 (p.(Gly1161Val)) and others

SM0024 (Male / 52 years old / MM R-ISS2 with OS of 121.29, PFS of 116.71 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (51.32 to 70.19);
- TMB at TP1 is 0.23; TMB at TP2 became 0.29
- Therapy: VCD, ASCT+VRD
- There were 3 clones in this patient that arose from a single founder clone 2. Numerous mutations emerged in this patient that evolved with rising cellular prevalence. Twelve

mutations were detected and consisted of F5 (p.(His1327Arg)), KRT6B (p.(Ile365Val)), HERC1 (p.(Asp76Glu)), GOLGA6A(p.(Gln505Glu)), ZNF705G (p.(Gly47Arg)) and others.

SM0025 (Male / 48 years old / MM R-ISS2 with OS of 179.57, PFS of 127.43 weeks)

- Evolution pattern: Branching
- Total clones= 5; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 2 (50.00 to 50.00); Falling clones (cellular prevalence at TP1 to TP2) = 1 (50.00 to 47.39)
- TMB at TP1 is 0.82; TMB at TP2 became 0.5
- Therapy: VCD
- Two founder clones (1,2) were enriched in CDKN1B (p.(Phe64Val)) and CSNK2A3 (p.(Arg280Gln)) in clone 1 that tended to decrease with progression and with stable levels of CACNA1G (p.(Leu1174Met)), MLF1 (p.(Ser102Tyr)) and RTP3 (p.(Asn74Ser)) in clone 2.

SM0067 (Female / 54 years old / MM R-ISS2 with OS of 70.14, PFS of 65.71 weeks)

- Evolution pattern: Branching
- Total clones= 5; 2 founder(s) (3, 2); Rising clones (cellular prevalence at TP1 to TP2) = 3 (28.66 to 36.80), 2 (0.00 to 42.50); ;
- TMB at TP1 is 0.2; TMB at TP2 became 1.42
- Therapy: VCD
- Founder clone 3 had abundant PDE4DIP (p.(His1598Arg)), CSTL1 (p.(Arg66Lys)) and FCRL6 (p.(Gln423Ter) rising mutations while reducing prevalence of KRTAP1-1 (p.(Pro58Arg)) and CSTL1 (p.(Arg66Lys)). The founder clone 2 had two rising mutations in OR4A16 (p.(Ile166Phe)) and MYH8 (p.(Lys638Asn)).

SM0082 (Male / 60 years old / MM R-ISS2 with OS of 275.86, PFS of 198.57 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (4, 1); Rising clones (cellular prevalence at TP1 to TP2) = 4 (22.66 to 44.09); Falling clones (cellular prevalence at TP1 to TP2) = 1 (32.52 to 0.00);
- TMB at TP1 is 0.82; TMB at TP2 became 0.77
- Therapy: VRD, ASCT
- This patient had two founder clones that branched to total 4 clones at the time of progression. Founder clone 1 had all falling mutations in USP31 (p.(Phe567Val)), METTL15 (p.(Asn31Lys)) and other genes, all of which diminished by progression. On the contrary, founder clone 4 had two mutations ZNF285 (p.(Lys292Glu)) and CCDC13 (p.(Arg25Trp)) that increased in prevalence further on progression.

SM0094 (Female / 44 years old / MM R-ISS2 with OS of 215.57, PFS of 67.86 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (3); Rising clones (cellular prevalence at TP1 to TP2) = 3 (41.72 to 59.76); ;
- TMB at TP1 is 2.42; TMB at TP2 became 0.58
- Therapy: RD, VCD_VD, CTD,VRD, CRP, PAD

- A single founder clone 3 was identified at diagnosis that evolved into three clones by TP2. The founder clone had multiple mutations in drivers such as FAT4 (rising p.(Ala807Val)) and PABPC1 (falling 3'UTR variant) and other rising mutations among LAMC1 (p.(Ile458Val)), NABP2 (p.(Glu118Lys)) and others.

SM0102 (Male / 48 years old / MM R-ISS3 with OS of 140.86, PFS of 45.00 weeks)

- Evolution pattern: Branching
- Total clones= 4; 3 founder(s) (3, 2, 4); Rising clones (cellular prevalence at TP1 to TP2) = 3 (33.33 to 33.33), 4 (0.00 to 21.39); Falling clones (cellular prevalence at TP1 to TP2) = 2 (20.47 to 0.00);
- TMB at TP1 is 88.1; TMB at TP2 became 91.85
- Therapy: VRD, VD
- Driver mutations in PDE4DIP (splice variant), tumor suppressor gene PIKR3 (p.(Asn329Lys)), oncogene CYP19A1, (3'UTR), MAP2K1 (splice variant), FANCA (p.(Gly501Ser)), SERPINB3 (p.(Gly351Ala)), PLCG1 (p.(Ile813Thr)), ALK (p.(Lys1491Arg)), DROSHA (3'UTR), PTCH1 (p.(Pro1315Leu)) were observed in clone 3. Clone 2 had NTRK1(p.(His604Tyr)), KRAS (3'UTR), PDPR (p.(Thr29Ala)), FAT1 (p.(Thr2261Met)), IL3 (p.(Pro27Ser)), PABPC1 (p.(Gly579Ser)) mutations. Founder clone 4 had NTRK1 (p.(Gly613Val)), PTPN14 (splice variant), EXO1 (p.(Glu589Lys)), BRCA1 (3'UTR) and other mutations.

SM0113 (Male / 61 years old / MM R-ISS2 with OS of 267.29, PFS of 267.29 weeks)

- Evolution pattern: Branching
- Total clones= 3; 2 founder(s) (2, 3); Rising clones (cellular prevalence at TP1 to TP2) = 2 (19.06 to 36.56); Falling clones (cellular prevalence at TP1 to TP2) = 3 (22.34 to 0.00);
- TMB at TP1 is 0.48; TMB at TP2 became 0.93
- Therapy: RD, VRD
- Representative mutations in founder clones 2 and 3 at diagnosis comprised of DNAH17 (p.(Arg879His)), LRP5 (splice variant), IRAK1 (p.(Asn345Ser)), ZNF98 (p.(Tyr350Cys)), ACOXL (p.(Thr255Met)), EXD3 (p.(Arg38Trp)) and others.

SM0152 (Male / 70 years old / MM R-ISS3 with OS of 238.00, PFS of 106.71 weeks)

- Evolution pattern: Branching
- Total clones= 4; 1 founder(s) (4); ; Falling clones (cellular prevalence at TP1 to TP2) = 4 (66.29 to 54.25);
- TMB at TP1 is 0.79; TMB at TP2 became 1.52
- Therapy: VTD-VD, CTD-RD
- A single founder clone 4 had mutations in driver HOXD13 (p.(Gly11Ala)), in MST1L (p.(Trp403Ter)), DHX58 (p.(Arg523Gln)), KLK14 (p.(Gln33Arg)) and others that diversified into total 4 clones by progression.

SM0172 (Female / 69 years old / MM R-ISS3 with OS of 51.86, PFS of 21.86 weeks)

- Evolution pattern: Branching

- Total clones= 6; 3 founder(s) (1, 4, 6); Rising clones (cellular prevalence at TP1 to TP2) = 1 (32.00 to 33.33), 6 (0.00 to 15.95); Falling clones (cellular prevalence at TP1 to TP2) = 4 (15.27 to 0.00);
- TMB at TP1 is 0.31; TMB at TP2 became 0.35
- Therapy: RD, VRD
- In this patient, three out of 6 clones were founders. Founder clone 1 had PLET1 (p.(Ser142Pro)), PABPC3 (p.(Met251Ile)), CCDC173 (5'UTR), clone 4 carried mutations in AK2 (3'UTR), SMARCB1 (p.(Val234Met)), CEL (p.(Ile488Thr)) whereas clone 6 had FCGBP (p.(Ala3916Val)), TTC30A (p.(Val446Ile)) and UGT1A5 (p.(Gly259Arg)).

SM0197 (Male / 45 years old / MM R-ISS3 with OS of 155.86, PFS of 50.00 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (45.78 to 50.31); ;
- TMB at TP1 was 2.19; TMB at TP2 became 1.39
- Therapy: VCD, VTD-DT,ASCT+VRD- RD
- Only one founder was detected at diagnosis. This clone 1 had 18 mutations, notably in drivers DIS3 (p.(Ile348Lys)), DICER1 (p.(Glu235Gly)), EPHA7 (p.(Met450Ile)), VWF (p.(Gly1922Ala)) and others.

SM0224 (Female / 61 years old / MM R-ISS2 with OS of 72.00, PFS of 72.00 weeks)

- Evolution pattern: Branching
- Total clones= 6; 3 founder(s) (5, 3, 4); Rising clones (cellular prevalence at TP1 to TP2) = 5 (33.33 to 33.33), 4 (0.00 to 33.33); Falling clones (cellular prevalence at TP1 to TP2) = 3 (33.33 to 0.00);
- TMB at TP1 is 48.4; TMB at TP2 became 23.23
- Therapy: VCD, RD
- Founder clone 5 had driver mutations in SUFU (c.1299T>C(p.(Ile433=))), PGR (p.(Ser344Thr)), CAMTA1 (p.(Asn1177Lys)), RHPN2 (p.(Gln384Arg)), SIRPA (p.(Gly75Ala)), BARD1 (p.(Arg378Ser)), ZNF292 (p.(Ile1740Val)). Clone 3 was characterized by mutations in PDE4DIP (p.(Arg171Lys)), ERCC5 (p.(Cys529Ser)), FANCM (p.(Ile1460Val)), PLCB4 (p.(Thr998Ala)), EP300 (p.(Ile997Val)), FAT4 (p.(Gly3526Asp)). Clone 4 had PDE4DIP (p.(Leu1272Phe)), CLIP (p.(Pro1403Leu)), EP400 (p.(Leu1741Gln)), TRAF3 (p.(Met129Thr)), BLM (p.(Pro868Leu), p.(Val1321Ile)) and other mutations.

SM0237 (Female / 52 years old / MM R-ISS2 with OS of 225.29, PFS of 225.29 weeks)

- Evolution pattern: Branching
- Total clones= 5; 2 founder(s) (3, 5); Rising clones (cellular prevalence at TP1 to TP2) = 3 (28.77 to 50.00); Falling clones (cellular prevalence at TP1 to TP2) = 5 (28.82 to 0.00);
- TMB at TP1 is 0.66; TMB at TP2 became 0.39
- Therapy: RD, VRD-VD, ASCT+VRD-RD
- Founder clone 5 had one major mutation PABPC3 (p.(Val119Phe) that reduced in prevalence on progression but the other founder clone 3 picked up prevalence of 4 mutations viz. RAB3GAP2 (p.(Asn570Ser)), TPTE (p.(Val68Asp)), RAB11FIP5 (p.(Arg461Trp)) and PBK (splice variant).

SM0267 (Male / 42 years old / MM R-ISS2 with OS of 235.14, PFS of 235.14 weeks)

- Evolution pattern: Branching
- Total clones= 2; 2 founder(s) (1, 2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.00 to 15.74); Falling clones (cellular prevalence at TP1 to TP2) = 1 (14.87 to 0.00);
- TMB at TP1 is 0.96; TMB at TP2 became 0.24
- Therapy: RD
- On diagnosis, founder clone 2 had 3 mutations BAGE2 (p.(Arg106Gln)), EPHA5 (p.(Lys626Glu)) and PCDH12 (p.(Gln500His)). The other founder clone 1 had multiple mutations e.g., PADI4 (p.(Gly112Ala)), PRAMEF1 (p.(Trp98Arg)), AP3S2 (p.(Phe23Leu)), CGB7 (5'UTR) and others

SM0294 (Male / 48 years old / MM R-ISS2 with OS of 241.71, PFS of 241.71 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (4, 2); Rising clones (cellular prevalence at TP1 to TP2) = 4 (29.98 to 36.03); Falling clones (cellular prevalence at TP1 to TP2) = 2 (50.00 to 0.00);
- TMB at TP1 is 0.31; TMB at TP2 became 0.63
- Therapy: VRD
- Founder clone 2 had mutations in KIAA0586 (p.(Leu1568Pro)) and GRK4 (p.(Arg65Leu)), both of which were lost by progression. Clone 4 became predominant by progression and most of mutations in clone 4 increased in cellular prevalence with time. These mutations were CDK11B (c.1959T>G(p.(Ala653=))), KRTAP4-11 (p.(Leu161Val)), TTC30A (p.(Val446Ile)), SENP2 (p.(Thr301Lys)), ZAN (p.(Ala2761Pro)) and NUTM2F (p.(Ala589Gly)).

SM0299 (Female / 53 years old / MM R-ISS2 with OS of 90.14, PFS of 40.86 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (1); ; Falling clones (cellular prevalence at TP1 to TP2) = 1 (77.14 to 36.45);
- TMB at TP1 is 0.26; TMB at TP2 became 0.17
- Therapy: RD
- This patient had a single founder clone 1 that had a falling mutation in SPRN (p.(Thr7Met)) and an almost constant maintained mutation in OBSCN (5'UTR).

SM0311 (Female / 52 years old / MM R-ISS2 with OS of 104.43, PFS of 94.00 weeks)

- Evolution pattern: Branching
- Total clones= 5; 1 founder(s) (3); ; Falling clones (cellular prevalence at TP1 to TP2) = 3 (100.00 to 90.80);
- TMB at TP1 is 0.79; TMB at TP2 became 0.14
- Therapy: VRD-VD, ASCT-VRD,VCD
- A single founder clone 3 had falling mutations in ALG10 (p.(Val19Ile)), GCSAML (5'UTR) and a consistent KLH5 (splice mutation)

SM0329 (Female / 54 years old / MM R-ISS2 with OS of 69.14, PFS of 67.86 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (2, 4); Rising clones (cellular prevalence at TP1 to TP2) = 2 (29.58 to 31.59), 4 (0.00 to 34.69);
- TMB at TP1 is 1.39; TMB at TP2 became 4.53
- Therapy: VD, VTD
- Two founder clones 2 and 4 were identified at diagnosis. Clone 2 had driver mutations in TP53 (p.(Arg158His)), MCM3AP (p.(Trp502Ter)), EGR1 (p.(Ser62Asn)). Similarly, clone 4 was mutated in multiple drivers such as KRAS (p.(Gly13Asp)), DNMT1 (p.(Ala1334Thr)), CNOT3 (3'UTR), KMT2C (p.(Tyr987His)) etc.

SM0339 (Male / 71 years old / MM R-ISS2 with OS of 100.43, PFS of 28.86 weeks)

- Evolution pattern: Branching
- Total clones= 3; 2 founder(s) (2, 3); Rising clones (cellular prevalence at TP1 to TP2) = 3 (0.00 to 19.73); Falling clones (cellular prevalence at TP1 to TP2) = 2 (45.66 to 18.93);
- TMB at TP1 is 1.74; TMB at TP2 became 0.33
- Therapy: VRD, RD
- Founder clone 3 showed an increase in prevalence while the other founder clone 2 reduced in cellular prevalence with time. Clone 2 had mutations such as those in F5 (p.(Arg740Ter)), RBL2 (p.(Gln783Ter)), HIST1H4D (p.(Ala70Val)) etc. While clone 3 had driver mutations in PARP4 (splice variant), IGLL5 (p.(Pro20His)) and others.

SM0343 (Male / 60 years old / MM R-ISS2 with OS of 123.57, PFS of 121.57 weeks)

- Evolution pattern: Branching
- Total clones= 3; 2 founder(s) (1, 3); Rising clones (cellular prevalence at TP1 to TP2) = 1 (8.65 to 35.34); Falling clones (cellular prevalence at TP1 to TP2) = 3 (10.74 to 0.00);
- TMB at TP1 is 0.86; TMB at TP2 became 0.69
- Therapy: VD, RD+H3:H31
- Three rising mutations were found in founder clone 1 (STK36 (p.(Leu434Pro)), GPR160 (p.(Ile262Thr)), KLHL38 (p.(Ile334Val))) that increased in prevalence from diagnosis to progression. On the contrary, founder clone 3 had mutations that reduced relatively with time. These included FLG (p.(Trp3555Arg)), CFP (p.(Pro237His)), FBXW11 (p.(Arg356Ser)) and others

SM0351 (Male / 58 years old / MM R-ISS2 with OS of 226.86, PFS of 108.86 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (1); ; Falling clones (cellular prevalence at TP1 to TP2) = 1 (71.36 to 68.79);
- TMB at TP1 is 1.13; TMB at TP2 became 1.44
- Therapy: RD
- One founder clone 1 was found with mutations that increased in prevalence (WDFY4 (p.(Leu841Met)), DIAPH3 (p.(Leu1034Ter)), BRAF (p.(Val600Glu))) or decreased with time (CABLES1 (p.(Lys496Arg)), CLOCK (p.(Ala400Gly)), KLHL31 (p.(Ala203Ser)) etc).

SM0370 (Female / 55 years old / MM R-ISS3 with OS of 228.00, PFS of 160.57 weeks)

- Evolution pattern: Branching
- Total clones= 4; 2 founder(s) (1, 2); Rising clones (cellular prevalence at TP1 to TP2) = 1 (21.95 to 25.48), 2 (0.00 to 26.65); ;
- TMB at TP1 is 0.27; TMB at TP2 became 0.57
- Therapy: RD, VRD-VD
- Driver mutations in BCL7A (p.(Arg4Gly)) in founder clone 1 and DOT1L(p.(Phe1474Tyr)), MLH1 (p.(Cys142Arg)) were observed in clone 2 among others.

SM0422 (Female / 45 years old / MM R-ISS2 with OS of 205.86, PFS of 146.00 weeks)

- Evolution pattern: Branching
- Total clones= 3; 2 founder(s) (1, 3); Rising clones (cellular prevalence at TP1 to TP2) = 3 (0.00 to 16.19); Falling clones (cellular prevalence at TP1 to TP2) = 1 (46.07 to 15.64);
- TMB at TP1 is 0.47; TMB at TP2 became 0.29
- Therapy: VRD, VD, VTD, VCD, CRP
- In this patient, founder clone 1 had falling mutations in FANK1 (p.(Gln4Ter)), DDX60L (p.(Cys336Tyr)) whereas clone 3 had rising mutations in CPED1 (p.(Ala551Gly), STAP2 (p.(Ala366Gly)), CETP (c.1212C>T(p.(Phe404=))) and others

SM0433 (Male / 72 years old / MM R-ISS2 with OS of 186.29, PFS of 183.29 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (3); ; Falling clones (cellular prevalence at TP1 to TP2) = 3 (69.20 to 47.65);
- TMB at TP1 is 1.51; TMB at TP2 became 1.11
- Therapy: VD, VRD, RD
- An individual founder clone 3 had rising variations in driver NRAS (p.(Gln61Arg)), PRDM4 (p.(His99Arg)), RBM5 (p.(Gly759Arg), p.(Arg633Thr), p.(Ser744Ile)), MAPK10 (p.(Val244Leu)). Mutations that decreased in prevalence in this clone with time included HCAR1 (p.(Val277Met)), OBSCN (p.(Val634Met)), CD163L1 (p.(Gly1074Cys)) and others.

SM0505 (Male / 60 years old / MM R-ISS2 with OS of 168.71, PFS of 72.00 weeks)

- Evolution pattern: Branching
- Total clones= 5; 2 founder(s) (3, 5); Rising clones (cellular prevalence at TP1 to TP2) = 3 (18.24 to 42.96), 5 (0.00 to 50.00);
- TMB at TP1 is 0.77; TMB at TP2 became 1.97
- Therapy: VCD, VD
- Two founder clones were observed at diagnosis. Clone 3 had multiple mutations while clone 5 had 4 mutations that emerged before progression. The latter were BRINP2 (p.(Val134Gly)), FAN1 (p.(Arg581Ter)), COL14A1 (p.(Pro1717Arg)) and FSD1L (p.(Phe57Leu)). Clone 3 had TRPC6 (p.(Gly20Arg)), RORC (p.(Leu501Val)), HDAC10 (p.(Asn142Lys)) and others

SM0510 (Male / 39 years old / MM R-ISS2 with OS of 48.86, PFS of 46.14 weeks)

- Evolution pattern: Branching

- Total clones= 3; 2 founder(s) (3, 1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (0.00 to 32.58); Falling clones (cellular prevalence at TP1 to TP2) = 3 (16.67 to 0.00);
- TMB at TP1 is 0.15; TMB at TP2 became 0.78
- Therapy: VRD
- Founder clone 1 was a rising clone with mutations in driver CIC (p.(Glu125Ter)), FAM171A1 (p.(Thr303Met)), TRPV4 (p.(Gly20Arg)), DNAH1 (p.(Tyr1899Cys)), MUC16 (p.(Pro14112His)), MLLT6 (p.(Pro45Thr)) etc. Cellular prevalence of mutations e.g., in PARP4 (5'UTR), SYNM (p..(Ala212Val)) and EXOC7 (3'UTR) were observed to fall with time in clone 3.

SM0546 (Female / 54 years old / MM R-ISS2 with OS of 143.71, PFS of 100.29 weeks)

- Evolution pattern: Branching
- Total clones= 2; 2 founder(s) (1, 2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.00 to 50.00); Falling clones (cellular prevalence at TP1 to TP2) = 1 (17.54 to 0.00);
- TMB at TP1 is 0.55; TMB at TP2 became 0.03
- Therapy: VRD, RD
- Founder Clone 2 had a single mutation in SF1 (p.(Pro64Ser)). Whereas founder clone 1 had several mutations in drivers CR1 (p.(Glu888Asp)), PTPRS (p.(Arg1798Cys)), BCORL1 (p.(Ile175Asn)), EGR1 (p.(Asn61Lys)), HIST1H1D (p.(Asn78Ser), p.(Ser87Arg)), FAM3C (p.(Ser75Gly)) and others

SM0581 (Female / 58 years old / MM R-ISS2 with OS of 138.14, PFS of 18.86 weeks)

- Evolution pattern: Branching
- Total clones= 4; 1 founder(s) (4); ; Falling clones (cellular prevalence at TP1 to TP2) = 4 (93.11 to 90.22);
- TMB at TP1 is 0.55; TMB at TP2 became 0.63
- Therapy: PD
- This patient had a single founder clone with a mutation in MYRFL (p.(Ser157Ala)) and in PPIAL4G (3'UTR)

SM0584 (Male / 67 years old / MM R-ISS2 with OS of 64.00, PFS of 51.00 weeks)

- Evolution pattern: Branching
- Total clones= 5; 2 founder(s) (4, 2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.01 to 47.04); Falling clones (cellular prevalence at TP1 to TP2) = 4 (32.58 to 21.86);
- TMB at TP1 is 2.47; TMB at TP2 became 1.54
- Therapy: RD
- Founder clone 4 had multiple mutations such as MTA2 (p.(Pro184Ala)), MUC5AC (p.(Gly1085Ser)), UNG (p.(Ala264Thr)), NCAPD2 (p.(Thr1331Ala)). The other founder clone 2 had mutations in NM1 (p.(Ser16Leu)) and others.

SM0588 (Male / 53 years old / MM R-ISS2 with OS of 97.57, PFS of 23.00 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (2); ; Falling clones (cellular prevalence at TP1 to TP2) = 2 (77.14 to 45.18);

- TMB at TP1 is 65.79; TMB at TP2 became 46.64
- Therapy: VRD
- Multiple driver mutations were present in a single founder clone 2. These consisted of actionable WRN (p.(Leu1074Phe)), ROS1 (splice variant), MAP3K1 (p.(Asp806Asn)), FBN2 (p.(Pro2784Leu), p.(Met2311Val)), ATXN7 (p.(Lys264Arg), p.(Val862Met)), ATR (p.(Arg2425Gln)), CUL3 p.(Val573Ile), FOXD4L1 (p.(Asn162Lys)) and others.

SM0660 (Male / 63 years old / MM R-ISS2 with OS of 166.71, PFS of 49.14 weeks)

- Evolution pattern: Branching
- Total clones= 4; 3 founder(s) (3, 1, 4); Rising clones (cellular prevalence at TP1 to TP2) = 4 (0.00 to 8.89); Falling clones (cellular prevalence at TP1 to TP2) = 3 (10.05 to 7.29), 1 (33.33 to 0.00);
- TMB at TP1 is 0.26; TMB at TP2 became 0.18
- Therapy: VRD, VD
- Of the 3 founder clones at diagnosis, only one clone 4 increased in cellular prevalence by progression and had mutations in LMAN2L (p.(Arg255Cys)), TIPARP (p.(Glu370Lys)) and WDFY3 (p.(Arg941Met)). The other clone 3 had LEPR (p.(Pro266Ser)) and NDST3 (p.(Lys498Thr)) mutations while the clone 1 had 3' UTR mutations in ASCC1, GIT2, CDH24 etc.

SM0678 (Male / 68 years old / MM R-ISS3 with OS of 133.00, PFS of 112.43 weeks)

- Evolution pattern: Branching
- Total clones= 4; 3 founder(s) (3, 4, 2); Rising clones (cellular prevalence at TP1 to TP2) = 3 (10.16 to 14.82), 2 (0.00 to 17.66); Falling clones (cellular prevalence at TP1 to TP2) = 4 (18.82 to 0.00);
- TMB at TP1 is 0.38; TMB at TP2 became 1.34
- Therapy: VCD, VD
- This patient had three founder clones at the time of diagnosis. Clone 3 had driver mutations in MAX (p.(Arg33Ter)), clone 4 in SLC45A3 (5'UTR), GREM1 (3'UTR), and clone 2 in PLCB4 (p.(Ile222Val)), FANCD2 (p.(Tyr632Cys)) and FGFR3(p.(Arg671Gly)).

SM0686 (Male / 63 years old / MM NA with OS of 141.00, PFS of 84.71 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (2); ; Falling clones (cellular prevalence at TP1 to TP2) = 2 (53.70 to 40.38);
- TMB at TP1 is 0.76; TMB at TP2 became 0.41
- Therapy: VCD, VD
- Only single founder clone was identified in this patient and had a mutation in tumor suppressor gene KLF2 (p.(Leu104Pro)), and in other genes PBX1 (p.(Tyr384Ter)) and MKNK2 (p.(Lys4Asn)).

SM0698 (Male / 44 years old / MM R-ISS2 with OS of 149.14, PFS of 54.29 weeks)

- Evolution pattern: Branching

- Total clones= 3; 1 founder(s) (2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (51.63 to 68.78); ;
- TMB at TP1 is 0.48; TMB at TP2 became 1.12
- Therapy: VCD, VD
- One founder clone was present at TP1 with multiple mutations in RIF1 (p.(Leu645His)), C6orf118 (p.(Lys327Met)), and many more

SM0726 (Male / 56 years old / MM R-ISS3 with OS of 126.14, PFS of 64.00 weeks)

- Evolution pattern: Branching
- Total clones= 3; 2 founder(s) (1, 3); Rising clones (cellular prevalence at TP1 to TP2) = 3 (0.00 to 18.19); Falling clones (cellular prevalence at TP1 to TP2) = 1 (50.00 to 0.00);
- TMB at TP1 is 0.19; TMB at TP2 became 0.35
- Therapy: VRD, VD
- Founder clone 5 had 5'UTR variations in ACTA2, STK39 and EPHB1 genes while clone 3 had mutations in PIK3C2A (p.(Asn1003Ser)), C1orf167 (p.(Gly1188Ser)), SPINK5 (p.(Arg711Gln)) and others.

SM0738 (Male / 61 years old / MM NA with OS of 143.43, PFS of 80.00 weeks)

- Evolution pattern: Branching
- Total clones= 5; 1 founder(s) (2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (100.00 to 100.00); ;
- TMB at TP1 is 0.85; TMB at TP2 became 1.1
- Therapy: VRD, RD
- A single founder dominated at diagnosis with mutations in APOA4 (p.(Arg220Cys)), TENM4 (p.(Arg2298Trp)), PCDHGC3 (p.(Val701Gly)) and 5'UTR variant in OSTF1 gene.

SM0740 (Male / 47 years old / MM R-ISS2 with OS of 124.57, PFS of 51.71 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (49.10 to 94.36); ;
- TMB at TP1 is 2.01; TMB at TP2 became 2.6
- Therapy: VRD, VD
- This patient also had a single founder clone carrying driver mutations in ENPEP (3'UTR), and PIM1 (p.(His6Leu), p.(Thr287Pro)) genes.

SM0755 (Male / 46 years old / MM R-ISS2 with OS of 126.86, PFS of 100.29 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (45.20 to 54.62); ;
- TMB at TP1 is 1.74; TMB at TP2 became 1.91
- Therapy: VCD, VRD

- One founder clone was detected at TP1 with several driver mutations such as MAX (p.(Arg35Cys)), FAT1 (p.(Phe3823Val)), PIM1 (p.(Ser74Ala)), RECQL4 (p.(Ser886Arg)) and NR4A3 (p.(Glu591Lys)).

SM0779 (Female / 70 years old / MM R-ISS2 with OS of 129.57, PFS of 85.14 weeks)

- Evolution pattern: Branching
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (0.00 to 32.99); Falling clones (cellular prevalence at TP1 to TP2) = 2 (13.43 to 0.00);
- TMB at TP1 is 0.48; TMB at TP2 became 1.74
- Therapy: VRD, RD
- At TP1, the founder clone 2 had mutations in EIF!AD (p.(Ala164Thr)), TAS2R43 (p.(Gly160Arg)), DVL3 (p.(Ser233Leu)) etc while the founder clone 1 had somatic mutations in driver genes such as KRAS (p.(Gln61His)), STAG2 (p.(Arg252Trp)) and CTNNB1 (p.(Asp162Glu))

SM0815 (Male / 62 years old / MM R-ISS2 with OS of 78.29, PFS of 36.29 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (3); ; Falling clones (cellular prevalence at TP1 to TP2) = 3 (44.95 to 33.44);
- TMB at TP1 is 2.97; TMB at TP2 became 1.02
- Therapy: VRD, VD
- Only one founder clone carrying mutations in MYH2 (p.(Glu1940Lys)), GAL3ST1 (p.(Arg354His)), PLXND1 (3'UTR), GRM4 (p.(Arg351Cys)) and TREML1 (p.(Pro269Leu)) was present at diagnosis.

SM1288 (Female / 48 years old / MM R-ISS2 with OS of 46.57, PFS of 26.71 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (2); ; Falling clones (cellular prevalence at TP1 to TP2) = 2 (68.21 to 46.28);
- TMB at TP1 is 1.09; TMB at TP2 became 0.86
- Therapy: VCD
- This patient possessed single founder clone with mutations in drivers TP53 (p.(Cys277Phe)), DCC (p.(Leu334Ter)) and BRAF (p.(Val600Glu)),

SM1547 (Male / 34 years old / MM R-ISS2 with OS of 60.29, PFS of 57.14 weeks)

- Evolution pattern: Branching
- Total clones= 3; 1 founder(s) (2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (54.63 to 55.53); ;
- TMB at TP1 is 1.88; TMB at TP2 became 1.67
- Therapy: VCD
- A single founder clone was identified with multiple mutations in NXPE1 (p.(Thr117Pro)), MMP26 (splice variant), NOS1 (p.(Arg904Gly)) and others

SM007 (Female/58 years old/MM R-ISS3 with OS of 221 weeks, PFS of 175 weeks)

- Evolution pattern: Branching
- Total clones= 9; 3 founder(s) (3, 8, 9); Rising clones (cellular prevalence at TP1 to TP2) = 3 (33.33 to 33.33); Falling clones (cellular prevalence at TP1 to TP2) = 8 (33.33 to 27.41), 9 (33.33 to 0.00);
- TMB at TP1 is 134.43; TMB at TP2 became 96.61
- Therapy: VCD; PCD
- Among several somatic mutations present in founder clone 1, an actionable driver mutation in NRAS (p.(Gly12Ala)) and another in FOXD4L1 (p.(Arg145Cys)) were noticed. Additional somatic mutations observed in founder clone 2 included KIAA0556 (p.(Ser368Asn)), MIPEP (p.(Ser368Asn)) and others

SM0052 (Male / 59 years old/MM R-ISS2 with OS of 242.29 weeks, PFS of 148.00 weeks)

Evolution pattern: Branching

- Total clones= 5; 3 founder(s) (3, 4, 5); Rising clones (cellular prevalence at TP1 to TP2) = 3 (0.00 to 32.75); Falling clones (cellular prevalence at TP1 to TP2) = 5 (32.99 to 32.64), 4 (32.11 to 0.00);
- TMB at TP1 is 132.12; TMB at TP2 became 119.99
- Therapy: DT, ASCT
- This patient has several driver mutations such as those in FAM186A (p.(Leu1233Pro), p.(Lys187Gln)), ZNF626 (p.(Lys180Asn)), MERTK (p.(Ile518Val)), IL3 (p.(Pro27Ser)) in founder clone 5, in PTPRC (p.(Asp543Asn)), KRAS (3'UTR), BRCA2 (p.(Asn289His)), CYP19A1 (p.(Arg264Cys)) in founder 4, and in NCOR2 (p.(Ala1699Thr)), KMT2B (p.(Asp2364Gly)) in founder clone 3.

Linear

SM0076 (Male / 72 years old / MM R-ISS2 with OS of 280.71, PFS of 252.71 weeks)

- Evolution pattern: Linear
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 2 (17.13 to 20.99), 1 (0.00 to 23.15); ;
- TMB at TP1 is 0.35; TMB at TP2 became 2.16
- Therapy: MPT
- Founder clone 2 carried mutations in PNPLA2 (p.(Ser170Ala)), MIXL1 (p.(Ala81Thr)) etc while founder clone 1 had mutations in actionable driver oncogene NRAS (p.(Gly12Ala)), FOXD4L1 (p.(Arg145Cys)) and many more.

SM0133 (Male / 50 years old / MM R-ISS2 with OS of 260.00, PFS of 260.00 weeks)

- Evolution pattern: Linear
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.31 to 29.50), 1 (0.00 to 49.93); ;
- TMB at TP1 is 1.36; TMB at TP2 became 105.47

- Therapy: VTD-VD
- Founder clone 2 had driver mutations such as TSG SUFU (p.(Arg280Gln)), actionable oncogene RET (p.(Lys989Arg)), TSG TET1 (p.(Ser193Thr), p.(Ala256Val)), NOTCH2 (p.(Asn2008Ser), p.(Asp1327Gly)), KRAS (3'UTR), FLT1 (p.(Lys337Gln)), TP53BP1 (p.(Lys1141Gln)), BRCA1 (p.(Ser1613Gly), p.(Lys1183Arg), p.(Glu1038Gly)), DNMT1 (p.(Ile327Val)) while founder clone 1 had numerous mutations in drivers such as CLIP1 p.(Asp1080Glu), MLH3 (p.(Pro844Leu)), STIL (p.(Ala86Val)) and CIITA (p.(Leu45Val)).

SM0138 (Male / 69 years old / MM R-ISS2 with OS of 181.14, PFS of 85.14 weeks)

- Evolution pattern: Linear
- Total clones= 3; 1 founder(s) (1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (82.81 to 97.65); ;
- TMB at TP1 is 79.67; TMB at TP2 became 80.72
- Therapy: RD
- One single founder clone was observed at diagnosis, which contained mutations in PDE4DIP (p.(Trp560Ter), p.(Arg295His)), PRRX1 (p.(Ser200Arg)), IKBKE (p.(Pro713Leu)), PTPN11 (p.(Asn18Ser)) and others,

SM0143 (Female / 43 years old / MM R-ISS2 with OS of 253.14, PFS of 139.71 weeks)

- Evolution pattern: Linear
- Total clones= 3; 2 founder(s) (3, 2); Rising clones (cellular prevalence at TP1 to TP2) = 3 (49.23 to 49.91), 2 (0.00 to 49.69); ;
- TMB at TP1 is 95; TMB at TP2 became 39.41
- Founder clone 3 had FANCA (p.(Gly809Asp)), MSH3 (p.(Ala1045Thr)), WRN(p.(Leu1074Phe)), founder clone 2 had TET1 (p.(Asp162Gly)), RBM15 (p.(Asn798Ser)), FAM46C (p.(His67Gln)) and additional driver mutations

SM0208 (Male / 54 years old / MM R-ISS2 with OS of 179.00, PFS of 132.71 weeks)

- Evolution pattern: Linear
- Total clones= 4; 2 founder(s) (3, 4); Rising clones (cellular prevalence at TP1 to TP2) = 4 (0.00 to 50.00); Falling clones (cellular prevalence at TP1 to TP2) = 3 (22.68 to 17.85);
- TMB at TP1 is 0.18; TMB at TP2 became 0.55
- Therapy: VRD-VD, ASCT+VRD-RD, CPT, DCEP
- Founder clone 3 was a falling clone with GUCY1A2(p.(Cys725Tyr)), TTF2 (p.(Lys167Glu)), whereas clone 4 was a rising founder clone with ZNF778 (p.(Tyr701Cys)), SLC35G4 (p.(Leu45Met)), and other mutations

SM0559 (Female / 31 years old / MM R-ISS2 with OS of 163.57, PFS of 22.00 weeks)

- Evolution pattern: Linear
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (0.00 to 19.21); Falling clones (cellular prevalence at TP1 to TP2) = 2 (17.43 to 0.05);
- TMB at TP1 is 0.16; TMB at TP2 became 0.37
- Therapy: VCD

- The founder clone 2 had mutations with falling prevalence (SDK2 (p.(Ala1499Gly)), ST8SIA3 (p.(Ala45Thr))) whereas founder clone 1 had mutations rising prevalence before progression (MUC5B (p.(Pro2830Leu)), MYH4 (p.(Ile1106Met)), etc.)

SM0664 (Male / 47 years old / MM R-ISS2 with OS of 101.71, PFS of 28.29 weeks)

Evolution pattern: Linear

- Total clones= 2; 2 founder(s) (1, 2); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.00 to 18.56); Falling clones (cellular prevalence at TP1 to TP2) = 1 (30.07 to 0.97);
- TMB at TP1 is 4.69; TMB at TP2 became 1.16
- Therapy: VRD, CTD, DCEP
- In this patient, founder clone 1 had driver mutations in FAT3 (p.(Ser3322Arg)), SPRTN (p.(Val183Asp)), MGA (p.(Ser1263Ter)), EP300 (p.(Asn607Thr)) while founder clone 2 had mutations in KMT2C (p.(Lys339Asn)), KMT5A (p.(Pro60Leu)), TRIM60 (p.(Trp44Arg)) and others.

SM0667 (Female / 65 years old / MM R-ISS2 with OS of 130.57, PFS of 89.29 weeks)

- Evolution pattern: Linear
- Total clones= 4; 1 founder(s) (4); Rising clones (cellular prevalence at TP1 to TP2) = 4 (82.50 to 91.33); ;
- TMB at TP1 is 0.24; TMB at TP2 became 0.96
- Therapy: VRD, CRD
- A single founder clone was present in this patient at TP1 and harboured mutations in LRRC378 (p.(Gly652Arg)) and POM121 (p.(Pro478Leu))

SM1595 (Female / 58 years old / MM R-ISS3 with OS of 95.86, PFS of 94.71 weeks)

- Evolution pattern: Linear
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 1 (0.00 to 21.40); Falling clones (cellular prevalence at TP1 to TP2) = 2 (20.47 to 10.83);
- TMB at TP1 is 0.91; TMB at TP2 became 3.14
- Therapy: VRD-VD, ASCT+VRD-RD
- This patient had mutations in founder clone 2 (such as PRAMEF1 (p.(Leu105Ter), (p.(Glu110Gly), CUL9 (p.(Glu377Ter))) while in founder clone 1 in KRAS (p.(Gly12Asp)), LRIG3 (p.(Val251Ile)), NBEA (p.(Arg2083His)) and others.

Stable with loss of clone

SM0115 (Female / 67 years old / MM R-ISS2 with OS of 220.00, PFS of 168.14 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (2, 1); ; Falling clones (cellular prevalence at TP1 to TP2) = 2 (33.84 to 0.58), 1 (50.00 to 0.00);
- TMB at TP1 is 54.83; TMB at TP2 became 0.53

- Therapy: RD, DT, CTD
- Founder clone 2 carried driver mutations in PDE4DIP (p.(Glu2001Gly)), PTPN14 (p.(Ile924Val)), HERC2 (p.(Val3327Met)), IGLL5 (p.(Thr211Ala)),, KMT2C (p.(Ala1685Ser), p.(Cys391Ter)). The other founder clone 1 had driver mutations in PGR (p.(Gln553Glu)), ATM (p.(His1380Tyr)), PRDM2 (p.(Ile586Thr)) , NUMA1 (p.(Ala794Gly)), KRAS (3'UTR), EXO1 (p.(Glu589Lys)), DIS3 (p.(Asn269Ser)) and others

SM0167 (Female / 66 years old / MM R-ISS3 with OS of 67.57, PFS of 34.00 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 1 founder(s) (1); ; Falling clones (cellular prevalence at TP1 to TP2) = 1 (100.00 to 0.17);
- TMB at TP1 is 78.34; TMB at TP2 became 1.09
- Therapy: VRD, RD
- This patient had a single founder clone harbouring mutations in driver TSG TET1 (p.(Asp162Gly)), PDE4DIP (p.(Arg1978His), NUMA1 (p.(Glu809Asp), FAT3 (p.(Asn2293Ser)), CR1 (p.(Pro1827Arg)), TSG ATXN2 (p.(Ser248Asn)) and others

SM0185 (Male / 63 years old / MM R-ISS2 with OS of 259.14, PFS of 147.00 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (2, 1); ; Falling clones (cellular prevalence at TP1 to TP2) = 2 (31.33 to 0.72), 1 (50.00 to 0.00);
- TMB at TP1 is 75.88; TMB at TP2 became 0.67
- Therapy: MP, MPT, RD
-

SM0266 (Male / 63 years old / MM R-ISS1 with OS of 184.14, PFS of 184.14 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 2 (0.92 to 29.01); Falling clones (cellular prevalence at TP1 to TP2) = 1 (16.69 to 0.00);
- TMB at TP1 is 0.63; TMB at TP2 became 0.47
- Therapy: VRD, VD
- Driver mutations in founder clone 2 included TSG TET1 (p.(Asn1018Ser)), CLIP1 (p.(Asp1080Glu)), PITRB (p.(Asp633Glu)), DNMT3B (c.1674T>C(p.(Tyr558=))), TSG FANCD2 (p.(Asn405Ser)), KMT2C (p.(Ala1685Ser)). Founder clone 1 had CPEB3 (p.(Ala499Gly)), PDE4DIP (p.(Val1371Ile)), LRP5 (p.(Val667Met)), FAT3(p.(Gln1726Arg)) and others

SM0353 (Female / 61 years old / MM R-ISS3 with OS of 202.43, PFS of 133.43 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (1, 2); Rising clones (cellular prevalence at TP1 to TP2) = 1 (14.09 to 17.57); Falling clones (cellular prevalence at TP1 to TP2) = 2 (18.61 to 0.00);
- TMB at TP1 is 1.08; TMB at TP2 became 0.34
- Therapy: VRD-VD, VCD-VD, CPT

- Founder clone 1 possessed driver mutations at TP1 (MYO5A (p.(Arg90Ser))), similarly, founder clone 2 had CACNA1D (p.(Ser1224Tyr)), FAT1 (p.(Val43Met)), NSD2 (p.(Met397Ile)) and BRAF (p.(Val600Glu)) actionable driver mutations

SM0471 (Female / 48 years old / MM R-ISS3 with OS of 220.43, PFS of 52.14 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 3; 2 founder(s) (3, 1); Rising clones (cellular prevalence at TP1 to TP2) = 3 (25.46 to 27.33); Falling clones (cellular prevalence at TP1 to TP2) = 1 (33.07 to 0.00);
- TMB at TP1 is 1.13; TMB at TP2 became 0.32
- Therapy: RD, CTD, DT
- In this case, at diagnosis, founder clone 3 was loaded with actionable driver mutations in BIRC3 (p.(Tyr31His)), etc. The other founder clone 1 also had actionable driver mutations in BARD1 (p.(Tyr87His)), FGFR3 (p.(Cys275Tyr)) and others including IGLL5 (p.(Gln22Ter)), TNFAIP3 (p.(Arg45Ter)) and HIST1H1E (p.(Ala116Val)).

SM0808 (Male / 70 years old / MM R-ISS3 with OS of 83.14, PFS of 31.00 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (2, 1); Rising clones (cellular prevalence at TP1 to TP2) = 2 (7.46 to 22.78); Falling clones (cellular prevalence at TP1 to TP2) = 1 (15.81 to 0.00);
- TMB at TP1 is 2.44; TMB at TP2 became 0.69
- Therapy: VCD, VTD
- On diagnosis, two driver somatic mutations were observed in founder clone 2 (NBEA (p.(Ser200Cys)), IRF4 (p.(Lys123Arg))) and a few in founder clone 1 (ARID5B (p.(Asn640Ser)), DIS3 (p.(Arg780Lys)), AXIN2 (p.(Arg841Gln)), actionable BRAF (p.(Val600Glu)) and others)

SM0145 (Male / 60 years old/MM R-ISS3 with OS of 251.14 weeks, PFS of 123.29 weeks)

- Evolution pattern: Stable with loss of clone
- Total clones= 2; 2 founder(s) (1, 2); Falling clones (cellular prevalence at TP1 to TP2) = 2 (34.89 to 1.28), 1 (50.00 to 0.00);
- TMB at TP1 is 126.3; TMB at TP2 became 0.97
- Therapy: VRD-VD, VCD-RD
- Driver mutations found in founder clone 2 included PARP4 (p.(His490Gln)), MAX (p.(Met1?)), actionable MLH3 (p.(Pro844Leu)), HERC2 (p.(Val3327Met)), ALK (p.(Glu588Ala)), NOTCH4 (p.(Gly534Ser), p.(Lys117Gln)) and others. The founder clone also possessed driver mutations such as TCF7L2 (p.(Pro495Ala), RET (p.(Gly691Ser), CCDC6 (p.(Pro470Thr), ARID5B (p.(Asn299Lys)), ATM (p.(Leu263Pro), p.(Ser707Pro)), KMT2A (p.(Arg3564Trp)), NOTCH2 (p.(His1160Arg)).