Supplementary

**Supplement Table 1. The combination of flow cytometry antibody panel.**

| Tube   | CD16-FITC | CD117-PE | CD34-PerCPCy5.5 | CD38-PECy7 | CD13-APC | HLA-DR-APCCy7 | CD11b-V450 | CD45-V500 |
|--------|-----------|----------|-----------------|------------|----------|----------------|------------|-----------|
| Tube 1 |           |          |                 |            |          |                |            |           |
| Tube 2 |           |          |                 |            |          |                |            |           |
| Tube 3 |           |          |                 |            |          |                |            |           |
| Tube 4 |           |          |                 |            |          |                |            |           |

**Supplement Table 2. List of 141 genes included in the targeted sequencing panel.**

| ABL1      | ANKRD26   | ARID1A   | ASXL1 | ASXL2 | ATG2B | ATM | B2M | BCL2 | BCL6 |
|-----------|-----------|----------|-------|-------|-------|-----|-----|------|------|
| BCOR      | BCORL1    | BIRC3    | BRAF  | BRINP3| BTK   | CALR| CARD11| CASP8| CBL  |
| CCND1     | CCND2     | CCND3    | CCR4  | CD28  | CD58  | CD798| CDC25C| CDKN1B| CDKN2A|
| CEBPA     | CNOT3     | CREBBP   | CRLF2 | CSF3R | CSNK1A1| CUX1| CXC4 | DDX3X| DDX41|
| DIS3      | DNM2      | DNMT3A   | DNMT3B| EED   | EGR1  | EP300| ETNK1| ETV6  | EZH2  |
| FAM46C    | FAT1      | FBXW7    | FGFR3 | FLT3  | GATA1 | GATA2| GATA3| GNA13 | ID3   |
| IDH1      | IDH2      | IKZF1    | IL7R  | IRF4  | JAK1  | JAK2 | JAK3 | KDM6A | KIT   |
| KLF2      | KMT2A     | KMT2D    | KRAS  | MAP2K1| MAPK1 | MAX  | MED12| MEF2B | MPL   |
| MYC       | MYD88     | NF1      | NOTCH1| NOTCH2| NPM1  | NRAS | NT5C2| PAX5  | PDGFRB|
| PHF6      | PIGA      | PLCG1    | PLCG2 | PPM1D | PRDM1 | PRKCB| PRPS1| PTEN  | PTPN11|
| RAD21     | RBBP6     | RELN     | RHOA  | RPL10 | RUNX1 | SETBP1| SETD2| SF1   | SF3B1 |
| SH2B3     | SMC1A     | SMC3     | SPEN  | SRP72 | SRSF2 | STAG2| STAT3| STAT5B| SUZ12 |
| TAL1      | TCF3      | TERT     | TET2  | TNFAIP3| TNFRSF14| TP53 | TPMT | TRAF3 | U2AF1 |
| USP7      | WHSC1     | WT1      | XPO1  | ZBTB7A| ZMYM3 | ZRSR2| NOTCH3| NOTCH4| PRPF8 |
| ZNF384    |           |          |       |       |       |      |      |       |      |
Supplement Table 3. List of 267 genes included in the targeted sequencing panel.

| ABCC1 | ABL1 | ANKRD26 | APC | ARID1A | ARID1B | ARID2 | ARID5B | ASXL1 | ASXL2 |
|-------|------|----------|-----|--------|--------|-------|--------|-------|-------|
| ATG2B | ATM  | ATRX     | B2M | BACH2  | BCL10  | BCL2  | BCL6   | BCL7A | BCOR  |
| BCORL1| BIRC3| BLM      | BPGM| BRAF   | BRCA1  | BRCA2 | BRIP1  | BTG1  | BTG2  |
| BTK   | CALR | CARD11   | CBL | CBLB   | BCLC   | CCND1 | CCND3  | CCR4  | CD28  |
| CD58  | CD79A| CD79B    | CDC25| CDKN1A| CDKN1B | CDKN2A| CDKN2B | CDKN2C| CEBSA |
| CHD2  | CHD8 | CITA     | CNOT3| CREBBP| CRLF2  | CSF1R | CSF3R  | CSMD1 | CSNK1A|
| CTCF  | CUX1 | CXCR4    | CYLD | DDX3X  | DDX41  | DIS3  | DKC1   | DNM2  | DNMT3A|
| DNMT3B| DTX1 | DUSP2    | EBF1| EED    | EGFR   | EGLN1 | EGR1   | ELANE | EP300 |
| EPHA7 | EPOR | ETNK1    | ETV6| EZH2   | FAM46C | FAS   | FAT1   | FAT4  | FBXO11|
| FBXW7 | FGFR3| FLT3     | FOXL1| FYN    | GAB2   | GATA1 | GATA2  | GATA3 | GF1   |
| GNA13 | GNA2 | GNAS     | GN1B | GSKIP  | H1-2   | H1-3  | H1-4   | H1-5  | HAX1  |
| HLA-A | HLA-C| HLA-DMB  | HNRNPK| HRAS  | HUEI   | HVEN1 | ID3    | IDH1  | IDH2  |
| IGLL5 | IKZF1| IKZF2    | IL7R| IRF2    | IRF2BP2| IRF4  | IRF8   | ITPKB | JAK1  |
| JAK2  | JAK3 | JUNB     | KDM6A| KIT    | KLF2   | KHL6  | KMT2A  | KMT2B | KMT2C |
| KMT2D | KRAS | KRT20    | LCOR| LMO2   | LTB    | LYN   | MAP2K1 | MAPK1 | MAX   |
| MCL1  | MED12| MEF2B    | MFHAS1| MPL   | MTOR   | MYC   | MYCN   | MYD88 | MYOM2 |
| NF1   | NFE2 | NFKBIA   | NOTCH1| NOTCH2| NOTCH3 | NOTCH4| NPM1   | NRAS  | NRAS  |
| NT5C2 | P2RY8| PALB2    | PAX5 | PDGFRA | PDGFRB | PDS5B | PHF6   | PIGA  | PIK3CA|
| PIK3CD| PIK3R1| PIM1     | PIM2 | PLCG1  | PLCG2  | POT1  | PPM1D  | PRDM1 | PRF1  |
| PRKCB | PRKD2| PRKD8    | PRPF8| PRPS1  | PSMB5  | PTEN  | PTPN1  | PTPN11| PTPRD |
| RAD12 | RASA2| RB1      | RBBP6| RELN   | RHOA   | RPL10 | RRAGC  | RUNX1 | SAMHD1|
| SBDS  | SETBP1| SETD1B   | SETD2| SETDB1 | SF1    | SF3B1 | SGK1   | SH2B3 | SH2D1A|
| SMARCA4| SMC1A| SMC3     | SMO  | SOCS1  | SPI40  | SPEN  | SRP72  | SRSF2 | STAG2 |
| STAT3 | STAT5B| STAT6    | SUFU | SUZ12  | SYK    | TAL1  | TBL1XR1| TCF3  | TERC  |
| TERT  | TET1 | TET2     | TMEM30A| TMSB4X| TNFAIP3| TNFRSF14| TOX   | TP53  | TPMT  |
| TRAF3 | U2AF1| UBE2A    | UBR5 | USP7   | VAV1   | VHL   | WHSC1  | WT1   | XBP1  |
| XPO1  | ZAP70| ZBTB7A   | ZF3P6L1| ZMYM3 | ZNF292 | ZRSR2 |        |       |       |
Supplement Table 4. Pairwise comparison of survival rates between WHO 2022 subtypes in MDS.

| P value | MDS-5q | MDS-SF3B1 | MDS-biTP53 | MDS-LB | MDS-h | MDS-IB1 | MDS-IB2 |
|---------|--------|-----------|------------|--------|-------|---------|---------|
| MDS-5q  | -      | -         | -          | -      | -     | -       | -       |
| MDS-SF3B1 | 0.208  | -         | -          | -      | -     | -       | -       |
| MDS-biTP53 | 0.038  | <0.001    | <0.001     | -      | -     | -       | -       |
| MDS-LB  | 0.389  | 0.237     | <0.001     | -      | -     | -       | -       |
| MDS-h   | 0.060  | 0.754     | <0.001     | 0.094  | -     | -       | -       |
| MDS-IB1 | 0.702  | <0.001    | <0.001     | <0.001 | <0.001| -       | -       |
| MDS-IB2 | 0.685  | <0.001    | <0.001     | <0.001 | <0.001| 0.707   | -       |
| MDS-f   | 0.073  | <0.001    | 0.548      | <0.001 | <0.001| 0.002   | 0.004   |

Abbreviations: WHO, World Health Organization; MDS: myelodysplastic syndromes (neoplasms); 5q−: isolated 5q deletion; biTP53: biallelic TP53 inactivation; LB: low blasts; MDS-h: MDS, hypoplastic; IB1/2: increased blasts type1/2; MDS-f: MDS with fibrosis.
### Supplement Table 5. Clinical and laboratory characteristics of MDS-IB1 and MDS-IB2 patients

| Characteristics                  | MDS-IB1 (n=161) | MDS-IB2 (n=103) | P value |
|----------------------------------|-----------------|-----------------|---------|
| Male, (%)                        | 117 (73)        | 73 (71)         | 0.780   |
| Age, years, median (IQR)         | 59 (48-65)      | 59 (52-65)      | 0.618   |
| Haemoglobin, g/l, median (IQR)   | 80 (67-98)      | 75 (60-87)      | 0.467   |
| WBC×10E+9/L, median (IQR)        | 2.40 (1.63-3.28)| 2.25 (1.53-3.94)| 0.825   |
| ANC×10E+9/L, median (IQR)        | 0.88 (0.52-1.79)| 0.74 (0.37-1.88)| 0.375   |
| PLT×10E+9/L, median (IQR)        | 61 (37-100)     | 41 (18-56)      | 0.090   |
| IPSS-R karyotype (%)             |                 |                 |         |
| Very Good                        | 3 (2.1)         | 2 (2.1)         |         |
| Good                             | 71 (50.4)       | 59 (62.8)       |         |
| Intermediate                     | 42 (29.8)       | 22 (23.4)       | 0.449   |
| Poor                             | 8 (5.7)         | 3 (3.2)         |         |
| Very poor                        | 17 (12.1)       | 8 (8.5)         |         |
| Normal karyotype (%)             | 69 (48.9)       | 55 (58.5)       | 0.182   |
| Complex karyotype (%)            | 22 (15.6)       | 10 (10.6)       | 0.334   |
| IPSS-R risk group (%)            |                 |                 |         |
| Very Low                         | 0               | 0               |         |
| Low                              | 5 (3.5)         | 4 (4.3)         | 0.326   |
| Intermediate                     | 37 (26.2)       | 17 (18.1)       |         |
| High                             | 60 (42.6)       | 38 (40.4)       |         |
| Very High                        | 39 (27.7)       | 35 (37.2)       |         |
| IPSS-M risk group (%)            |                 |                 |         |
| Very Low                         | 1 (0.7)         | 1 (1.1)         |         |
| Low                              | 9 (6.4)         | 6 (6.4)         |         |
| Moderate low                     | 16 (11.3)       | 4 (4.3)         | 0.189   |
| Moderate High                    | 15 (10.6)       | 10 (10.6)       |         |
| High                             | 53 (37.6)       | 28 (29.8)       |         |
| Very High                        | 47 (33.3)       | 45 (47.9)       |         |

Abbreviations: MDS: myelodysplastic syndromes (neoplasms); IB1/2: increased blasts type 1/2; WBC, white blood cell count; ANC, absolute neutrophil count; PLT, platelet count; IPSS-R, Revised International Prognostic Scoring; IPSS-M, International Prognostic Scoring Systems-Molecular.
Median OS for MDS-IB1 and MDS-IB patients were 24 and 26 months, respectively. Survival rate between MDS-IB1 and MDS-IB2 patients were comparable (P=0.707).

Abbreviations: MDS: myelodysplastic syndromes (neoplasms); IB1/2: increased blasts type1/2; OS: overall survival.

Supplement Figure 1. Kaplan–Meier curves for Overall Survival in MDS-IB1 and MDS-IB2 patients.
Supplement Table 6. Clinical and laboratory characteristics of MDS-IB, MDS-biTP53 and MDS-f patients

| Characteristics                        | MDS-IB* (n=264) | MDS-f (n=42) | MDS-biTP53 (n=53) | P1     | P2     | P3     |
|----------------------------------------|-----------------|--------------|-------------------|--------|--------|--------|
| Male, (%)                              | 190 (72)        | 30 (71.4)    | 32 (60.4)         | 0.720  | 0.064  | 0.286  |
| Age, years, median (IQR)               | 59 (48-65)      | 59 (52-65)   | 60 (54-64)        | 0.867  | 0.516  | 0.618  |
| Haemoglobin, g/l, median (IQR)         | 80 (67-98)      | 75 (60-87)   | 72 (59-82)        | 0.023  | <0.001 | 0.467  |
| WBC×10E+9/L, median (IQR)              | 2.40 (1.63-3.28)| 2.25 (1.53-3.94) | 2.82 (1.70-3.57) | 0.772  | 0.323  | 0.825  |
| ANC×10E+9/L, median (IQR)              | 0.88 (0.52-1.79)| 0.74 (0.37-1.88) | 1.04 (0.49-2.02) | 0.333  | 0.236  | 0.375  |
| PLT×10E+9/L, median (IQR)              | 61 (37-100)     | 41 (18-56)   | 45 (29-108)       | <0.001 | 0.207  | 0.090  |
| IPSS-R karyotype (%)                   |                 |              |                   |        |        |        |
| Very Good                              | 5 (2.1)         | 0            | 0                 |        |        |        |
| Good                                   | 130 (55.3)      | 14 (43.8)    | 5 (9.8)           |        |        |        |
| Intermediate                           | 64 (27.2)       | 10 (31.3)    | 2 (3.9)           | 0.487  | <0.001 | <0.001 |
| Poor                                   | 11 (4.7)        | 2 (6.3)      | 4 (7.8)           |        |        |        |
| Very poor                              | 25 (10.6)       | 6 (18.8)     | 40 (78.4)         |        |        |        |
| Normal karyotype (%)                   | 124 (52.8)      | 11 (34.4)    | 3 (5.9)           | 0.060  | <0.001 | 0.001  |
| Complex karyotype (%)                  | 32 (13.6)       | 6 (18.8)     | 42 (82.4)         | 0.423  | <0.001 | <0.001 |
| IPSS-R risk group (%)                  |                 |              |                   |        |        |        |
| Very Low                               | 0               | 0            | 0                 |        |        |        |
| Low                                    | 9 (3.8)         | 2 (6.3)      | 2 (3.9)           | 0.227  | <0.001 | 0.150  |
| Intermediate                           | 54 (23)         | 3 (9.4)      | 4 (7.8)           |        |        |        |
| High                                   | 98 (41.7)       | 14 (43.8)    | 12 (23.5)         |        |        |        |
| Very High                              | 74 (31.5)       | 13 (40.6)    | 33 (64.7)         |        |        |        |
| IPSS-M risk group (%)                  |                 |              |                   |        |        |        |
| Very Low                               | 2 (0.9)         | 0            | 0                 |        |        |        |
| Low                                    | 15 (6.4)        | 4 (12.5)     | 0                 |        |        |        |
| Moderate low                           | 20 (8.5)        | 0            | 0                 | 0.183  | <0.001 | <0.001 |
| Moderate High                          | 25 (10.6)       | 1 (3.1)      | 1 (2)             |        |        |        |
| High                                   | 81 (34.5)       | 10 (31.3)    | 2 (3.9)           |        |        |        |
| Very High                              | 92 (39.1)       | 17 (53.1)    | 48 (94.1)         |        |        |        |

* MDS-IB1 and MDS-IB2 were merged into MDS-IB

p1, p value for MDS-IB vs. MDS-f; p2, value for MDS-IB vs. MDS-biTP53; p3, p value for MDS-f vs. MDS-biTP53.

Abbreviations: MDS: myelodysplastic syndromes(neoplasms); biTP53: biallelic TP53 inactivation; IB1/2: increased blasts type1/2; MDS-f: MDS with fibrosis; WBC, white blood cell count; ANC, absolute neutrophil
count; PLT, platelet count; IPSS-R, Revised International Prognostic Scoring System; IPSS-M, International Prognostic Scoring Systems-Molecular.
Supplement Table 7. Clinical and laboratory characteristics of MDS-LB and MDS-h patients

| Characteristics                  | MDS-LB (n=293) | MDS-h (n=80) | P value |
|----------------------------------|----------------|--------------|---------|
| Male, (%)                        | 181 (61.8)     | 54 (67.5)    | 0.364   |
| Age, years, median (IQR)         | 52 (40-62)     | 52 (38-60)   | 0.543   |
| Haemoglobin, g/l, median (IQR)   | 82 (67-99)     | 78 (65-98)   | 0.343   |
| WBC×10E+9/L, median (IQR)        | 2.68 (1.96-4.00)| 2.40 (1.76-3.29)| 0.004   |
| ANC×10E+9/L, median (IQR)        | 1.26 (0.81-2.16)| 1.04 (0.66-1.59)| 0.004   |
| PLT×10E+9/L, median (IQR)        | 62 (32-131)    | 40 (23-80)   | 0.027   |
| IPSS-R karyotype (%)             |                |              |         |
| Very Good                        | 3 (1.1)        | 1 (1.4)      |         |
| Good                             | 157 (59.2)     | 43 (58.9)    |         |
| Intermediate                     | 72 (27.3)      | 20 (27.4)    | 0.107   |
| Poor                             | 13 (4.9)       | 8 (11)       |         |
| Very poor                        | 20 (7.5)       | 1 (4.8)      |         |
| Normal karyotype (%)             | 137 (51.7)     | 41 (56.2)    | 0.511   |
| Complex karyotype (%)            | 30 (11.3)      | 8 (11)       | 1.000   |
| IPSS-R risk group (%)            |                |              |         |
| Very low                         | 15 (5.7)       | 7 (9.6)      |         |
| Low risk                         | 104 (39.2)     | 19 (26)      | 0.182   |
| Intermediate                     | 110 (41.5)     | 36 (49.3)    |         |
| High                             | 28 (10.6)      | 10 (13.7)    |         |
| Very high                        | 8 (3.0)        | 1 (1.4)      |         |
| IPSS-M risk group (%)            |                |              |         |
| Very Low                         | 8 (3)          | 4 (5.5)      |         |
| Low                              | 72 (27.2)      | 18 (24.7)    |         |
| Moderate low                     | 61 (23)        | 21 (28.8)    | 0.737   |
| Moderate High                    | 55 (20.8)      | 15 (20.5)    |         |
| High                             | 50 (18.9)      | 10 (13.7)    |         |
| Very High                        | 19 (7.2)       | 5 (6.8)      |         |

Abbreviations: MDS: myelodysplastic syndromes(neoplasms); LB: low blasts; MDS-h: MDS, hypoplastic; WBC, white blood cell count; ANC, absolute neutrophil count; PLT, platelet count; IPSS-R, Revised International Prognostic Scoring System; IPSS-M, International Prognostic Scoring Systems-Molecular.
Supplement Figure 2. Kaplan–Meier curves for Overall Survival in MDS-LB and MDS-h patients.

Median OS for both MDS-LB and MDS-h were unreached. MDS-h patients had a trend of better prognosis compared with MDS-LB patients (P=0.094).

Abbreviations: MDS: myelodysplastic syndromes (neoplasms); LB: low blasts; MDS-h: MDS, hypoplastic; OS: overall survival.
Supplement Table 8. Clinical and laboratory characteristics of MDS-LB-SLD and MDS-LB-MLD patients.

| Characteristics                     | MDS-LB-SLD (n=34) | MDS-LB-MLD (n=259) | P value |
|-------------------------------------|-------------------|--------------------|---------|
| Male, (%)                           | 18 (52.9)         | 163 (62.9)         | 0.266   |
| Age, years, median (IQR)            | 58 (44-62)        | 51 (40-62)         | 0.413   |
| Haemoglobin, g/l, median (IQR)      | 93 (80-120)       | 81 (66-98)         | 0.001   |
| WBC×10E+9/L, median (IQR)           | 3.80 (2.60-4.92)  | 2.57 (1.91-3.84)   | 0.002   |
| ANC×10E+9/L, median (IQR)           | 2.14 (1.22-3.04)  | 1.21 (0.79-1.99)   | 0.001   |
| PLT×10E+9/L, median (IQR)           | 60 (31-133)       | 62 (32-131)        | 0.950   |
| IPSS-R karyotype (%)                |                   |                    |         |
| Very Good                           | 0                 | 3 (1.3)            |         |
| Good                                | 20 (66.7)         | 137 (58.3)         |         |
| Intermediate                        | 7 (23.3)          | 65 (27.7)          | 0.590   |
| Poor                                | 0                 | 13 (5.5)           |         |
| Very poor                           | 3 (10)            | 17 (7.2)           |         |
| Normal karyotype (%)                | 17 (56.7)         | 115 (51.5)         | 0.699   |
| Complex karyotype (%)               | 3 (10)            | 27 (11.5)          | 1.000   |
| IPSS-R risk group (%)               |                   |                    |         |
| Very low                            | 6 (20)            | 9 (3.8)            |         |
| Low                                 | 14 (46.7)         | 90 (38.3)          | 0.003   |
| Intermediate                        | 7 (23.3)          | 103 (43.8)         |         |
| High                                | 2 (6.7)           | 26 (11.1)          |         |
| Very high                           | 1 (3.3)           | 7 (3)              |         |
| IPSS-M risk group (%)               |                   |                    |         |
| Very Low                            | 3 (10)            | 5 (2.1)            |         |
| Low                                 | 15 (50)           | 57 (24.3)          |         |
| Moderate low                        | 5 (16.7)          | 56 (23.8)          | 0.004   |
| Moderate High                       | 4 (13.3)          | 51 (21.7)          |         |
| High                                | 3 (10)            | 47 (20)            |         |
| Very High                           | 0                 | 19 (8.1)           |         |

Abbreviations: MDS: myelodysplastic syndromes (neoplasms); LB-SLD/MLD: low blasts with single lineage dysplasia/multilineage dysplasia; WBC, white blood cell count; ANC, absolute neutrophil count; PLT, platelet count; IPSS-R, Revised International Prognostic Scoring System; IPSS-M, International Prognostic Scoring Systems-Molecular.
Supplement Figure 3. Kaplan–Meier curves for Overall Survival in MDS-LB-SLD and MDS-LB-MLD patients.

Median OS for both MDS-LB-SLD and MDS-LB-MLD were unreached. MDS-LB-SLD patients had a better prognosis compared with MDS-LB-MLD patients (P=0.023).

Abbreviations: MDS: myelodysplastic syndromes (neoplasms); LB: low blasts; SLD: single lineage dysplasia; MLD: multilineage dysplasia; OS: overall survival.