Supplementary material

Oral decitabine cedazuridine with and without venetoclax in higher-risk myelodysplastic syndromes or chronic myelomonocytic leukemia: a propensity score–matched study

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Supplementary Tables

Supplementary Table 1. Clinical trials included in this study

DEC-C cohort		DEC-C-Ven cohort
Phase 2 (NCT02103478)	**Phase 3 (ASCERTAIN) (NCT03306264)**	**Phase 1/2 (NCT04655755)**
Phase 2	Phase 3	Phase 1/2
Multicentric	Multicentric	Unicentric
Open-label	Open-label	Open-label
Randomized	Randomized	Not randomized
≥ 18 yo	≥ 18 yo	≥ 18 yo
ECOG 0-2	ECOG 0-1	Not specified
IPSS Int 1 IPSS Int 2 IPSS high	IPSS Int 1 IPSS Int 2 IPSS high	IPSS Int 2 IPSS high
Treatment-naïve or 1 cycle prior HMA permitted	Treatment-naïve or 1 cycle prior HMA permitted	Treatment-naïve
Initial n of patients: 138	Initial n of patients: 173	Initial n of patients: 53

Dose confirmation stage
• **Seq A (n = 25)**
  • C1: oDec 35 mg & Ced 100 mg x 5 d
  • C2: IV Dec 20 mg/m^2 x 5 d
  • C3 & onwards: DEC-C x 5 d
• **Seq B (n = 25)**
  • C1: IV Dec 20 mg/m^2 x 5 d
  • C2: oDec 35 mg & Ced 100 mg x5 d
  • C3 & onwards: DEC-C x 5 d
Fixed-dose combination stage
• **Seq A (n = 16)**
• **Seq B (n = 14)**
	Crossover
	• **Seq A (n = 69)** (3 withdrew consent, 3 discontinued)
	  • C1: DEC-C x 5 d
	  • C2: IV Dec 20 mg/m^2 x 5 d
	  • C3 & onwards: DEC-C x 5 d
	• **Seq B (n = 69)** (2 withdrew consent, 2 discontinued)
	  • C1: IV Dec 20 mg/m^2 x 5 d
	  • C2: DEC-C x 5 d
	  • C3 & onwards: DEC-C x 5 d
		Dose escalation
		• **Dose level 0 (n = 3)**
		  • C1 & onwards: DEC-C x 5 d & Ven 200 mg 1-14 d)
		• **Dose level 1 (n = 6)**
		  • C1 & onwards: DEC-C x 5 d Ven 400 mg 1-14 d)
		Dose expansion (n = 44)
		• C1 & onwards: DEC-C x 5 d Ven 400 mg 1-14 d)

80 patients treated 63 MDS 17 CMML	133 patients received at least 1 dose 117 MDS 16 CMML	53 patients treated 46 MDS 6 CMML 1 aCML

Ced: Cedazuridine; Dec: decitabine; DEC-C: fixed-dose oral decitabine plus cedazuridine; oDec: oral decitabine.

Supplementary Table 2. Next-generation sequencing coverage (DEC-C cohort)

Obtained from:

https://genomictestingcooperative.com/genomic-tests/hematology-profile/

ABL1	*CREBBP*	*GRIN2A*	*NOTCH1*	*SMARCA4*
ABRAXAS1	*CRLF2*	*H3-3A (H3F3A)*	*NOTCH2*	*SMARCB1*
ACVR1B	*CSF1R*	*H3C2 (HIST1H3B)*	*NOTCH3*	*SMC1A*
AKT1	*CSF3R*	*HGF*	*NPM1*	*SMC3*
AKT2	*CTCF*	*HNF1A*	*NRAS*	*SMO*
AKT3	*CTNNA1*	*HOXB13*	*NSD1*	*SOCS1*
ALK	*CTNNB1*	*HRAS*	*NSD2 (WHSC1)*	*SOX2*
AMER1	*CUX1*	*HSP90AA1*	*NTHL1*	*SOX9*
ANKRD26	*CXCR4*	*ID3*	*NTRK1*	*SPOP*
APC	*CYLD*	*IDH1*	*NTRK2*	*SRC*
AR	*DAXX*	*IDH2*	*NTRK3*	*SRSF2*
ARAF	*DDR2*	*IGF1R*	*PAK3*	*STAG2*
ARID1A	*DDX41*	*IKZF1*	*PALB2*	*STAT3*
ARID1B	*DICER1*	*IKZF3*	*PAX5*	*STAT5B*
ARID2	*DNM2*	*IL7R*	*PBRM1*	*STK11*
ASXL1	*DNMT3A*	*INHBA*	*PDGFRA*	*SUFU*
ATM	*DOT1L*	*IRF4*	*PDGFRB*	*SUZ12*
ATR	*EED*	*JAK1*	*PHF6*	*TAL1*
ATRX	*EGFR*	*JAK2*	*PIK3CA*	*TCF3*
AURKA	*EGLN1*	*JAK3*	*PIK3R1*	*TENT5C (FAM46C)*
AURKB	*ELANE*	*KAT6A*	*PIK3R2*	*TERC*
AURKC	*EP300*	*KDM5C*	*PIM1*	*TERT*
AXIN1	*EPAS1*	*KDM6A*	*PLCG1*	*TET2*
AXIN2		*KDR*	*PMS1*	*TGFBR2*

B2M	*EPHA3*	*KEAP1*	*PMS2*	*TMEM127*
BAP1	*EPHA5*	*KIT*	*POLD1*	*TNFAIP3*
	ERBB2	*KMT2A*	*POLE*	*TNFRSF14*
BCL2	*ERBB3*	*KMT2B*	*POT1*	*TP53*
BCL2L1	*ERBB4*	*KMT2C*	*PPM1D*	*TRAF3*
BCL6	*ERG*	*KMT2D*	*PPP2R1A*	*TSC1*
BCOR	*ESR1*	*KRAS*	*PRDM1*	*TSC2*
BCORL1	*ETNK1*	*LRP1B*	*PRKAR1A*	*TSHR*
BCR	*ETV6*	*MAP2K1*	*PRKDC*	*U2AF1*
BIRC3	*EXO1*	*MAP2K2*	*PRPF8*	*U2AF2*
BLM	*EZH2*	*MAP2K4*	*PRSS1*	*UBA1*
	FANCA	*MAP3K1*	*PTCH1*	*VHL*
BRAF	*FANCC*	*MAP3K14*	*PTEN*	*WT1*
BRCA1	*FANCD2*	*MAPK1*	*PTPN11*	*XPO1*
BRCA2	*FANCE*	*MCL1*	*RAC1*	*XRCC2*
BRIP1	*FANCF*	*MDM2*	*RAD21*	*XRCC3*
BTK	*FANCG*	*MDM4*	*RAD50*	*ZNF217*
CALR	*FAS*	*MED12*	*RAD51*	*ZRSR2*
CARD11	*FBXW7*	*MEF2B*	*RAD51C*	
CBL	*FGF4*	*MEN1*	*RAD51D*	
CBLB	*FGF6*	*MET*	*RAF1*	
CBLC	*FGFR1*	*MITF*	*RB1*	
CCND1	*FGFR2*	*MLH1*	*RET*	
CCND3	*FGFR3*	*MPL*	*RHEB*	
CCNE1	*FGFR4*	*MRE11 (MRE11A)*	*RHOA*	
CD274 (PD-L1)	*FH*	*MSH2*	*RIT1*	
CD79A	*FLCN*	*MSH3*	*RNF43*	
CD79B	*FLT3*	*MSH6*	*ROS1*	
CDC73	*FLT4*	*MTOR*	*RUNX1*	

CDH1	*FOXL2*	*MUTYH*	*SAMD9*	
CDK12	*FUBP1*	*MYC*	*SAMD9L*	
CDK4	*GALNT12*	*MYCL*	*SDHA*	
CDK6	*GATA1*	*MYCN*	*SDHB*	
	GATA2	*MYD88*	*SDHAF2*	
CDKN2A	*GATA3*	*NBN*	*SDHC*	
CDKN2B	*GEN1*	*NF1*	*SDHD*	
CDKN2C	*GNA11*	*NF2*	*SETBP1*	
CEBPA	*GNAQ*	*NFE2*	*SETD2*	
CHEK1	*GNAS*	*NFE2L2*	*SF3B1*	
CHEK2	*GNB1*	*NFKBIA*	*SMAD2*	
CIC	*GREM1*	*NKX2-1*	*SMAD4*	

Supplementary Table 3. Next-generation sequencing coverage (DEC-C Ven cohort)

Gene	Exons (codons) tested
ANKRD26(NM_014915)	1 (1-6)
ASXL1 (NM_015338)	11-12 (362-1542)
ASXL2 (NM_018263)	11-12 (381-1436)
BCOR (NM_017745)	2-4 (1-512), 4-6 (514-1080), 7 (1122-1124), 7 (1091-1099), 7-15 (1124-1722)
BCORL1 (NM_021946)	1-6 (1-1261), 6 (1264-1323), 6-11 (1326-1600), 11-12 (1614-1699), 12 (1706-1712)
BRAF (NM_004333)	11 (439-478), 15 (581-620)
BRINP3 (NM_199051)	2-8 (1-471), 8 (475-767)
CALR (NM_004343)	9 (352-418)
CBL (NM_005188)	7-9 (336-477)
CBLB (NM_170662)	7-10 (282-469)
CBLC (NM_012116)	7-9 (336-454), 10 (464-475)
CEBPA (NM_004364)	1 (1-56), 1 (59-91), 1 (96), 1 (128-143), 1 (146-175), 1 (178-201), 1 (249-358)
CREBBP (NM_004380)	2-8 (29-608), 9-10 (615-705), 12-16 (724-1084), 17-31 (1094-1943), 31 (1950-2235), 31 (2238-2443)
CSF3R (NM_156039)	14 (575-622), 17 (681-864)
CUX1 (NM_181552)	2-6 (11-172), 6-9 (174-241), 10-12 (248-359), 13-14 (367-408)
DDX41 (NM_016222)	1-10 (1-366), 11 (369-410), 12-17 (420-623)
DNMT3A (NM_022552)	8-22 (286-862), 23 (866-913)
EED (NM_003797)	1-2 (1-69), 2-8 (71-287), 9-12 (289-442)
ELANE (NM_001972)	1-2 (5-46), 2 (69-75), 4-5 (123-268)
ETNK1 (NM_018638)	3 (228-275)
ETV6 (NM_001987)	1-6 (1-378), 7-8 (385-453)
EZH2 (NM_004456)	2-5 (1-158), 6 (162-205), 7 (209-217), 8-13 (243-512), 14 (516-538), 14-19 (547-732), 20 (752)
FBXW7 (NM_033632)	9-12 (413-708)
FLT3 (NM_004119)	11-17 (437-709), 18-20 (736-847)
GATA1 (NM_002049)	2-3 (1-84)
GATA2 (NM_032638)	2-5 (1-377), 5-6 (379-481)
GFI1 (NM_005263)	2 (2-39)
GNAS (NM_000516)	8 (200-202), 11 (315-324)
HNRNPK (NM_002140)	3-7 (1-96), 7 (101-106), 8-17 (111-465)
HRAS (NM_005343)	2-3 (1-60), 3-4 (87-150)
IDH1 (NM_005896)	4 (132-133)
IDH2 (NM_002168)	4 (125-178)
IKZF1 (NM_006060)	2-8 (1-443), 8 (445-518)
IL2RG (NM_000206)	1-2 (1-45), 2-8 (51-340), 8 (360-370)
IL7R (NM_002185)	5-7 (180-292)
JAK1 (NM_002227)	3-9 (3-445), 10 (453-465), 10-22 (470-1023), 22-24 (1026-1123)
JAK2 (NM_004972)	10 (405-442), 12-14 (505-622), 16 (665-711), 18 (762-802)
JAK3 (NM_000215)	2-23 (1-1069)

KDM6A (NM_021140)	1-19 (1-971), 19-21 (976-1070), 22-29 (1080-1402)
KIT (NM_000222)	8-9 (411-514), 11 (550-592), 17 (788-828)
KMT2A (NM_005933)	2-4 (145-1075), 4-13 (1081-1561), 14-15 (1566-1665), 27 (2178-2195), 27 (2201-2362), 27 (2365-2715), 27 (2721-3216), 27 (3219-3327), 27 (3336-3505), 27 (3521-3582)
KRAS (NM_004985)	2-4 (1-150)
MAP2K1 (NM_002755)	2 (27-90), 3 (98-146)
MPL (NM_005373)	10 (490-522), 12 (552-636)
NF1 (NM_001042492)	2-4 (21-160), 5 (165-190), 6 (201-218), 8-13 (244-468), 13-14 (478-547), 15-17 (568-667), 18 (674-728), 18-22 (746-992), 23-26 (997-1146), 26-30 (1160-1330), 30-31 (1353-1378), 31-34 (1382-1493), 34-35 (1512-1550), 35 (1563-1575), 36-38 (1601-1868), 39 (1870-1884), 39-40 (1886-1947), 40-47 (1952-2322), 47-49 (2325-2438), 50-51 (2441-2491), 51-52 (2494-2555), 53-58 (2580-2840)
NOTCH1 (NM_017617)	26 (1529-1600), 26-28 (1604-1795), 34 (2061-2228), 34 (2234-2274), 34 (2290-2309), 34 (2290-2556), 34 (2061-2228), 34 (2234-2274), 34 (2309-2556)
NPM1 (NM_002520)	11 (283-295)
NRAS (NM_002524)	2-4 (1-150)
PAX5 (NM_016734)	1-10 (1-392)
PHF6 (NM_032458)	2-3 (1-79), 4-10 (81-366)
PIGA (NM_002641)	2 (1-6), 2-5 (15-396), 6 (399-485)
PML (NM_033238)	3 (201-255)
PRPF40B (NM_001031698)	2-19 (2-609), 19-20 (611-658), 20-24 (661-807), 25-26 (815-893)
PTEN (NM_000314)	7-8 (212-340)
PTPN11 (NM_002834)	3-4 (46-125), 7 (253-285), 12 (460-462), 12-13 (465-533)
RAD21 (NM_006265)	2-12 (1-540), 13 (544-560), 14 (569-632)
RARA (NM_000964)	6-7 (211-338)
RUNX1 (NM_001754)	2-9 (1-419), 9 (426-437), 9 (456-474)
SETBP1 (NM_015559)	4 (838-885)
SF1 (NM_004630)	1-2 (1-31), 2 (39-54), 3-12 (57-524), 13 (544-578), 13 (596-600), 13 (605-640)
SF3A1 (NM_005877)	2-7 (22-322), 7-9 (355-424), 9-12 (427-646), 13-16 (651-794)
SF3B1 (NM_012433)	13-16 (574-790)
SH2B3 (NM_005475)	2 (1-40), 2 (43-119), 2 (132-164), 2-6 (233-374), 6-8 (380-576)
SMC1A (NM_006306)	1-25 (1-1234)
SMC3 (NM_005445)	1 (1-5), 2-6 (19-110), 6-11 (113-299), 11-15 (308-477), 15-16 (498-504), 16-17 (507-580), 17-19 (591-706), 20-25 (708-975), 25 (979-1035), 26-29 (1038-1217)
SRSF2 (NM_003016)	1 (1-38), 1 (45-121)
STAG1 (NM_005862)	2 (1-5), 3-5 (10-101), 5-12 (121-392), 13-20 (402-703), 21-22 (724-738), 22-27 (740-953), 27 (955-979), 28 (985-1008), 29-34 (1022-1259)
STAG2 (NM_006603)	2-8 (1-273), 9-16 (287-518), 16 (521-539), 17-22 (547-751), 23-33 (756-1232)
STAT3 (NM_139276)	17 (489-509), 17-22 (521-715)
STAT5A (NM_003152)	3-6 (1-177), 6-7 (181-189), 8-20 (261-795)
STAT5B (NM_012448)	16 (636-673)

SUZ12 (NM_015355)	1 (20-44), 1 (46-84), 2 (92-97), 4-5 (129-169), 7-11 (198-431), 12-16 (468-740)
TERC (NR_001566)	1 (1-36)
TERT (NM_198253)	1-2 (1-172), 2 (258-342), 2 (349-474), 2-4 (477-630), 4-5 (633-692), 6 (711-749), 6-12 (753-954), 12-16 (957-1133)
TET2 (NM_001127208)	3 (1-77), 3 (91-92), 3 (98-815), 3 (829-853), 3-10 (867-1453), 10-11 (1465-2003)
TP53 (NM_000546)	2 (1-25), 4-11 (80-394)
U2AF1 (NM_006758)	2 (15-44), 6 (117-161)
U2AF2 (NM_007279)	1-5 (1-161), 6-12 (163-437), 12 (441-476)
WT1 (NM_024426)	1 (1-5), 1 (7-63), 1-10 (127-518)
ZRSR2 (NM_005089)	1-4 (1-90), 5 (105-130), 6-8 (134-257), 9-11 (260-419), 11 (465-483)

Supplementary Table 4. Characteristics of unmatched cohorts

Characteristic	DEC-C cohort (n = 117)	DEC-C-Ven cohort (n = 52)	*P* value
Age, median (range) [years]	71 (40-90)	71 (27-94)	.965
Race, n (%)			
Asian	2 (2)	3 (6)	1
Black or African-American	2 (2)	0	1
White	109 (93)	49 (94)	1
Other/not reported	3 (3)	0	1
Male sex, n (%)	77 (66)	37 (71)	.613
ECOG performance status			
0	48 (41)	21 (40)	1
1	64 (55)	25 (48)	1
2	4 (3)	6 (12)	.286
Not available	1 (1)	0	-
WHO diagnosis, n (%)			
MDS-EB1	51 (44)	9 (17)	**.002**
MDS-EB2	44 (38)	37 (71)	**< .001**
CMML	22 (19)	6 (12)	1
Hemoglobin, median (range) [g/L]	92 (64-149)	92 (62-144)	.403
Neutrophil count, median (range) [x 10^9 cells/L]	0.9 (0.1-43.8)	0.9 (0.1-11.3)	.156
Platelet count, median (range) [x 10^9 cells/L]	61 (8-570)	70 (15-407)	.938
Bone marrow blasts, median (range) [%]	9 (5-19)	12 (6-18)	**<.001**
Cytogenetic category, n (%)			
Very low	2 (2)	0	1
Low	48 (41)	19 (37)	.811
Intermediate	19 (16)	15 (29)	1
High	8 (7)	6 (12)	1
Very high	19 (16)	12 (23)	1
IPSS			
Intermediate-1	48 (41)	0	**< .001**
Intermediate-2	37 (32)	38 (73)	**< .001**
High	29 (25)	14 (27)	1
IPSS-R, n (%)			
Very low	0	0	-
Low	4 (3)	0	1
Intermediate	27 (23)	6 (12)	.175
High	30 (26)	16 (32)	1
Very high	35 (30)	28 (56)	.104
Not available	21 (18)	0	-
IPSS-M, n (%)			
Very low	0	0	-
Low	12 (10)	0	.093
Intermediate low	4 (3)	1 (2)	1
Intermediate high	7 (6)	3 (6)	1
High	17 (15)	17 (33)	.547
Very high	51 (44)	31 (60)	1

Supplementary Table 5. Responses by the IWG-2023 criteria

Response, n (%)	DEC-C-Ven cohort (n = 51)
ORR	41 (80)
CR	29 (54)
CR-uni	6 (12)
CR-bi	5 (12)
CR-h	1 (2)
SD/PD	9 (18)
NE	1 (2)

ORR: Overall response rate, CR-uni: CR unilineage, CR-bi: CR bilineage, CR-h: CR with partial hematologic recovery, SD: Stable disease, PD: progressive disease, NE: not evaluable

Supplementary Figures

Supplementary Fig. 1. (A) Mutations and cytogenetic findings in the DEC-C and DEC-C-Ven non-matched cohorts. (B) IPSS-M score distribution in the DEC-C and DEC-C-Ven non-matched cohorts.

Supplementary Fig. 2. (A) Standardized mean differences of the variables used for propensity score matching, before (purple) and after matching (green). (B) Propensity score of matched and unmatched individuals of each cohort. (C) Distribution of the propensity score distance of individuals in the DEC-C and DEC-C cohorts, before and after matching.

Supplementary Fig. 3. Response rate and univariate analyses of OS and EFS in selected subgroups of patients.

Supplementary Fig. 4. OS and EFS of the DEC-C vs DEC-C-Ven cohorts with censoring at last follow-up (tick) or at HSCT (point).

Supplementary Fig. 5. (A) OS of the DEC-C vs DEC-C-Ven cohorts by disease (MDS or CMML). (B) EFS of the DEC-C vs DEC-C-Ven cohorts by disease (MDS or CMML). (C) OS of the DEC-C vs DEC-C-Ven cohorts by IPSS-R (I: intermediate, H: high, VH: very high). (D) EFS of the DEC-C vs DEC-C-Ven cohorts by IPSS-R (I: intermediate, H: high, VH: very high). (E) OS of the DEC-C vs DEC-C-Ven cohorts by IPSS-M (H: high, VH: very high). (F) EFS of the DEC-C vs DEC-C-Ven cohorts by IPSS-M (H: high, VH: very high).

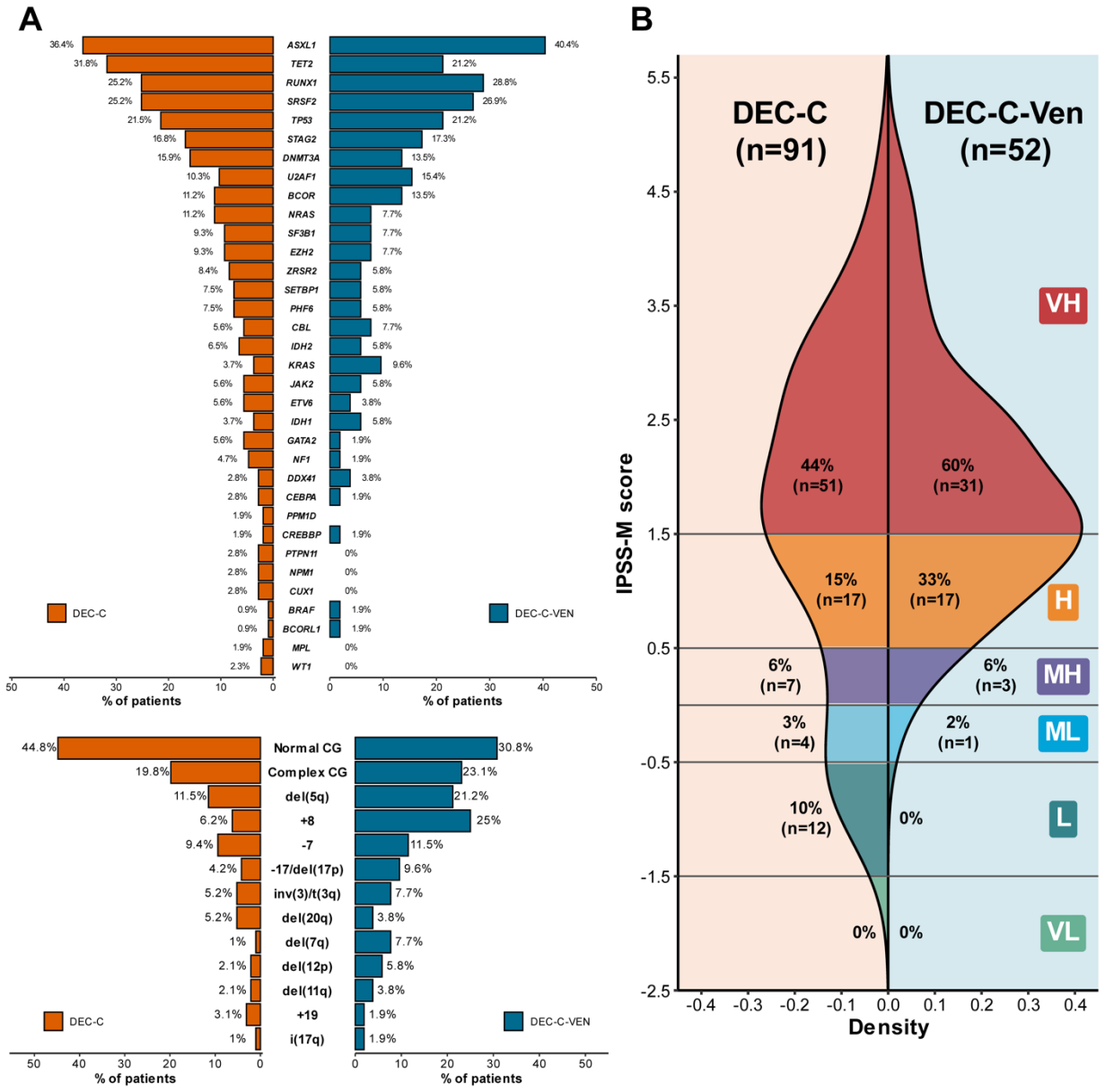
Supplementary Fig. 6. (A) OS of the DEC-C vs DEC-C-Ven cohorts by *ASXL1* mutation (wt: wild-type, mut: mutated). (B) EFS of the DEC-C vs DEC-C-Ven cohorts by *ASXL1* mutation (wt: wild-type, mut: mutated). (C) OS of the DEC-C vs DEC-C-Ven cohorts by *TP53* mutation (wt: wild-type, mut: mutated). (D) EFS of the DEC-C vs DEC-C-Ven cohorts by *TP53* mutation (wt: wild-type, mut: mutated).

Supplementary Fig. 7. Cumulative incidence (CI) of death vs HSCT as competing events.

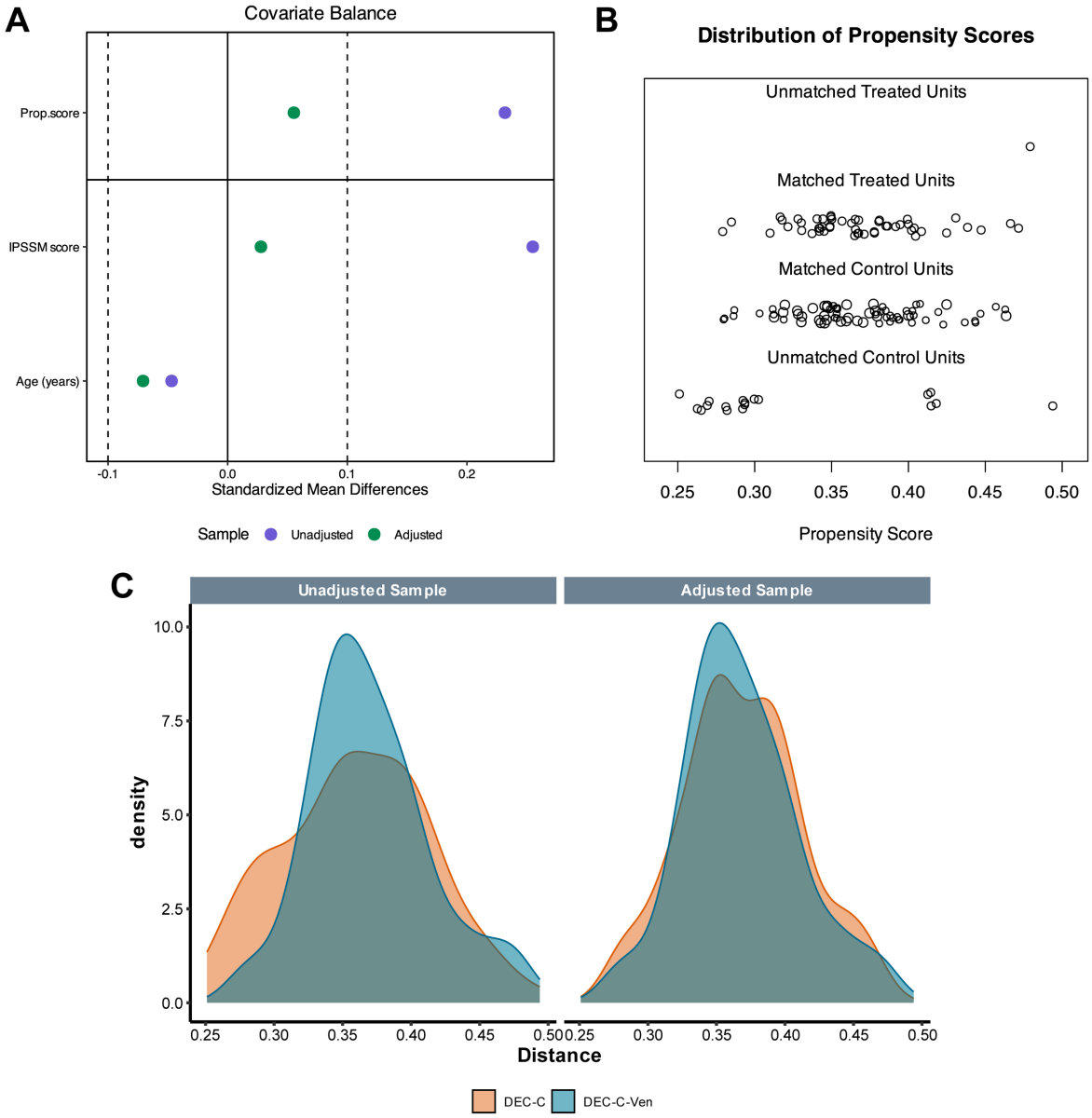
Supplementary Fig. 8. (A) OS of the DEC-C vs DEC-C-Ven cohorts after HSCT. (B) EFS of the DEC-C vs DEC-C-Ven cohorts after HSCT. (C) Cumulative incidence (CI) of death and relapse as competing events in DEC-C and DEC-C-Ven cohorts.

Supplementary Fig. 9. (A) Absolute neutrophil count (ANC) at each timepoint during the first cycle. (C) Platelet count at each timepoint during the first cycle. * $P < 0.05$, ** $P < 0.01$

Supplementary Fig. 1. Mutations in each cohort

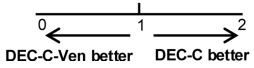


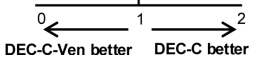
Supplementary Fig. 2. Propensity score performance



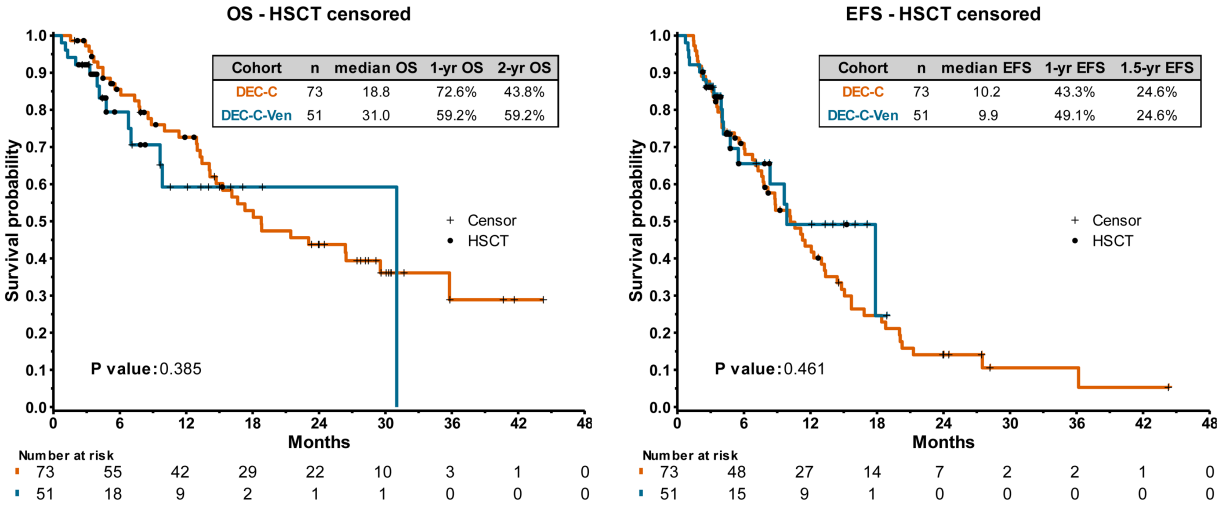
Supplementary Fig. 3. Outcomes by group

	Response rate			Overall survival (OS)				Event-free survival (EFS)			
	n of responders/total n (%)			n of events/total n (%)		Univariate analysis for OS		n of events/total n (%)		Univariate analysis for EFS	
Variable	DEC-C	DEC-C-VEN	P val	DEC-C	DEC-C-VEN	HR (95% CI)	P val	DEC-C	DEC-C-VEN	HR (95% CI)	P val
All	47/73 (64)	46/51 (90)	0.002	43/73 (59)	21/51 (41)	1.04 (0.61-1.77)	0.889	63/73 (86)	26/51 (51)	0.6 (0.38-0.94)	0.028
Sex											
Female	18/28 (64)	13/15 (87)	0.164	20/28 (71)	4/15 (27)	0.55 (0.18-1.63)	0.28	27/28 (96)	5/15 (33)	0.3 (0.12-0.78)	0.014
Male	29/45 (64)	33/36 (92)	0.004	23/45 (51)	17/36 (47)	1.34 (0.72-2.54)	0.368	36/45 (80)	21/36 (58)	0.8 (0.46-1.38)	0.417
Age											
<70	20/30 (67)	20/21 (95)	0.017	14/30 (47)	8/21 (38)	1.53 (0.61-3.85)	0.361	25/30 (83)	10/21 (48)	0.62 (0.3-1.3)	0.209
>70	27/43 (63)	26/30 (87)	0.033	29/43 (67)	13/30 (43)	0.77 (0.4-1.48)	0.429	38/43 (88)	16/30 (53)	0.58 (0.32-1.04)	0.069
Disease											
CMML	11/14 (79)	6/6 (100)	0.521	7/14 (50)	2/6 (33)	1.35 (0.26-7.13)	0.723	11/14 (79)	2/6 (33)	0.45 (0.1-2.09)	0.308
MDS	36/59 (61)	40/45 (89)	0.002	36/59 (61)	19/45 (42)	0.99 (0.56-1.73)	0.966	52/59 (88)	24/45 (53)	0.6 (0.37-0.97)	0.038
BM Blasts											
<10	24/40 (60)	10/11 (91)	0.075	24/40 (60)	5/11 (46)	1.22 (0.46-3.23)	0.696	35/40 (88)	8/11 (73)	1.01 (0.46-2.18)	0.987
≥10	23/33 (70)	36/40 (90)	0.038	19/33 (62.2)	16/40 (40)	1.05 (0.52-2.09)	0.9	28/33 (85)	18/40 (45)	0.5 (0.28-0.92)	0.026
IPSS-R											
High	14/25 (56)	15/16 (94)	0.013	14/25 (56)	5/16 (31)	0.53 (0.19-1.51)	0.237	22/25 (88)	5/16 (31)	0.23 (0.08-0.6)	0.003
Very High	18/29 (62)	25/29 (86)	0.07	20/29 (69)	14/29 (48)	1.34 (0.65-2.77)	0.427	26/29 (90)	19/29 (66)	0.89 (0.49-1.61)	0.698
IPSS-M											
Mod. High	4/5 (80)	3/3 (100)	1	1/5 (20)	1/3 (33)	1.49 (0.09->10)	0.778	4/5 (80)	1/3 (33)	0.47 (0.05-4.27)	0.504
High	11/17 (65)	16/17 (94)	0.085	10/17 (58)	7/17 (41)	1.84 (0.64-5.31)	0.258	15/17 (88)	8/17 (47)	0.54 (0.23-1.28)	0.161
Very High	27/46 (59)	26/30 (87)	0.011	31/46 (67)	13/30 (43)	0.72 (0.37-1.37)	0.317	40/46 (87)	17/30 (57)	0.56 (0.31-0.99)	0.046
Cytogenetics											
Normal	21/30 (69)	16/16 (100)	0.018	10/30 (53)	6/16 (38)	1.87 (0.67-5.21)	0.23	22/30 (73)	6/16 (38)	0.62 (0.25-1.55)	0.309
del(5q)	8/10 (80)	10/11 (91)	0.586	8/10 (80)	6/11 (55)	1.15 (0.39-3.4)	0.807	9/10 (90)	8/11 (73)	1.13 (0.43-2.97)	0.801
-7/del(7q)	5/7 (71)	9/10 (90)	0.537	6/7 (86)	5/10 (50)	0.71 (0.19-2.65)	0.606	7/7 (100)	6/10 (60)	0.54 (0.18-1.64)	0.279
+8	3/4 (75)	12/13 (92)	0.426	3/4 (75)	5/13 (39)	0.66 (0.13-3.45)	0.627	4/4 (100)	8/13 (62)	0.77 (0.2-2.92)	0.701
Complex	11/14 (79)	11/12 (92)	0.598	11/14 (79)	6/12 (50)	1 (0.35-2.85)	0.997	13/14 (92)	9/12 (75)	1.1 (0.46-2.61)	0.836
Mutations											
ASXL1	22/30 (73)	20/20 (100)	0.015	16/30 (53)	6/20 (30)	0.61 (0.24-1.55)	0.296	24/30 (80)	6/20 (30)	0.29 (0.12-0.72)	0.007
BCOR	3/11 (27)	7/7 (100)	0.004	7/11 (64)	3/7 (43)	0.37 (0.08-1.8)	0.218	10/11 (91)	3/7 (43)	0.15 (0.03-0.7)	0.016
IDH2	1/5 (20)	3/3 (100)	0.143	3/5 (60)	0/3 (0)	0 (0->10)	0.999	4/5 (80)	0/3 (0)	0 (0->10)	0.999
SRSF2	10/16 (63)	12/13 (92)	0.093	8/16 (50)	5/13 (39)	1.36 (0.42-4.39)	0.611	14/16 (88)	6/13 (46)	0.61 (0.23-1.63)	0.322
STAG2	7/13 (54)	9/9 (100)	0.046	7/13 (54)	3/9 (33)	0.8 (0.2-3.14)	0.749	11/13 (85)	3/9 (33.3)	0.2 (0.05-1.01)	0.052
TET2	15/22 (68)	11/11 (100)	0.067	12/22 (55)	6/11 (55)	1.49 (0.55-4.02)	0.431	17/22 (77)	6/11 (55)	0.85 (0.33-2.21)	0.743
TP53	11/18 (61)	10/11 (91)	0.11	14/18 (78)	6/11 (55)	0.87 (0.33-2.31)	0.784	16/18 (89)	8/11 (73)	0.84 (0.36-1.97)	0.696

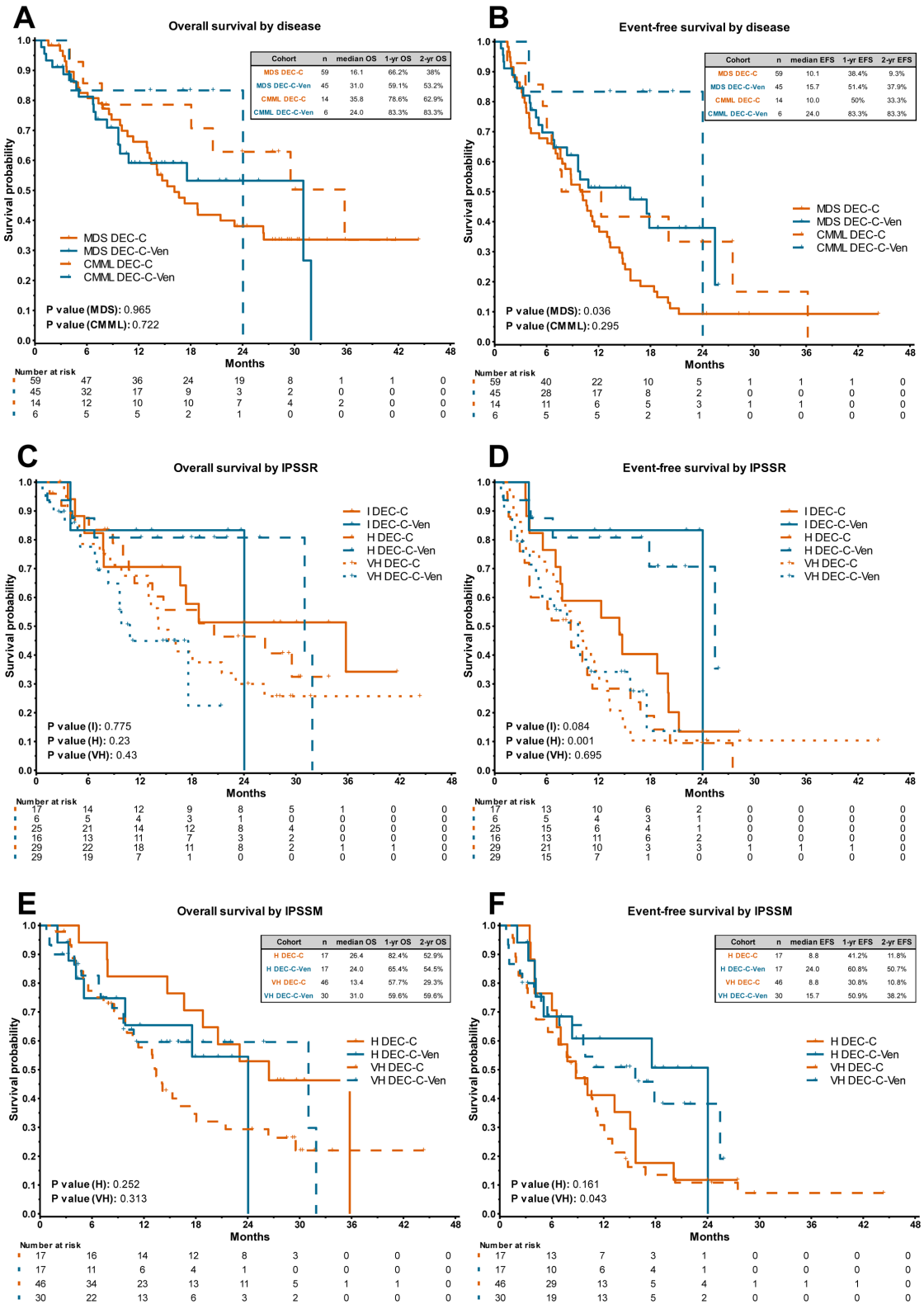




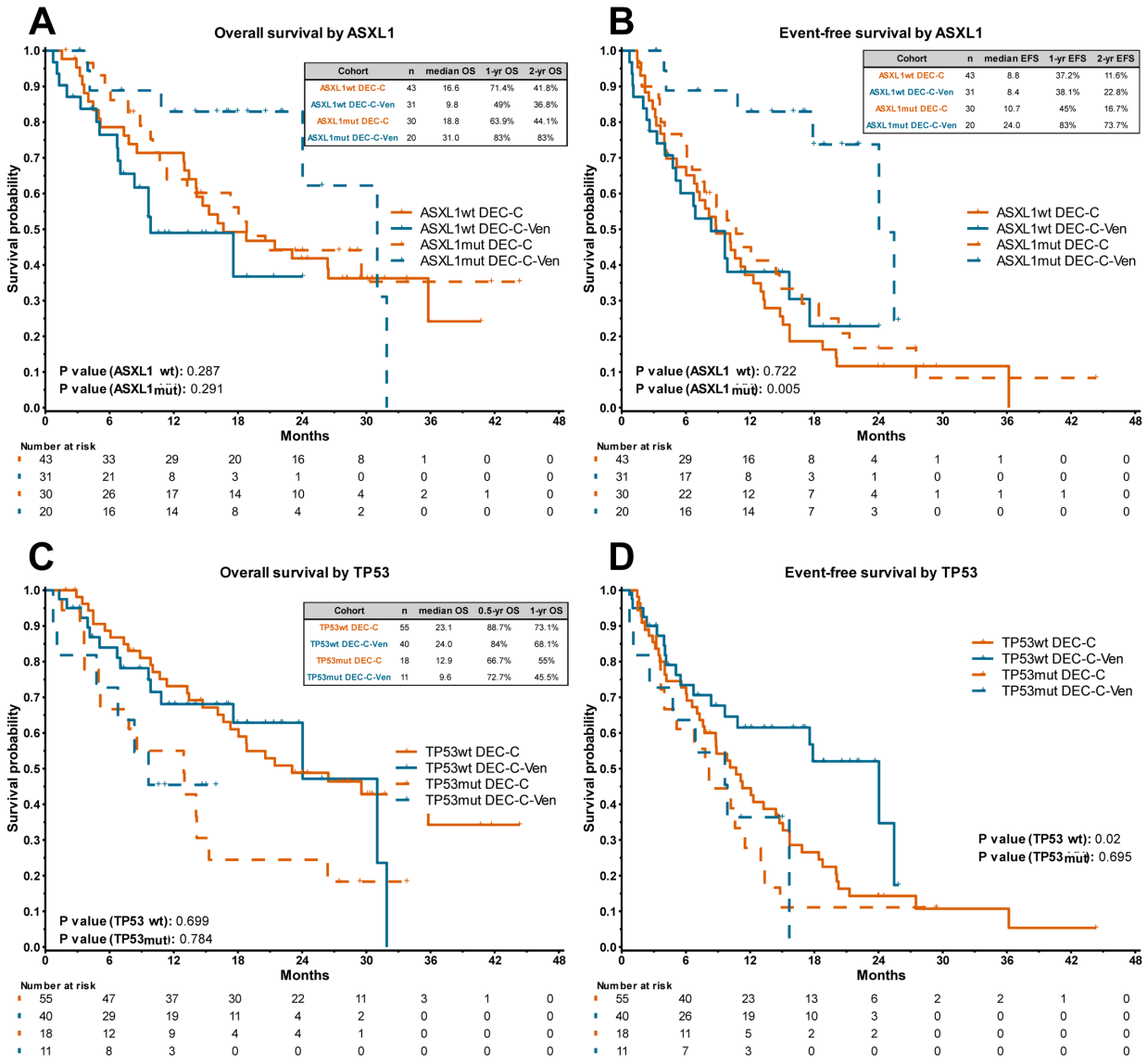
Supplementary Fig. 4. OS and EFS, censored at HSCT



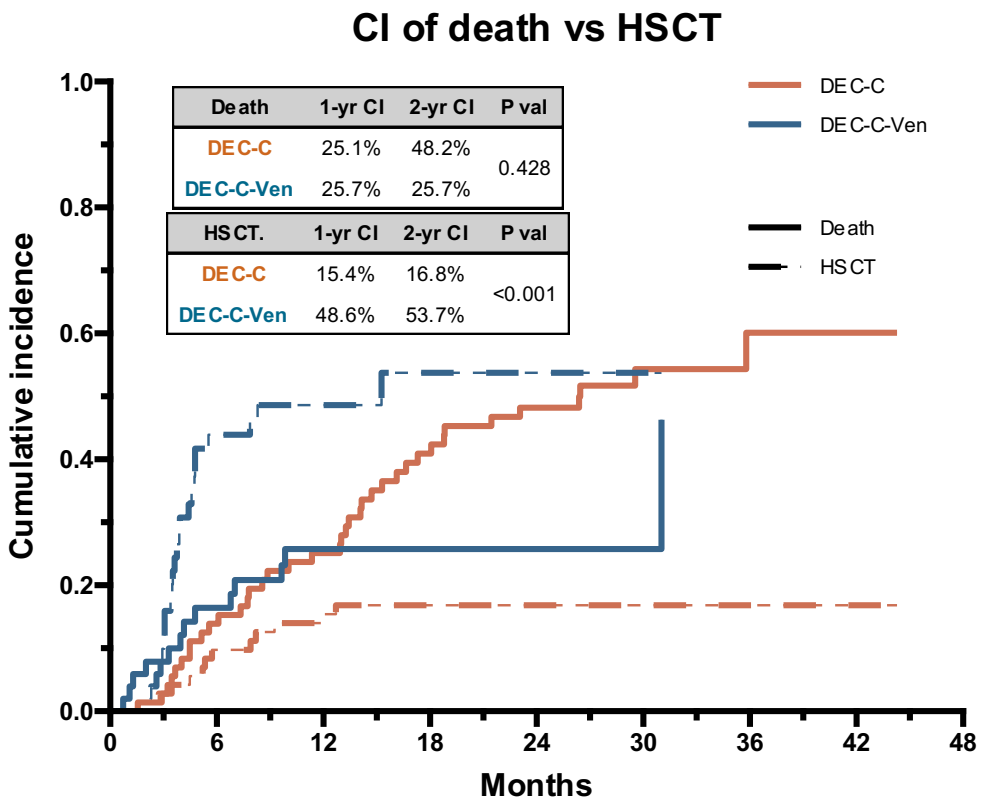
Supplementary Fig. 5. OS and EFS of specific subgroups – I



Supplementary Fig. 6. OS and EFS of specific subgroups – II



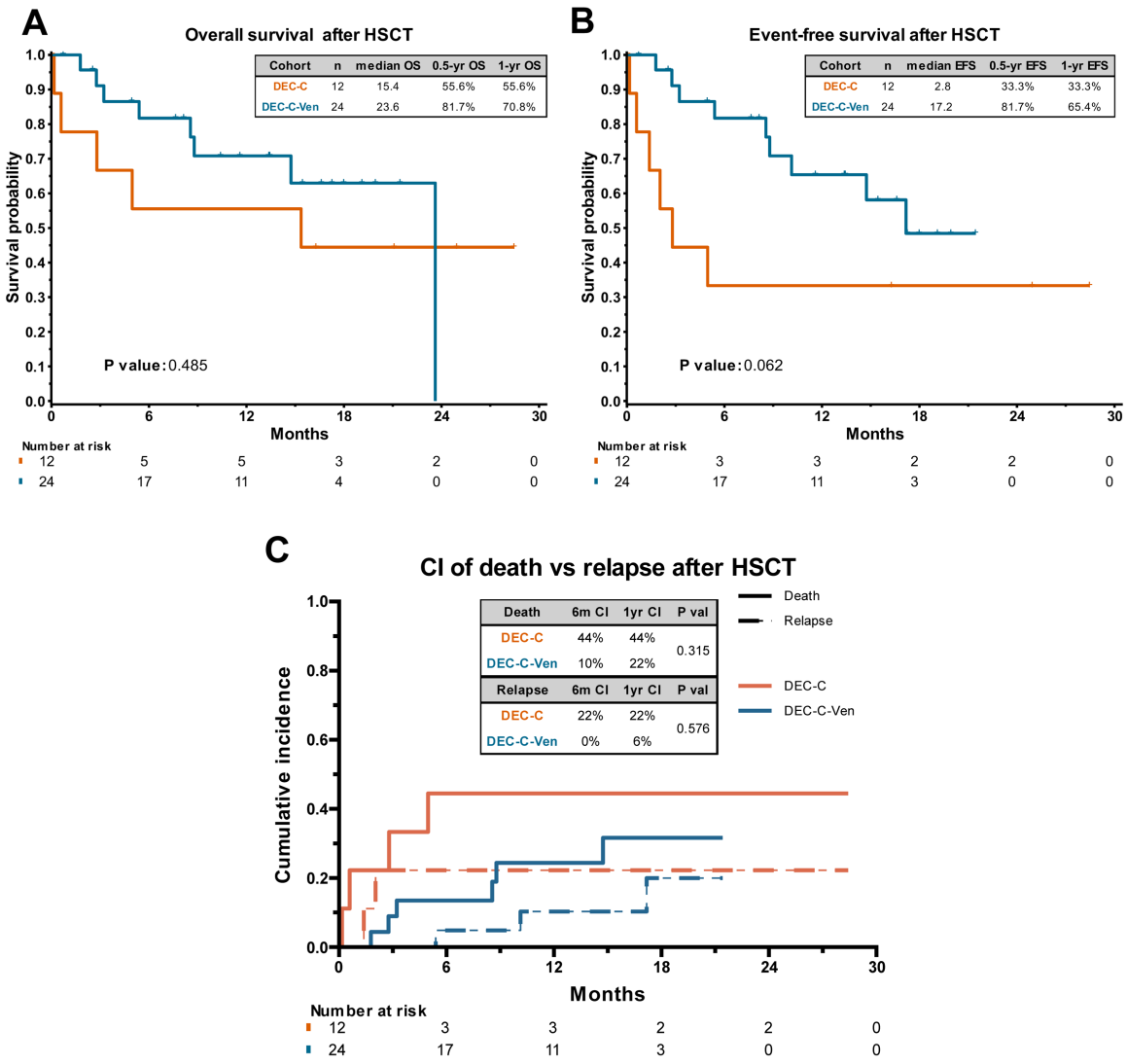
Supplementary Fig. 7. Cumulative incidence of death vs HSCT



Death	1-yr CI	2-yr CI	P val
DEC-C	25.1%	48.2%	0.428
DEC-C-Ven	25.7%	25.7%	

HSCT.	1-yr CI	2-yr CI	P val
DEC-C	15.4%	16.8%	<0.001
DEC-C-Ven	48.6%	53.7%	

Supplementary Fig. 8. Survival after HSCT



Supplementary Fig. 9. Blood counts on C1