Comprehensive Cancer Center
Tübingen-Stuttgart

Post ASH 2023 San Diego

AML/MDS

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EBERHARD KARLS
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TÜBINGEN

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State of the Art AML

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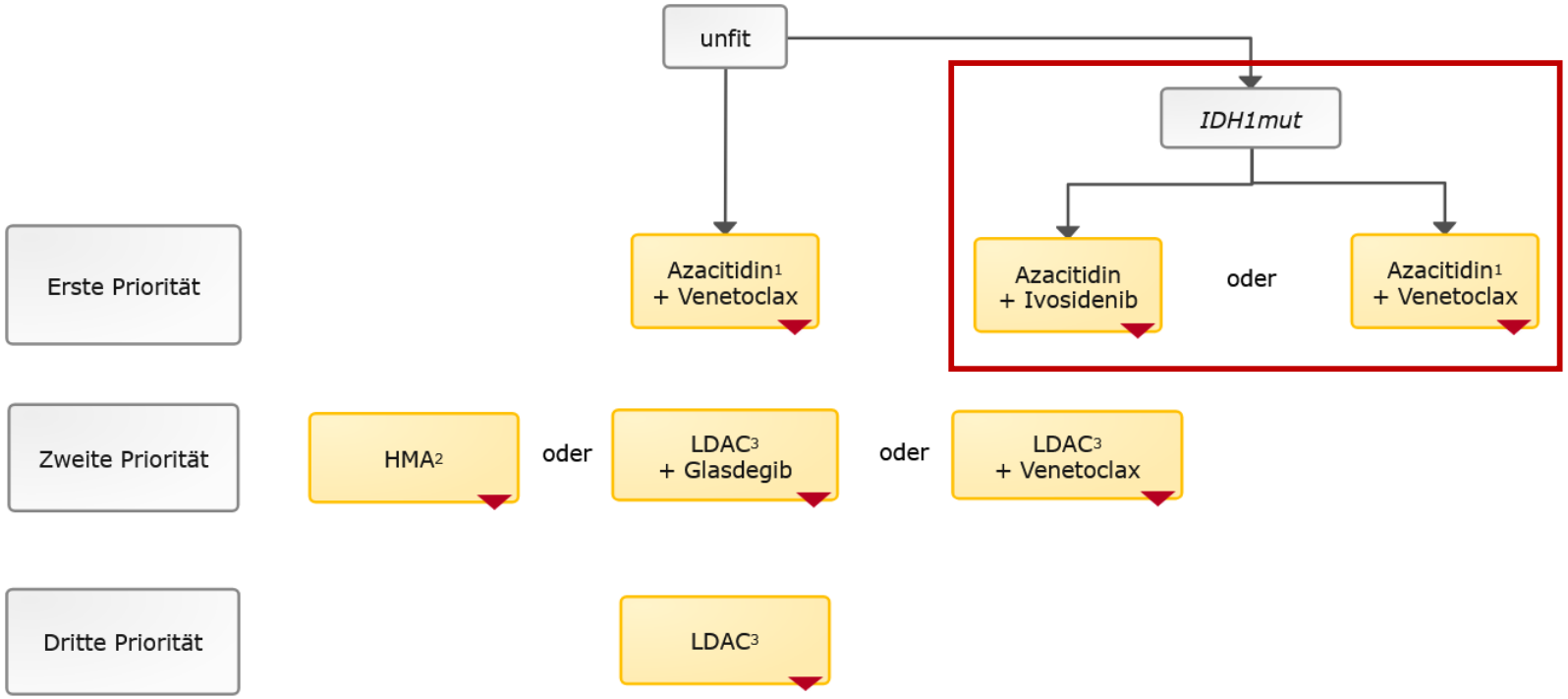
Therapie-Optionen für die **Primärtherapie unfitter Patienten**



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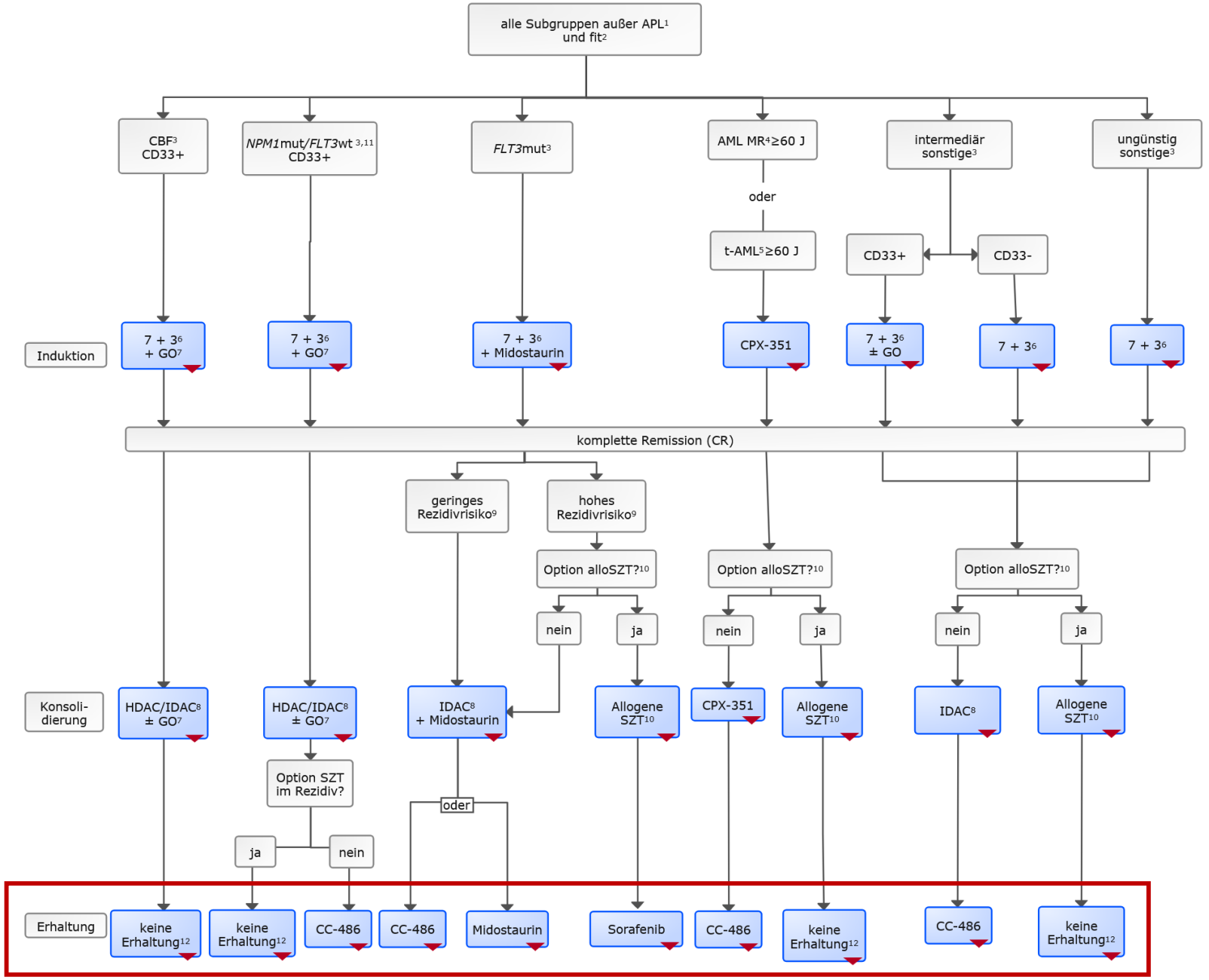
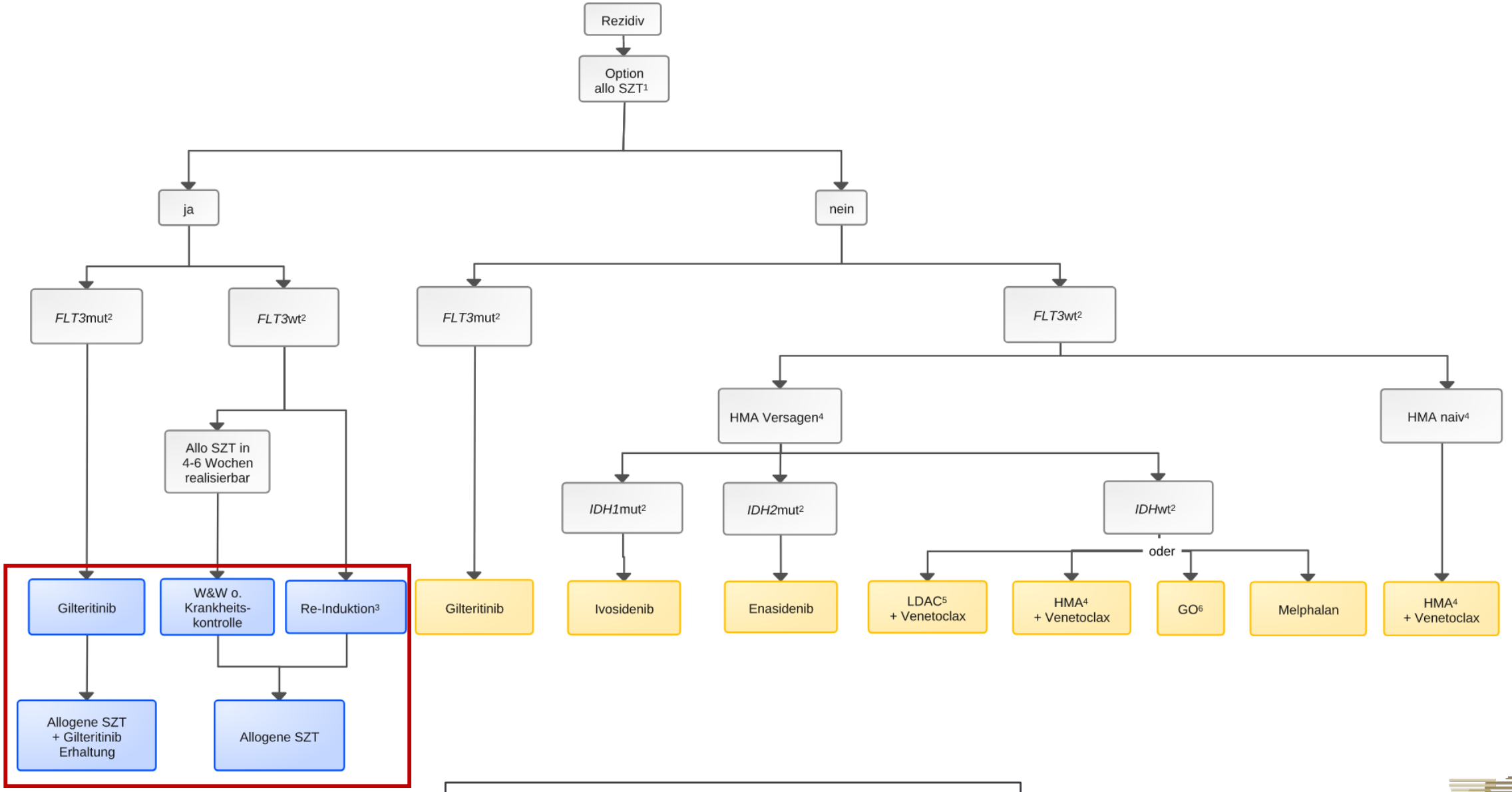


Algorithmus für die initiale Entscheidung bei **Erstdiagnose**

Therapie-Algorithmus für die **Rezidivtherapie**



AML/MDS

- **Induktionschemotherapie bei AML**
  - CPX-351
  - Chemotherapie und Venetoclax
  - NPM1-Leukämie, APL
- **Zielgerichtete Therapien bei AML**
  - Tripletts: HMA/Venetoclax +

    Ivosidenib, Enasidenib, Revumenib, Quizartinib
- **MDS**
  - Inflammasom-Inhibitor, Luspatercept, Imetelstat
  - Vidaza/Venetoclax für HR-MDS

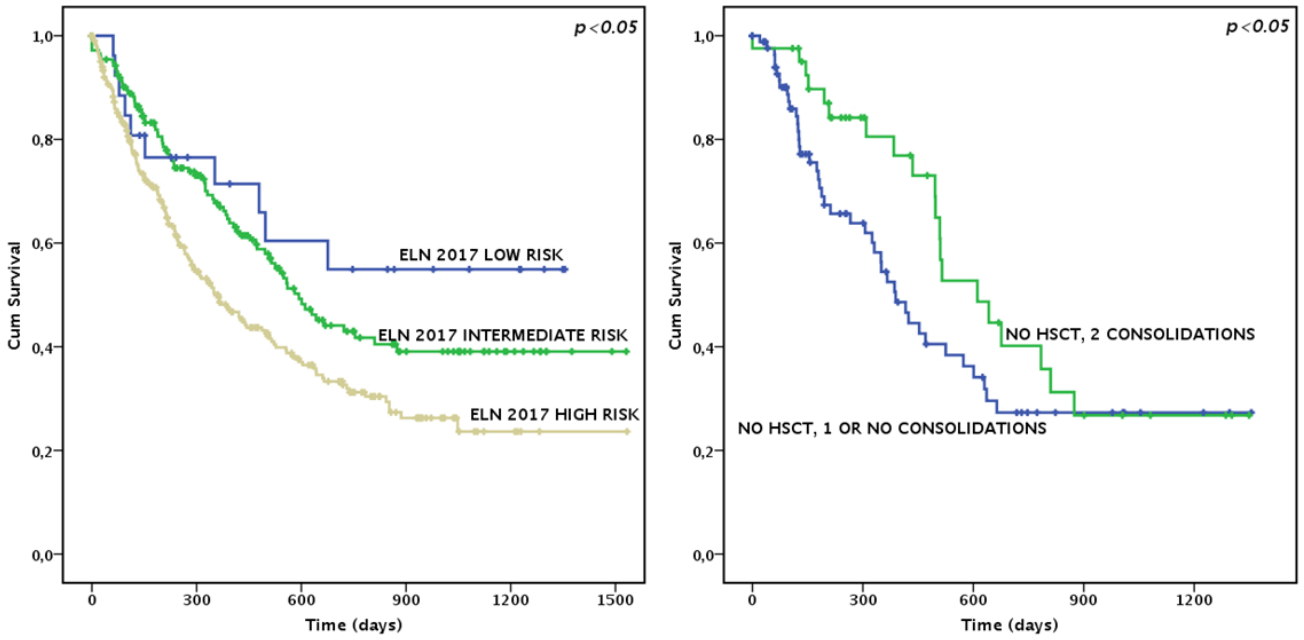
615. Acute Myeloid Leukemias: Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies: Long-Term Outcomes for Children and Adults Diagnosed With AML/APL

731 Optimal Duration of CPX-351 Treatment and Best Timing for Consolidation with Allogeneic Stem Cell Transplantation: Evidence from a Large Real-World Italian Study

Fabio Guolo et al.

Clinic of Hematology, Department of Internal Medicine (DiMI), University of Genoa, Genoa, Italy

Figure 1:
A) Overall Survival in All Patients according to ELN 2017 risk score
B) Overall Survival according to number of consolidations in non HSCT patients (landmark analysis)



- 513 ältere Pat. (median 65,6 Jahre) mit **s-AML oder t-AML** aus 38 italienischen Zentren seit 2019
- NPM1 (n=31), FLT3-ITD (n=24), 10,6%
- 58% CR-Rate nach Induktion 1
- HSZT in 1. CR bei 166 Patienten
- Statistik-Analyse: **HSZT, sobald CR erreicht**, weitere CPX-351-Behandlung nur nützlich ohne HSZT

615. Acute Myeloid Leukemias: Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster III

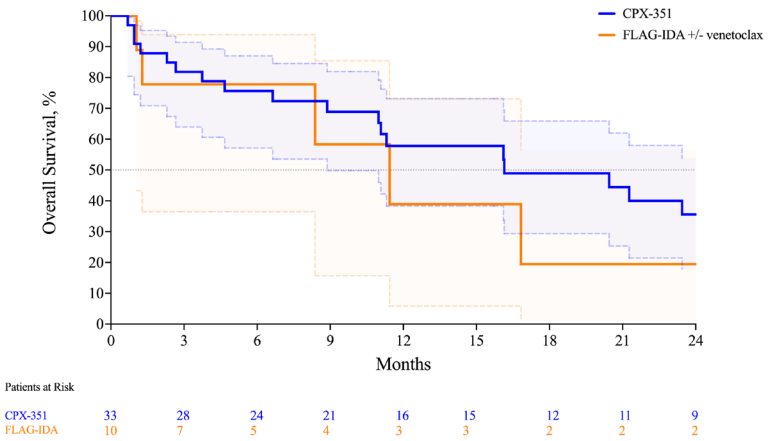
4269 CPX-351 Versus FLAG-IDA with or without Venetoclax in Previously Untreated and Relapsed or Refractory Acute Myeloid Leukemia

A. Demographics of the CPX-351 and FLAG-IDA cohorts

First-Line	CPX-351 (N = 33)	FLAG-IDA (N=10)	Significance
Age — years (%)	65 (28–72)	61 (34–68)	p = 0.093
Sex — male (%)	15 (45.5)	4 (40.0)	p > 0.999
Race — White (%)	22 (66.7)	7 (70.0)	p > 0.999
ECOG — (range)	1 (0–2)	0 (0–1)	p = 0.007
CCI — (range)	5 (2–14)	5 (2–11)	p = 0.484
ELN 2022 Adverse — (%)*	21 (65.6)	5 (55.6)	p = 0.701
AlloSCT — (%)	13 (39.4)	4 (40.0)	p > 0.999
Relapsed or Refractory	**CPX-351 (N = 10)**	**FLAG-IDA (N = 96)**	**Significance**
Age — years (%)	57.6 (20–78)	52 (21–72)	p = 0.619
Sex — male (%)	5 (50.0)	52 (54.2)	p > 0.999
Race — White (%)	7 (70.0)	62 (65.3)	p > 0.999
ECOG — (range)	1 (0–2)	1 (0–3)	p = 0.462
CCI — (range)	4 (2–9)	3 (0–7)	p = 0.720
ELN 2022 Adverse — (%)*	6 (66.7)	43 (46.7)	p = 0.310

*ELN 2022 risk was not evaluable at diagnosis for one patient in each cohort in the first-line setting.

B. Overall survival of patients treated with first-line CPX-351 or FLAG-IDA with or without venetoclax



Ian Bouligny et al.

Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

- Patienten mit neuer oder r/r AML 2013-2023
- **Neue AML:** CPX-351 (n=33): ECOG signifikant schlechter,
  FLAG-IDA (3/10 mit Venetoclax)
  MRD negativ: 33,3% mit CPX-351 und 50% mit FLAG-IDA
  OS: p=0,129 (Abbildung B)
- **r/r AML:** CPX-351 (n=10), 16/96 Patienten **FLAG-IDA-Venetoclax**
  MRD negativ: 50% mit CPX-351 und 66,7% mit FLAG-IDA
  OS: p=0,561

Hohe Rate von MRD-Negativität, Überleben nicht signifikant verschieden

615. Acute Myeloid Leukemias: Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies: Improving Intensive Chemotherapy Regimens for Treatment of AML

969 Venetoclax Combined with Daunorubicin and Cytarabine (2 + 6) in Acute Myeloid Leukemia: Updated Results of a Phase II Trial

Table 1 Response Assessment

	Overall (n=70)	Favorable risk (n=32) *	Intermediate risk (n=9) *	Adverse risk (n=29) *
Overall response rate (CR+CRi+PR)	92.9% (65/70)	96.0% (31/32)	77.8% (7/9)	93.1% (27/29)
composite complete remission rate	90.0% (63/70)	96.0% (31/32)	77.8% (7/9)	86.2% (25/29)
CR	87.1% (61/70)	96.0% (31/32)	77.8% (7/9)	79.3% (23/29)
CRi	2.9% (2/70)	0	0	6.9% (2/29)
PR	2.9% (2/70)	0	0	6.9% (2/29)
Died	1.4% (1/70)	0	0	3.4% (1/29)
MRD (-) after induction by flow cytometry	89.5% (51/57)			
Responders that received allo-HSCT	6/69 (8.7%)			
Time to blood cell count recovery after induction, days				
Time to absolute neutrophil count ≥ 0.5×10^9/L, days	13 (5-36)			
Time to absolute platelet count ≥ 30×10^9/L, days	13 (8-48)			
Even free survival,				
Median, months	NR	NR	NR	NR
12-month, % (95% CI)	81.0%			
Overall survival				
Median, months	NR	NR	NR	NR
12-month, % (95% CI)	84.9%			

Data are n (%). NR, not reached; CR, complete remission. Cri, complete remission with incomplete blood cell count recovery; PR, partial remission; Allo-HSCT, allogeneic-haematopoietic stem cell transplantation; MRD, measurable residual disease. *European Leukemia Net 2022 risk category.

Figure 1

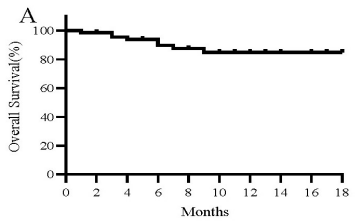


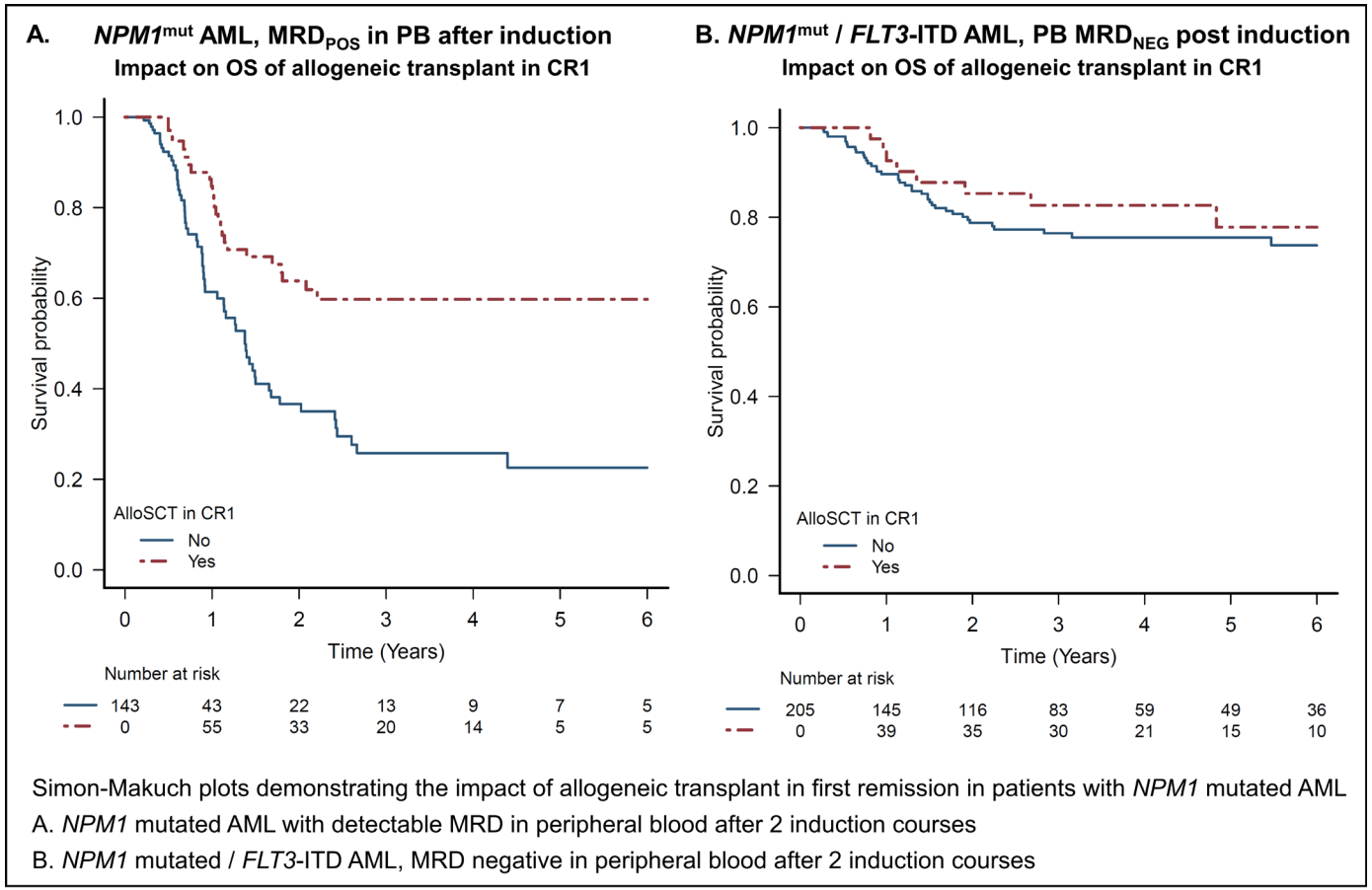
Figure 1 legend: The Kaplan-Meier plot of overall survival (OS) of all patients.

Xiaohui Suo et al.

Department of Hematology, Handan Central Hospital, Handan, Hebei, China, 056000, Handan, China

- 70 Patienten mit **Venetoclax und DA (2+6)** behandelt (<60 Jahre)
- 29/70 ungünstig und 9/70 intermediär nach ELN 2022
- **89,5% CR-Rate nach Induktion I mit MRD-Negativität**
- 1/70 Patienten verstorben
- Median der Neutrophilen- und Thrombozytenerholungszeit 13 Tage (5-36 und 8-48)
- 12-Monats-Überleben 84,9%

425 The Benefit of Allogeneic Transplant in 1st Complete Remission in *NPM1* Mutated AML with or without *FLT3* ITD Is Restricted to Those Testing MRD Positive after Induction – an Analysis of the UK NCRI AML17 and AML19 Studies



Simon-Makuch plots demonstrating the impact of allogeneic transplant in first remission in patients with *NPM1* mutated AML

A. *NPM1* mutated AML with detectable MRD in peripheral blood after 2 induction courses

B. *NPM1* mutated / *FLT3*-ITD AML, MRD negative in peripheral blood after 2 induction courses

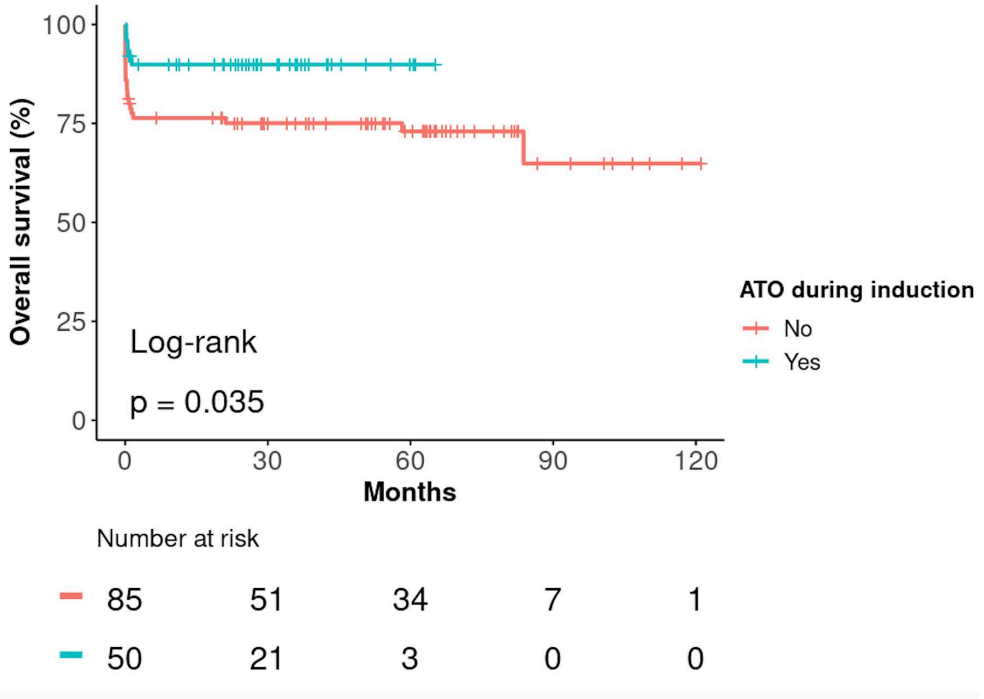
Jad Othman et al.

Department of Medical and Molecular Genetics, King's College London, London, United Kingdom

- Patienten mit ***NPM1*^mut AML mit CR/CRi** und einem MRD-Ergebnis nach Zyklus 2
- **MRD-positive Patienten: 3-jähriges OS 61 % mit allo-SZT vs. 24 % ohne SZT, p<0,001, Abbildung A**
- Allo-SZT in CR1 bot keinen Überlebensvorteil für MRD-negative Patienten, p=0,4
- kein Allo-Vorteil, wenn MRD-negative Patienten mit hohem (>0,5) FLT3-ITD-Allelverhältnis betrachtet, p = 0,50

1471 Impact of Arsenic Trioxide in the Treatment of Higher Risk Acute Promyelocytic Leukemia

Audrey Da Rocha et al. Hematology Department, CHU Amiens, Amiens, France



- Hoch-Risiko-APL (n=135) aus 12 französischen Zentren
- Arzt-Entscheidung: **ATRA/ATO** (n=50), ATRA/Chemo (n=85)
- **OS mit ATO-Behandlung nach 3 Jahren 89,9% versus 75,1%**
- weniger Kardiotoxizität und weniger sekundäre myeloische Neoplasien erwartet

AML/MDS

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968 Phase Ib/2 Study of Oral Decitabine/Cedazuridine (ASTX727) and Venetoclax in Combination with the Targeted Mutant IDH1 Inhibitor Ivosidenib or the Targeted Mutant IDH2 Inhibitor Enasidenib: 2023 Update

Himachandana Atluri et al.

Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Table 1: Response rates in Newly Diagnosed and Relapsed/Refractory Patients

Response Rates						
	All (n = 50)		Newly Diagnosed (n=24)		Relapsed/Refractory (n = 26)	
	IDH1 (n= 20)	**IDH2** (n=30)	**IDH1** (n=10)	**IDH2** (n=14)	**IDH1** (n=10)	**IDH2** (n=16)
CRc	14 (70)	21 (70)	9 (90)	14 (100)	5 (50)	7 (44)
MRD (-) CR	13 (65)	16 (53)	8 (80)	13 (93)	5 (50)	3 (19)

Data reported as n (%)

Table 2: Prior Therapies in patients with R/R AML

Prior Therapy (R/R AML, n=26)			
	IDH1 (n=10)	**IDH2** (n=16)	**CRc**
Prior HMA + VEN	6 (60)	12 (75)	5 (27)
HMA/VEN/IDHi naive	1 (10)	2 (13)	2 (66)
Prior IDHi	4 (40)	3 (19)	5 (71)
No VEN exposure	3 (30)	4 (25)	6 (85)

Data reported as n (%)

- ASTX727: orale Kombination aus Decitabin und Cedazuridin (35 mg/100 mg) mit Bioäquivalenz zu i.v. Decitabin
- **orales Triplett-Regime** von ASTX727 (Tag 1-5) + VEN (Tag 1-14) in Kombination mit Ivosidenib oder Enasidenib
- 50 Patienten (medianes Alter 72 Jahre), die mediane Nachbeobachtungszeit war 11,0 Monate für neue Diagnose (ND) Patienten und 14,6 Monate für R/R-Patienten
- NW: indirekte Hyperbilirubinämie (6 %, Enasidenib), Mukositis Grad 3 (4%), Differenzierungssyndrom (10 %) ,TLS (4%)
- **Sicheres Protokoll für IDH-mutierte AML mit hohen Raten von MRD-negativer CR**

58 Early Results of the Phase I/II Study Investigating the All-Oral Combination of the Menin Inhibitor Revumenib (SNDX-5613) with Decitabine/Cedazuridine (ASTX727) and Venetoclax in Acute Myeloid Leukemia (SAVE)

Ghayas C. Issa et al.

Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

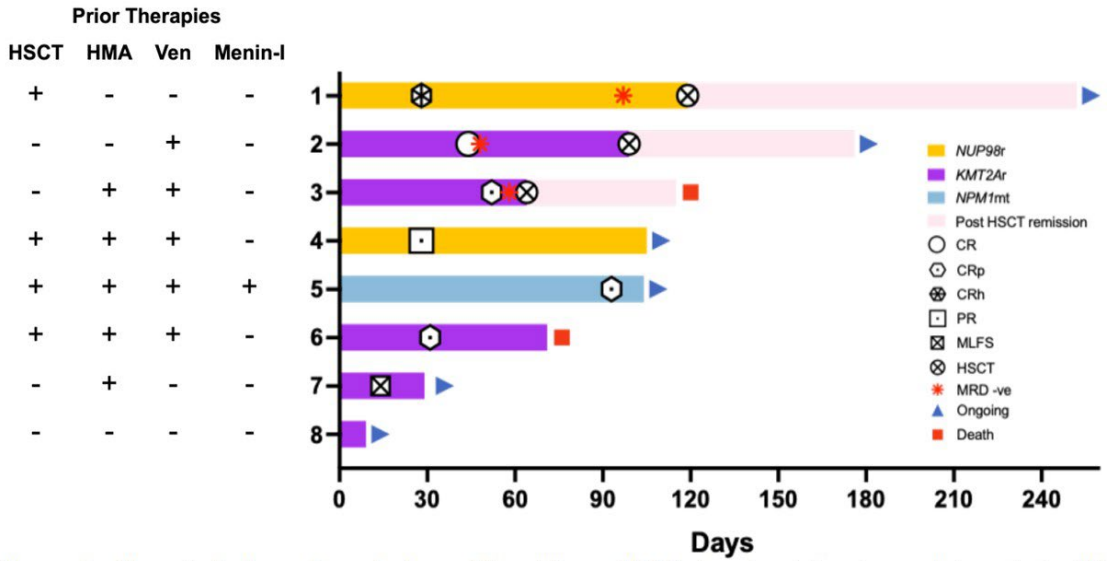

Figure 1: Characterization of remissions. Abbreviations: HSCT, hematopoietic stem cell transplant; HMA, hypomethylating agent; Ven, venetoclax; Menin-I, menin inhibitor

- Revumenib (ehemals SNDX-5613) ist ein oraler Inhibitor der Menin-KMT2A-Interaktion bei hochrefraktären akuten Leukämien (Issa GC, Nature 2023)
- auch wirksam bei *Nucleoporin 98* (*NUP98r*) oder Mutation des *Nucleophosmin-1-Gens* (*NPM1mt*)
- 8 Patienten, medianes Alter 27 Jahre (12-62 Jahre)
- ASTX727 (**Decitabin/Cedazuridin, Tag 1-5) mit Venetoclax (Tag 1-5) und Revumenib** in verschiedenen Dosisstufen
- NW: febrile Neutropenie (63 %), Thrombozytopenie, Hyperphosphatämie (63 %), Übelkeit (63 %) und AST/ALT-Erhöhung (25 %), Differenzierungssyndrom (2 Patienten)
- **7/8 morphologische Remission, 3/7 MRD-**

158 Phase I/II Study of Quizartinib, Venetoclax, and Decitabine Triple Combination in FLT3-ITD Mutated AML

Table 1. Baseline Clinical and Molecular Characteristics

Characteristics	Relapse/Refractory (N=40) N (%), Median [Range]	Frontline (N=10) N (%), Median [Range]
Age-years	58 [19-86]	70 [65-85]
Gender- Male	24 (60)	4 (40)
Diagnosis, AML		
De novo	29 (72)	3 (30)
Secondary	8 (20)	5 (50)
Therapy related	3 (8)	2 (20)
Prior therapies, median	3 [1-5]	n/a
HMA + VEN	22 (55)	n/a
HMA + VEN + FLT3i	13 (33)	n/a
Gilteritinib	31 (78)	n/a
≥1 prior FLT3i	34 (85)	n/a
ASCT, yes	16 (40)	n/a
Karyotype		
Diploid	16 (40)	4 (40)
Adverse	11 (28)	3 (30)
Other	13 (32)	3 (30)
FLT3 mutations		
ITD	40 (100)	10 (100)
ITD allelic ratio	0.42 [0.01-10.3]	0.45 [0.3-1.8]
ITD allelic frequency,%	30 [1-91]	31 [21-65]
ITD + D835	1 (3)	0 (0)
ITD + F691L	1 (3)	0 (0)
Other mutations*		
DNMT3A	19 (49)	4 (40)
NPM1	11 (28)	1 (10)
WT1	16 (41)	0 (0)
TET2	9 (23)	2 (20)
RAS/MAPK	12 (23)	1 (10)
RUNX1	11 (30)	4 (40)
IDH1/2	6 (16)	1 (10)
TP53	1 (3)	1 (10)

-1 pt with no baseline molecular data excluded from molecular subcategory, mutations >10% shown except TP53

*RAS/MAPK pathway mutations: RAS/PTPN11/CBL/NF1/BRAF

Table 2. Response Rates and Outcomes

Response*, N (%)	Relapsed/Refractory (N=40)	Frontline (N=10)
CRc	27 (68)	10 (100)
CR	5 (13)	7 (70)
CRi	8 (20)	3 (30)
MLFS	14 (35)	0 (0)
Day 14 BM blasts ≤5%¥	19 (48)	10 (100)
Best MRD, anytime		
Flow Cytometry (-)	7/24 (29)	7/9 (78)
FLT3 PCR (-)	8/22 (36)	9/10 (90)
30-day mortality	0 (0)	0 (0)
60-day mortality	3 (8)	0 (0)
Bridge to ASCT	13 (33)	4 (40)

*Response assessment by modified IWG criteria – Cheson et al. J Clin Oncol. 2003 Dec 15;21(24):4642-9

¥Including acellular or aplastic bone marrow

Musa Yilmaz et al.

Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

- 50 Patienten, darunter 40 R/R und 10 neue AML, FLT3-ITD-mutiert
- 10 Tage **Decitabin** zur Induktion, gefolgt von 5 Tagen in den folgenden Zyklen
- Patienten mit KM-Blasten ≤5% am Tag 14 **Venetoclax** beendet, bei >5% bis Tag 21
- **Quizartinib** täglich verabreicht

- **neue AML: alle CRc (7 CR, 3 CRi)**
- Bei den 31/40 Gilteritinib-exponierten Patienten betrugen CR+CRi 23%, medianes Gesamtüberleben 6,9 Monate und 1-Jahres-Überleben 21 %.

State of the Art MDS

Therapie bei Myelodysplastischen Neoplasien (Niedrigrisiko)

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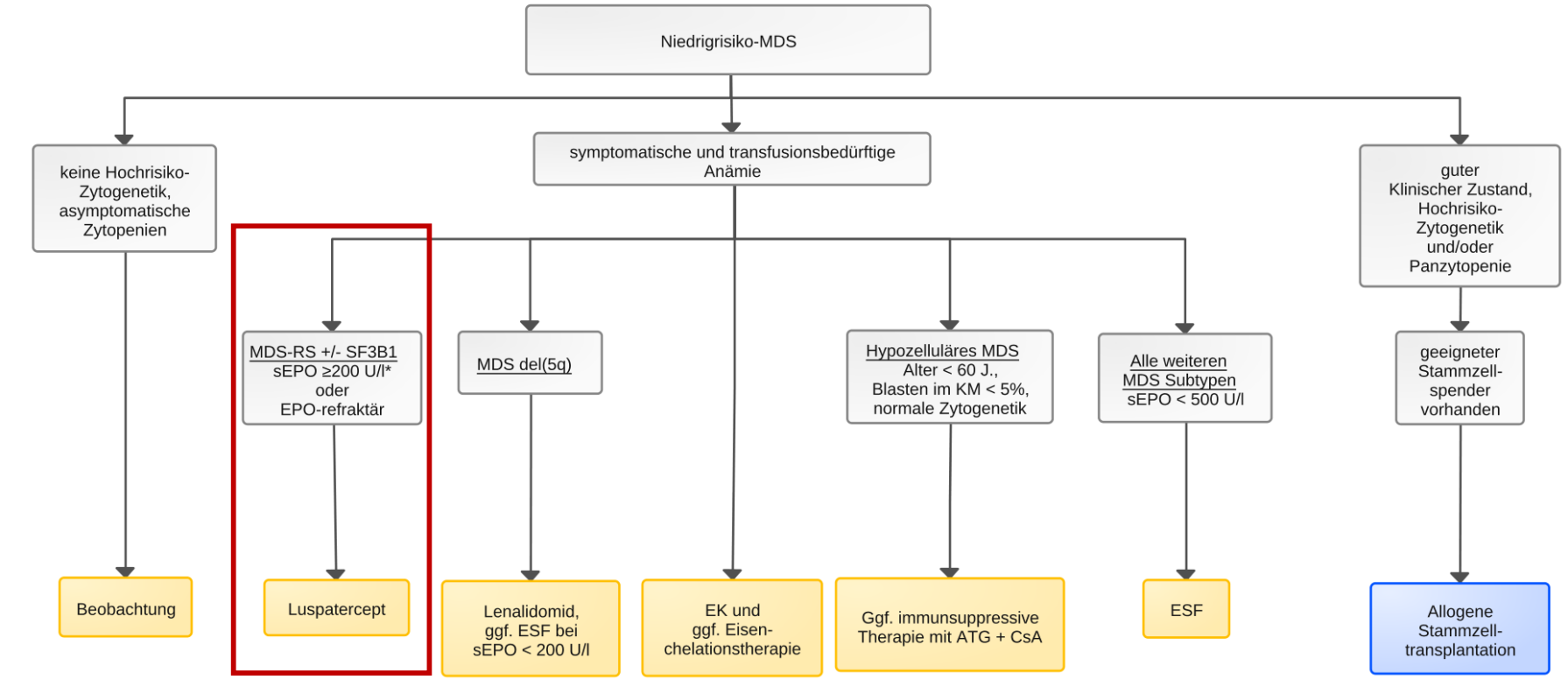

Legende:

palliativ, kurativ.

MDS-RS: MDS mit Ringsideroblasten; SF3B1+ (positiv): Mutation im SF3B1-Gen, SF3B1- (negativ): keine Mutation im SF3B1-Gen (Wildtyp); sEPO: Erythropoetinspiegel im Serum; ATG: Antithymozytenglobulin, CsA: Cyclosporin. ESF: Erythropoese stimulierende Faktoren

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  - Vidaza/Venetoclax für HR-MDS

1417 The Dual Inflammasome/Myddosome Inhibitor HT-6184 Restores Erythropoiesis in MDS/AML

Emma Rabinovich et al. Department of Bone Marrow Transplant, Memorial Sloan Kettering Cancer Center, New York, NY

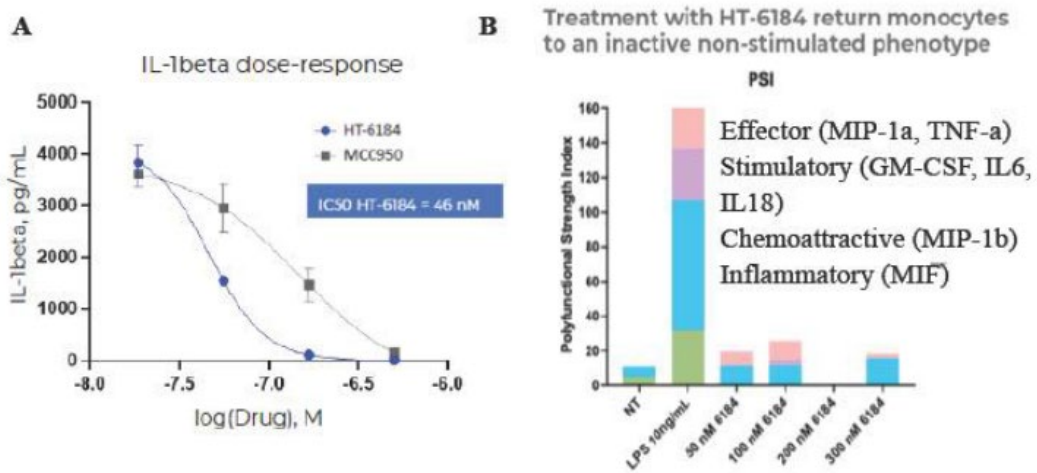


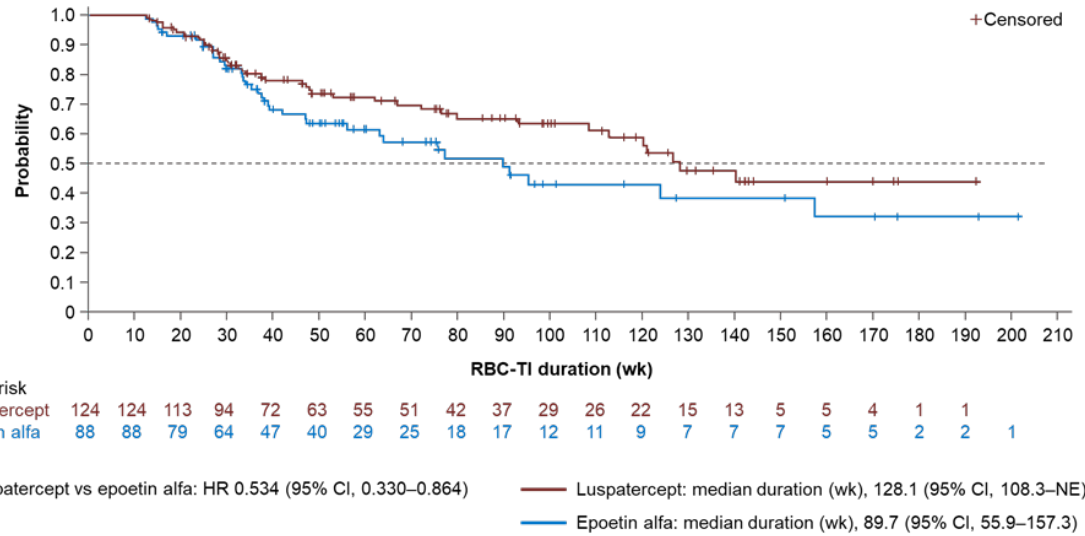
Fig 1: HT-6184 is a potent inhibitor of inflammasome in monocytes: HT-6184 inhibits IL-1b secretion from monocytes more effectively when compared to other inhibitors of the inflammasome pathway (A). HT-6184 reverts monocytes to a non-inflammatory phenotype when examined with single cell proteomics (Isoplexis system)

- Das NLRP3-Inflammasom ist einer der wichtigsten biologischen Treiber für die ineffektive Hämatopoese und Entzündung beim MDS
- Die zelluläre Expression der Inflammasom-Komponenten Caspase-1 und IL-18 ist in MDS-Proben im Vergleich zu gesunden Kontrollen signifikant hochreguliert
- **HT-6184** ist ein potenter allosterischer Inhibitor des Inflammasom-Gerüstproteins NEK7
- HT-6184 hob in humanen Monozyten die Produktion von IL-1β und IL-6 auf und versetzte menschliche **Monozyten in einen weniger entzündlichen Zustand**
- Die Behandlung von primären MDS/AML-Knochenmarkproben (N=10) mit HT-6184 in Methylzellulosekulturen führt zu einer deutlichen **Erhöhung der erythroiden Differenzierung und reduzierte myelomonozytäre Kolonien** in der Mehrzahl der Proben.

193 Efficacy and Safety of Luspatercept Versus Epoetin Alfa in Erythropoiesis-Stimulating Agent (ESA)-Naive Patients (Pts) with Transfusion-Dependent (TD) Lower-Risk Myelodysplastic Syndromes (LR-MDS): Full Analysis of the COMMANDS Trial

Figure. Duration of RBC-TI ≥ 12 wk for the ITT population (A) and subgroup analysis of the primary endpoint (B)

A



B

	Luspatercept	Epoetin Alfa
Overall, n/N (%)	110/182 (60.4%)	63/181 34.8%
***SF3B1* mutated, n/N (%)**	80/114 (70.2%)	33/101 (32.7%)
***SF3B1* non-mutated, n/N (%)**	29/65 (44.6%)	26/72 (36.1%)
sEPO ≤ 200 U/L, n/N (%)	96/145 (66.2%)	59/144 (41.0%)
sEPO > 200 U/L, n/N (%)	14/37 (37.8%)	4/37 (10.8%)
RS+, n/N (%)	87/133 (65.4%)	38/130 (29.2%)
RS−, n/N (%)	23/49 (46.9%)	25/50 (50.0%)

CI, confidence interval; ITT, intent to treat; NE, not estimable; RBC-TI, red blood cell transfusion independence; RS, ring sideroblast; sEPO, serum erythropoietin; wk, week.

Guillermo Garcia-Manero et al.

Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX

- MDS mit niedrigen Risiko mit < 5 % Knochenmarkblasten, sEPO < 500 U/L und transfusionsabhängig
- 182 Patienten für **Luspatercept** und 181 Patienten für Epoetin-alfa randomisiert
- Der primäre Endpunkt (TU > 12 Wochen) wurde mit 110 (60,4 %) Patienten im Luspatercept-Arm gegenüber 63 (34,8 %) im Epoetin-alfa-Arm erreicht ($p < 0{,}0001$)
- **Die mediane Dauer der Erythrozyten-TU ≥ 12 Wochen war mit Luspatercept länger als mit Epoetin-alfa: 128,1 Wochen versus 89,7 Wochen**

194 Efficacy of Imetelstat in Achieving Red Blood Cell Transfusion Independence (RBC-TI) across Different Risk Subgroups in Patients with Lower-Risk Myelodysplastic Syndromes (LR-MDS) Relapsed/Refractory (R/R) to Erythropoiesis-Stimulating Agents (ESAs) in IMerge Phase 3 Study

Table. Risk subgroup analysis of RBC-TI rates.

	Imetelstat (n = 118)	Placebo (n = 60)	*P* value[a]
All patients, n	118	60	
8-week RBC-TI, n (%)	47 (39.8)	9 (15.0)	<.001
24-week RBC-TI, n (%)	33 (28.0)	2 (3.3)	<.001
1-year RBC-TI, n (%)	16 (13.6)	1 (1.7)	.012
IPSS			
Low, n	80	39	
8-week RBC-TI, n (%)	32 (40.0)	8 (20.5)	.034
24-week RBC-TI, n (%)	23 (28.8)	2 (5.1)	.003
1-year RBC-TI, n (%)	10 (12.5)	1 (2.6)	.082
Intermediate-1, n	38	21	
8-week RBC-TI, n (%)	15 (39.5)	1 (4.8)	.004
24-week RBC-TI, n (%)	10 (26.3)	0	.009
1-year RBC-TI, n (%)	6 (15.8)	0	.048
IPSS-R cytogenetic risk			
Good/very good, n	89	47	
8-week RBC-TI, n (%)	33 (37.1)	8 (17.0)	.014
24-week RBC-TI, n (%)	22 (24.7)	2 (4.3)	.002
1-year RBC-TI, n (%)	9 (10.1)	1 (2.2)	.071
Intermediate, n	22	9	
8-week RBC-TI, n (%)	12 (54.5)	1 (11.1)	.029
24-week RBC-TI, n (%)	9 (40.9)	0	.024
1-year RBC-TI, n (%)	5 (22.7)	0	.152
IPSS-R			
Very low, n	3	2	
8-week RBC-TI, n (%)	0	0	NE
24-week RBC-TI, n (%)	0	0	NE
1-year RBC-TI, n (%)	0	0	NE
Low, n	87	46	
8-week RBC-TI, n (%)	37 (42.5)	9 (19.6)	.008
24-week RBC-TI, n (%)	26 (29.9)	2 (4.3)	<.001
1-year RBC-TI, n (%)	10 (11.5)	1 (2.2)	.064
Intermediate, n	20	8	
8-week RBC-TI, n (%)	7 (35.0)	0	.055
24-week RBC-TI, n (%)	5 (25.0)	0	.091
1-year RBC-TI, n (%)	4 (20.0)	0	.131
High, n	1	0	
8-week RBC-TI, n (%)	1 (100.0)	0	NE
24-week RBC-TI, n (%)	0	0	NE
1-year RBC-TI, n (%)	0	0	NE
IPSS-M			
Very low/low, n	69	33	
8-week RBC-TI, n (%)	33 (47.8)	7 (21.2)	.017
24-week RBC-TI, n (%)	24 (34.8)	1 (3.0)	<.001
1-year RBC-TI, n (%)	10 (14.5)	0	.025
Moderate low/moderate high, n	29	16	
8-week RBC-TI, n (%)	6 (20.7)	1 (6.3)	.167
24-week RBC-TI, n (%)	3 (10.3)	0	.154
1-year RBC-TI, n (%)	2 (6.9)	0	.248
High/very high, n	5	3	
8-week RBC-TI, n (%)	2 (40.0)	0	.157
24-week RBC-TI, n (%)	0	0	NE
1-year RBC-TI, n (%)	0	0	NE

*P value based on Cochran-Mantel-Haenszel controlling for prior RBC transfusion burden (≤6 vs >6 U of RBCs) and IPSS risk group (low vs intermediate-1) applied to randomization, for comparison between treatment arms (imetelstat vs placebo) within each specific risk group.

Rami S. Komrokji et al.

Moffitt Cancer Center, Tampa, FL

- **Imetelstat** (Telomerase-Inhibitor) für Erythrozyten-Transfusionsabhängiges LR-MDS, R/R oder nicht geeignet für Epo
- **Patienten, die Imetelstat erhielten, zeigten signifikant höhere Raten von ≥8-wöchigen, ≥24-wöchigen und ≥1-jährigen Erythrozyten-TU** im Vergleich zu Patienten, die Placebo erhielten (39,8 v. 15 %, 28 v. 3,3 % und 13,6 v 1,7 %).

- Weitere Subgruppenanalysen zeigten, dass Imetelstat in verschiedenen Risikountergruppen durchweg höhere TU-Ansprechraten als Placebo aufwies, unabhängig vom Klassifikationssystem.

1868 Combination of Venetoclax and Azacitidine in Patients with Treatment-Naive, High-Risk Myelodysplastic Syndromes with Responses Leading to Stem Cell Transplantation

Table. Demographics and Baseline Characteristics for Patients Who Received SCT

Characteristic	N=51
Treatment regimen, n (%)	
Ven 100 mg for 14 days + Aza	4 (8)
Ven 200 mg for 14 days + Aza	1 (2)
Ven 400 mg for 14 day + Aza	46 (90)
Median age, years (range)	64 (26–78)
<65 years, n (%)	31 (61)
≥65 years, n (%)	20 (39)
≥75 years, n (%)	1 (2)
ECOG PS, n (%)[a]	
0	29 (58)
1	21 (42)
IPSS-R cytogenetic risk, n (%)	
Very good	0 (0)
Good	21 (41)
Intermediate	17 (33)
Poor	3 (6)
Very poor	10 (20)
Baseline mutations, n/N (%)	
ASXL1	16/38 (42)
RUNX1	11/38 (29)
TP53	7/38 (18)
SRSF2	9/38 (24)
Best response before transplantation, n (%)	
CR	21 (41)
mCR	23 (45)
mCR with HI, n/n (%)	7/23 (30)
PR	0
SD	7 (14)

[a]ECOG PS missing for 1 patient.

Aza, azacitidine; CR, complete remission; ECOG PS, Eastern Cooperative Oncology Group performance status; HI, Hematological Improvement; SCT, stem cell transplantation; mCR, marrow complete remission; PR, partial response; SD, stable disease; Ven, venetoclax.

Guillermo Garcia-Manero et al.

University of Texas MD Anderson Cancer Center, Houston, TX

- Patienten mit behandlungsnaiven HR-MDS; IPSS Risikokategorien von Int-2 oder hoch, <20 % Blasten im Knochenmark
- **Eine Knochenmark-CR (mCR) wurde bei 23 von 51 (45,1 %) Patienten erreicht und die kombinierte Ansprechrate (mCR mit hämatologischer Verbesserung) betrug 30,4 % (7/23).**
- mediane Zeit bis zum besten Gesamtansprechen für Ven+Aza betrug 2 Monate
- Patienten, die sich einer Transplantation unterzogen: Überleben 64,7 % (33/51)

AML/MDS

- **AML**
  - schnelle molekulare Primärdiagnostik und MRD-Diagnostik
  - CPX-351: ein Zyklus vor allogener Transplantation günstig
  - Venetoclax mit reduzierter Chemotherapie kombinieren (z.B. 2 + 6)
  - ATRA/ATO auch bei HR-APL
  - Venetoclax-Protokolle mit oralem Decitabin und einem zielgerichteten Kombinationspartner gut wirksam

- **MDS**
  - LR-MDS: Transfusionssparend: Luspatercept, Imetelstat, IPSS-M!

Klinische Studien Med. II:

Kurztitel	Indikation	Fallzahl	Rekrutierungsstand
AMLSG 30-18	Neu diagnostizierte akute myeloische Leukämie und intermediäres bzw. ungünstiges genetisches Risiko **3+7 versus CPX351**	**n = 882**	**n = 607/882** Stand 11/2023 Tübingen **n = 17**
VENSWITCH	Phase-II-Studie zur (frühen) Salvage-Kombinationstherapie mit Intensiviertem **Venetoclax und Decitabin bei rezidivierter/refraktärer AML**	**n = 27**	**n = 1/27** Stand 11/2023 Tübingen **n = 1**
AMLSG 29-18 (HOVON 150 AML)	Neu diagnostizierte Akute Myeloische Leukämie (AML) oder myelodysplastisches Syndrom mit Exzess von Blasten-2 (MDS-EB2) mit IDH1 oder IDH2 Mutation, eligibel für **intensive Chemotherapie** **Ivosidenib/Placebo** Enasidenib/Placebo (**geschlossen**)	**n = 968** (484 mit IDH1 und 484 mit IDH2)	**n = 385/484 IDH1** **n = 484/484 IDH2** Stand 11/2023 Tübingen **n = 3**
AMLSG 31-19	A Randomized, Placebo-Controlled Phase III Study of Induction and Consolidation **Chemotherapy With Venetoclax in Adult Patients With Newly** Diagnosed Acute Myeloid Leukemia or Myelodysplastic Syndrome With Excess Blasts-2	**n = 650**	Tübingen **n = 3**

Vielen Dank für Ihre Aufmerksamkeit

Universitätsklinikum Tübingen