HEMATOLOGY
& ONCOLOGY

San Juan City Hospital
VA Caribbean Healthcare System

Triplet; New Frontier in AML Therapy?

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Fellow Hematology-Oncology

HISTORY OF PRESENT ILLNESS

46 year old female with no medical hx of systemic disease.

Started with general malaise and fatigue for 2 weeks.

Decided to visit her primary care physician.

PAST MEDICAL HISTORY

No history of systemic disease

OBGYN

- GOPO
- Regular menses

Toxic Habits

- Alcohol: Denied
- Tobacco: Denied
- Illicit Drug: Denied

PHYSICAL EXAMINATION

General

- Well nourished, Alert and Active
- No acute distress

Neck

- Supple, No JVD, No goiter.
- No lymphadenopathy

Lymph Nodes

- None palpable

Abdomen

- No palpable masses
- No hepatomegaly, splenomegaly

Skin

- Petechias at lower extremities

Neurologic

- No gross motor or sensory deficit.

LABORATORY

- **Complete blood count:**
  - **WBC: 82 x10^3/mm^3**
  - **Hgb: 8.0 g/dL**
  - Hct: 24.4%
  - **Plt: 19 x10^3/mm3**
- **Peripheral Smear:**
  - **85% Blasts**

PT, PTT, Fibrinogen: WNL

- **Blood Chemistry:**
  - ✓ **Creatinine-> 0.85**
  - ✓ **No Electrolyte Disturbances**

Other Labs:

Uric Acid: 7.5

BM Aspiration and Biopsy

BONE MARROW BIOPSY

HYPERCELLULAR BONE MARROW WITH 83% BLASTS

CG: t(6;9)(p22;q34)/*DEK-NUP214*

POSITIVE: FLT3-ITD (AR 0.5)

NEGATIVE: IDH1, IDH2, NPMI (MYELOID PANEL)

INDUCTION CHEMOTHERAPY

CYTARABINE + IDARUBICIN

- CYTARABINE (200MG/M2) D 1-7
- IDARUBICIN (12 MG/M2) D 1-3

MIDOSTAURIN

- 50 MG BID (DAYS 8-21)

BONE MARROW BIOPSY DAY 28

BONE MARROW WITH 10% BLASTS

CG: t(6;9)(p22;q34)/*DEK-NUP214*

POSITIVE: FLT3-ITD (AR 0.5)

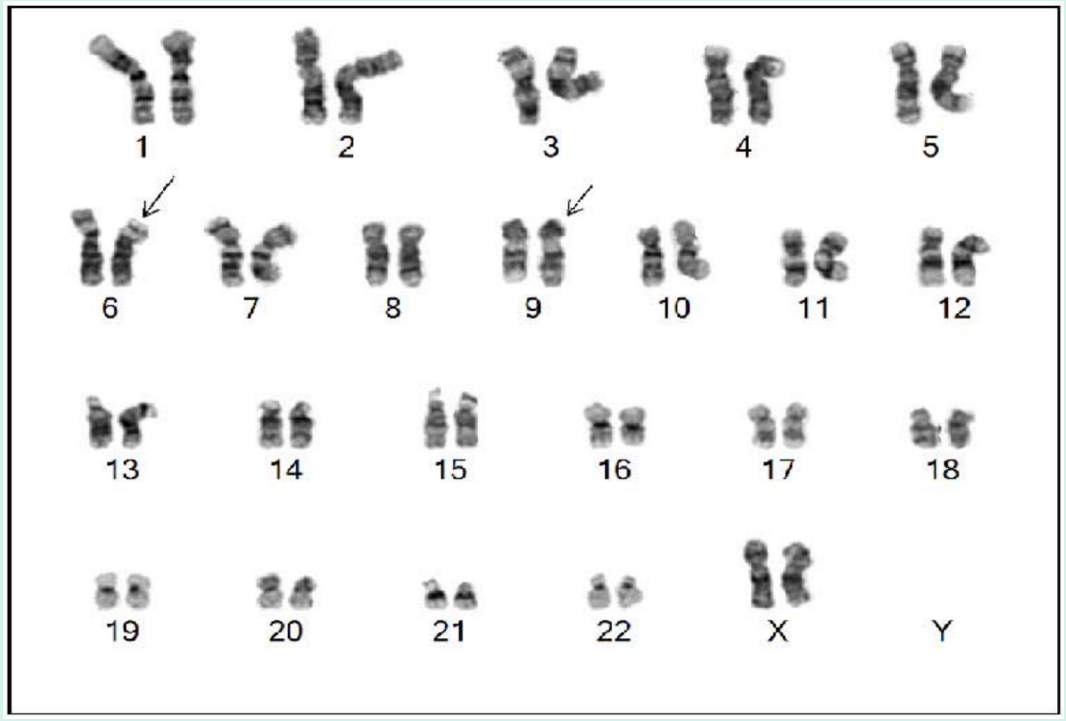
NEGATIVE: IDH1, IDH2, NPMI (MYELOID PANEL)

European Journal of Haematology

Original Article

The kinetics of relapse in *DEK-NUP214*-positive acute myeloid leukemia patients

Hans B. Ommen, Aurore Touzart, Elisabeth MacIntyre, Wolfgang Kern, Torsten Haferlach, Claudia Haferlach, Khalid Tobal, Peter Hokland, Susanne Schnittger



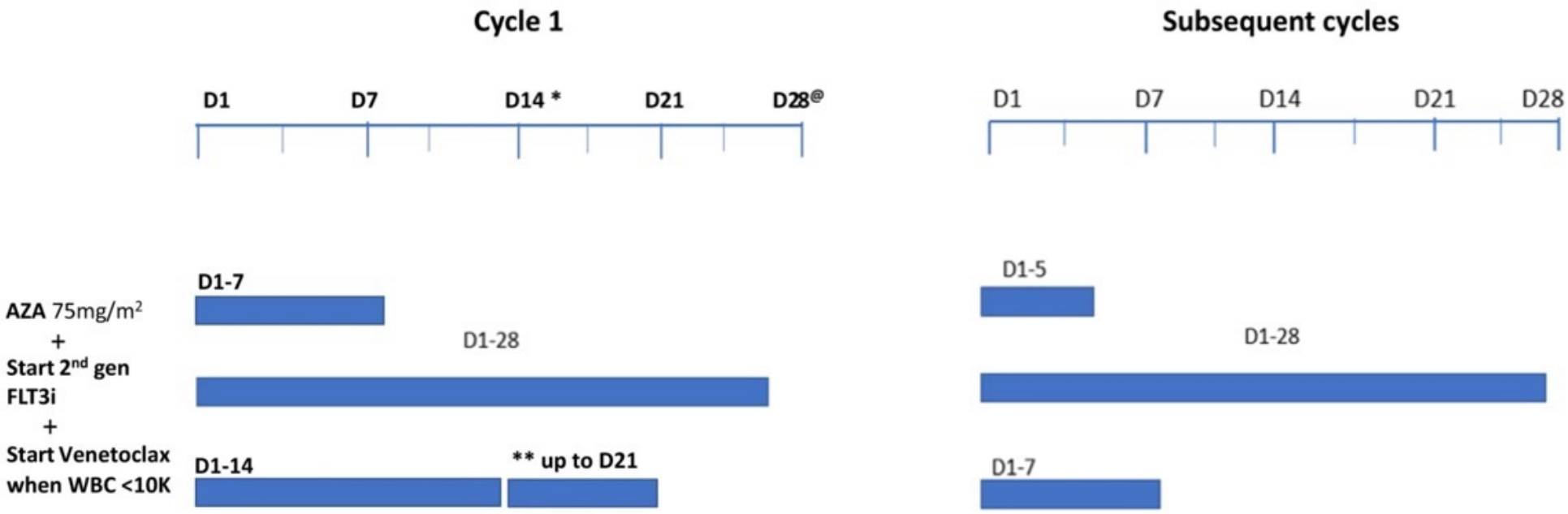
T(6;9)(P22;Q34)
DEK-NUP214

+1% OF AML

+CHEMOTHERAPY RESISTANCE

+POOR OUTCOME

+FAILURE TO THERAPY


Cycle 1
D1
D7
D14 *
D21
D28@
Subsequent cycles
D1
D7
D14
D21
D28
AZA 75mg/m2
+
Start 2nd gen FLT3i
+
Start Venetoclax when WBC <10K
D1-7
D1-28
D1-14
** up to D21
D1-5
D1-28
D1-7

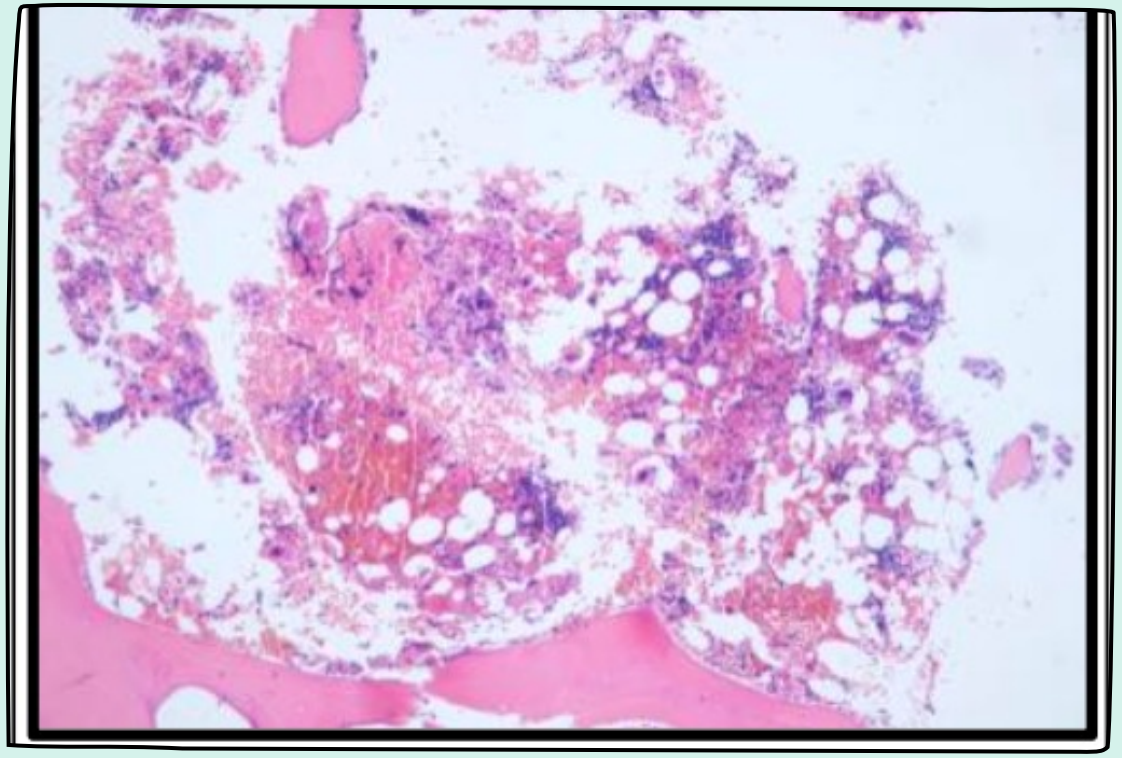
AZA-VEN-GILT

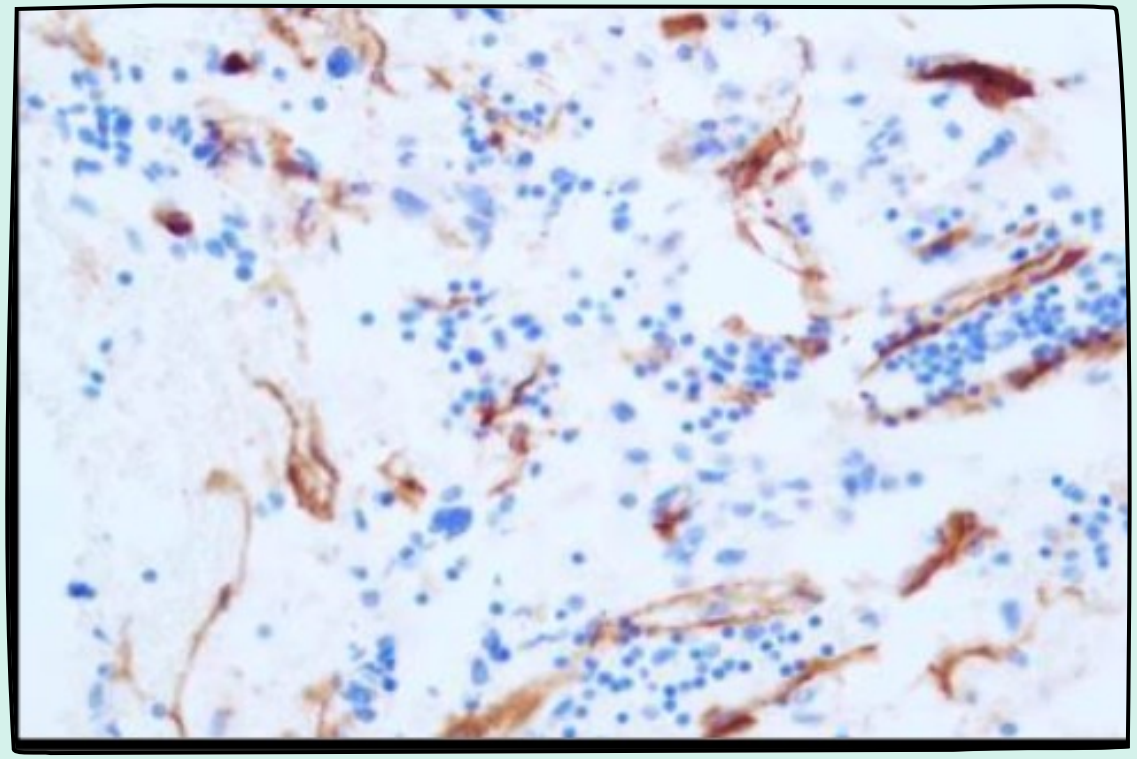
BM BIOPSY DAY 14

HYPOCELLULAR WITH LESS THAN 5% BLASTS

t(6;9)(p22;q34)/*DEK-NUP214*

POSITIVE: FLT3-ITD (AR 0.3)





BONE MARROW BIOPSY AFTER 3RD CYCLE

BONE MARROW BIOPSY

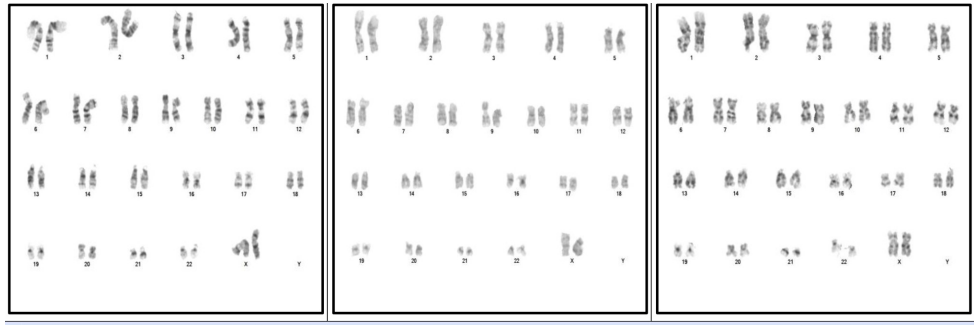
BONE MARROW WITH 1 % BLAST

CG: NORMAL FEMALE KARYOTYPE

NEGATIVE: FLT3-ITD

NEGATIVE: IDH1, IDH2, NPMI (MYELOID PANEL)

Pan-Myeloid Panel (70 Genes)									
Hotspot Genes (23)			**Full Genes (17)**			**Fusion Driver Genes (30)**			
ABL1	*IDH1*	*NRAS*	*ASXL1*	*PHF6*	*ZRSR2*	*ABL1*	*FUS*	*MYH11*	*TFE3*
BRAF	*IDH2*	*PTPN11*	*BCOR*	*PRPF8*		*ALK*	*HMGA2*	*NTRK3*	
CBL	*JAK2*	*SETBP1*	*CALR*	*RB1*		*BCL2*	*JAK2*	*NUP214*	
CSF3R	*KIT*	*SF3B1*	*CEBPA*	*RUNX1*		*BRAF*	*KMT2A (MLL)*	*NUP98*	
DNMT3A	*KRAS*	*SRSF2*	*ETV6*	*SH2B3*		*CCND1*	*KMT2A-PTD*	*PDGFRA*	
FLT3	*MPL*	*U2AF1*	*EZH2*	*STAG2*		*CREBBP*	*MECOM*	*PDGFRB*	
GATA2	*MYD88*	*WT1*	*IKZF1*	*TET2*		*EGFR*	*MET*	*RARA*	
HRAS	*NPM1*		*NF1*	*TP53*		*ETV6*	*MLLT10*	*RBM15*	
						FGFR1	*MLLT3*	*RUNX1*	
						FGFR2	*MYBL1*	*TCF3*	



Normal Karyo (C-1,Cell #7)	Normal Karyo (C-2,Cell #18)	Normal Karyo (C-1,Cell #8)

ISCN RESULTS: **46,XX[20]; Normal Female Karyotype**

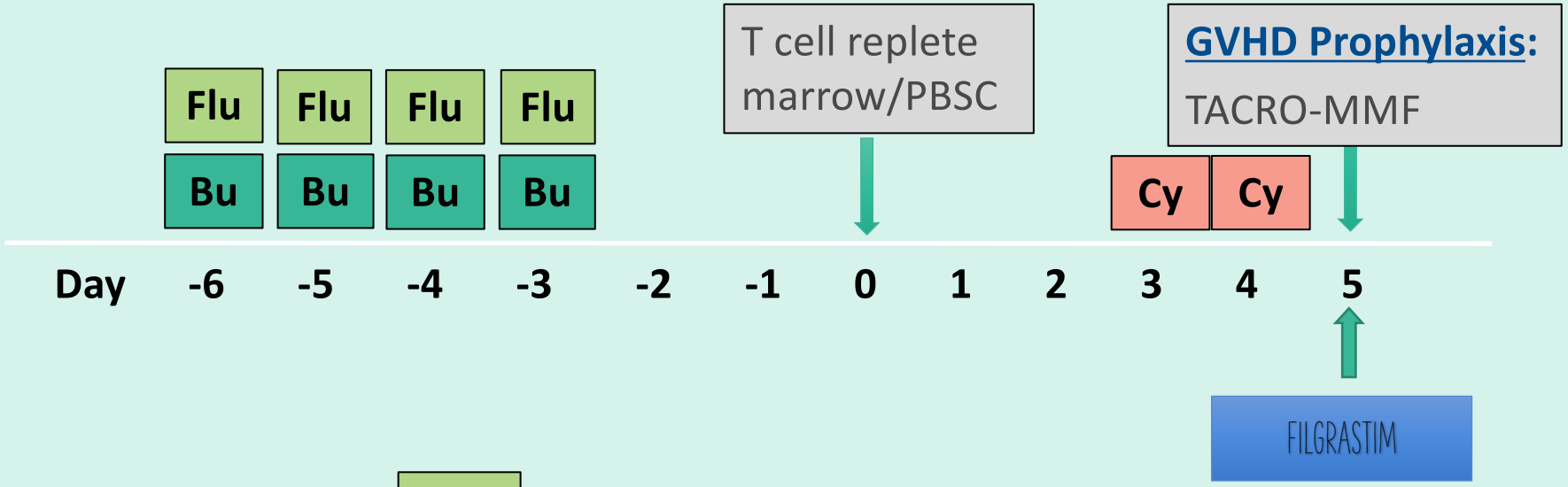
METHOD: (G-Banding)

No. of cells with <44 / 44 / 45 / 46 / 47 />47 chromosomes 0 2 1 17 0 0	G-Banding Average Resolution:400		
Cells counted: 20	Cells analyzed:20	Cells captured:20	Cells karyotyped:4

MOLECULAR DIAGNOSIS (FLT3 by Fragment Analysis)

BM: No FLT3 Internal Tandem Duplications (ITD) and Tyrosine Kinase Domain (TKD) Mutations

COMPLETE CYTOGENETIC AND MOLECULAR REMISSION



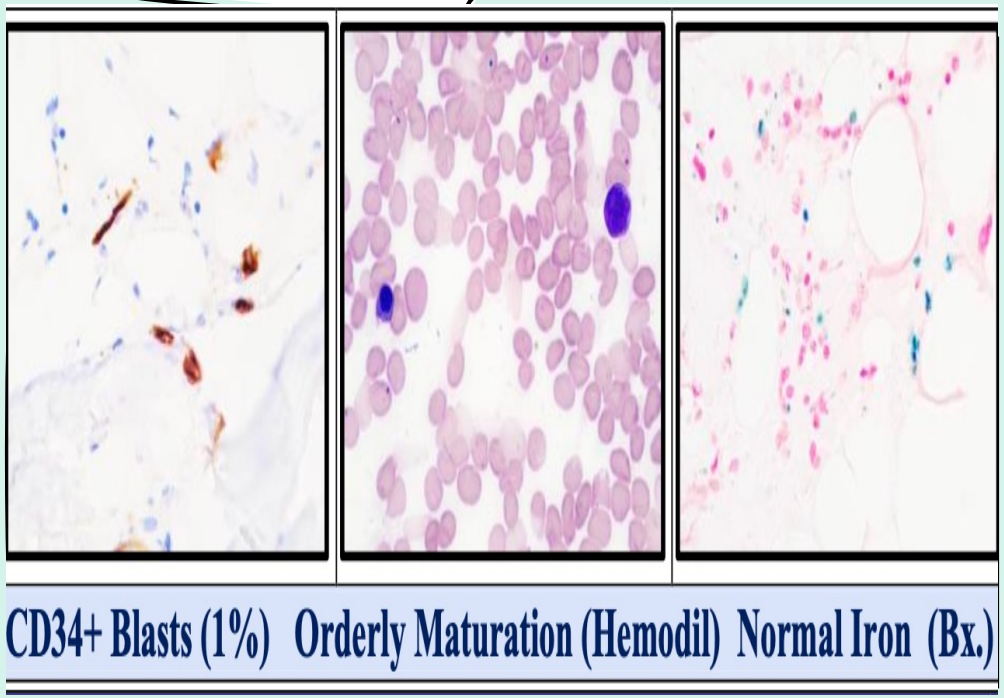
Flu Fludarabine 30 mg/m^2 IV daily

Bu Busulfan 75 mg/m^2 IV daily (PK AUC 3150)

Cy Cyclophosphamide 50 mg/kg IV daily

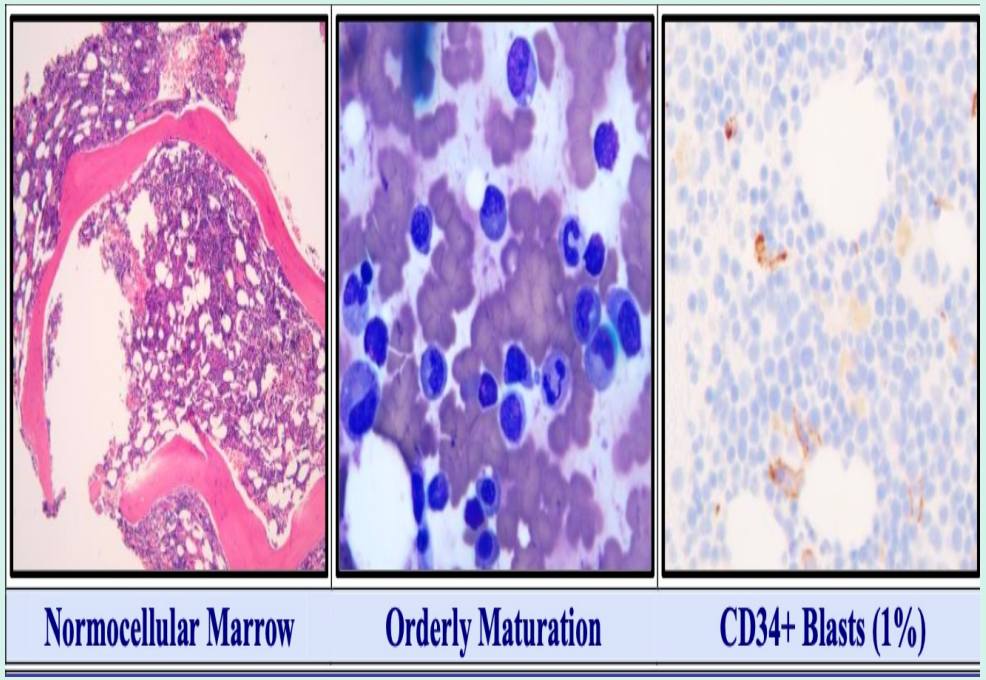
HAPLOIDENTICAL-ALLO-HSCT

BM BIOPSY DAY 30



CD34+ Blasts (1%) Orderly Maturation (Hemodil) Normal Iron (Bx.)

BM BIOPSY DAY 100



Normocellular Marrow Orderly Maturation CD34+ Blasts (1%)

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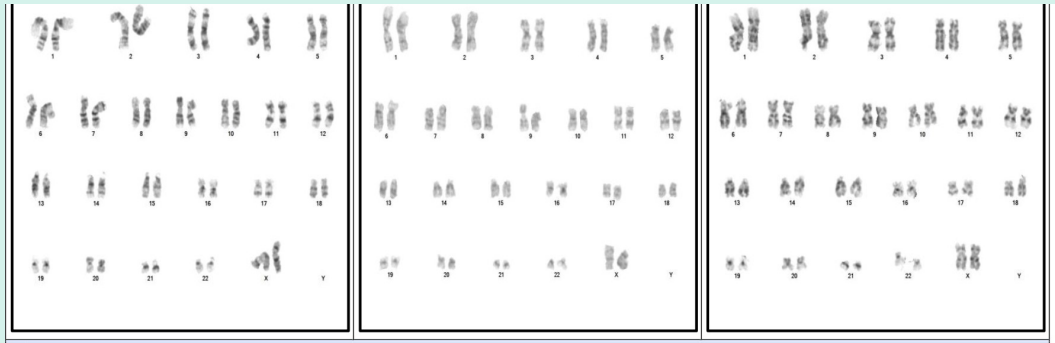

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CASE SUMMARY

AML, FLT3-ITD WITH t(6;9)(p22;q34)/DEK-NUP214

REFRACTORY TO IC WITH FLT3 inhibitor

THE TRIPLE: AZA-VEN-GILT

TAKE HOME MESSAGE

TREATMENT OF AML NEED TO BE BASE ON MOLECULAR AND CYTOGENETICS

REGIMEN COMBINATIONS HAS EFFECT AGAINST CHEMOTHERAPY RESISTANCE

TRIPLETS REGIMEN ARE THE NEW FRONTIER IN AML

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