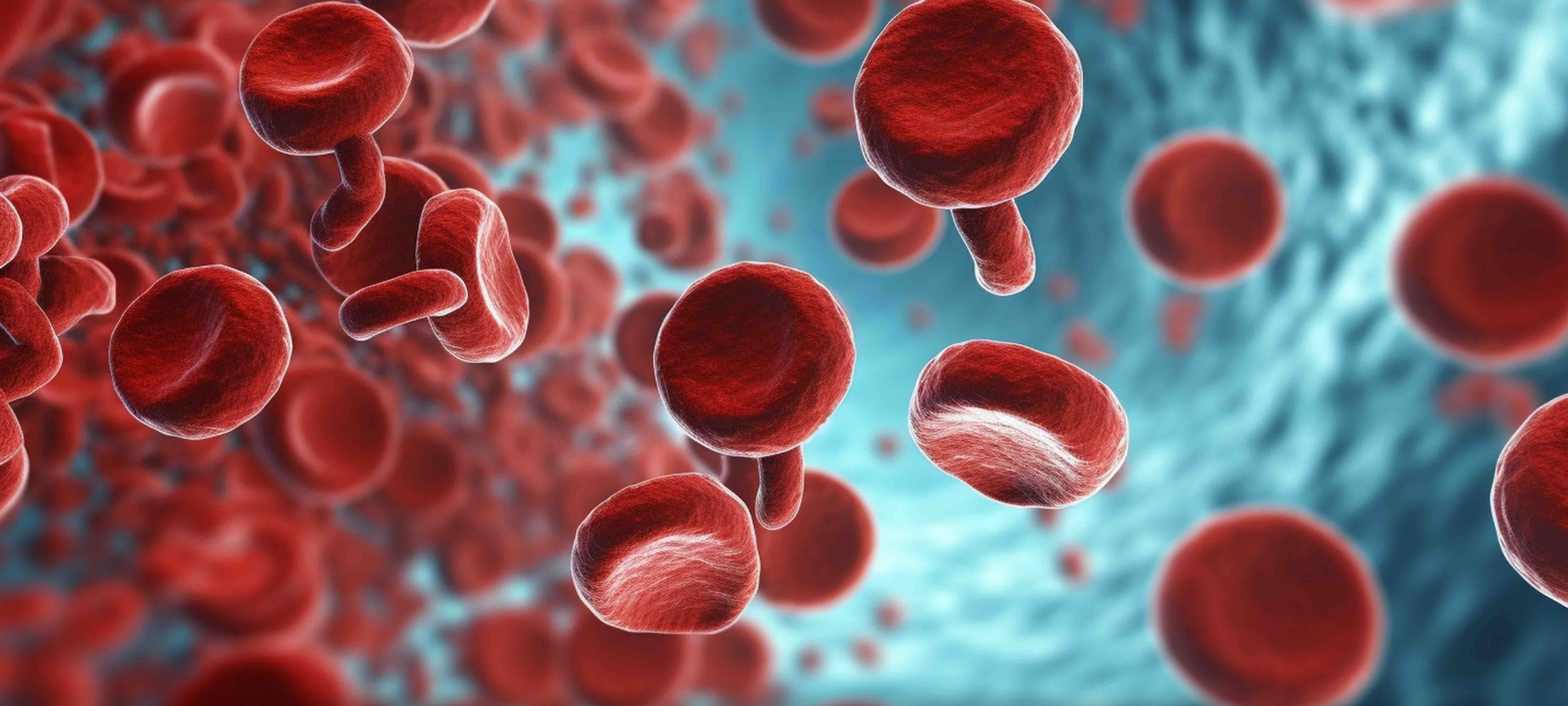




HEMATOLOJİ GÜNCELLEME



MİYELODİSPLASTİK SENDROM

En sık sebep idiyopatiktir

- ◆ En sık sitogenetik anomali 5q delesyonudur → İyi prognoz göstergesi
- ◆ 12p veya 20q delesyonu, SF3B1 mutasyonu → İyi prognoz göstergesi
- ◆ 11q delesyonu ve Y kromozom delesyonu → Çok iyi prognoz göstergesi
- ◆ 3q delesyonu, p53 mutasyonu, RINX1 / ASXL1 mutasyonu → Kötü prognoz göstergesi
- ◆ Alkilleyici ajanlar → Radyasyon benzeri etki mekanizması → MDS → AML (en sık AML-M5)
- ◆ DNA topoizomerez inhibitörü kullanımı
- ◆ Down sendromu, Trizomi 8, Fanconi aplastik anemisi

REPORTED FREQUENCY OF GENETIC LESIONS IN MDS

Gene	%	Location	Function
<i>SF3B1</i>	28	2q33	Splicing factor
<i>TET2</i>	21	4q24	Control of cytosine hydroxy-methylation
<i>ASXL1</i>	14	20q11	Epigenetic regulator
<i>SRSF2</i>	12	17q25	Splicing factor
<i>RUNX1</i>	9	21q22	Transcription factor
<i>TP53</i>	8	17p13	Transcription factor

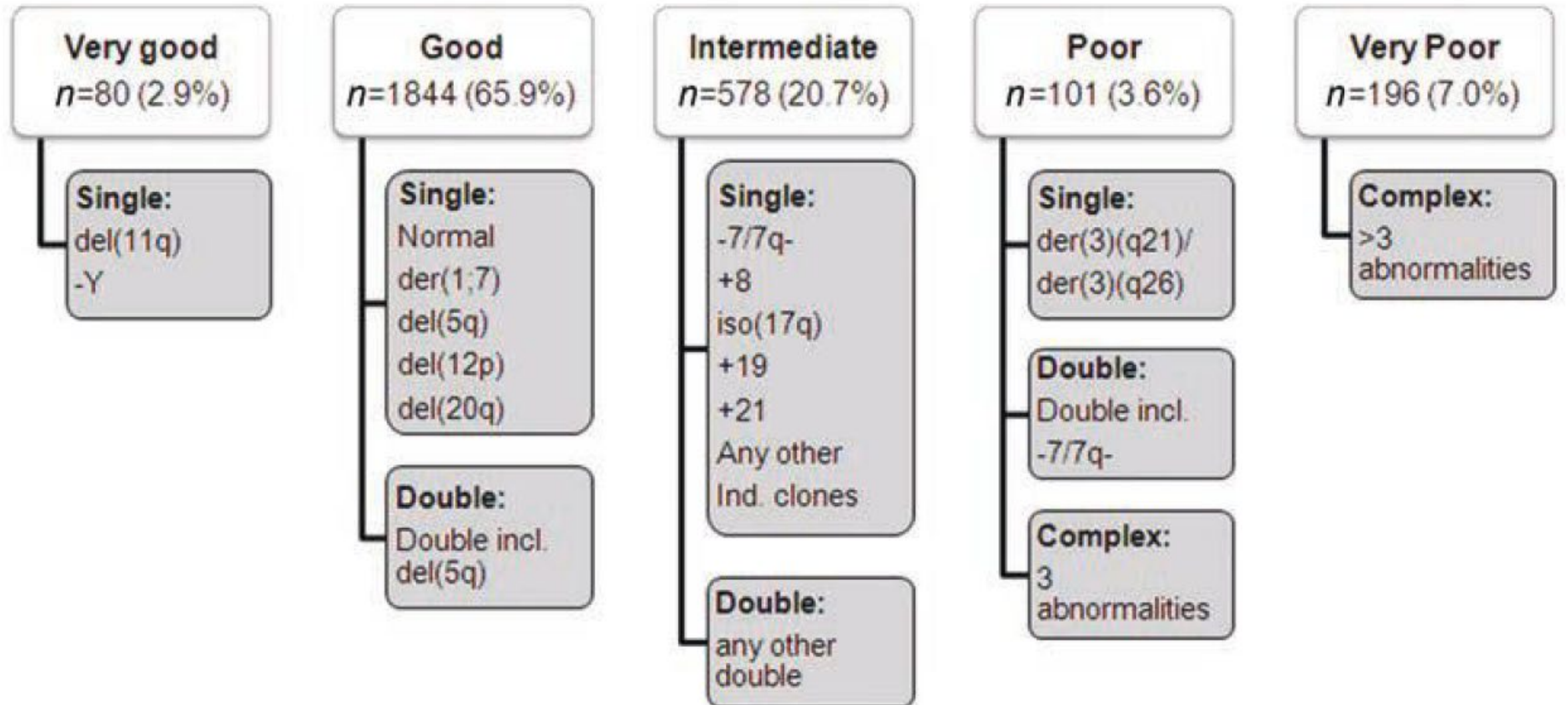


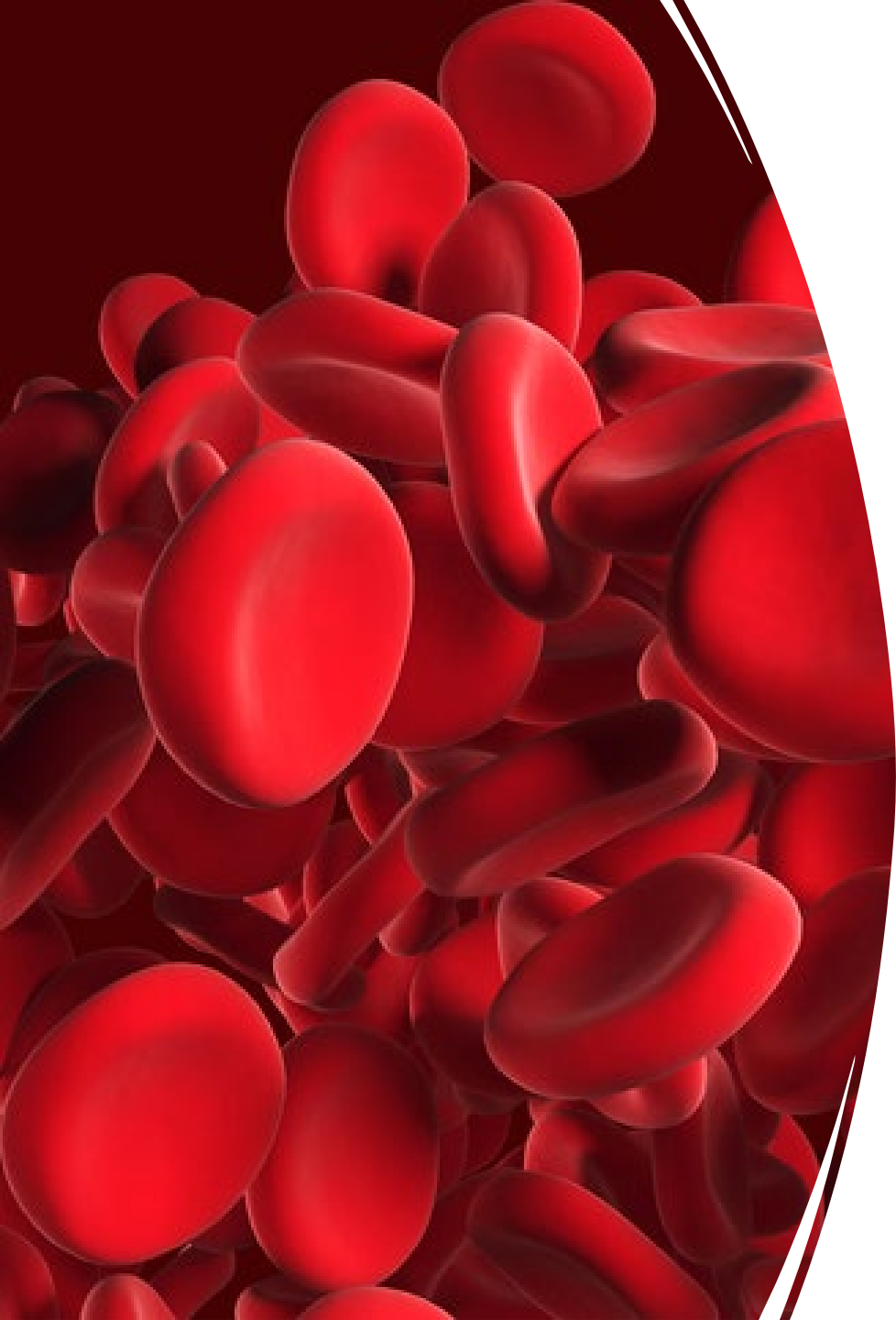
TABLE 102-5 World Health Organization (WHO) Classification of Myelodysplastic Syndromes (MDS)/Neoplasms

NAME	RING SIDEROBLASTS	MYELOBLASTS	KARYOTYPE
MDS with single lineage dysplasia (MDS-SLD)	<15% (<5%) ^a	BM <5%, PB <1%, no Auer rods	Any, unless fulfills all criteria for MDS with isolated del(5q)
MDS with multilineage dysplasia (MDS-MLD)	<15% (<5%) ^a	BM <5%, PB <1%, no Auer rods	Any, unless fulfills all criteria for MDS with isolated del(5q)
MDS with ring sideroblasts (MDS-RS)			
MDS-RS with single lineage dysplasia (MDS-RS-SLD)	≥15% / ≥5% ^a	BM <5%, PB <1%, no Auer rods	Any, unless fulfills all criteria for MDS with isolated del(5q)
MDS-RS with multilineage dysplasia (MDS-RS-MLD)	≥15% / ≥5% ^a	BM <5%, PB <1%, no Auer rods	Any, unless fulfills all criteria for MDS with isolated del(5q)
MDS with isolated del(5q)	None or any	BM <5%, PB <1%, no Auer rods	del(5q) alone or with 1 additional abnormality except -7 or del(7q)
MDS with excess blasts (MDS-EB)			
MDS-EB-1	None or any	BM 5–9% or PB 2–4%, no Auer rods	Any
MDS-EB-2	None or any	BM 10–19% or PB 5–19% or Auer rods	Any
MDS, unclassifiable (MDS-U)			
• with 1% blood blasts	None or any	BM <5%, PB = 1%, no Auer rods	Any
• with single lineage dysplasia and pancytopenia	None or any	BM <5%, PB = 1%, no Auer rods	Any
• based on defining cytogenetic abnormality	<15%	BM <5%, PB = 1%, no Auer rods	MDS-defining abnormality
Refractory cytopenia of childhood	None	BM <5%, PB <2%	Any

Luspatercept, geç evre eritropoezi güçlendirerek MDS'deki anemiye düzelten ajanıdır. TGF-beta süper ailesi ligandlarını bağlayarak anormal Smad2/3 sinyalini azaltır. Ring sideroblastları olan, SF3B1 içeren MDS'de en etkilidir

İvosidenib IDH1 mutasyonu tespit edilen nükseden veya dirençli MDS'nin tedavisi için FDA tarafından onaylanmıştır

İmetelstat düşük riskli MDS hastalarında, özellikle del(5q) anormalliği olmayan hastalarda transfüzyona ihtiyacını azaltan antisens oligonükleotid telomeraz inhibitörüdür



AKUT LÖSEMİLERE GİRİŞ

TABLE 168-1 WORLD HEALTH ORGANIZATION
CLASSIFICATION OF ACUTE LEUKEMIAS
(2016)

Acute Myeloid Leukemia (AML) and Related Neoplasms

AML with recurrent genetic abnormalities
 AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
 AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
 APL with *PML-RARA*
 AML with t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*
 AML with t(6;9)(p23;q34.1); *DEK-NUP214*
 AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*
 AML (megakaryoblastic) with t(1;22)(p13.3;q13.3); *RBM15-MKL1*
Provisional entity: AML with BCR-ABL1
 AML with mutated *NPM1*
 AML with biallelic mutations of *CEBPA*
Provisional entity: AML with mutated RUNX1
 AML with myelodysplasia-related changes
 Therapy-related myeloid neoplasms

B-Lymphoblastic Leukemia/Lymphoma

B-lymphoblastic leukemia/lymphoma, NOS
 B-lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
 B-lymphoblastic leukemia/lymphoma with t(9;22)(q34.1;q11.2); *BCR-ABL1*
 B-lymphoblastic leukemia/lymphoma with t(v;11q23.3); *KMT2A* rearranged
 B-lymphoblastic leukemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
 B-lymphoblastic leukemia/lymphoma with hyperdiploidy
 B-lymphoblastic leukemia/lymphoma with hypodiploidy
 B-lymphoblastic leukemia/lymphoma with t(5;14)(q31.1;q32.3); *IL3-IGH*
 B-lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
Provisional entity: B-lymphoblastic leukemia/lymphoma, BCR-ABL1-like
Provisional entity: B-lymphoblastic leukemia/lymphoma with iAMP21

T-Lymphoblastic Leukemia/Lymphoma

Provisional entity: Early T-cell precursor lymphoblastic leukemia
Provisional entity: Natural killer (NK) cell lymphoblastic leukemia/lymphoma

AML, NOS

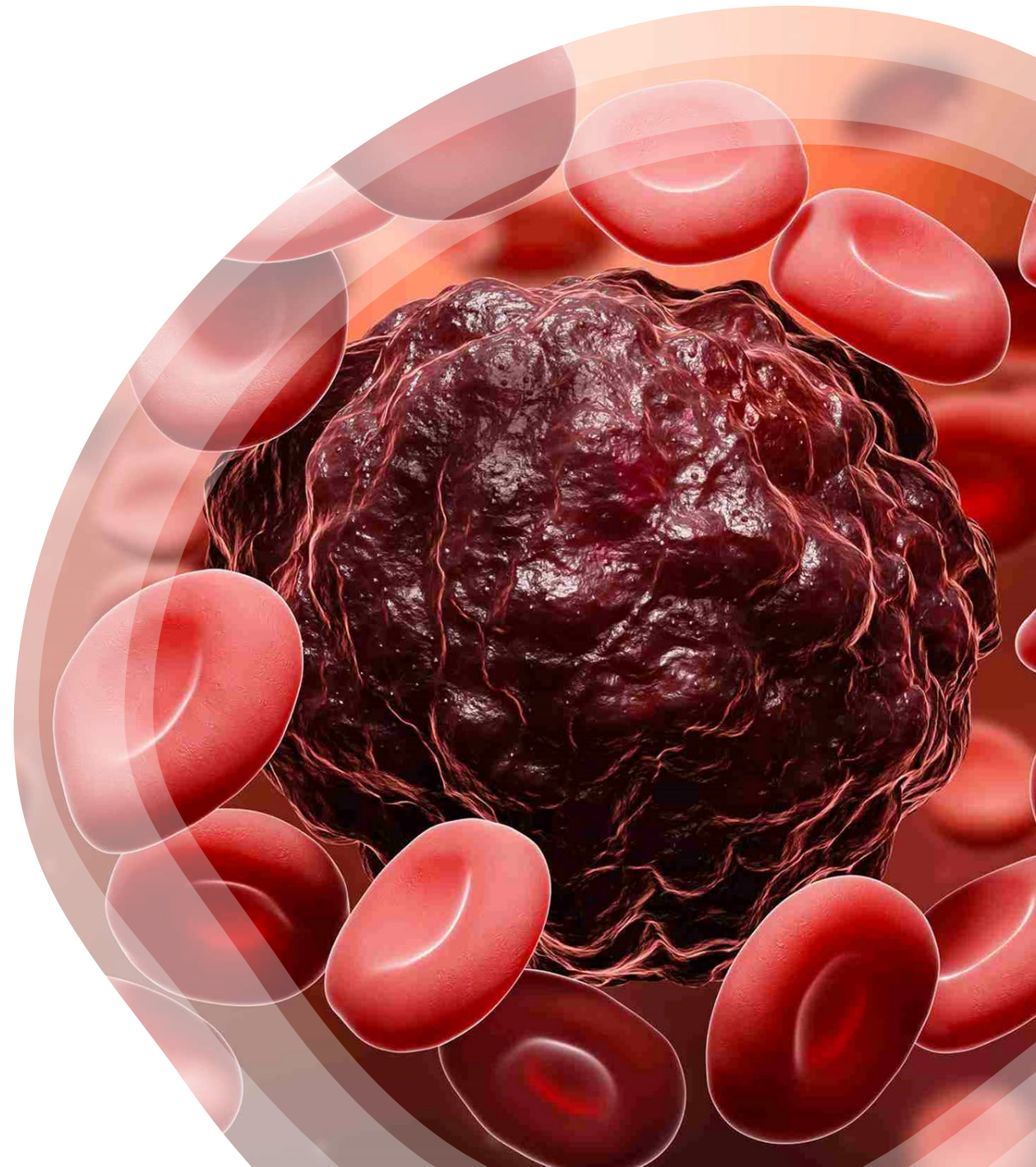
AML with minimal differentiation
 AML without maturation
 AML with maturation
 Acute myelomonocytic leukemia
 Acute monoblastic/monocytic leukemia
 Pure erythroid leukemia
 Acute megakaryoblastic leukemia
 Acute basophilic leukemia
 Acute panmyelosis with myelofibrosis
 Myeloid sarcoma
 Myeloid proliferations related to Down syndrome
 Transient abnormal myelopoiesis (TAM)
 Myeloid leukemia associated with Down syndrome

Blastic Plasmacytoid Dendritic Cell Neoplasm

Acute Leukemias of Ambiguous Lineage

Acute undifferentiated leukemia
 Mixed phenotype acute leukemia (MPAL) with t(9;22)(q34.1;q11.2); *BCR-ABL1*
 MPAL with t(v;11q23.3); *KMT2A* rearranged
 MPAL, B/myeloid, NOS
 MPAL, T/myeloid, NOS

AKUT LENFOBLASTİK LÖSEMİ



SUBTYPES	MARKER	INCIDENCE	FREQUENT CYTOGENETIC ABERRATIONS	GENETIC ABERRATIONS AND FUSION TRANSCRIPTS	CLINICAL CHARACTERISTICS	RELAPSE KINETICS AND LOCALIZATION
B-lineage ALL (B-ALL)	HLA-DR+, TdT+, CD19+, and/or CD79a+, and/or CD22+	76%				
Pro B-ALL	No additional differentiation markers Frequent myeloid coexpression (>50%) CD10–	12%	t(4;11) (q21;q23)	70% <i>ALL1-AF4</i> (20% <i>Flt3</i> in MLL+)	High WBC (>100,000/ μ L) (26%)	Mainly BM (>90%)
Common ALL	CD10+	49%	t(9;22)(q34;q11) del(6q)	33% <i>BCR-ABL</i> with 54% <i>IKFZ1</i> del >25% <i>CDKN2A/B</i>	Higher age >50 years (24%)	Mainly BM (>90%) Prolonged relapse kinetics (up to 5–7 years)
Pre-B-ALL	CD10 $\pm$, cyIg+	11%	t(9;22)(q34;q11) t(1;19)(q23;p13)	4% t(1;19)/ <i>PBX-E2A</i>		
Mature B-ALL	CD10 $\pm$, sIg+	4%	t(8;14)(q24;q32) t(2;8)(p12;q24) t(8;22)(q24;q11)		Higher age >55 years (27%) Frequent organ involvement (32%) and CNS involvement (13%)	Frequent CNS (10%) Short relapse kinetics (up to 1–1.5 years)
T-lineage ALL (T-ALL)	cyCD3 or sCD3	24%	t(10;14)(q24;q11) t(11;14)(p13;q11)	50% <i>NOTCH1B</i> 33% <i>HOX11b</i> 5% <i>HOX11L2b</i> 4% <i>NUP213-ABL1</i>	Younger age (90% <50 years) Frequent mediastinal tumors (60%) Frequent CNS involvement (8%) High WBC (>50/ μ L) (46%)	Frequent CNS (up to 10%) Extramedullary (6%) Intermediate relapse kinetics (up to 3–4 years) When relapsed, fast progression
Early Pro/ Pre T-ALL	No additional differentiation markers, mostly CD2–	6%				
Cortical T-ALL	CD1a+, sCD3 $\pm$	12%				
Mature T-ALL	sCD3+, CD1a–	6%				

İyi prognoz kriterleri

† (8;21), † (15;17), inv 16, CEPBA , NPM 1, miR-181 alfa ↑

Kötü prognoz

FLT-3 ITD

TABLE 168-2

2017 EUROPEAN LEUKEMIA NET
CYTOGENETIC/MOLECULAR RISK
STRATIFICATION OF AML

SUBSET	
Favorable	t(8;21)(q22;q22.1); <i>RUNX1-RUNX1T1</i> inv(16)(p13.1;q22) or t(16;16)(p13.1;q22); <i>CBFB-MYH11</i> Mutated <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i> ^{low*} Biallelic mutated <i>CEBPA</i>
Intermediate	Mutated <i>NPM1</i> and <i>FLT3-ITD</i> ^{high*} Wild-type <i>NPM1</i> without <i>FLT3-ITD</i> or with <i>FLT3-ITD</i> ^{low*} (without adverse-risk genetic lesions) t(9;11)(p21.3;q23.3); <i>MLLT3-KMT2A</i> [†] Cytogenetic abnormalities not classified as favorable or adverse
	t(6;9)(p23;q34.1); <i>DEK-NUP214</i> t(v;11)(v;q23.3); <i>KTM2A</i> rearranged T(9;22)(q34.1;q11.2); <i>BCR-ABL1</i>
Adverse	inv(3)(q21.3;q26.2) or t(3;3)(q21.3;q26.2); <i>GATA2</i> , <i>MECOM (EVI1)</i> -5 or del(5q); -7; -17/abnl(17p) Complex karyotype, [‡] monosomal karyotype Wild-type <i>NPM1</i> and <i>FLT3-ITD</i> ^{high*}
Adverse	Mutated <i>RUNX1</i> [§] Mutated <i>ASXL1</i> [§] Mutated <i>TP53</i>

TABLE 87-3. Commonly Mutated Genes in Cytogenetically Normal Acute Myelogenous Leukemia

Mutated Gene	Approximate Frequency in AML with Normal Karyotype (%)	Implication	Comments	References
<i>NPM1</i>	50	More-favorable outcomes	Most frequently mutated gene in AML. Allogenic transplantation not needed in first remission if this mutation occurs in absence of mutated <i>FLT3-ITD</i>	173–179
<i>FLT3-ITD</i>	40	Less-favorable outcomes		173, 174, 184–191
<i>DNMT3A</i>	20	Less-favorable outcomes	Seen more often in AML patients with normal cytogenetics. Mutant <i>NPM1</i> , <i>FLT3-ITD</i> , and <i>IDH1</i> have been found more frequently in AML patients with <i>DNMT3A</i> mutations compared to those with wild-type <i>DNMT3A</i>	192–199
<i>RUNX1</i>	15	Less-favorable outcomes		200–205
<i>TET2</i>	15	Less-favorable outcomes	Coincidence of mutated <i>TET2</i> with <i>NPM1</i> mutation in the absence of <i>FLT3-ITD</i> mutation predicts a less-favorable outcome	206–209
<i>CEBPα</i>	15	More-favorable outcomes	Only cases with double mutations associated with favorable outcomes	173, 210–214
<i>NRAS</i>	10	Little effect on prognosis		200
<i>IDH1</i> or <i>IDH2</i>	10	Little effect on outcomes	More frequent in AML patients with normal cytogenetics. Frequently associated with <i>NPM1</i> . Adverse prognostic factor if present with mutated <i>NPM1</i> without <i>FLT3-ITD</i> . Serum 2-hydroxyglutarate levels indicate high probability of <i>IDH</i> mutation	193, 215–223
<i>MLL-PTD</i>	8	Less-favorable outcomes		200
<i>WT1</i>	6	Less-favorable outcomes	More frequent in females than in males (6.6 vs 4.7%; $P = 0.014$) and in patients <60 than in patients >60 years ($P < 0.001$)	225, 226
<i>FLT3-TKD</i>	6	Little effect on outcomes	May appear after use of FLT3-ITD inhibitor	186, 190

Klinik:

Erişkinlerde en sık görülen lösemi → B lenfosit kökenli lösemidir

Matür B lenfositlerin kontrolsüz klonal çoğalmasıdır

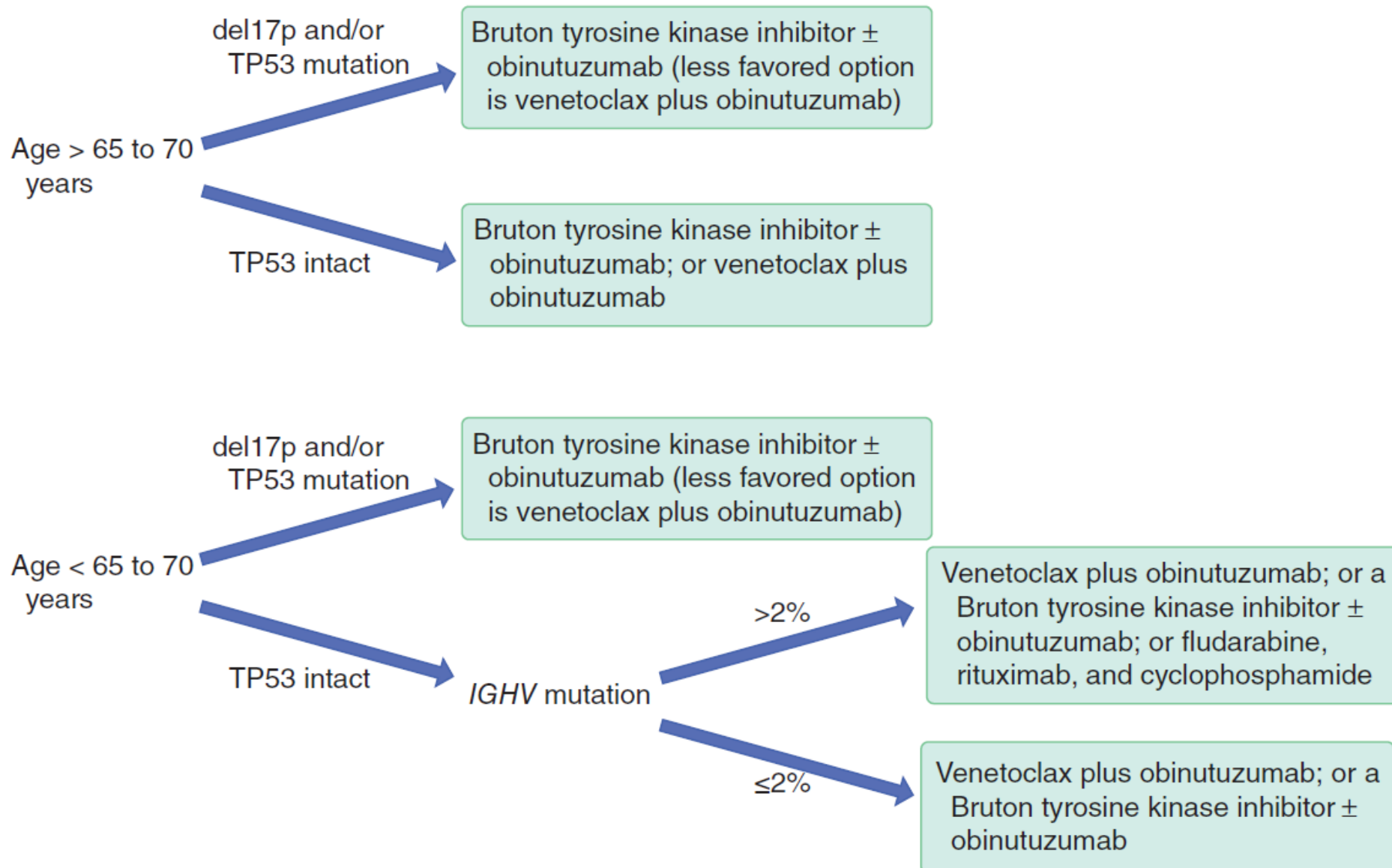
En sık sitogenetik anomali 13q delesyonudur → İyi prognoz (diğer tüm delesyonlar kötü prognoz)

INCIDENCE OF GENOMIC ABNORMALITIES AND ASSOCIATED CLINICAL FEATURES IN CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)

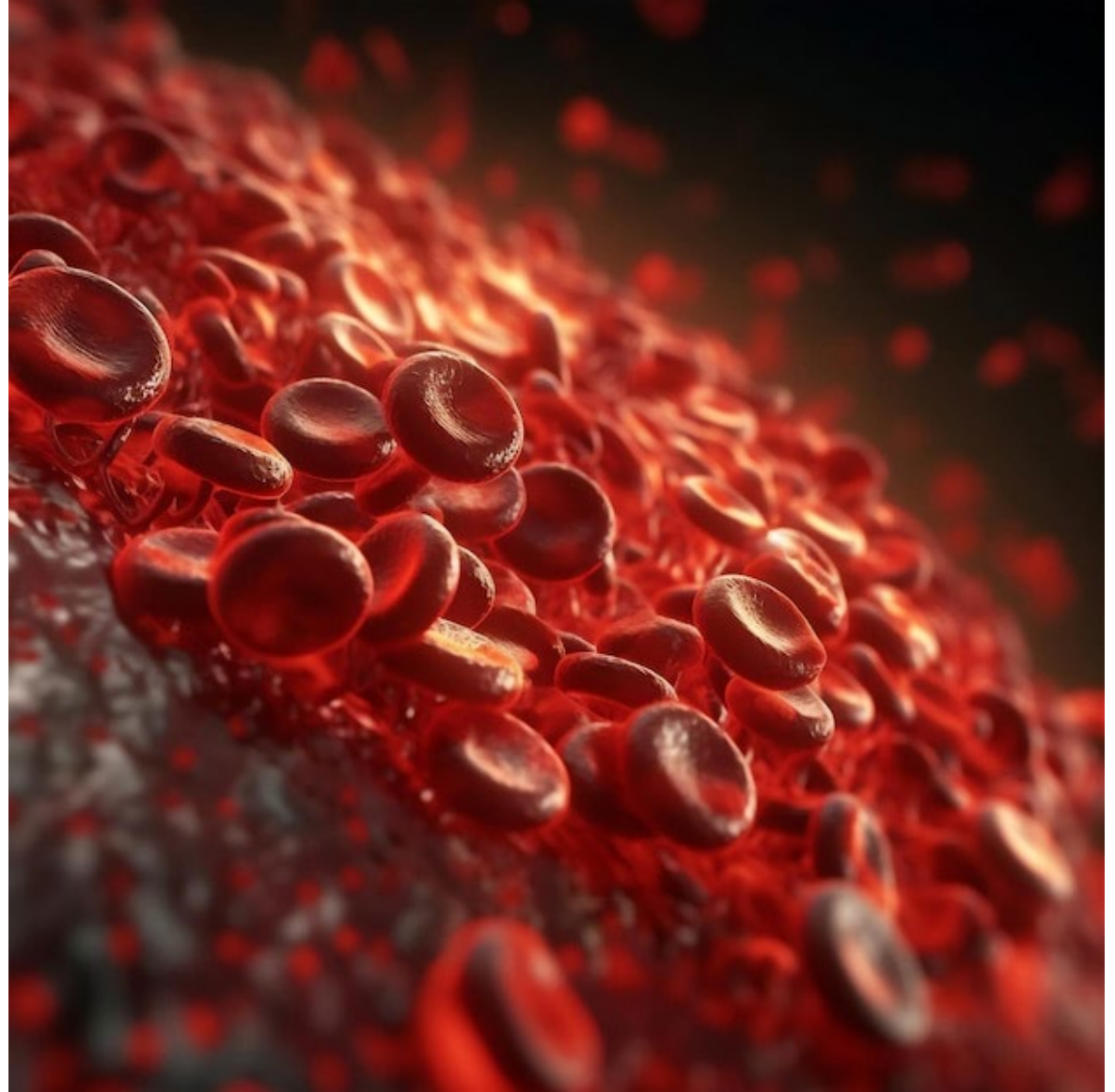
Genomic Abnormality	Incidence (%)		Affected Genes	Clinical Features
	Classical Cytogenetics ^a	Fluorescence in Situ Hybridization ^b		
Normal	50 ^c	18	—	—
13q deletion	10	55	<i>Rb, MiR-15a, MiR-16-1</i>	Good prognosis
11q deletion	8	18	<i>ATM</i> <i>SF3B1</i>	Younger; bulky lymphadenopathy; poor prognosis
12q trisomy	13	16	<i>MDM2</i> <i>NOTCH1</i>	"Atypical" morphology; end-stage disease
17p deletion	4	7	<i>TP53</i>	CLL/PLL morphology; drug resistance; very poor prognosis

Flow sitometride CD 19, 20, 21, 23 ve CD 5 pozitif izlenir
Tanı için kemik iliği aspirasyon/biyopsi yapma şartı yoktur

TABLE 107-2 Typical Immunophenotype of CLL Compared with Other B Cell Malignancies						
DISEASE	CD5	CD10	CD19	CD20	CD23	CYCLIN D1
CLL	+	–	+	+ (dim)	+	–
Mantle cell lymphoma	+	–	+	+ (mod/bright)	–	+
Marginal zone lymphoma	–/+	–	+	+ (mod/bright)	–/+	–
Follicular lymphoma	–	+	+	+	+	–



HAIRY CELL LÖSEMI



BRAF %90 vakada pozitif → Artık BRAF inhibitörleri de verilebilir !!

Kemik iliğinde fibrozis → Dry tap

TABLE 110-3 Differential Diagnosis of “Dry Tap”—Inability to Aspirate Bone Marrow

Dry taps occur in about 4% of attempts and are associated with:

Metastatic carcinoma infiltration	17%
Chronic myeloid leukemia	15%
Myelofibrosis	14%
Hairy cell leukemia	10%
Acute leukemia	10%
Lymphomas, Hodgkin’s disease	9%
Normal marrow	Rare

Tedavi: Asemptomatik vakalarda tedavi gerekmez

Semptomatik vakalarda klorodeoksiadenozin verilir

◆ Rituksimab, INF ve splenektomi yapılabilir

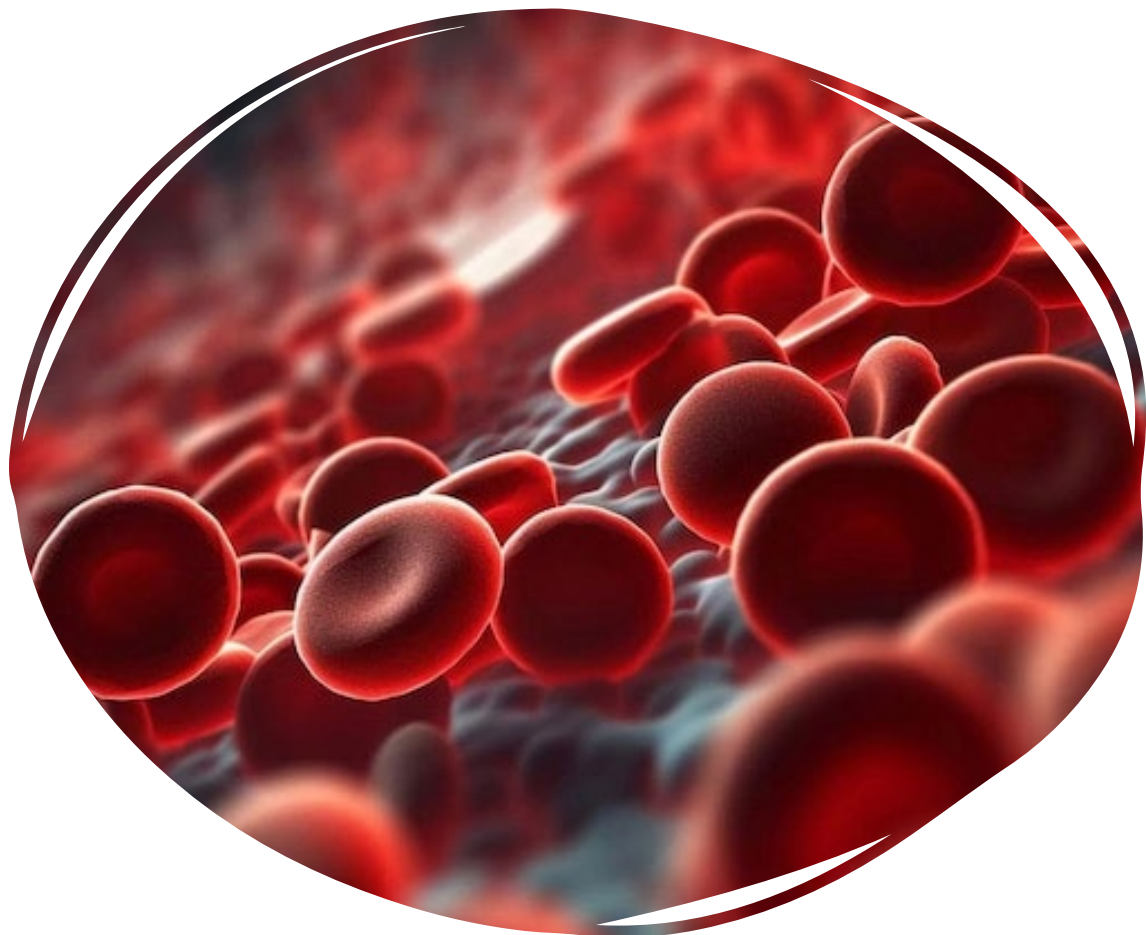
Dirençli vakalar → OKİT

SUGGESTED TREATMENT REGIMENS^{a,b}

INITIAL THERAPY ^{c,d,e,f}	
Preferred Regimens	Useful in Certain Circumstances (consider for patients who are unable to tolerate purine analogs including frail patients and those with active infection)
• Purine analogs ▸ Cladribine ± rituximab ▸ Pentostatin	• Vemurafenib ± anti-CD20 monoclonal antibody (mAb)^g

RELAPSED/REFRACTORY THERAPY ^{c,e,f}			
	Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances
Less than complete response after initial treatment OR Relapse <2 years	• Clinical trial • Dabrafenib* + trametinib (if not previously treated with BRAF inhibitor) • Vemurafenib^{h,*} ± rituximab (if not previously given)	• Peginterferon-alfa 2aⁱ • Alternative purine analog ± rituximab	• Rituximab, if unable to receive purine analog
Relapse ≥2 years	• Retreatment with initial purine analog + rituximab • Alternative purine analog + rituximab		• Rituximab, if unable to receive purine analog

PROGRESSIVE DISEASE AFTER RELAPSED/REFRACTORY THERAPY ^{e,f}		
Preferred Regimens	Other Recommended Regimens	Useful in Certain Circumstances (for patients with disease resistant to BRAF inhibitor therapy):
• Clinical trial • Dabrafenib* + trametinib (if not previously treated with BRAF inhibitor) • Vemurafenib* ± rituximab	• Ibrutinib • Zanubrutinib	• Venetoclax ± rituximab



HODGKIN LENFOMA

TABLE 172-1 WORLD HEALTH ORGANIZATION
CLASSIFICATION OF HODGKIN LYMPHOMA
SUBTYPES

SUBTYPE NAME	FREQUENCY (%)*
Classic Hodgkin lymphoma	
Nodular sclerosing	60
Lymphocyte rich	3
Mixed cellularity	9
Lymphocyte depleted	1
Nodular lymphocyte-predominant Hodgkin lymphoma	8
Hodgkin lymphoma, not otherwise classifiable	19

TABLE 89–2. Indolent Lymphomas

Disseminated lymphomas/leukemias

Chronic lymphocytic leukemia

Hairy cell leukemia

Lymphoplasmacytic lymphoma

Splenic marginal zone B-cell lymphoma

Plasma cell myeloma/plasmacytoma

T-cell large granular lymphocytic leukemia

Nodal lymphomas

Follicular lymphoma

Nodal marginal zone B-cell lymphoma

Small lymphocytic lymphoma

Nodular lymphocyte predominant Hodgkin lymphoma

Extranodal lymphomas

Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) type

TABLE 89–3. Aggressive Lymphomas

Immature B-cell neoplasms

B-lymphoblastic leukemia/lymphoma

Mature B-cell neoplasms

Burkitt lymphoma/leukemia

Diffuse large B-cell lymphoma

Follicular lymphoma grade III

Mantle cell lymphoma

High-grade B-cell lymphoma (NOS or double hit) classical Hodgkin lymphoma

Immature T-cell neoplasms

T-lymphoblastic leukemia/lymphoma

Peripheral T- and natural killer (NK)-cell neoplasms

T-cell prolymphocytic leukemia/lymphoma

Aggressive NK cell leukemia/lymphoma

Adult T-cell lymphoma/leukemia (associated with HTLV-1 [human T-cell leukemia virus type 1])

Extranodal NK/T-cell lymphoma

Enteropathy-associated T-cell lymphoma

Hepatosplenic T-cell lymphoma

Subcutaneous panniculitis-like T-cell lymphoma

Peripheral T-cell lymphomas, not otherwise specified

Angioimmunoblastic T-cell lymphoma

Follicular T-cell lymphoma

Anaplastic large cell lymphoma, ALK+ and ALK–

Immune deficiency-associated lymphoproliferative disorders

INFECTIONS AND ASSOCIATIONS WITH LYMPHOMA

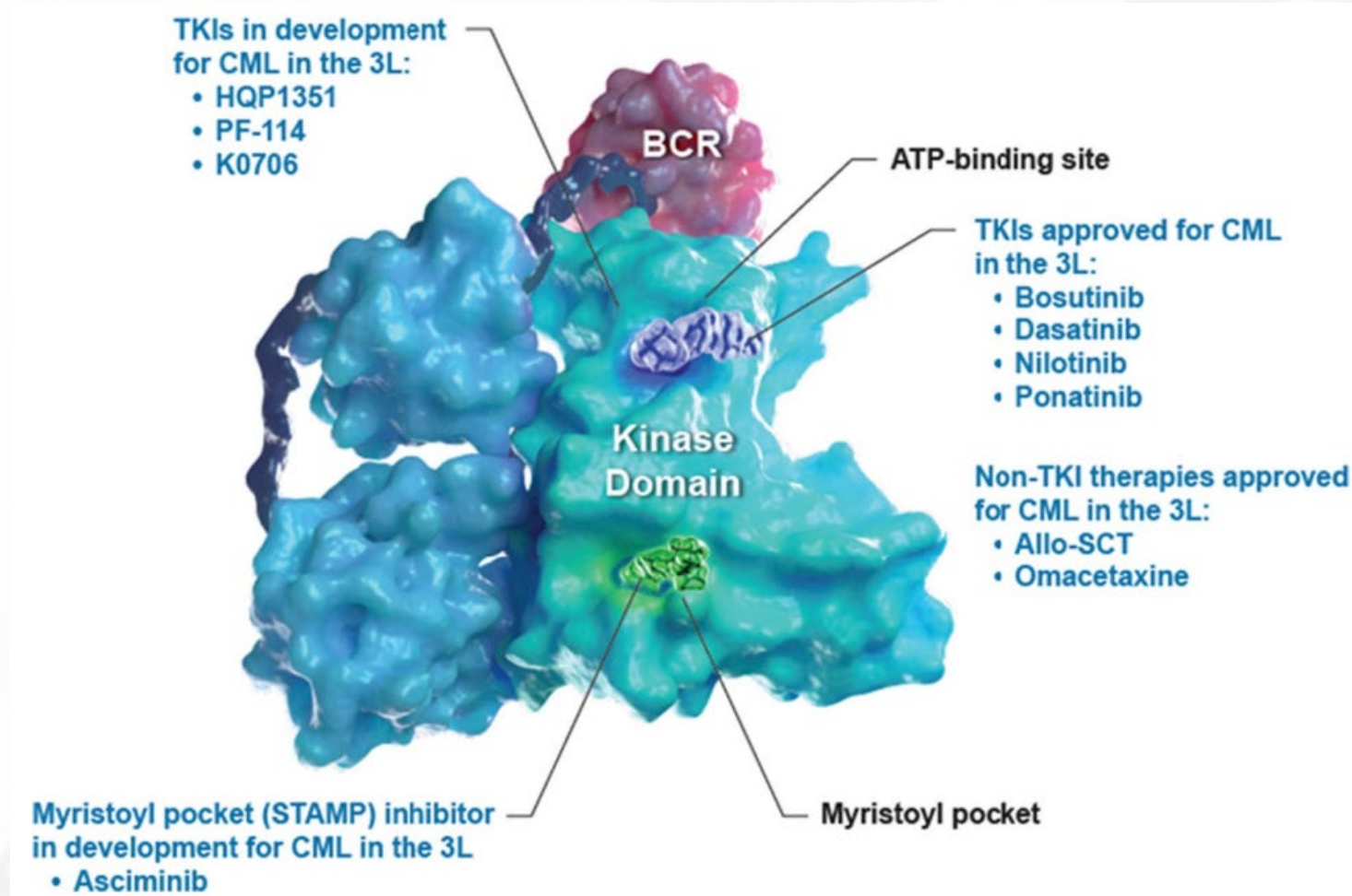
Agent	Lymphoma Type(s)
Epstein-Barr virus (EBV)	Burkitt lymphoma (Africa) Posttransplant lymphoproliferative disorders Acquired immunodeficiency syndrome–related lymphoma (central nervous system, others) Natural killer/T cell nasal lymphoma Hodgkin lymphoma Diffuse large B cell lymphoma of the elderly
Human T-lymphotropic virus I (HTLV-1)	Adult T cell leukemia/lymphoma
Human herpes virus 8/Kaposi sarcoma–associated herpes virus	Primary effusion lymphoma Plasmablastic lymphoma
<i>Helicobacter pylori</i>	Gastric MALToma ^a
Hepatitis B virus	Diffuse large B cell lymphoma
Hepatitis C virus	Splenic marginal zone lymphoma; other B cell lymphomas
<i>Campylobacter jejuni</i>	Immunoproliferative small intestinal disease ^a
<i>Borrelia burgdorferi</i>	Primary cutaneous B cell lymphoma ^a
<i>Chlamydia psittaci</i>	Ocular adnexal lymphoma ^a

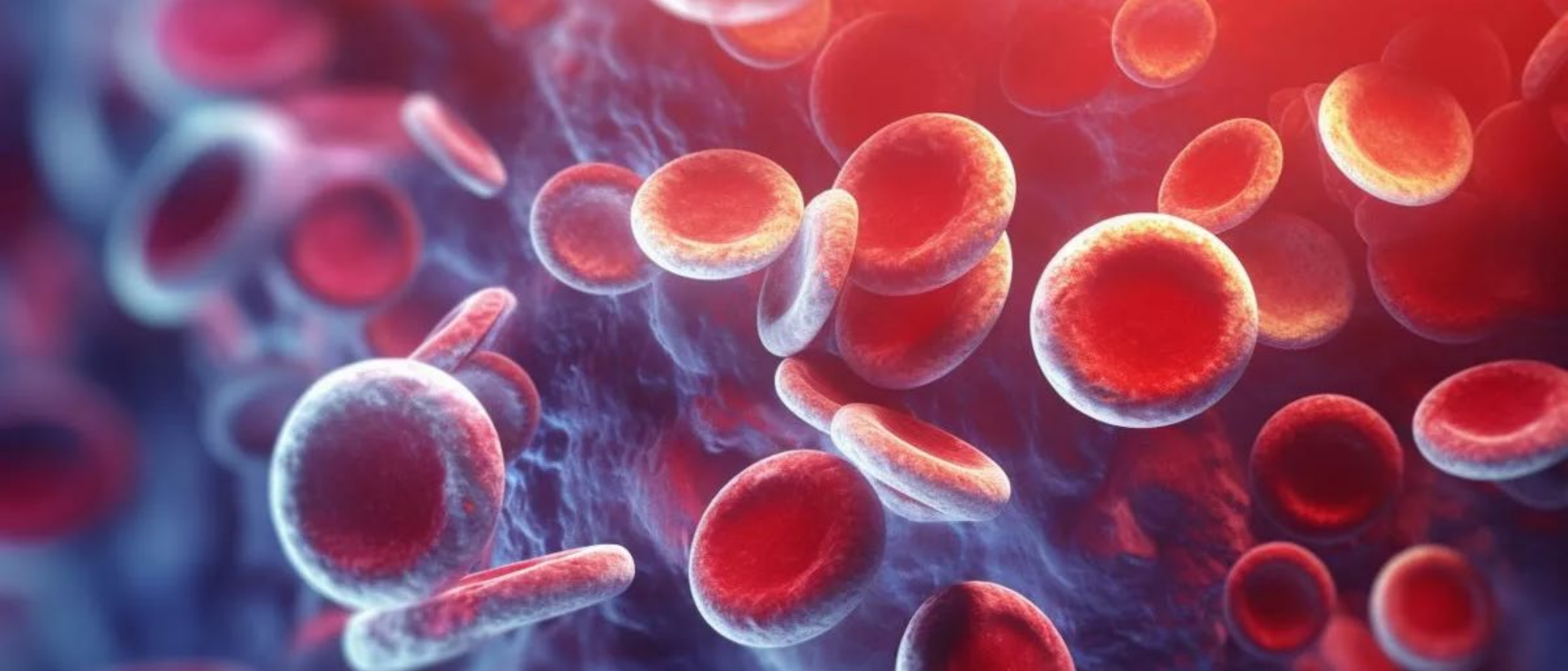
TABLE 108-3 Diseases or Exposures Associated with Increased Risk of Development of Malignant Lymphoma

Inherited immunodeficiency disease	Autoimmune disease
Klinefelter's syndrome	Sjögren's syndrome
Chédiak-Higashi syndrome	Celiac sprue
Ataxia-telangiectasia syndrome	Rheumatoid arthritis and systemic lupus erythematosus
Wiskott-Aldrich syndrome	Chemical or drug exposures
Common variable immunodeficiency disease	Phenytoin
Acquired immunodeficiency diseases	Dioxin, phenoxy herbicides
Iatrogenic immunosuppression	Radiation
HIV-1 infection	Prior chemotherapy and radiation therapy
Acquired hypogammaglobulinemia	

TABLE 108-4 Genetic Features of B- and T-Cell Lymphomas		
GENETIC FEATURE	GENES	LYMPHOMA
t(8;14) t(2;8) t(8;22)	<i>MYC/IgH</i> <i>MYC/Igκ</i> <i>MYC/Ig λ</i>	Burkitt's lymphoma
t(11;14)	<i>BCL1 (CCND1)/IgH</i>	Mantle cell lymphoma; multiple myeloma
t(14;18) t(3;14)	<i>BCL2/IgH</i> <i>BCL6/IgH</i>	Follicular lymphoma, diffuse large B-cell lymphoma (DLBCL)
t(11;18) t(1;14) t(14;18) t(3;14)	<i>API2/MALT1</i> <i>BCL10/IgH</i> <i>MALT1/IgH</i> <i>FOXP1/IgH</i>	MALT lymphoma
Trisomy 3 7q21 deletion	Unknown <i>CDK6</i>	Splenic marginal zone lymphoma
t(9;14) 6q21 deletion	<i>PAX5/IgH</i> Unknown	Lymphoplasmacytic lymphoma
inv(14) t(14;14)	<i>TCRα/TCL1</i>	Peripheral T-cell lymphoma, NOS; T-PLL
t(2;5) t(1;2) t(2;3) t(2;17) inv(2)	<i>NPM1/ALK</i> <i>TPM3/ALK</i> <i>TFG/ALK</i> <i>CTLC/ALK</i> <i>AT1C/ALK</i>	Anaplastic large-cell lymphoma (ALCL)
Trisomy 3 Trisomy 5	Unknown Unknown	Angioimmunoblastic T-cell lymphoma
Isochromosome 7q	Unknown	Hepatosplenic T-cell lymphoma

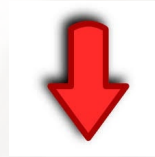
Hipotiroidi ve hipertansiyon tüm tirozin kinaz inhibitörlerin ortak yan etkisidir





MULTİPLE MİYELOM

isatuksimab



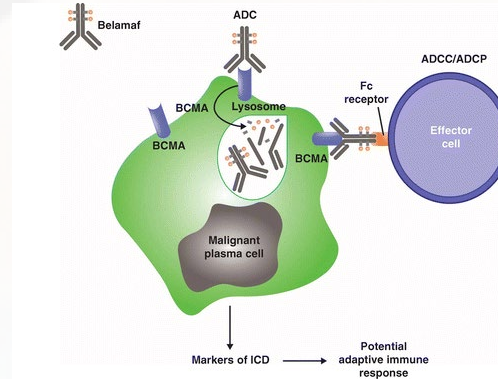
**Daratumumab gibi CD
38 monoklonal antikor**



Belantamab



**B hücresi maturasyon
antijenini (BCMA) hedef
alan ilaç**



Selineksor



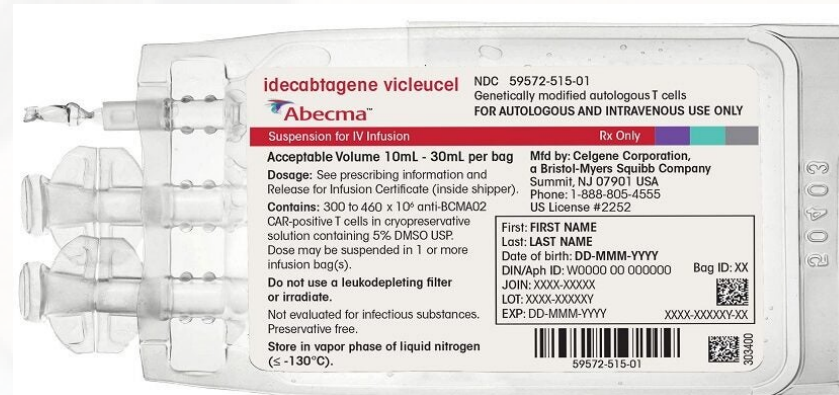
Selektif nükleer eksport inhibisyonu



IdecabtaGENe vicleucel



FDA onaylı ilk hücre bazlı gen tedavisi



HEMOSTAZ



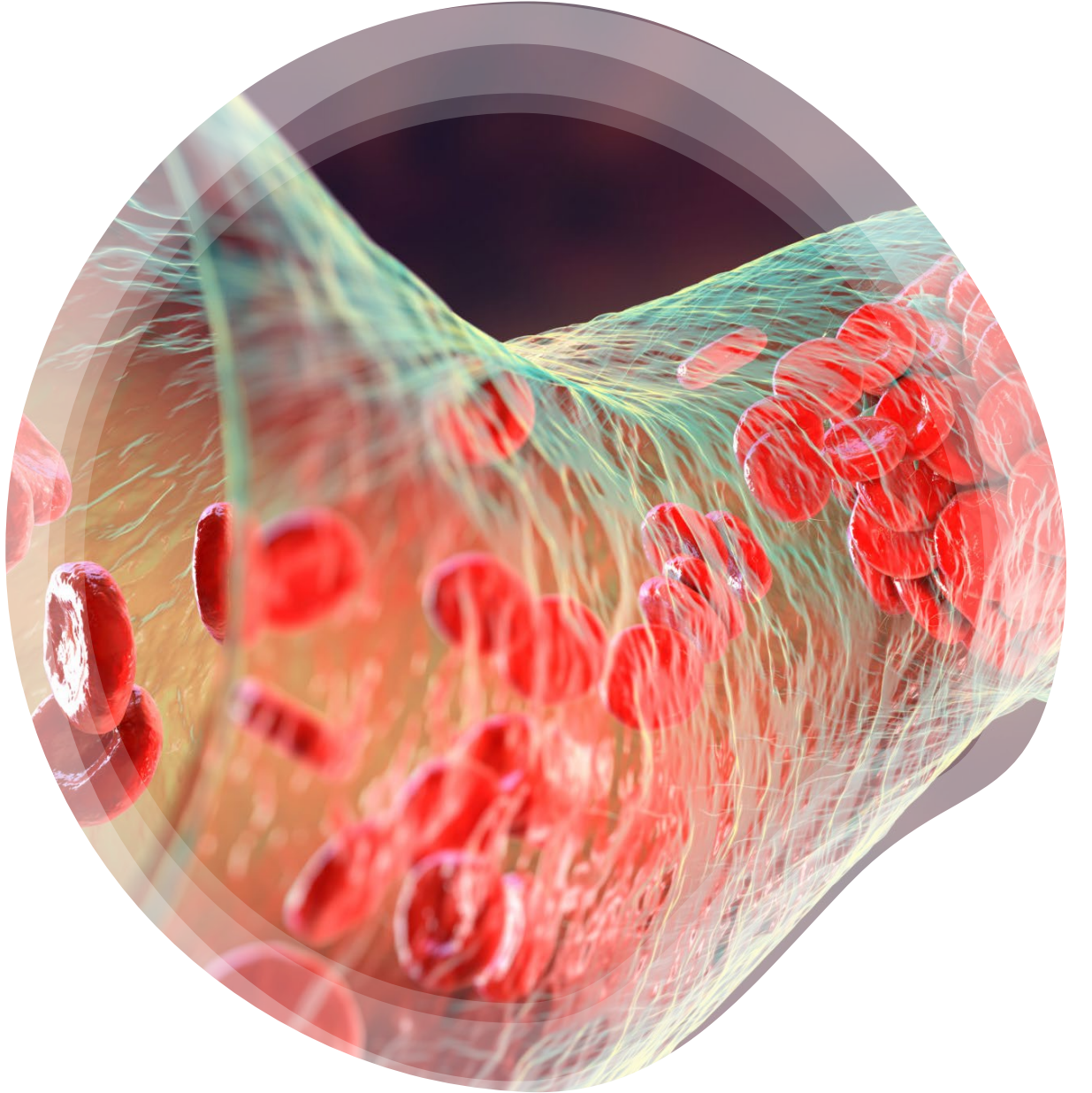
TABLE 6.3 Classification of von Willebrand Disease

Type	Inheritance	Frequency of VWD Type ^a	VWF Activity	RIPA	Multimer Pattern
Type 1 (classic)	Autosomal	70%–75%	↓	↓	Uniformly ↓ All multimers present
1C	Autosomal dominant	Uncertain	↓	↓	Normal
Type 2					
2A	Autosomal dominant (and recessive)	10%–15%	↓	↓	↓ Large and intermediate multimers
2B	Autosomal dominant	5%	↓	↑	↓ Large multimers
2M	Autosomal dominant (and recessive)	<5%	↓	↓	Normal multimers
2N	Autosomal recessive	Rare	Normal	Normal	Normal multimers
Type 3 (severe)	Autosomal recessive	Rare	↓↓	↓↓	Undetectable (usually cannot be visualized)

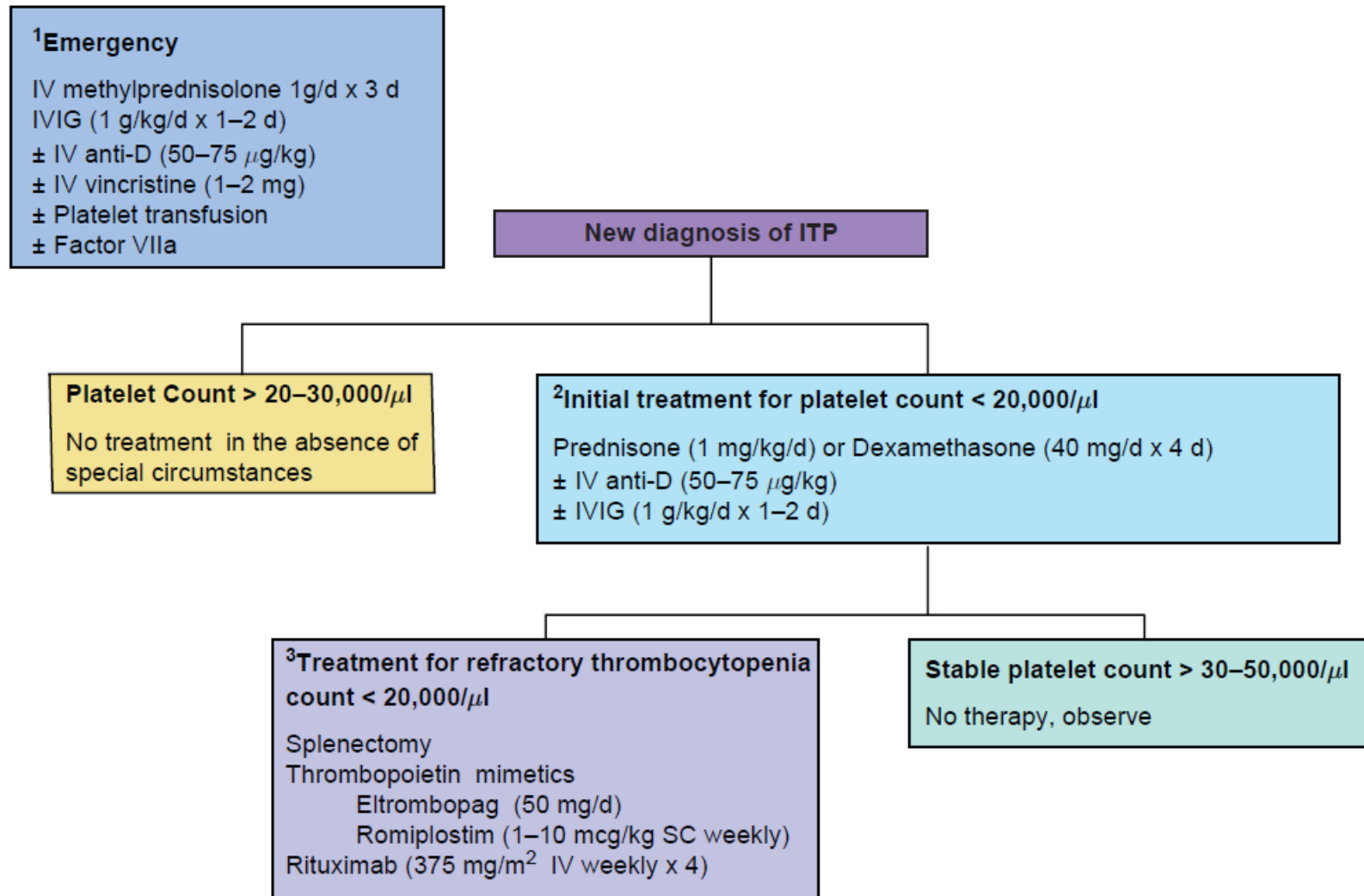
Ağır Hemofili A → Faktör 8 düzeyi < %1
Orta Hemofili A → Faktör 8 düzeyi > %2-5
Hafif Hemofili A → Faktör 8 düzeyi > %5-30

Type of Bleed	Goal of Therapy (% of Normal Clotting Factor Activity Level)
Joint	>30–50
Dental	>30–50
Genitourinary	50
Gastrointestinal	50
Muscle	>80
Intracranial	100

İMMÜN TROMBOSİTOPENİK PURPURA



Tedavi: En temel tedavi kortikosteroidlerdir → İlk tercih



TRANSFÜZYON



Bir ünite kan 450 cc'dir → Eritrosit süspansiyonu ise 325 ml'dir

◆ Eritrosit süs. 1-6 C'de 35-42 gün saklanır → Sitrat, fosfat, adenin ve dekstroza eklenir

Taze donmuş plazma, lökosit, trombosit ve kriyopresipitat için kan grubu uyumu gereklidir

Tam kan ve eritrosit süspansiyonu verilirken öncesinde mutlaka cross-match yapılmalıdır

◆ Cross-match diğer kan ürünleri için geçerli değildir

◆ Çok acil transfüzyonda 0 Rh (-) eritrosit kan grubu ve cross-match yapılmadan verilebilir

**Hangi kan ürünlerinin
transfüzyonunda **Rh uyumu**
aranmaz??**

- * Trombosit**
- * Kriyopresipitat**
- * Taze donmuş plazma**

Riskli bireylerde transfüzyon ilişkili graft-versus-host hastalığını engellemek amacıyla aşağıdaki **kan ürünlerinden hangisinin transfüzyon öncesi ışınlanmasına gerek yoktur?**

- A. Tam kan transfüzyonu
- B. Eritrosit transfüzyonu
- C. Trombosit transfüzyonu
- D. Kriyopresipitat
- E. Granülosit transfüzyonu

İşinlanabilen Kan Ürünleri

- * Trombositler
- * Granülosit
- * Tam kan / Eritrosit

İşinlanmayan Kan Ürünleri

- * Kök hücreler
- * Kriyopresipitat
- * Taze donmuş plazma

TABLE 162-4 EVIDENCE-BASED TRANSFUSION TRIGGERS

BLOOD COMPONENT	COMMONLY ACCEPTED INDICATIONS	TYPICAL INCREASE
RBC	Hb <7.0 g/dL Hb < 8.0 g/dL acute coronary syndrome/myocardial infarction	Hb: 1 g/dL or Hct: 3% after one unit of RBC
Platelets	<10,000/ μ L hospitalized adult patients with therapy-induced hypoproliferative thrombocytopenia <20,000/ μ L if febrile/septic, central venous catheter, or other minor procedures <50,000/ μ L if surgery, lumbar puncture, invasive procedure, or active bleeding <100,000/ μ L neurosurgery or central nervous system bleeding	30-60,000/ μ L after one platelet dose (a single apheresis component or 4-6 whole blood derived platelet concentrates [3×10^{11} platelets])
Plasma	Massive transfusion (plasma : RBC: 1 : 2) INR >2.0 prior to invasive procedure Replacement fluid for plasma exchange for thrombotic thrombocytopenic purpura	10-15 mL/kg increases factor levels by $\approx$ 20%
Cryoprecipitate	Fibrinogen <150 mg/dL with bleeding	$\approx$ 7 mg/dL increase in fibrinogen per unit

Hb = hemoglobin; Hct = hematocrit; ICH = intracranial hemorrhage; INR = international normalized ratio; PCC = prothrombin complex concentrate; RBC = red blood cell.

TABLE 162-2 NONINFECTIOUS TRANSFUSION-ASSOCIATED EVENTS

TRANSFUSION-ASSOCIATED ADVERSE EVENT	RISK PER UNIT TRANSFUSED IN THE UNITED STATES
Acute hemolytic transfusion reaction	≈1 : 110,000 transfusions
Febrile nonhemolytic transfusion reaction	≈1 : 1100
Allergic transfusion reaction	≈1 : 1200 ≈1 : 15,500 severe
Transfusion-associated circulatory overload	≈1 : 9000
Transfusion-related acute lung injury	≈1 : 140,000
Hypotensive transfusion reactions	≈1 : 32,000
Transfusion-associated dyspnea	≈1 : 28,000
Delayed hemolytic transfusion reaction	≈1 : 32,000
Delayed serologic transfusion reaction	≈1 : 8000
Transfusion-associated graft-versus-host disease	<1 : 10,000,000
Post-transfusion purpura	≈1 : 10,000,000

Transfusion-Related Acute Lung Injury TRALI is characterized by the occurrence or worsening of hypoxia and noncardiogenic pulmonary edema with bilateral interstitial infiltrates on chest x-ray during or within 6 h after transfusion, although delayed cases may occur up to 72 h later. Frequency of TRALI is BC dependent and ranges, on average, from 0.5 to 10 per 10^5 BCs. TRALI may be difficult to distinguish from other causes of hypoxia, such as circulatory overload, and is among the most common causes of transfusion-related fatalities. Treatment is supportive only. TRALI usually results from the transfusion of donor plasma that contains high-titer anti-HLA class II Abs that bind recipient cognate Ag. Anti-HLA class I and anti-human neutrophil antigen (HNA) Abs may also be involved. TRALI mediated by cytokines and chemokines in the absence of an HLA-mediated interaction may occur also. Leukocytes, especially when primed by either a bacterial moiety such as lipopolysaccharide or a cytokine/chemokine, aggregate in the pulmonary vasculature and release inflammatory mediators. The transfusion of plasma and PCs from male donors and nulliparous or parous female donors without anti-HLA Abs has significantly reduced the risk of TRALI where implemented. Recipient factors associated with an increased risk of TRALI include smoking, chronic alcohol use, shock, liver surgery (transplantation), cancer surgery, mechanical ventilation, and positive fluid balance.