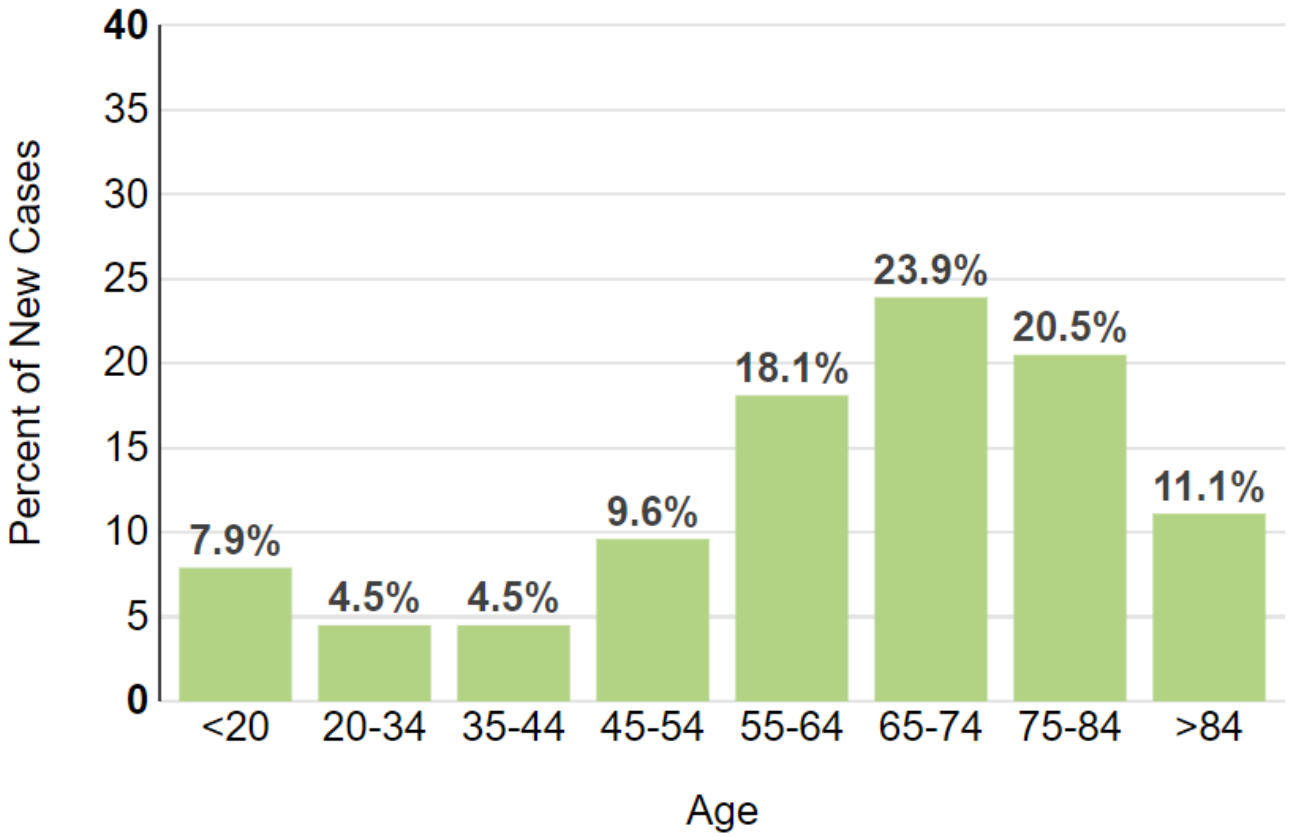
Akut Lösemilerde Ülkemizde Karşılanmayan İhtiyaçlar ve Riskler

	Common Types of Cancer	Estimated New Cases 2019	Estimated Deaths 2019
1.	Breast Cancer (Female)	268,600	41,760
2.	Lung and Bronchus Cancer	228,150	142,670
3.	Prostate Cancer	174,650	31,620
4.	Colorectal Cancer	145,600	51,020
5.	Melanoma of the Skin	96,480	7,230
6.	Bladder Cancer	80,470	17,670
7.	Non-Hodgkin Lymphoma	74,200	19,970
8.	Kidney and Renal Pelvis Cancer	73,820	14,770
9.	Uterine Cancer	61,880	12,160
10.	**Leukemia**	**61,780**	**22,840**

Leukemia represents 3.5% of all new cancer cases in the U.S.

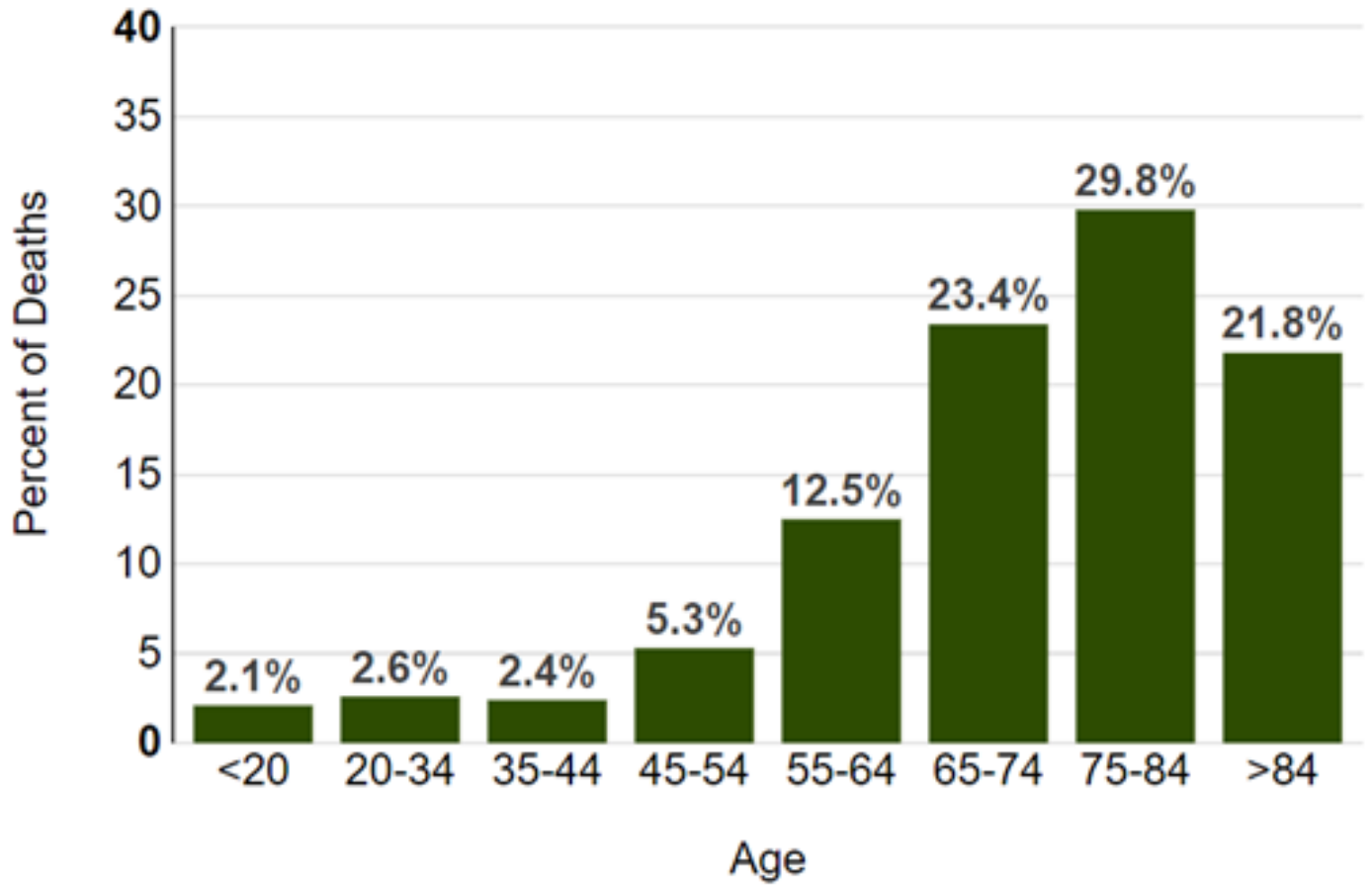
14,1/100 bin



Leukemia is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis
67

SEER 21 2012-2016, All Races, Both Sexes



The percent of leukemia deaths is highest among people aged 75-84.

Median Age At Death
75

International Agency for Research on Cancer

World Health Organization

Country-specific data source: Ankara Cancer Registry, Antalya Cancer Registry, Bursa Cancer Registry, Edirne Cancer Registry, Erzurum Cancer Registry, Eskisehir Cancer Registry, Izmir Cancer Registry, Samsun Cancer Registry, Trabzon Cancer Registry

Numbers at a glance

Total population

81 916 866

Number of new cases

210 537

Number of deaths

116 710

Number of prevalent cases (5-year)

470 851

Turkey

Source: Globocan 2018

Incidence, Mortality and Prevalence by cancer site

	New cases				Deaths				5-year prevalence (all ages)	
Cancer	Number	Rank	(%)	Cum.risk	Number	Rank	(%)	Cum.risk	Number	Prop.
Lung	34 703	1	16.5	4.48	33 683	1	28.9	4.43	32 632	39.84
Breast	22 345	2	10.6	4.80	5 452	5	4.7	1.14	68 288	164.37
Prostate	17 332	3	8.2	5.16	5 165	6	4.4	0.93	39 103	96.86
Thyroid	13 033	4	6.2	1.42	742	21	0.64	0.09	45 836	55.95
Stomach	11 934	5	5.7	1.45	10 006	2	8.6	1.19	16 369	19.98
Colon	11 286	6	5.4	1.35	7 971	3	6.8	0.89	27 043	33.01
Bladder	11 235	7	5.3	1.46	4 222	10	3.6	0.46	31 746	38.75
Rectum	8 403	8	4.0	1.06	2 025	14	1.7	0.24	21 682	26.47
Pancreas	6 473	9	3.1	0.79	6 416	4	5.5	0.79	4 033	4.93
Leukaemia	6 029	10	2.9	0.62	4 681	8	4.0	0.50	16 566	20.22
Brain, nervous system	5 909	11	2.8	0.67	5 084	7	4.4	0.60	15 135	18.48
Non-Hodgkin lymphoma	5 733	12	2.7	0.68	2 886	11	2.5	0.34	15 839	19.34
Corpus uteri	5 463	13	2.6	1.35	1 051	20	0.90	0.24	17 269	41.57
Kidney	4 728	14	2.2	0.61	2 484	12	2.1	0.31	11 640	14.21
Liver	4 362	15	2.1	0.52	4 307	9	3.7	0.52	3 127	3.82
Larynx	3 820	16	1.8	0.50	1 847	15	1.6	0.23	10 608	12.95
Ovary	3 729	17	1.8	0.84	2 191	13	1.9	0.51	9 901	23.83
Cervix uteri	2 356	18	1.1	0.51	1 280	17	1.1	0.28	6 683	16.09
Multiple myeloma	2 331	19	1.1	0.31	1 509	16	1.3	0.20	5 432	6.63
Lip, oral cavity	1 948	20	0.93	0.24	452	25	0.39	0.05	5 356	6.54
Gallbladder	1 763	21	0.84	0.22	1 153	19	0.99	0.13	1 924	2.35
Melanoma of skin	1 622	22	0.77	0.18	669	22	0.57	0.07	4 809	5.87
Hodgkin lymphoma	1 565	23	0.74	0.16	239	26	0.20	0.03	5 610	6.85
Testis	1 560	24	0.74	0.27	204	27	0.17	0.04	5 644	13.98
Oesophagus	1 470	25	0.70	0.18	1 255	18	1.1	0.15	1 419	1.73
Nasopharynx	922	26	0.44	0.10	513	24	0.44	0.06	2 861	3.49
Mesothelioma	825	27	0.39	0.11	597	23	0.51	0.08	884	1.08
Salivary glands	511	28	0.24	0.06	99	30	0.08	0.01	1 239	1.51
Kaposi sarcoma	473	29	0.22	0.05	44	32	0.04	0.00	1 213	1.48
Anus	342	30	0.16	0.04	37	33	0.03	0.00	889	1.09
Vulva	262	31	0.12	0.06	100	29	0.09	0.02	757	1.82
Hypopharynx	247	32	0.12	0.03	112	28	0.10	0.01	425	0.52
Oropharynx	203	33	0.10	0.03	77	31	0.07	0.01	606	0.74
Vagina	98	34	0.05	0.02	20	34	0.02	0.00	268	0.65
Penis	19	35	0.01	0.00	4	35	0.00	0.00	63	0.16
All cancer sites	210 537	-	-	22.77	116 710	-	-	13.08	470 851	574.79

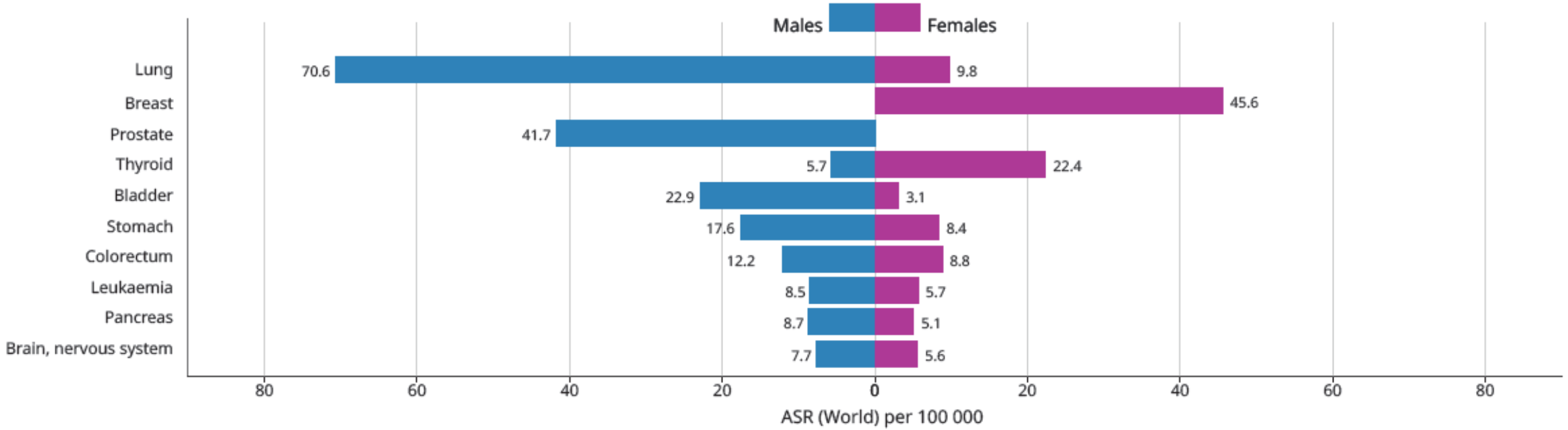
International Agency for Research on Cancer

World Health Organization

Turkey

Source: Globocan 2018

Age-standardized (World) incidence rates per sex, top 10 cancers



Akut Lösemi –DSÖ Sınıflaması

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
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

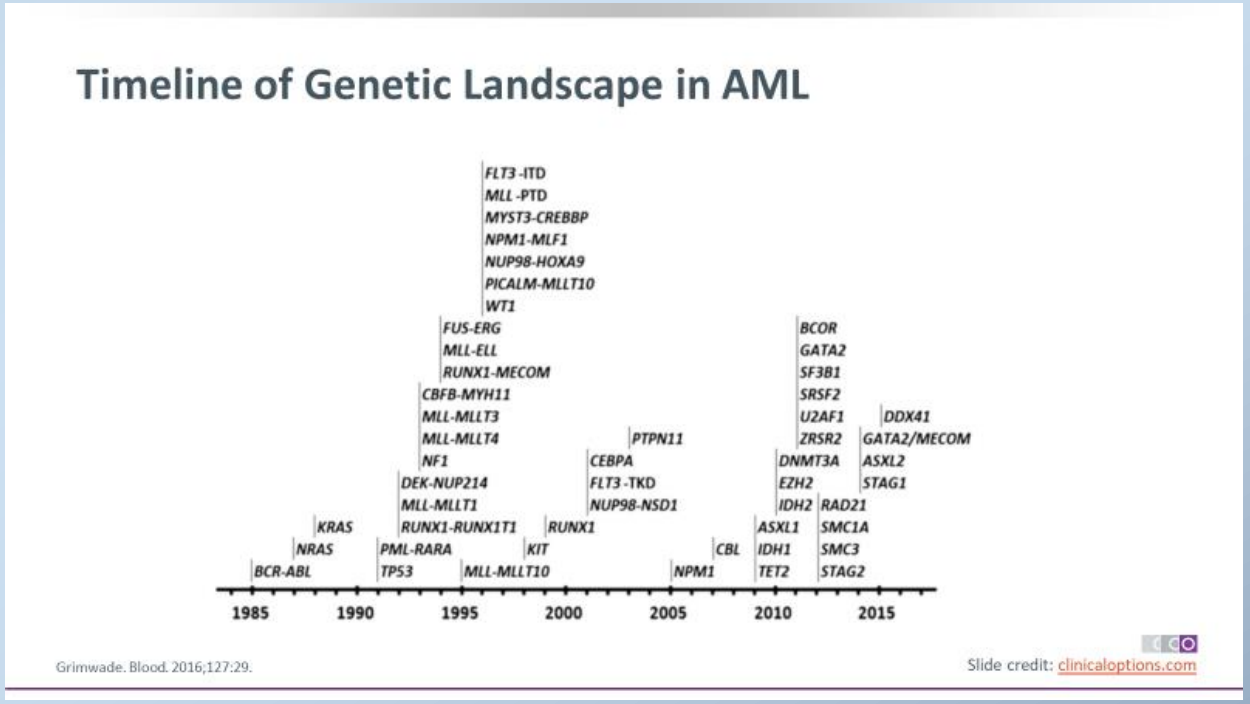
Blastic plasmacytoid dendritic cell neoplasm
Acute leukemias of ambiguous lineage
Acute undifferentiated leukemia
Mixed phenotype acute leukemia (MPAL) with t(9;22)(q34.1;q11.2); *BCR-ABL1*
MPAL with t(v;11q23.3); *KMT2A* rearranged
MPAL, B/myeloid, NOS
MPAL, T/myeloid, NOS
B-lymphoblastic leukemia/lymphoma
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

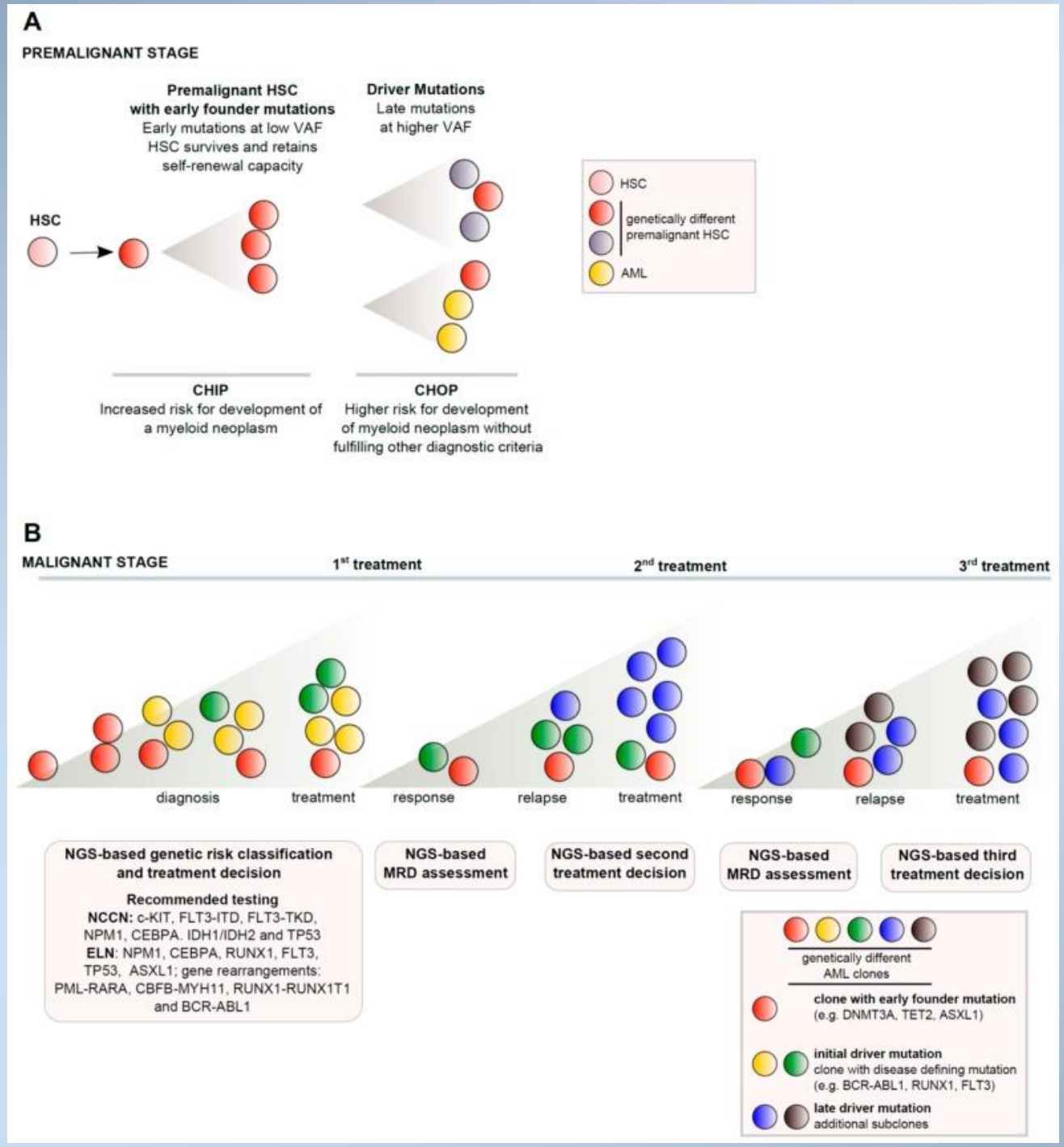
Lösemi Tanısı İçin…

- Hikaye-Fizik muayene
- Kan sayımı-Periferik yayma
- Kemik iliği aspirasyon-biyopsi
- İmmun Tiplendirme (Akan hücre ölçer ve/veya immunhistokimya)
- Genetik
  - Konvansiyonel genetik inceleme
  - PCR
  - iFİSH
  - NGS

NGS (Gelecek Nesil Sekanslama)

- Önceki yöntemlerin yerine alan geniş panel genom çalışmasına izin veren moleküler yöntem.
  - Tümörün genomik heterojenitesi
  - Spesifik moleküler biyobelirleyiciler
  - Tedaviye karar verme
  - Yeni ilaçların keşfine olanak sağlama
  - MRD izlemi




A
PREMALIGNANT STAGE
Premalignant HSC
with early founder mutations
Early mutations at low VAF
HSC survives and retains
self-renewal capacity
Driver Mutations
Late mutations
at higher VAF
HSC
genetically different
premalignant HSC
AML
CHIP
Increased risk for development of
a myeloid neoplasm
CHOP
Higher risk for development
of myeloid neoplasm without
fulfilling other diagnostic criteria
B
MALIGNANT STAGE
1st treatment
2nd treatment
3rd treatment
diagnosis
treatment
response
relapse
treatment
response
relapse
treatment
NGS-based genetic risk classification
and treatment decision
Recommended testing
NCCN: c-KIT, FLT3-ITD, FLT3-TKD,
NPM1, CEBPA. IDH1/IDH2 and TP53
ELN: NPM1, CEBPA, RUNX1, FLT3,
TP53, ASXL1; gene rearrangements:
PML-RARA, CBFB-MYH11, RUNX1-RUNX1T1
and BCR-ABL1
NGS-based
MRD assessment
NGS-based second
treatment decision
NGS-based
MRD assessment
NGS-based third
treatment decision
genetically different
AML clones
clone with early founder mutation
(e.g. DNMT3A, TET2, ASXL1)
initial driver mutation
clone with disease defining mutation
(e.g. BCR-ABL1, RUNX1, FLT3)
late driver mutation
additional subclones

Yetişkin ALL de Risk Faktörleri

- > 30 yaş
- Lökosit sayısı: B-ALL de > 30x10^9/L; T-ALL de > 100 x10^9/L
- Ph+, *BCR-ABL* translokasyonu
- Ph-benzeri ALL
- Diğer kromozomal anormallikler
  - t(4;11), 11q23+, *MLL* rearanjmanı
  - Hipodiploidi (≤ 44 kromozom)
- SSS tutulumu
- İndüksiyon sonrası MRH pozitifliği (> 10^{-4} ya da % 0,01)

AML de Risk Faktörleri

- Biyolojik
  - Kötü Sitogenetik
    - Monosomiler
    - Kompleks (≥ 3) anormallikler
    - inv(3); t(3;3); t(6;9); t(6;11); t(9;22); 17p
  - Diğer sitogenetik özellikler (örn: 11q23)
  - Gen ifadesinde değişiklikler
  - Tekrarlayan tek gen mutasyonları
- Klinik Değişkenler
  - Öncesinde hematolojik bozukluklar
  - Tanıda ileri yaş
  - Sitotoksik ilaçlara maruziyet ve/veya radyoterapi
  - Cinsiyet
  - Eşlik eden medikal hastalıklar

Schiller. Hematology Am Soc Hematol Educ Program. 2013;2013:201. Rücker. Leukemia. 2013;27:353.
Deschler. Cancer. 2006;107:2099.

Sitogenetik ve Moleküler Anormalliklere Göre AML de Risk Sınıflaması (ELN Önerisi)

Risk Status	Sitogenetikler	Moleküler Anormallikler
İyi	t(8;21)(q22;q22.1); RUNX1-RUNX1T1 inv(16)(p13.1q22) ya da t(16;16)(p13.1;q22); CBFB-MYH11	NPM1 mutasyonu (FLT3-ITD mut yok veya FLT3-ITD^{düşük} yada Biallelik CEBPA mutasyonu
Orta	t(9;11)(p21.3;q23.3); MLLT3-KMT2A İyi veya kötü riske dahil edilemeyen sitogenetik anormallikler	NPM1 mutasyonu ve FLT3-ITD^{yüksek} Wild-tip NPM1 fakat FLT3-ITD mut yok yada FLT3-ITD^{düşük} (Kötü genetik özellik yok)
Kötü	t(6;9)(p23;q34.1); DEK-NUP214 t(v;11q23.3); KMT2A yeniden düzenlenme t(9;22)(q34.1;q11.2); BCR-ABL1 inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); GATA2,MECOM(EVI1) -5 or del(5q); -7; -17/abn(17p) Kompleks karyotip, monozomal karyotip	Wild-tip NPM1 ve FLT3-ITD^{yüksek} RUNX1 mutasyonu ASXL1 mutasyonu TP53 mutasyonu

Düşük: Düşük allelik oran (< 0.5); Yüksek: Yüksek allelik oran (≥ 0.5).

Döhner. Blood. 2017;129:424.

Akut lösemilerde Moleküler Belirteçlerin Kliniğe Yansıması

- Prognoz
- Törapötik seçim: Hedefi belirleme
- MRH takibi için belirleyici
- Preempitif tedaviye karar verme-Allo-HKHN gibi
- Kemodirenç ve nüks mekanizmaları ile ilgili bilgi sahibi olma
- Nüksde tedaviye karar verme

Grimwade. Blood. 2016;127:29.

Slide credit: clinicaloptions.com

Tanıda Zorluklar

- Çoğu merkezde günümüzde hematolog var-
- Ancak tanı için yeterli donanım-ekipman, tecrübeli personel?
- Genetik sonuca ulaşma süresi?

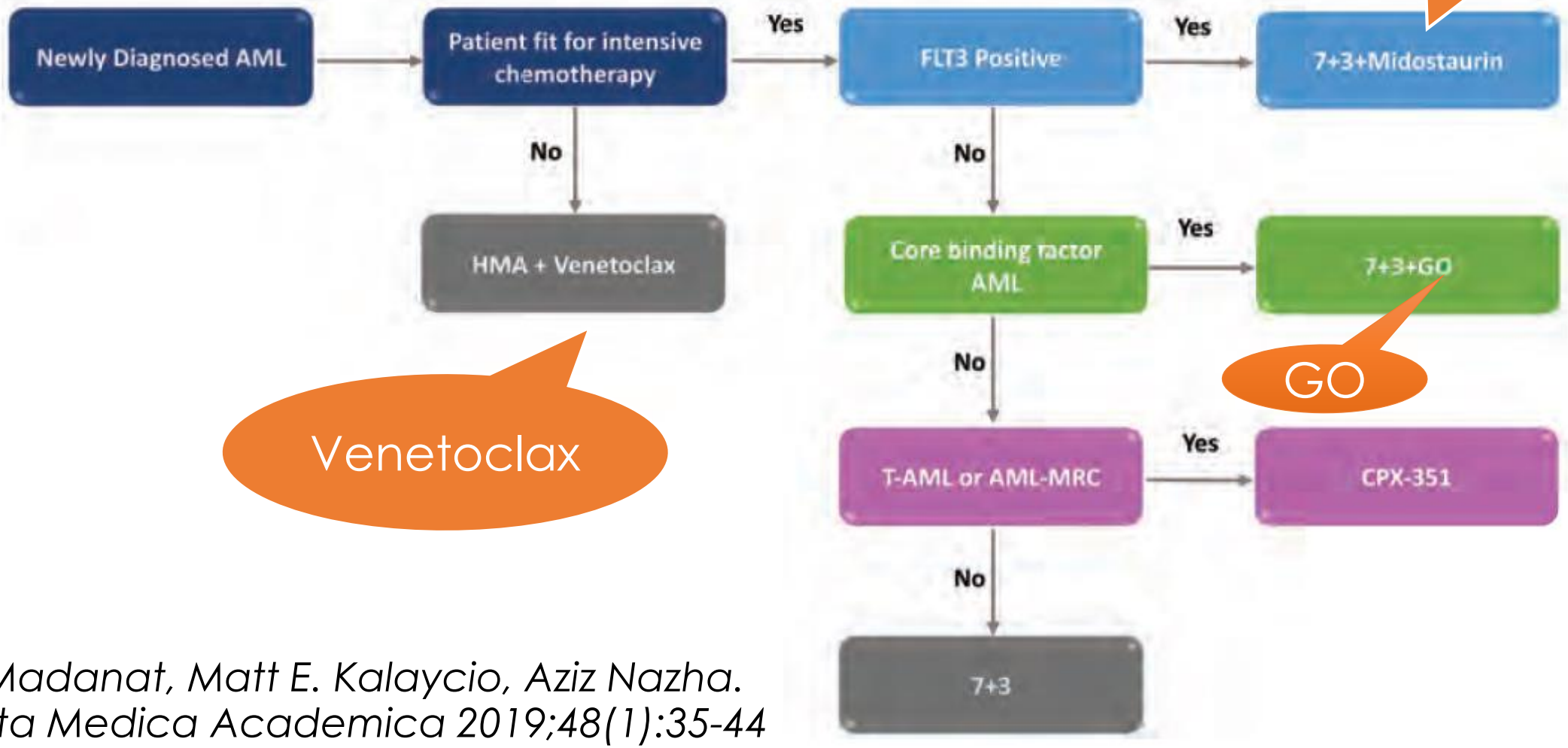
Tanı tamam…

- Tedavi
- HLA tiplendirme

Tedavi de zorluklar

- Etkin ancak kabul edilebilir toksisite
- İlaca erişim
- Geri ödeme sorunları
- Destek tedavileri

AML de Tedavi Algoritması



Midostaurin

Venetoclax

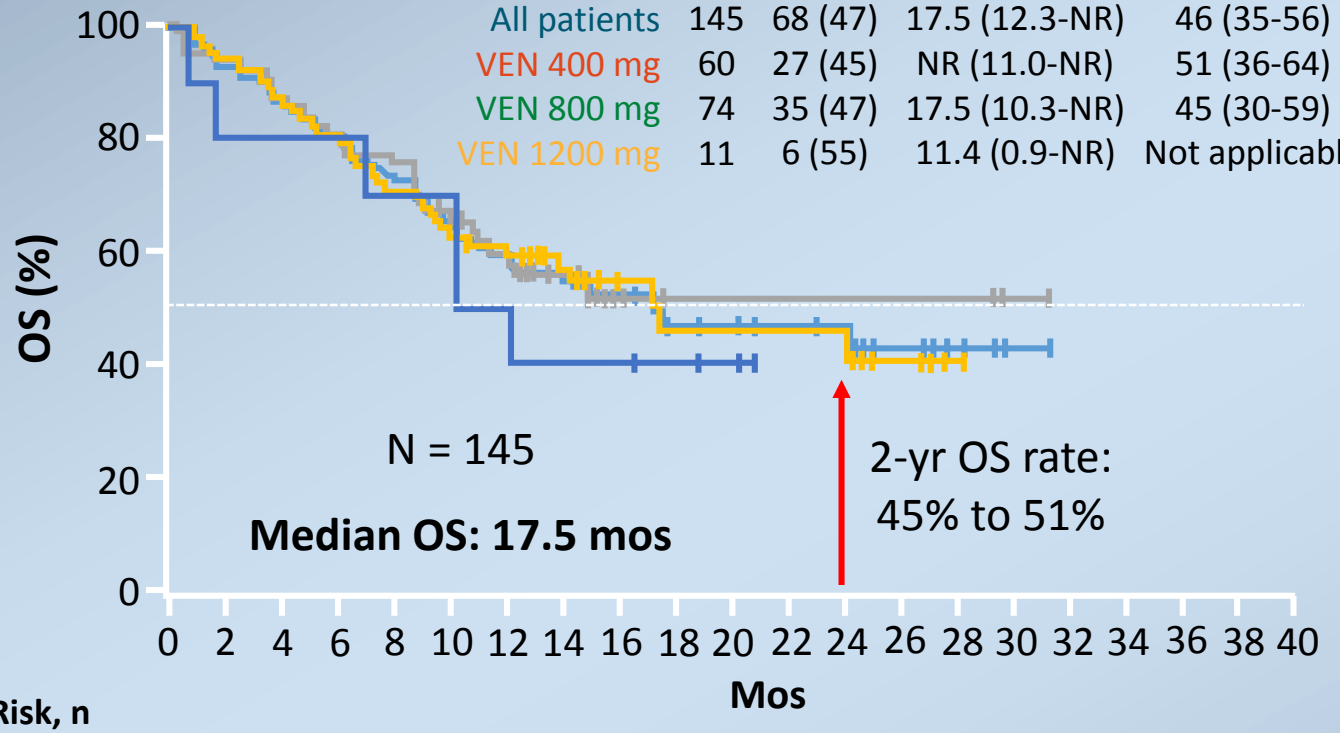
GO

F. Madanat, Matt E. Kalaycio, Aziz Nazha. Acta Medica Academica 2019;48(1):35-44

Venetoclax + Hypomethylating Agents for Unfit AML

OS[1]

	n	Events, n (%)	Median OS, Mos (Range)	2-Yr OS Rate, % (Range)
All patients	145	68 (47)	17.5 (12.3-NR)	46 (35-56)
VEN 400 mg	60	27 (45)	NR (11.0-NR)	51 (36-64)
VEN 800 mg	74	35 (47)	17.5 (10.3-NR)	45 (30-59)
VEN 1200 mg	11	6 (55)	11.4 (0.9-NR)	Not applicable



Patients at Risk, n

All patients	145	133	124	115	102	89	73	53	25	16	15	13	12	7	4	2
VEN 400 mg	60	56	52	48	45	38	30	20	8	3	3	3	3	3	3	2
VEN 800 mg	74	69	64	59	50	44	38	29	13	10	10	10	9	4	1	
VEN 1200 mg	11	8	8	8	7	7	5	4	4	3	2					

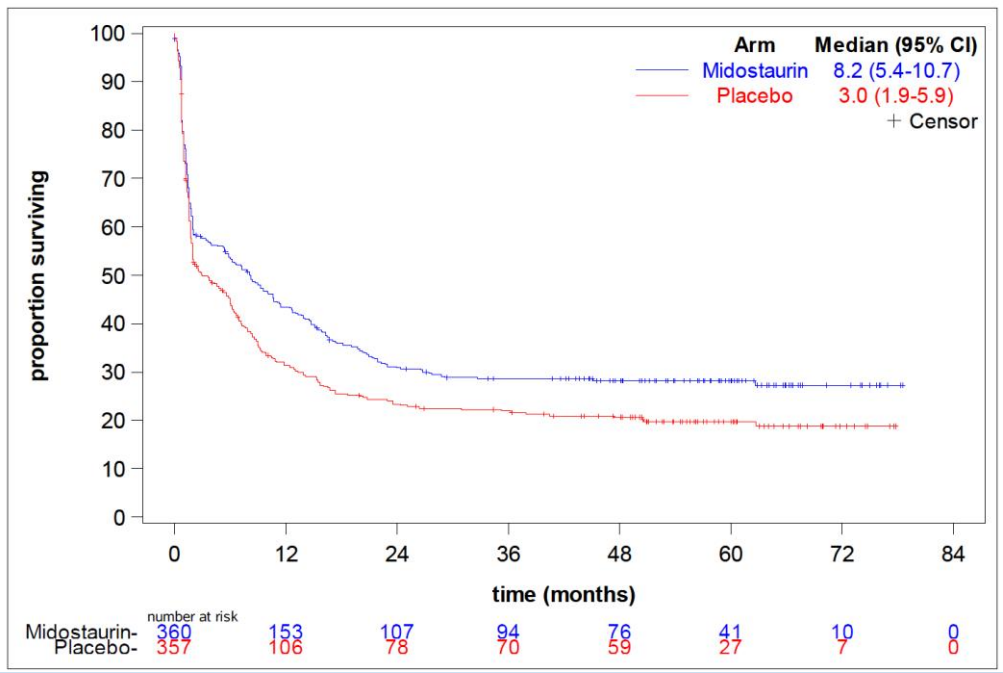
Regimen	CR/CRi, %	mOS, Mos	OS Rate, %
Azacitidine [2]	27.8	10.4	At 1 yr: 46.5
Decitabine [3]	17.8	7.7	NR
Venetoclax + HMA [1]	67	17.5	At 1 yr: 59 At 2 yrs: 46

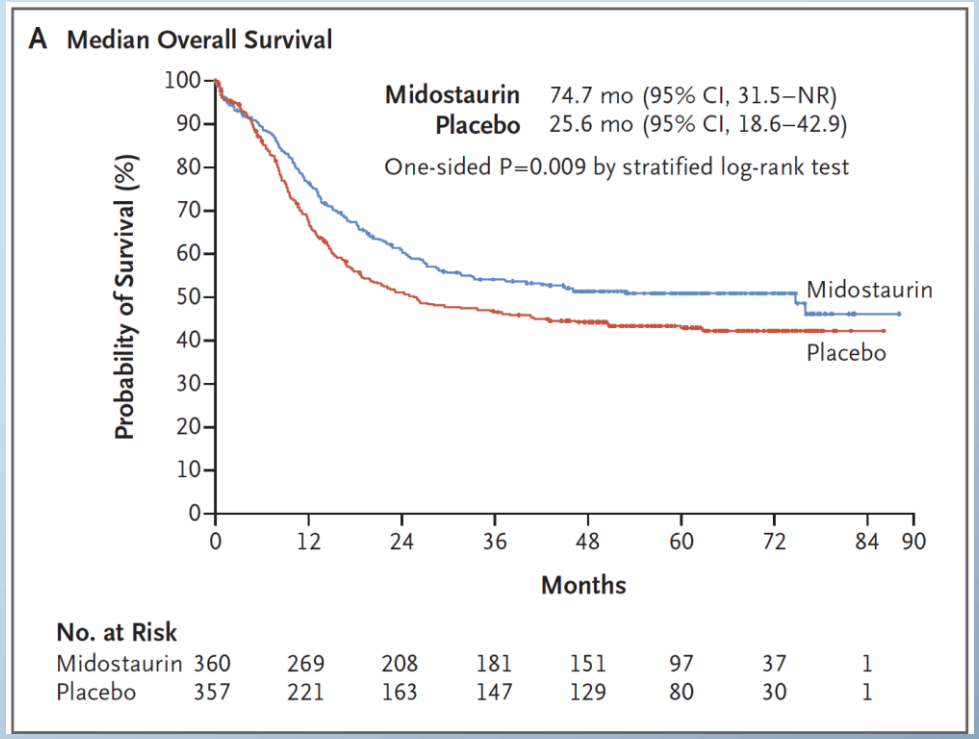
1. DiNardo. Blood. 2019;133:7. 2. Dombret. Blood. 2015;126:291. 3. Kantarjian. JCO. 2012;30:2670.

Slide credit: clinicaloptions.com

Midostaurin plus Chemotherapy for Acute Myeloid Leukemia with a *FLT3* Mutation

R.M. Stone, S.J. Mandrekar, B.L. Sanford, K. Laumann, S. Geyer, C.D. Bloomfield, C. Thiede, T.W. Prior, K. Döhner, G. Marcucci, F. Lo-Coco, R.B. Klisovic, A. Wei, J. Sierra, M.A. Sanz, J.M. Brandwein, T. de Witte, D. Niederwieser, F.R. Appelbaum, B.C. Medeiros, M.S. Tallman, J. Krauter, R.F. Schlenk, A. Ganser, H. Serve, G. Ehninger, S. Amadori, R.A. Larson, and H. Döhner





N Engl J Med 2017;377:454-64.

Yeni Tanı ALL de tedavi

- Fit hastalarda özellikle Pediatrik rejimlere benzer tedaviler
- Rituximab CD20+ B-ALL
- TKİ eklenmesi Ph+ ALL
- İlk sıra tedaviye yeni ilaçların eklenmesi ile ilgili çalışmalar devam etmekte (blinatumomab/inotuzumab ozogamicin)
- MRH ALL tedavisine yön vermede önemli
- Blinatumomab ile MRH tedavisine yönlenme önemli- % 80 oranında MRH yı düzeltmekte

Yüksek Riskli ALL/AML ve/veya Standart Riskli AML de…

- Allo-HKHN ile konsolidasyon
- Ülkemizde verici bulmada sorunlar günümüzde azaldı
  - TÜRKÖK -600 bin verici, 1400 nakil
  - Haplo nakiller
- Yaş sınırı yok.
- Fit olup-olmama var.

Nüks/Dirençli Lösemide Tedavi

- Kurtarma kemoterapileri: FLAG, EMA, CLAG gibi
- Yeni ilaçlar

Nüks/Dirençli ALL de Tedavi

ALL nüksten sonra Sağkalım: MRC UKALLXII/E2993

	Hasta	Olay
Akraba Tx	42	32
AD Tx	65	52
Oto	13	11

- ALL:
  - T-ALL de Nelarabin
  - B-ALL de blinatumomab, İnotuzumab
  - Ph+ ALL de Ponatinib
  - CAR-T hücre

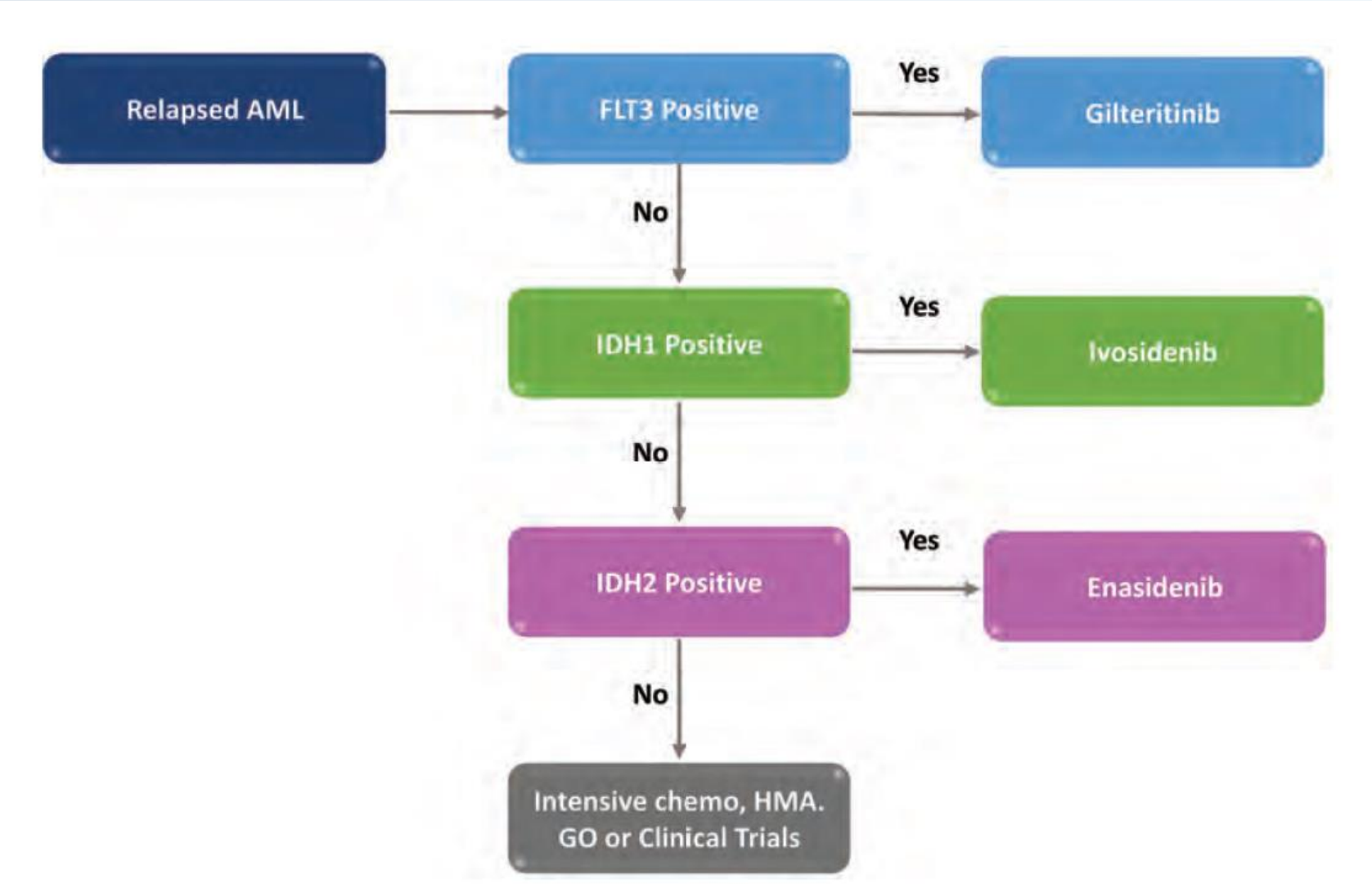
How to pick a winner? ASH 2018

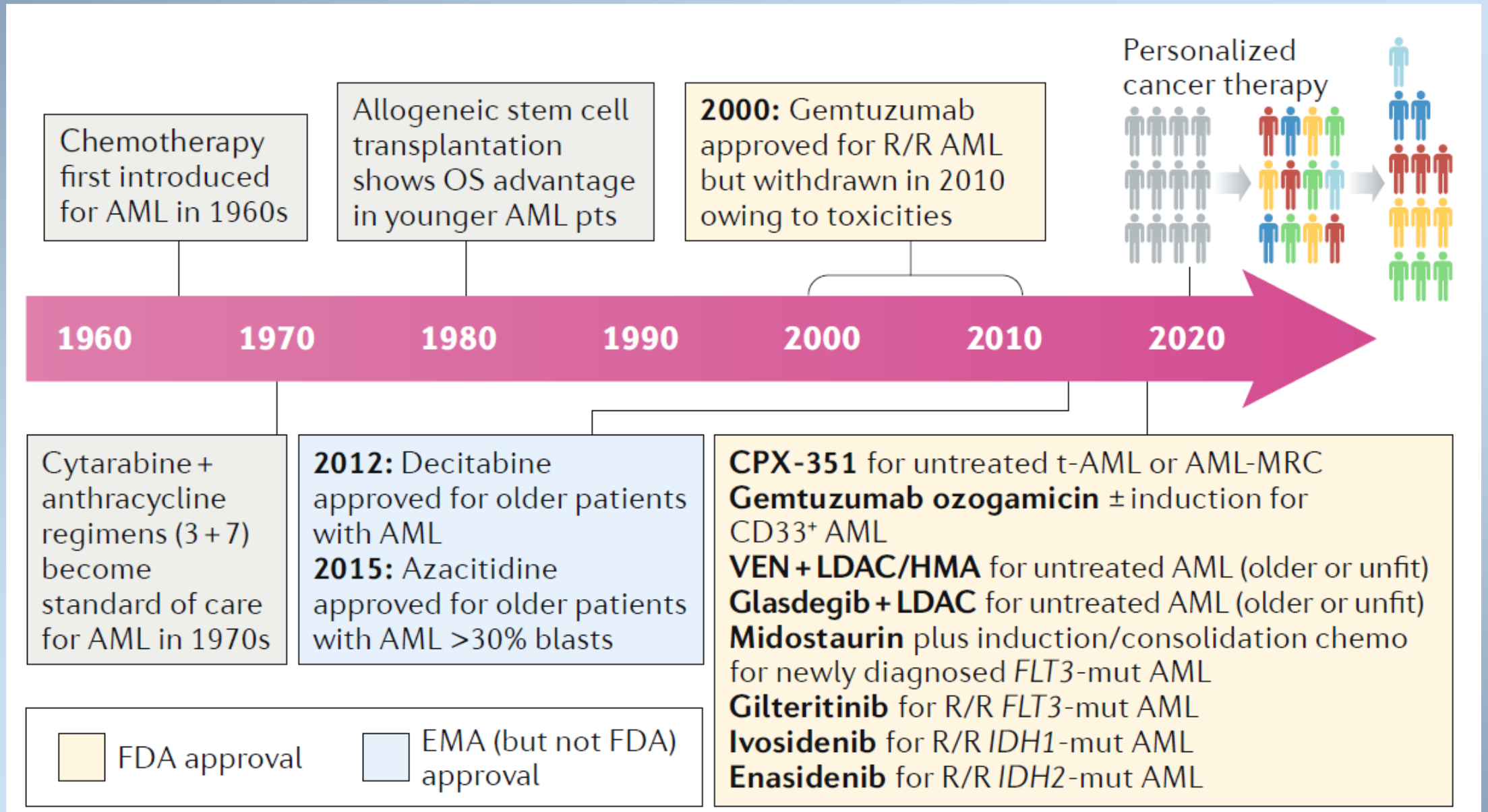
- İki ilacın doğrudan karşılaştırması yok
- Faz 3 çalışmalarda hasta popülasyonlarının önceki tedavileri farklı
- Düşük tümör yükü (<% 50 blast) ve hastaya tx planlanıyorsa: **Blinatumomab**
- Yüksek tümör yükü (blast >%50) veya SSS tutulumu olanlarda: **İnotuzumab**

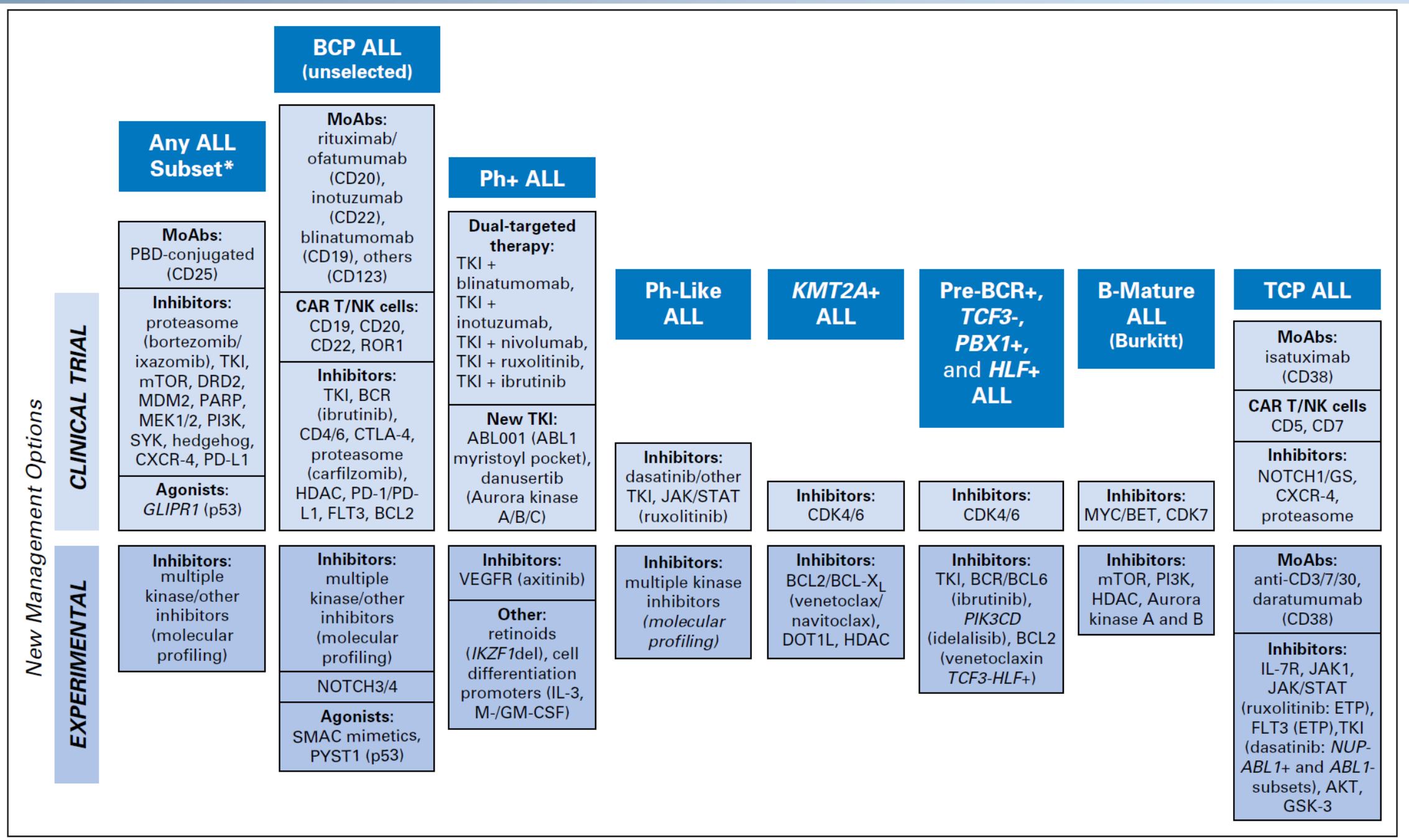
B-Hücre ALL Tisagenlecleucel Başvurusu

- **First CAR T-hücre immünoterapisine Ağustos 2017 de FDA onay alındı:**
  - Dirençli veya ≥2 nüks B hücreli prekürsör ALL de 25 yaşına kadar olan hastalarda

Nüks/Dirençli AML de Tedavi




Chemotherapy first introduced for AML in 1960s
Allogeneic stem cell transplantation shows OS advantage in younger AML pts
2000: Gemtuzumab approved for R/R AML but withdrawn in 2010 owing to toxicities
Personalized cancer therapy
1960
1970
1980
1990
2000
2010
2020
Cytarabine + anthracycline regimens (3 + 7) become standard of care for AML in 1970s
2012: Decitabine approved for older patients with AML
2015: Azacitidine approved for older patients with AML >30% blasts
CPX-351 for untreated t-AML or AML-MRC
Gemtuzumab ozogamicin ± induction for CD33⁺ AML
VEN + LDAC/HMA for untreated AML (older or unfit)
Glasdegib + LDAC for untreated AML (older or unfit)
Midostaurin plus induction/consolidation chemo for newly diagnosed *FLT3*-mut AML
Gilteritinib for R/R *FLT3*-mut AML
Ivosidenib for R/R *IDH1*-mut AML
Enasidenib for R/R *IDH2*-mut AML
FDA approval
EMA (but not FDA) approval


New Management Options
CLINICAL TRIAL
EXPERIMENTAL
Any ALL Subset*
MoAbs: PBD-conjugated (CD25)
Inhibitors: proteasome (bortezomib/ixazomib), TKI, mTOR, DRD2, MDM2, PARP, MEK1/2, PI3K, SYK, hedgehog, CXCR-4, PD-L1
Agonists: GLIPR1 (p53)
Inhibitors: multiple kinase/other inhibitors (molecular profiling)
BCP ALL (unselected)
MoAbs: rituximab/ofatumumab (CD20), inotuzumab (CD22), blinatumomab (CD19), others (CD123)
CAR T/NK cells: CD19, CD20, CD22, ROR1
Inhibitors: TKI, BCR (ibrutinib), CD4/6, CTLA-4, proteasome (carfilzomib), HDAC, PD-1/PD-L1, FLT3, BCL2
Inhibitors: multiple kinase/other inhibitors (molecular profiling)
NOTCH3/4
Agonists: SMAC mimetics, PYST1 (p53)
Ph+ ALL
Dual-targeted therapy: TKI + blinatumomab, TKI + inotuzumab, TKI + nivolumab, TKI + ruxolitinib, TKI + ibrutinib
New TKI: ABL001 (ABL1 myristoyl pocket), danusertib (Aurora kinase A/B/C)
Inhibitors: VEGFR (axitinib)
Other: retinoids (IKZF1del), cell differentiation promoters (IL-3, M-/GM-CSF)
Ph-Like ALL
Inhibitors: dasatinib/other TKI, JAK/STAT (ruxolitinib)
Inhibitors: multiple kinase inhibitors (molecular profiling)
KMT2A+ ALL
Inhibitors: CDK4/6
Inhibitors: BCL2/BCL-XL (venetoclax/navitoclax), DOT1L, HDAC
Pre-BCR+, TCF3-, PBX1+, and HLF+ ALL
Inhibitors: CDK4/6
Inhibitors: TKI, BCR/BCL6 (ibrutinib), PIK3CD (idelalisib), BCL2 (venetoclaxin TCF3-HLF+)
B-Mature ALL (Burkitt)
Inhibitors: MYC/BET, CDK7
Inhibitors: mTOR, PI3K, HDAC, Aurora kinase A and B
TCP ALL
MoAbs: isatuximab (CD38)
CAR T/NK cells CD5, CD7
Inhibitors: NOTCH1/GS, CXCR-4, proteasome
MoAbs: anti-CD3/7/30, daratumumab (CD38)
Inhibitors: IL-7R, JAK1, JAK/STAT (ruxolitinib: ETP), FLT3 (ETP),TKI (dasatinib: NUP-ABL1+ and ABL1-subsets), AKT, GSK-3

Hasta ve hastalık takibinde zorluklar

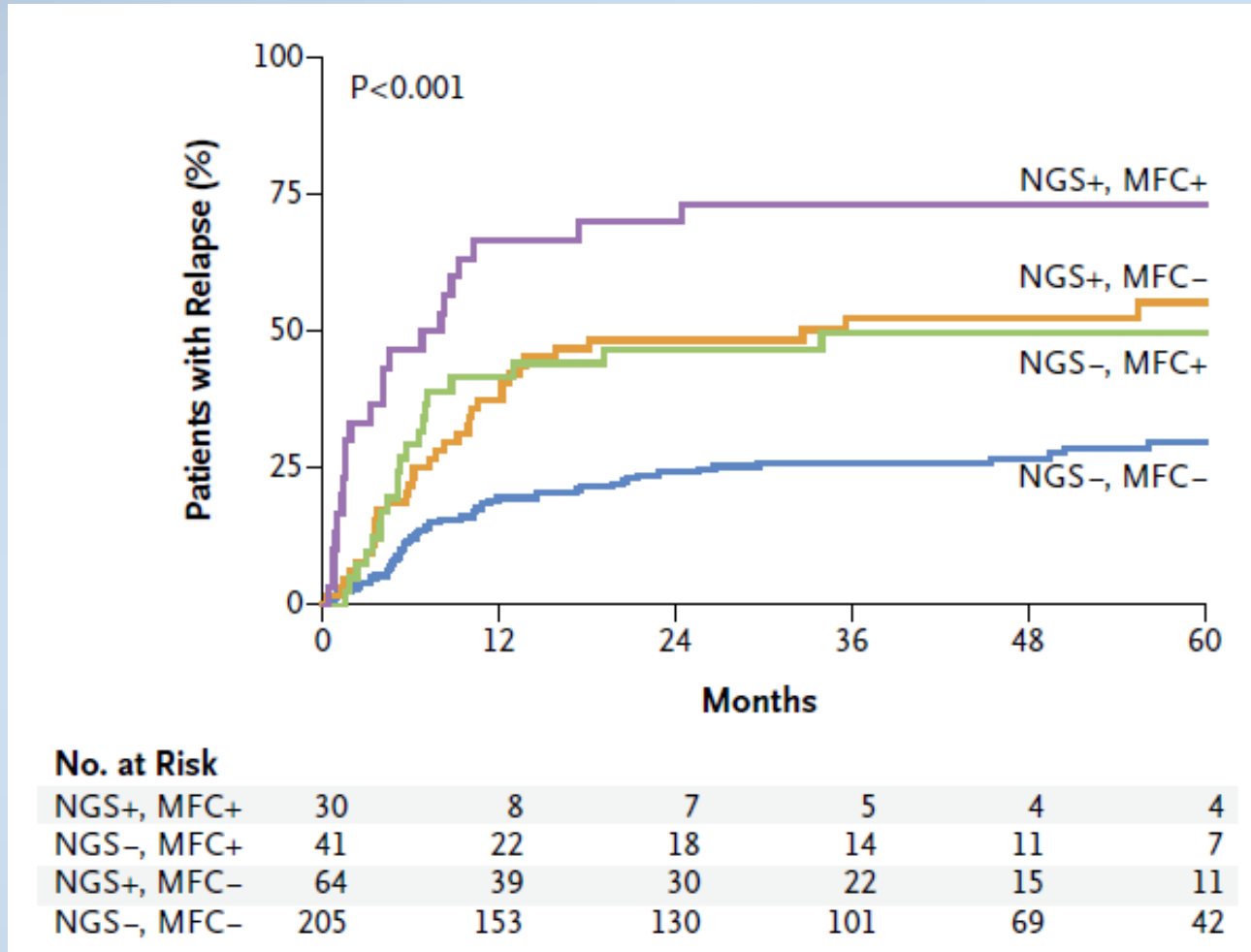
- Ölçülebilir kalıntı hastalık takibi

Parametre	Akan Hücre Ölçer	ASO-PCR	NGS
Sensivite	10^{-4} (to 10^{-5})	10^{-4} to 10^{-5}	10^{-6}
Örnekler	Taze	Taze veya donmuş	Taze veya donmuş
Kullanılabilirlilik	Geniş oranda	Geniş oranda değil	Merkezi referans lab
Özelleştirme	Gerekmiyor	Hastaya özgü prob ve primerler	Gerekmiyor
Maliyet	Kısmen pahalı	Pahalı	Pahalı

FDA 28 Eylül 2018 de ClonoSEQ analizi ilk NGS yöntemini ALL ve MM da onayladı

AML Nüksü- NGS ve Akan Hücre Ölçer

- Uyum: % 69.1



No. at Risk						
NGS+, MFC+	30	8	7	5	4	4
NGS–, MFC+	41	22	18	14	11	7
NGS+, MFC–	64	39	30	22	15	11
NGS–, MFC–	205	153	130	101	69	42

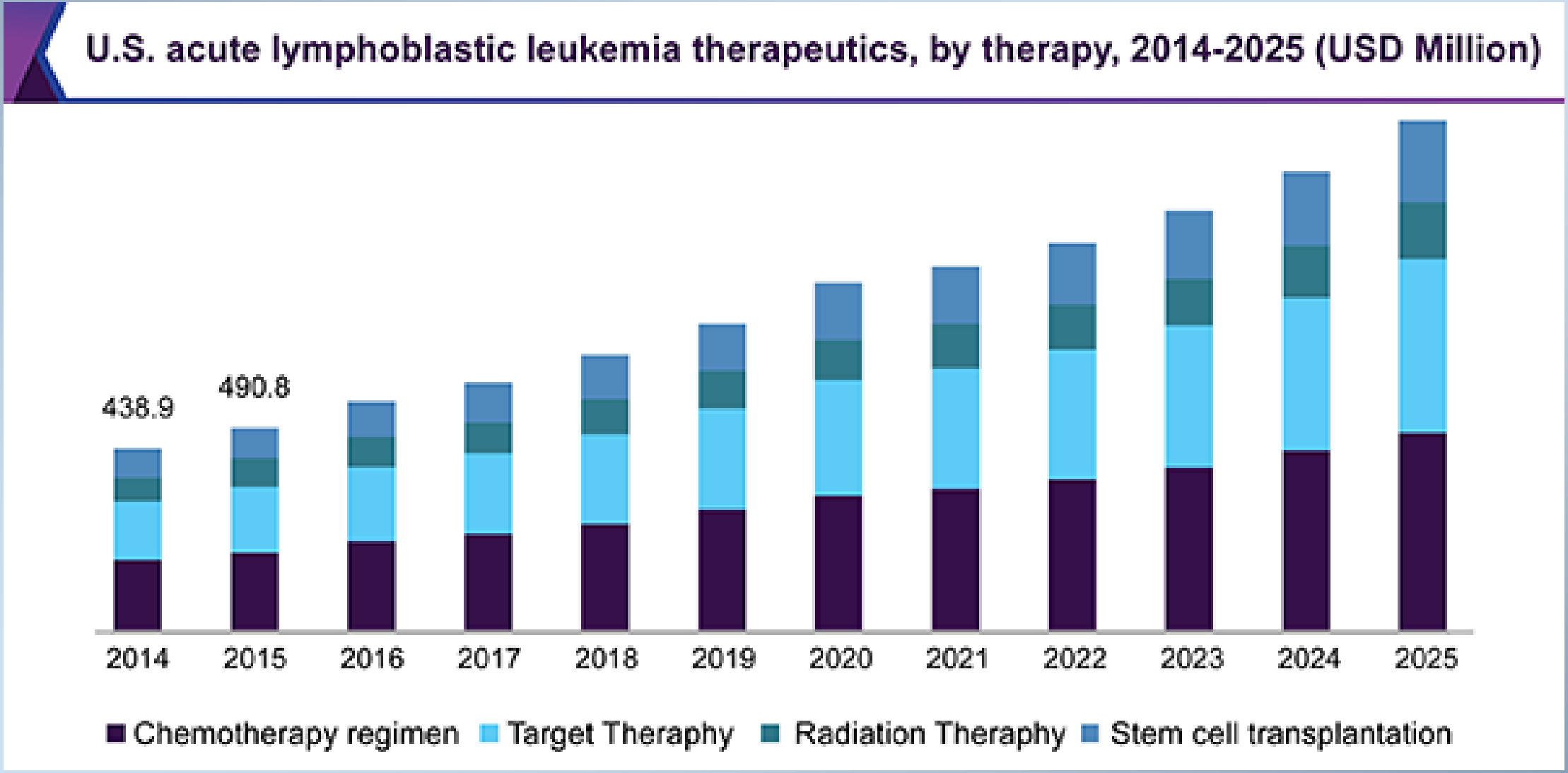
Jongen-Lavrencic. NEJM. 2018;378:1189.

Ekonomik Yükü

- Lösemiler kanserlerin yaklaşık % 3,5
- ABD 2008-2015 geri dönük çalışmada: AML tanılı 26344 hastada
- Toplam maliyet 352.138 $/hasta/yıl
- 45-59 yaş arası 377.423 $; 60 yaş 320.465 $

Hagiwara M, Sharma A, Chung KC, Delea TE. Burden of acute myeloid leukemia (AML) in a U.S. commercially insured population. *J Clin Oncol*. 2017;35:15(suppl):e18330-e18330.

Ekonomik Yükü

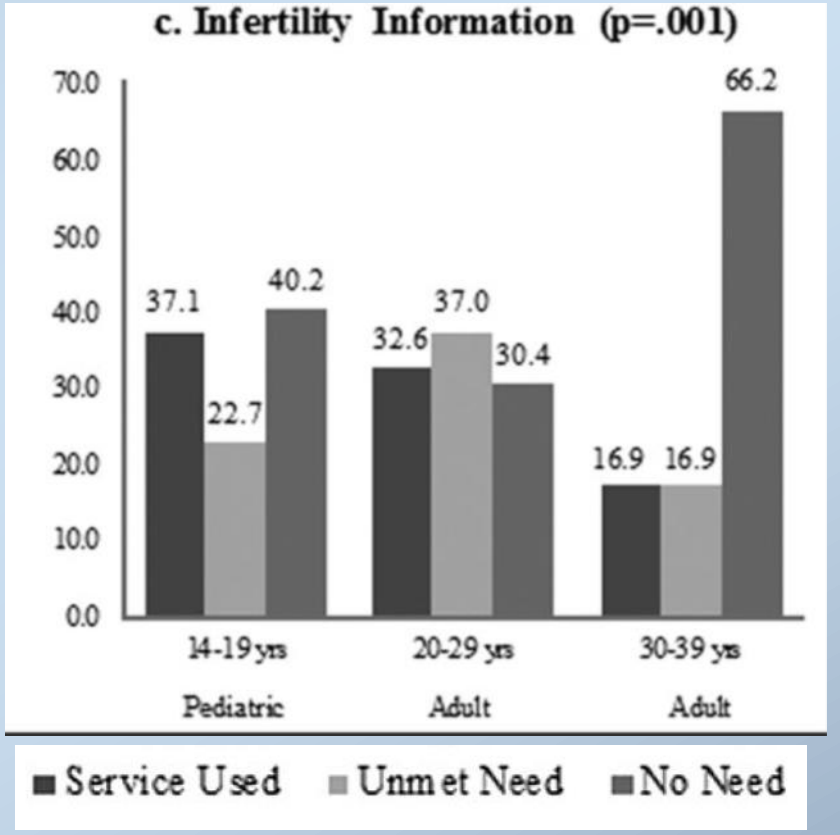


Hasta için Karşılanmayan İhtiyaçlar

- Yaşam kalitesi
- Psikososyal destek
  - % 68 anksiyete ve depresyon
- Maddi kayıp
- Fertilite
- İkincil primer maligniteler

Unmet Need	No.	%
Sexual issues	292	41
Handling medical living expenses	379	38
Emotional difficulties	399	37
Employment problems	268	32
Health insurance problems	404	30
Child care needs	116	29
Family problems	320	28
Difficulties with social and leisure activities	366	25
Cancer-related physical needs	375	18
Medical information	468	18
Social support from friends	438	18
Spiritual needs	358	14
Medical staff support	468	8
Transportation needs	393	8

Parry C, et al. Identification and Correlates of Unmet Service Needs in Adult Leukemia and Lymphoma Survivors After Treatment. JCO 2012



Brad J. Zebrack, et al. Psychosocial Service Use and Unmet Need Among Recently Diagnosed Adolescent and Young Adult Cancer Patients. Cancer 2013;119:201-14.

Fertility After Allogeneic Hematopoietic Stem Cell Transplantation: A 23-Year Review From A Tertiary Hospital

Pinar ATACA ATILLA[1], Erden ATILLA[1], Elif EDIBOGLU[2], Sinem C. BOZDAG[1], Selami K. TOPRAK[1], Onder ARSLAN[1], Muhit OZCAN[1],Gunhan GURMAN[1], Pervin TOPCUOGLU[1]

Table 2. Clinical characteristics and pregnancy complications of survivors reporting pregnancies after allo-HSCT

Variables		Female (n= 6)	Male (n= 20)
Pregnancy outcomes, n (%)			
Live births	6 (100%)	18 (90%)	
Miscarriage	1 (17%)	8 (30%)	
Stillbirth	1 (17%)	1 (5%)	
Pregnancy complications, n (%)			
Preeclampsia	1 (17%)	-	
Gestational diabetes	1 (17%)	1 (5%)	
Gestational hypertension	-	1 (5%)	
Mean time to pregnancy, months (range)	63 (8-108)	68 (4-144)	
Median Age at first post-HCT pregnancy, years (range)	30 (22-38)	32 (22-48)	
Diagnosis, n (%)			
Acute leukemia	1 (17%)	9 (45%)	
Chronic myeloproliferative disease	1 (17%)	10 (50%)	
Bone marrow failure	4 (66%)	1 (5%)	
Conditioning Regimen, n (%)			
Cyclophosphomide	6 (100%)	20 (100%)	
ATG (antithymocyte globulin)	4 (66%)	1 (5%)	
Fludarabine	1 (17%)	1 (5%)	
Busulphan	2 (34%)	17 (85%)	
TBI (total body irradiation)	-	1 (5%)	

UHOD *Number: 3 Volume: 26 Year: 2016*

Sekonder malignite gelişimi

- Topluma göre AML hastalarında % 17; ALL hastalarında % 43 daha fazla kanser gelişimi
- N=5091 6 ayda % 3 (Medyan: 37,5 y)
- Tedavi tamamlandıktan sonra 6 ayda % 0,5; 14 ayda % 25 ; 37,5 ayda % 50 ve 87,5 ayda % 75

Ghimire KB, Shah BK. Second primary malignancies in adult acute myeloid leukemia—a US population-based study. Anticancer Res. 2014;34(7):3855-3859; Second primary malignancies in adult acute lymphoblastic leukemia: a US population-based study. Blood. 2014 Sep 18;124(12):2000-1.

Klinik Çalışmalar İlaçlara Erken Erişimi Sağlamakta…

Çalışmalar	**Mevcut Durum**
A Study Of Two Inotuzumab Ozogamicin Doses in Relapsed/ Refractory Acute Lymphoblastic Leukemia Transplant Eligible Patients	Recruiting
Phase 3 Trial of Blinatumomab vs Standard Chemotherapy in Pediatric Subjects With HR First Relapse B-precursor ALL	Recruiting
Blinatumomab Versus Standard of Care Chemotherapy in Patients With Relapsed or Refractory Acute Lymphoblastic Leukemia (ALL)	Terminated
A Study of Cusatuzumab Plus Azacitidine in Participants With Newly Diagnosed Acute Myeloid Leukemia Who Are Not Candidates for Intensive Chemotherapy	Recruiting
A Global Study of the Efficacy and Safety of Midostaurin + Chemotherapy in Newly Diagnosed Patients With FLT3 Mutation Negative (FLT3-MN) Acute Myeloid Leukemia (AML)	Recruiting

Klinik Çalışmalar İlaçlara Erken Erişimi Sağlamakta…

Çalışmalar	**Mevcut Durum**
Pevonedistat Plus Azacitidine Versus Single-Agent Azacitidine as First-Line Treatment for Participants With Higher-Risk Myelodysplastic Syndromes (HR MDS), Chronic Myelomonocytic Leukemia (CMML), or Low-Blast Acute Myelogenous Leukemia (AML)	Recruiting
A Study of Venetoclax in Combination With Azacitidine Versus Azacitidine in Treatment Naïve Subjects With Acute Myeloid Leukemia Who Are Ineligible for Standard Induction Therapy	Active, not recruiting
An Efficacy and Safety Study of AG-221 (CC-90007) Versus Conventional Care Regimens in Older Subjects With Late Stage Acute Myeloid Leukemia Harboring an Isocitrate Dehydrogenase 2 Mutation	Recruiting
An Efficacy and Safety Study of Decitabine (DACOGEN) Plus Talacotuzumab (JNJ-56022473; Anti CD123) Versus Decitabine (DACOGEN) Alone in Participants With Acute Myeloid Leukemia (AML) Ineligible for Intensive Chemotherapy	Completed

Klinik Çalışmalar İlaçlara Erken Erişimi Sağlamakta…

Çalışmalar	**Mevcut Durum**
A Study of ASP2215 Versus Salvage Chemotherapy in Patients With Relapsed or Refractory Acute Myeloid Leukemia (AML) With FMS-like Tyrosine Kinase (FLT3) Mutation	Active, not recruiting
Efficacy of Oral Azacitidine Plus Best Supportive Care as Maintenance Therapy in Subjects With Acute Myeloid Leukemia in Complete Remission	Active, not recruiting
Efficacy and Safety of Panobinostat (LBH589) in Patients With Refractory de Novo or Secondary Acute Myelogenous Leukemia (AML)	Completed

- 23 yaşında Erkek
- Ağustos 2014: Pre-B ALL tanısı
- COG-ALL 0232 protokolü ile remisyon
- Ağustos 2017: nüks ve erken erişim programı ile blinatumumab ile indüksiyon sonrası -Remisyon
- 26/10/2017: tam uyumlu erkek kardeşinden Allojeneik hematopoetik kök hücre nakli
- 05/01/2018: kimerizm kaybı ile nüks: FLAG-IDA ile tam yanıtlı, MRD negatif
- 12/04/2018: $1x10^6$ CD3(+) ile DLI
- 10/05/2018: $5x10^6$ CD3(+) ile DLI
- 06/07/2018: $10x10^6$ CD3(+) ile DLI
- DLI sonrası GVHD gelişmedi, MRD negatif
- 16. ayda yaygın kemik ağrısı ile nüks
- 24/12/2018: FLAG sonrası MRD negatif tam yanıtlı
- 13/03/2019: nüks (%13 lenfoblast Kİ'de)
- 29/05/2019: Blinatumumab 1 kür verildi
- 21/06/2019: Kİ'de %12 lenfoblast
- 11/07/2019: inotuzumab klinik çalışmasına dahil edildi
- 2. kürü tamamlandı ve hasta MRD negatif remisyonda
- Tam uyumlu erkek kardeşinden 2. Allojeneik hematopoetik kök hücre nakli için hazırlıkları devam ediyor