

Leukemia Akut

Modul Hematologi-Onkologi

Narator

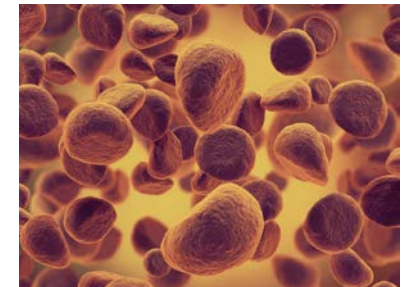
dr. Fikri Ichsan Wiguna

Narasumber

Dr. dr. Ikhwan Rinaldi, Sp.PD-KHOM, M.Epid



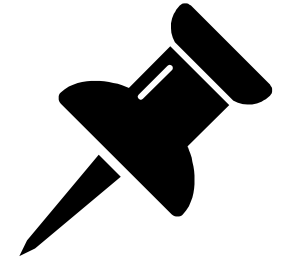
Universitas Indonesia
2019



Sumber gambar:

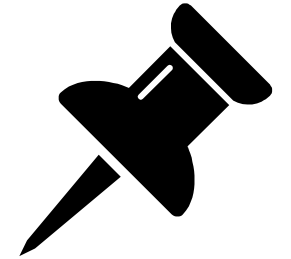
- tuke.co.ke
- Medicalnewstoday.com

Tujuan Pembelajaran



- Peserta didik mampu mengetahui dan memahami definisi, dan faktor risiko leukemia akut
- Peserta didik mampu membedakan dan mengenali tipe-tipe leukemia akut
- Peserta didik mampu mengetahui prinsip dasar terapi dan terapi dasar leukemia

Konten Pembahasan



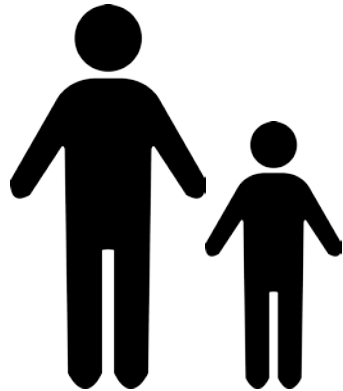
- Definisi
- Faktor penyebab
- Klasifikasi leukemia akut
- Diagnosis leukemia akut
- Prinsip dasar terapi



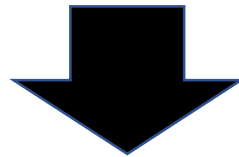
PEMAHAMAN DASAR



Definisi



Sel prekursor
hematopoietik



Proliferasi
tidak terkontrol

WHY?

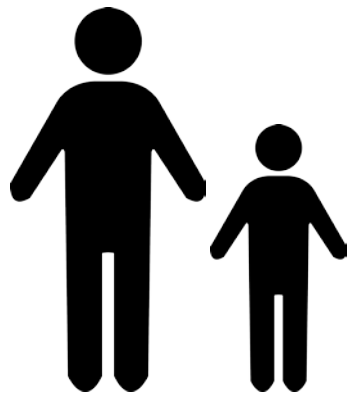
Perubahan
regulasi siklus sel
prekursor hematopoietik

Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731–738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
3. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* 2016; 127:2375.
4. Matutes E, Pickl WF, Van't Veer M, et al. Mixed-phenotype acute leukemia: clinical and laboratory features and outcome in 100 patients defined according to the WHO 2008 classification. *Blood* 2011; 117:3163.

Faktor Penyebab

Hereditas



Radiasi



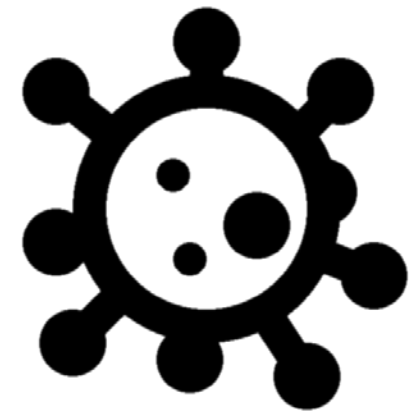
Bahan kimia



Obat



Virus

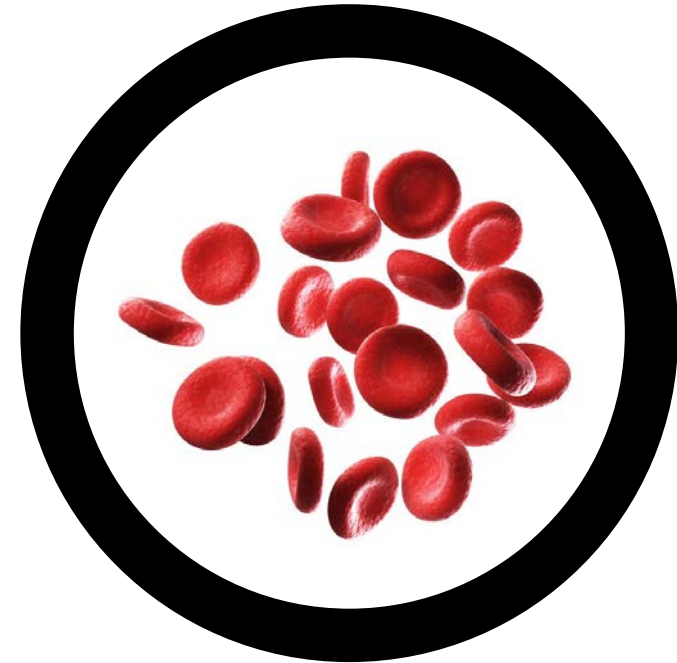


Sumber:

5. Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, editors. Harrison's principle of internal medicine. 19th ed. McGraw-Hill Education; 2015.

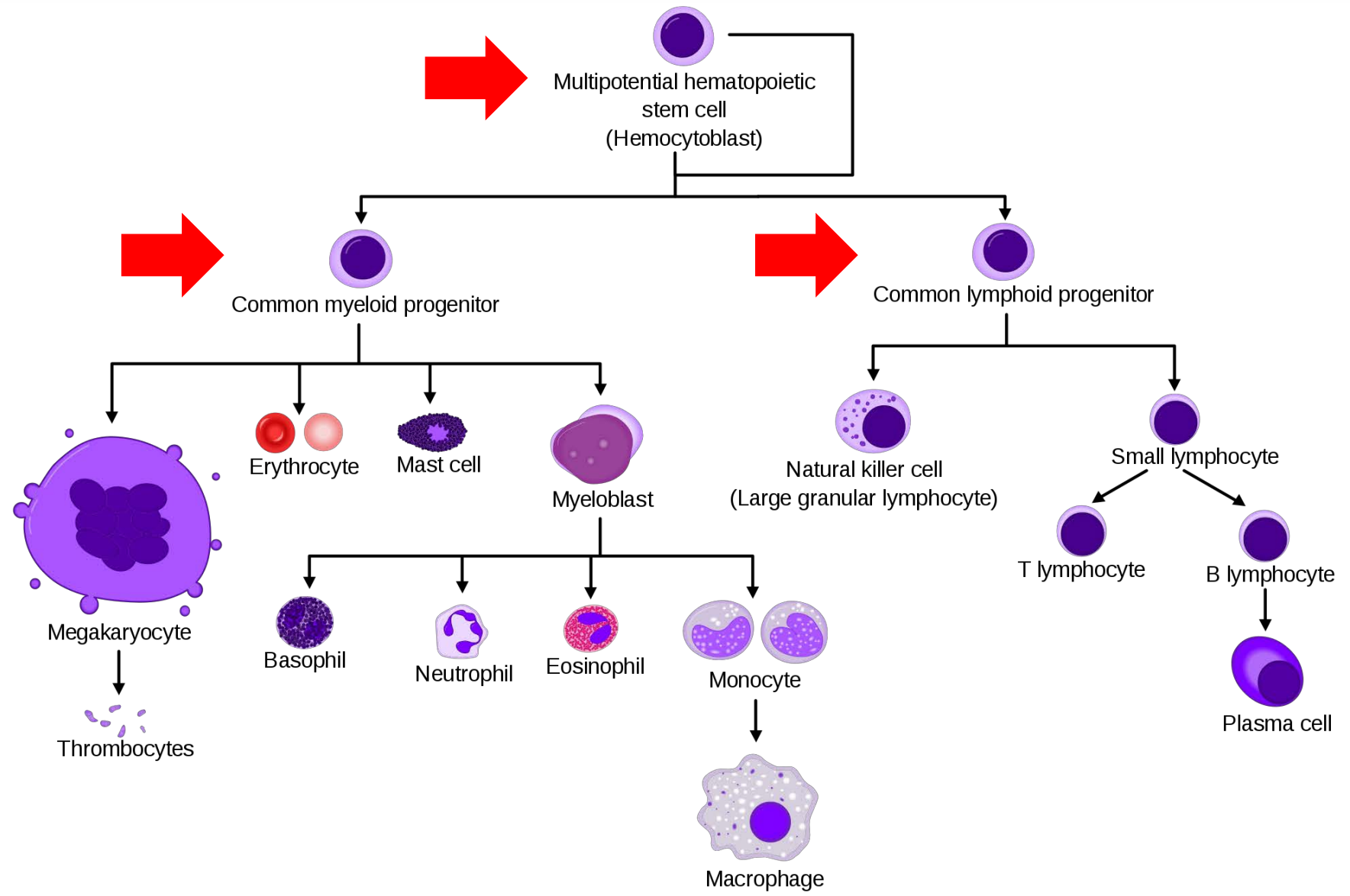
Sel Hematopoietik

- Hematopoiesis terbentuk di **sumsum tulang**
- Sel punca multipoten berdiferensiasi menjadi:
 1. Eritrosit
 2. Platetelt
 3. Neutrofil
 4. Eosinofil
 5. Basofil
 6. Monosit
 7. Limfosit B dan T
 8. *Natural Killer cells* (NK cell)
 9. Sel dendritik



Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731-738.
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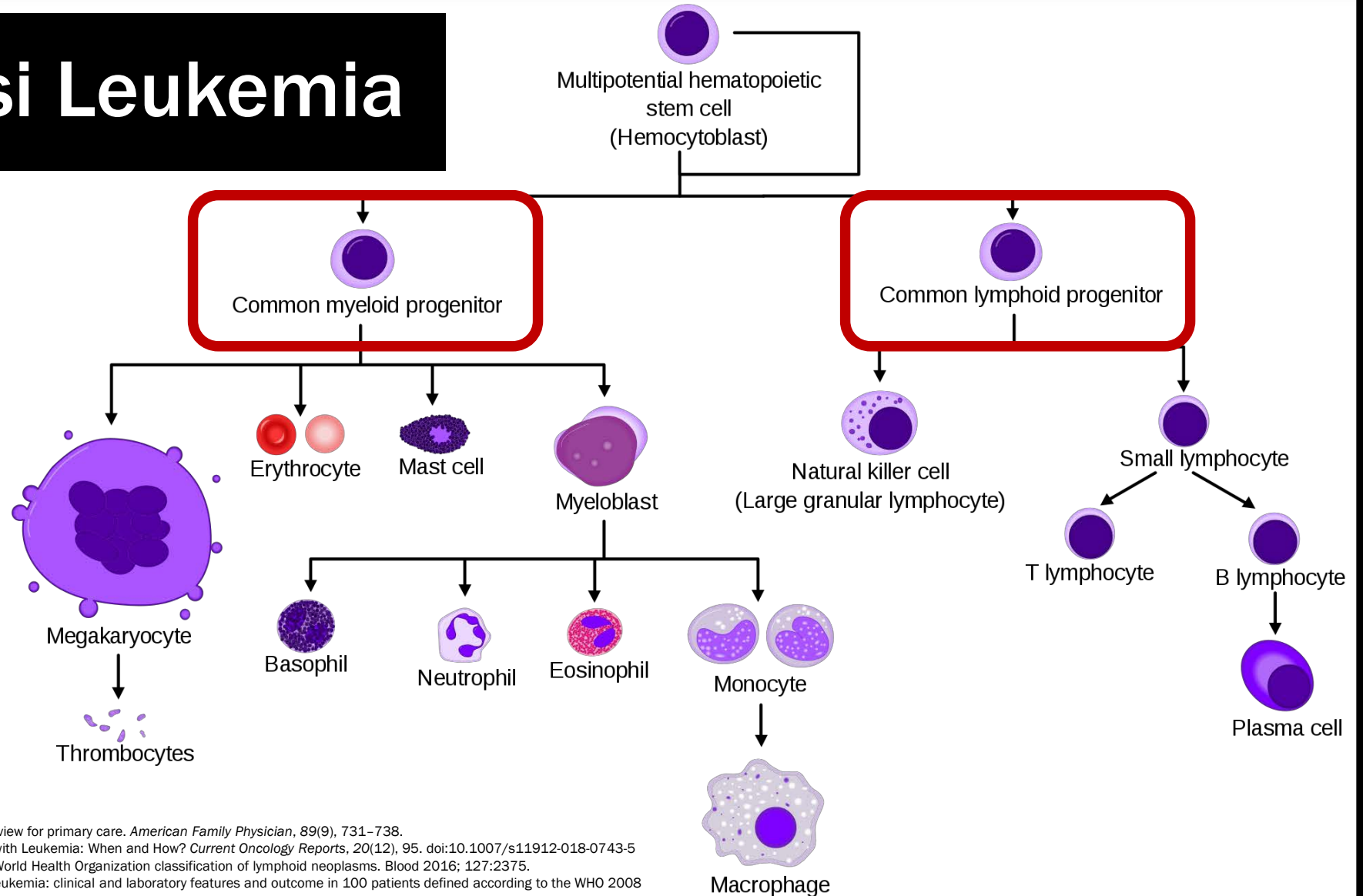
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Klasifikasi Leukemia

**Acute Lymphoid
Leukemia
ALL**

**Acute Myeloid
Leukemia
AML**



Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731-738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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4. Matutes E, Pickl WF, Van't Veer M, et al. Mixed-phenotype acute leukemia: clinical and laboratory features and outcome in 100 patients defined according to the WHO 2008 classification. *Blood* 2011; 117:3163.



DIAGNOSIS



Karakteristik Leukemia

Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731–738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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Subtipe	AML	ALL
Populasi	80% kasus ditemukan pada usia dewasa	Pada anak-anak dan dewasa muda (53% kasus ditemukan pada usia <20 tahun)
Gejala dan temuan	<ul style="list-style-type: none">• Demam, fatigue, turunnya berat badan, pendarahan dan memar• Hepatosplenomegali dan limfadenopathy (jarang)	<ul style="list-style-type: none">• Demam, lethargi pendarahan, nyeri atau kelemahan muskuloskeletal• Hepatosplenomegali dan limfadenopati

Karakteristik Leukemia

Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731–738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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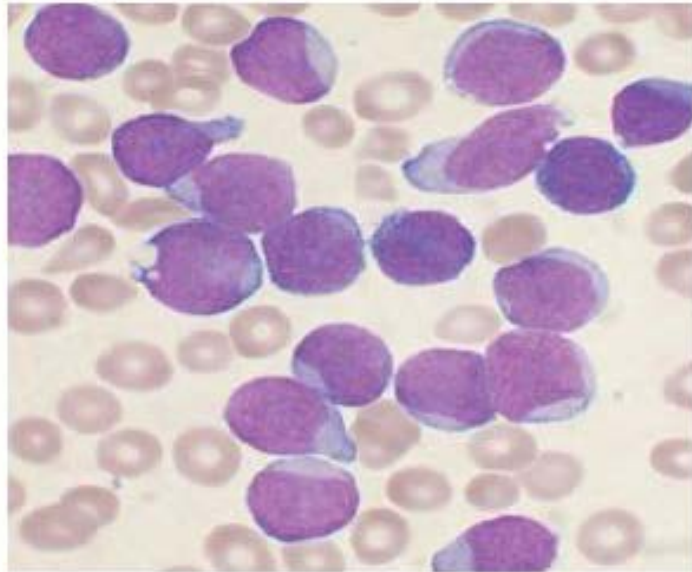
Subtipe	AML	ALL
Deskripsi	<ul style="list-style-type: none">• Sel blast tipe myeloid pada apusan darah tepi atau pada aspirasi sumsum tulang• Auer rods pada apusan darah tepi	Sel blast tipe limfoid / tidak terdiferensiasi pada apusan darah tepi atau pada aspirasi sumsum tulang

Karakteristik Leukemia

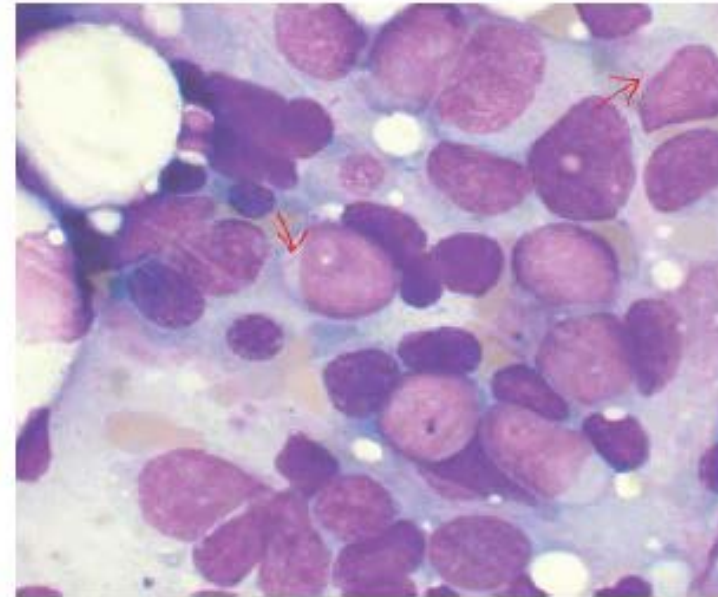
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1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731-738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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**ALL
(B cells)**



**AML
(Auer rods)**



Karakteristik Leukemia

Subtipe	AML	ALL
Rerata survival selama 5 tahun	<ul style="list-style-type: none">• <50 tahun: 75%• >50 tahun: 14%	<ul style="list-style-type: none">• <50 tahun: 75%• >50 tahun: 25%

Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731–738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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4. Matutes E, Pickl WF, Van't Veer M, et al. Mixed-phenotype acute leukemia: clinical and laboratory features and outcome in 100 patients defined according to the WHO 2008 classification. *Blood* 2011; 117:3163.

Diagnosis

Sumber:

6. Hoelzer D, Bassan R, Dombret H, Fielding A, Ribera J, Buske C. Acute lymphoblastic leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2016;27:v69–82.
7. Fey M, Buske C. Acute myeloblastic leukaemias in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24:vi138–43.

	ALL	AML
Morfologi sumsum tulang / darah perifer	Sel blast limfoid / tidak terdiferensiasi ($\geq 20\%$)	Sel blast myeloid $\geq 20\%$
Cairan serebrospinal	Keterlibatan SSP	
immunophenotyping	Membedakan galur sel B atau sel T	Menentukan tipe AML
Sitogenetik	Membedakan ALL tipe Ph+ atau Ph-	Menentukan tipe AML berdasarkan kelainan kromosom
Pemeriksaan lain	HLA typing, uji MRD	Cytochemistry, molecular genetics (deteksi mutasi), fungsi ginjal dan hati, status koagulasi, radiologi

Faktor Risiko ALL dan AML

Sumber:

6. Hoelzer D, Bassan R, Dombret H, Fielding A, Ribera J, Buske C. Acute lymphoblastic leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2016;27:v69-82.
7. Fey M, Buske C. Acute myeloblastic leukaemias in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2013;24:vi138-43.

High risk ?

ALL | AML

Faktor Risiko ALL

Sumber:

6. Hoelzer D, Bassan R, Dombret H, Fielding A, Ribera J, Buske C. Acute lymphoblastic leukaemia in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2016;27:v69–82.

Table 2. High-risk factors in adult ALL

Risk factors	Risk subsets (notes)	Recommendations
Patient-related		
– Age (years)	– >40/55/65	Mandatory
– Performance status (ECOG score)	– >1	Highly recommended
Disease-related		
– WBC ($\times 10^9/l$)	– >30 (B-lineage)/>100 (T-lineage)	Mandatory
– Immunophenotype (B-T-subsets)	– Pro-B/early and mature-T	Mandatory
– Cytogenetics (karyotype)	– Ph+/t(4;11)+/other adverse	Mandatory
– Genetics	– BCR-ABL1+/MLL+/PBX-E2A+/ Ph-like/IKZF1del/ETP/unmutated NOTCH1	Mandatory Recommended for new clinical trials
– Miscellaneous	– Central nervous system involvement	Mandatory
Response dynamics		
– corticosteroid sensitivity (blast count after pre-phase)	– Poor prednisone response ($\geq 1 \times 10^9/l$)	Recommended
– early blast cell response (BM morphology)	– Day 8–15 blasts $\geq 5\%$	Recommended
– time to CR (no. of courses)	– >1 cycle (late CR)	Mandatory
– MRD (molecular/LAIP)	– MRD+ (post-induction)	Mandatory

ALL, acute lymphoblastic leukaemia; ECOG, Eastern Cooperative Oncology Group; WBC, white blood cells; Ph+, Philadelphia-positive; Ph, Philadelphia; ETP, early T-cell precursor; BM, bone marrow; CR, complete remission; MRD, minimal residual disease; LAIP, leukaemia-associated immunophenotype.

Faktor Risiko AML

Sumber:

7. Fey M, Buske C. Acute myeloblastic leukaemias in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24:vi138-43.

Favourable	APL with t(15;17) CBF-AML with t(8;21) or inv 16 Biallelic CEBP α mutation with normal cytogenetics Normal karyotype with NPM mutation and no FLT3 ITD
Intermediate	AML with normal cytogenetics and no adverse molecular features FLT3 ITD with normal karyotype
Adverse	Complex karyotype abnormalities (>3) Monosomal karyotype



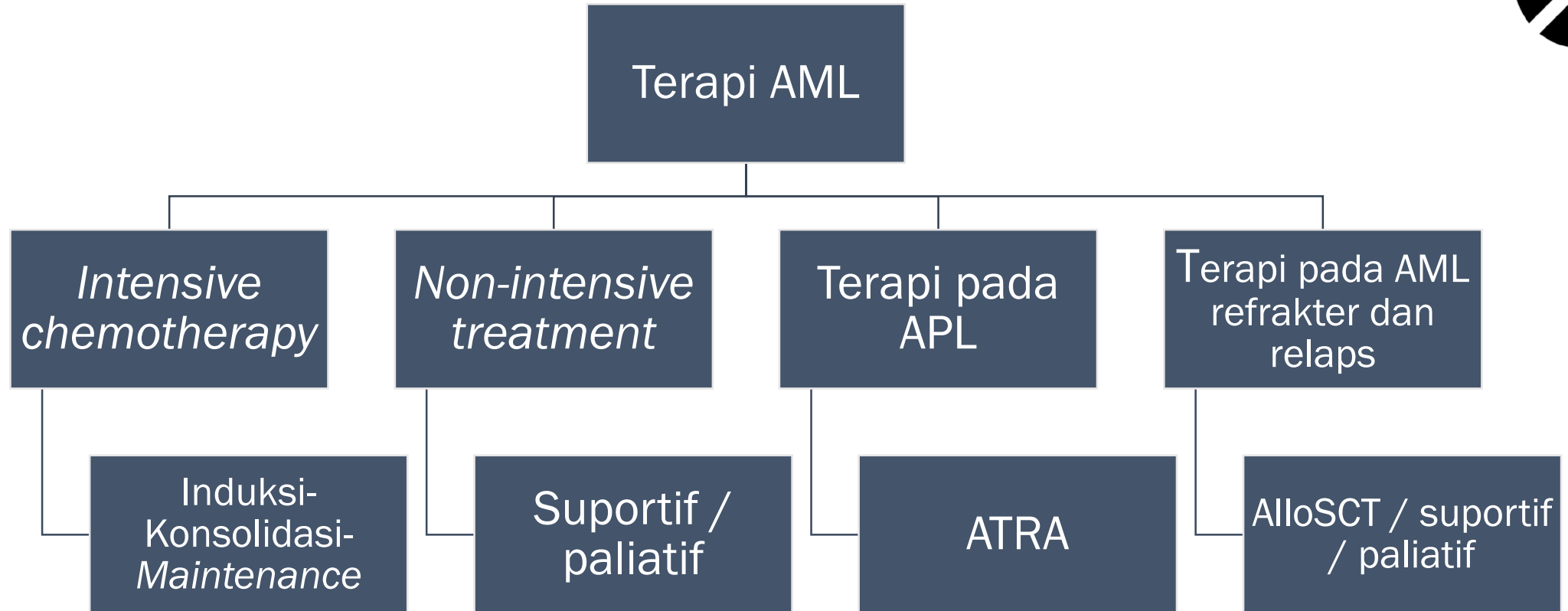
TERAPI



Prinsip Terapi

Sumber:

7. Fey M, Buske C. Acute myeloblastic leukaemias in adult patients: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24:vi138-43.



Prinsip Terapi

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Terapi ALL

- Terapi pre-fase
- Terapi suportif
- Terapi induksi
- Terapi konsolidasi
- *Maintenance therapy*
- Profilaksis SSP
- *Targeted therapy*

Respons Terapi

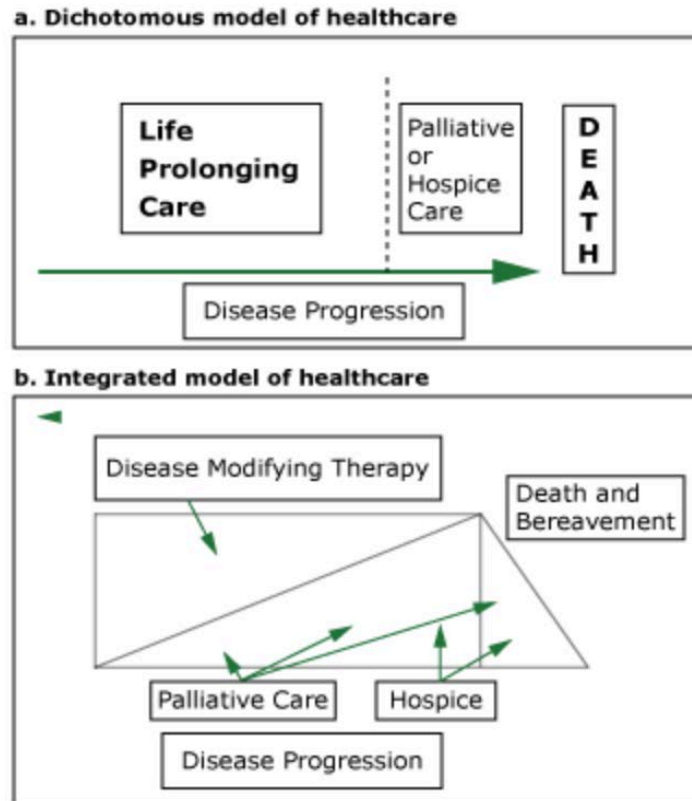
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1. Remisi komplit
 - Tidak ditemukannya lagi sel leukemik pada sumsum tulang
 - Gejala dan tanda klinis tidak ditemukan
 - Jumlah sel darah normal
 - Jumlah sel blast di sumsum tulang atau di darah tidak lebih dari 5%
2. Refrakter
 - Masih terdapat sedikit sel leukemik meskipun sudah dilakukan terapi intensif
3. Relaps
 - Sel leukemik kembali ditemukan setelah remisi komplit tercapai

Asesmen Kebutuhan Asuhan Paliatif



Adapted from National Consensus Project for Quality Palliative Care (2004).
Clinical practice guidelines for quality palliative care.
<http://www.nationalconsensusproject.org>.

- Bertujuan untuk meningkatkan kualitas hidup.
- Asuhan paliatif melibatkan kolaborasi interdisipliner.
- Asuhan paliatif harus diberikan beriringan dengan perawatan lainnya.
- Komponen fisik, mental, sosioekonomi, dan spiritual harus diperhatikan.

Sumber:

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731-738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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Kesimpulan

Leukemia akut merupakan kelompok keganasan yang ditandai dengan **peningkatan sel blast**. Leukemia akut juga merupakan penyakit dengan manifestasi klinis yang **tidak spesifik** sehingga cukup sulit untuk mendiagnosis leukemia. Diperlukan **beberapa modalitas** pemeriksaan untuk menegakkan diagnosis leukemia. Sementara itu, terapi leukemia juga sangat **bergantung dengan tipe dan progresi penyakit** yang diderita.

Daftar Pustaka

1. Davis, A. S., Viera, A. J., & Mead, M. D. (2014). Leukemia: An overview for primary care. *American Family Physician*, 89(9), 731–738.
2. Vidal, M., Hui, D., & Bruera, E. (2018). Palliative Care in Patients with Leukemia: When and How? *Current Oncology Reports*, 20(12), 95. doi:10.1007/s11912-018-0743-5
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Terima Kasih

Semoga bermanfaat!

Jangan lupa untuk mengerjakan latihan soal ya!