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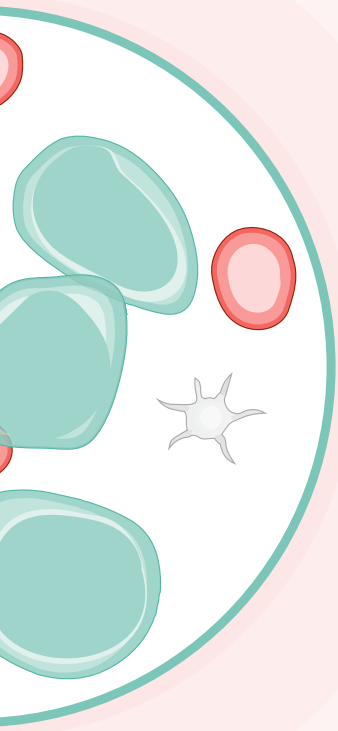
AML POSES A CRITICAL CLINICAL CHALLENGE



A growing global burden

Acute myeloid leukemia (AML) is the most common acute leukemia in adults, accounting for **~23.1% of all leukemia cases worldwide** (2017) [1]

It is highly aggressive with poor survival outcomes:

- 5-year relative survival: **32.9%** [2]
- With current SOC, this falls to **<10-15%** in older patients (≥60 years) [3]
- Once patients relapse, median overall survival drops **<6 months** [4]

The global burden has escalated over recent decades, with morbidity and mortality continuing to rise [5]:

In the US alone, projections for 2025 estimate **~22,010 new diagnoses** and **~11,090 deaths** [6]

Median age of diagnosis: **68 years** in US [7]

Incidence higher **in men** [5]

Most common potential risk factors related to AML: **smoking, previous chemo- or radiotherapies, history of blood disorders, genetic disorders** [5]

These poor outcomes are driven by limited treatment options and the underlying complexity of AML biology.

AML: Acute Myeloid Leukemia; SOC: Standard of Care; US: United States.

COMPLEXITY OF THE DISEASE

Similarity between AML blasts and normal hematopoietic cells [10]

Genetic and molecular heterogeneity [10]

Clonal evolution and therapy resistance [11]

Bone marrow niche protects leukemic cells [12]

AML: Acute Myeloid Leukemia.

What exactly is AML?

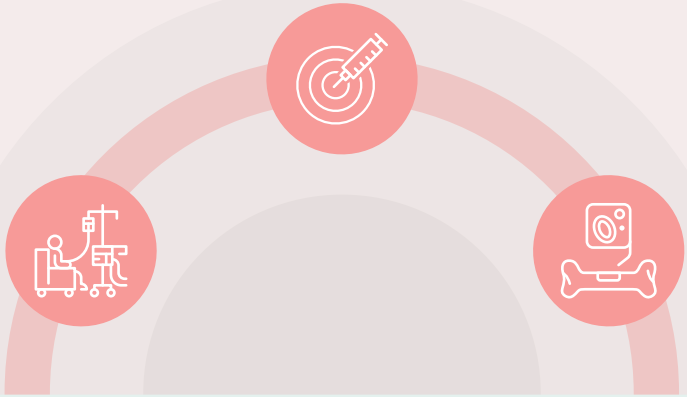
AML is [8,9]

- A blood and bone marrow cancer that predominantly impacts older adults
- A heterogeneous and malignant clonal disorder of the bone marrow/hematopoietic system
- Driven by chromosomal rearrangements and gene mutations in hematopoietic stem and progenitor cells
- Characterized by an accumulation of undifferentiated myeloid blasts
- Associated with impaired production of normal blood cells

THE CURRENT TREATMENT LANDSCAPE

Types of treatment available

Targeted therapies [14]



Chemotherapy and Hypomethylating Agents (HMAs) [13]

Stem Cell Transplantation [15]

Where current therapies fall short

Survival is poorest in **older** (<15% 5-year survival in patients ≥60 years) [3] **and R/R AML patients** (OS <6 months) [4]
Yet treatment choices remain limited

~30–35% relapse rates in younger patients with favorable risk factors, but **~80%** in older patients with adverse risk factors [16]

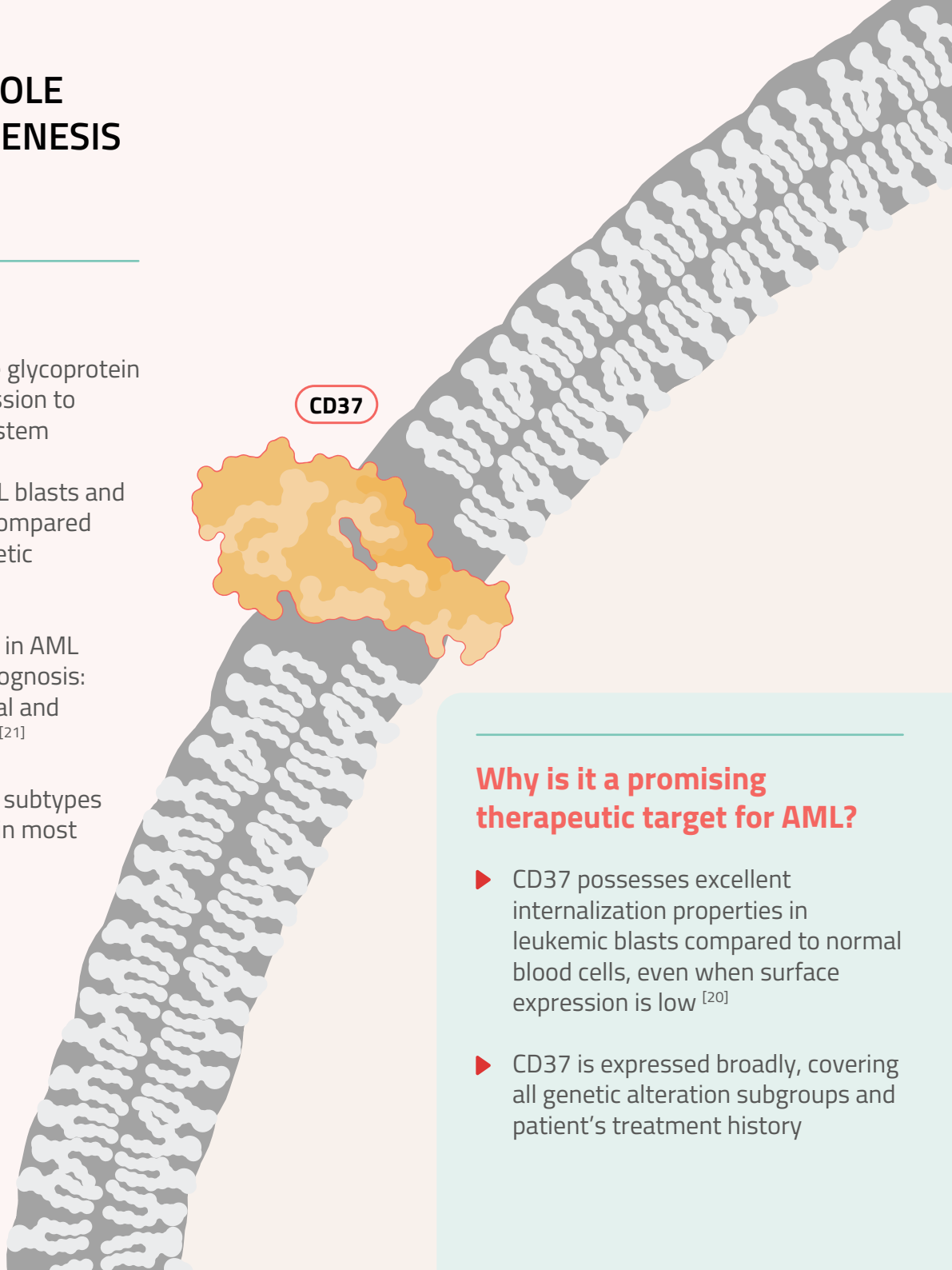
More than **50%** of patients with AML are ineligible for intensive chemotherapy regimens [17]

AML: Acute Myeloid Leukemia; HMA: Hypomethylating Agent; OS: Overall Survival; R/R: Relapsed or Refractory.

CD37 PLAYS A ROLE IN AML PATHOGENESIS

CD37 expression

- CD37 is a cell-surface glycoprotein with restricted expression to the hematopoietic system
- Overexpressed in AML blasts and leukemic stem cells compared to normal hematopoietic stem cells [18–20]
- Prognostic biomarker in AML related to the poor prognosis: shorter overall survival and disease-free survival [21]
- Expressed in multiple subtypes of AML [18-20] – found in most primary AML blasts



Why is it a promising therapeutic target for AML?

- CD37 possesses excellent internalization properties in leukemic blasts compared to normal blood cells, even when surface expression is low [20]
- CD37 is expressed broadly, covering all genetic alteration subgroups and patient's treatment history

AML: Acute Myeloid Leukemia.

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