

Current status of Acute Myeloid Leukemia in Spain: Results from a Delphi study on its epidemiology, disease management and unmet clinical needs.

Montesinos P¹, Colorado M², Esteve J³, López JL⁴, Pérez JA⁵, Sanz MA¹, Serrano J⁶, Sierra J⁷, Cebollero MA⁸, Ortiz V⁹, Gil A⁹

¹Hospital Universitario Politécnico de la Fe, Valencia; ²Hospital Universitario Marqués de Valdecilla, Santander; ³Hospital Clínico y Provincial, Barcelona; ⁴Hospital Universitario Fundación Jiménez Díaz, Madrid; ⁵Hospital Universitario Virgen del Rocío, Sevilla; ⁶Hospital Universitario Reina Sofía, Córdoba; ⁷Hospital de la Santa Creu i Sant Pau, Barcelona; ⁸Jazz Pharmaceuticals Iberia S.L.; ⁹Omakase Consulting S.L.

INTRODUCTION AND OBJECTIVES

Acute myeloid leukemia (AML) is a rare disease featuring a heterogeneous, hematologic malignant neoplasm. It is characterized by a group of molecular, cytogenetic and clinical entities which may lead to myoblast proliferation, resulting in a reduce number of the three key blood components (red blood cells, white blood cells and platelets), increasing the risk of hemorrhage, infection and mortality.

AML is a **rapidly progressing** disease that **rises in frequency with age**². In Spain, as it happens with many other rare diseases, the available information regarding AML is limited, highlighted by the lack of published data. The current study aims to evaluate the epidemiology of AML in Spain, determine the AML affected-patient flow in the National Healthcare System, understand its **management** and identify the **leading unmet patient-needs**. The main objective is to come up with a series of guidelines to increase AML knowledge and help achieve the desired clinical outcome.

METHODS

- Systematic literature review through the NCBI and PubMed biomedical databases as well as grey literature resources.
- The information collected was complemented and verified via interviews with two Spanish AML experts. Gathered information was employed to develop a two-round Delphi experiment (December 2017 and January 2018, respectively) accomplished by a group of 17 hematologists with practical experience in treating AML patients from 17 different sites representing 11 different Spanish regions. The results were presented, discussed and ratified by an expert panel made up of 8 medical experts in February 2018. The epidemiologic data were estimated by extrapolating the number of patients registered by each participant, by the total population covered by their respective site, and previously also extrapolated by the Autonomous community using data from the National Institute of Statistics.³

RESULTS

EPIDIMIOLOGY

AML incidence has increased in the past 5 years.



Figure 1. Evolution of AML incidence in the past 5 years.

DISEASE IMPACT

- Survival** Survival rates depend on the patient's age and AML subtype. The average survival is of approximately 16.5 months. Patients belonging to the subgroup aged ≥ 65 years and with secondary ALM have an average survival of about 6.8 months. It is understood that **38% of AML patients reach the stage of transplantation of hematopoietic progenitors**.
- Quality of Life** AML has a **high impact in the patient's quality of life**. It may be affected through all treatment phases, specially during intensive induction therapy and transplant.
- Resources** The current and conventional treatment of AML in Spain is administered in a hospital setting. Patients who receive said treatment are required to be hospitalized due to its challenging administration method (24h continuous perfusion over 7 days) and needed monitoring.

AML PATIENT FLOW IN THE NATIONAL HEALTHCARE SYSTEM

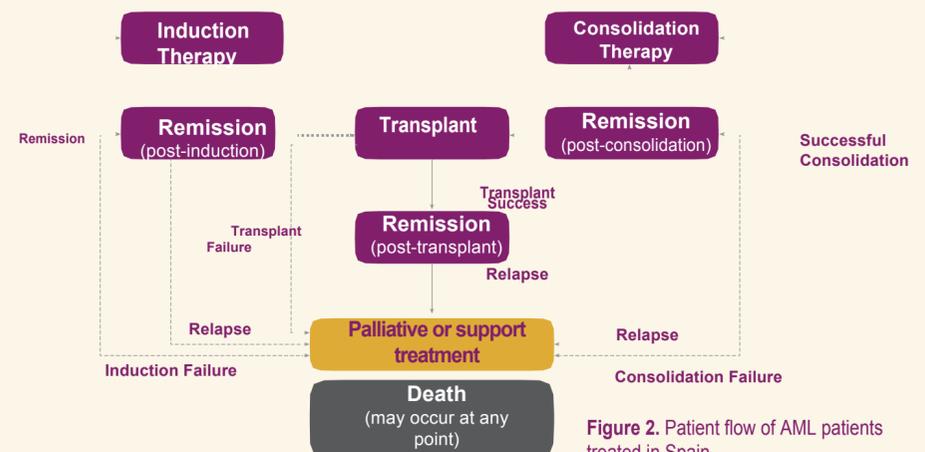
There are **2 main clinical branches** that defer patients with AML to a specialized hematologist: **1/ Primary Care**; **2/ Emergency Department**.

On average patients **visit de doctor 3 times** before they are given an AML diagnosis. A precise **diagnosis** requires at least **4 tests**, which include **conventional and molecular tests**; the most important being **bone marrow aspiration, complete blood count and immunophenotyping** (flow cytometry)

Not all Spanish sites have the equipment needed to carry out molecular tests.

In Spain **77% of patients** who go through **intensive induction therapy**, only receive **1 cycle** of chemotherapy. **34% of patients** aged < 65 who undergo **consolidation therapy** receive **1 cycle** of chemotherapy, while **32% receive 2 cycles**; while **56% of patients** aged ≥ 65 receive **only 1 cycle**.

Both **intensive induction therapy** and **consolidation therapy** are administered in a **hospital setting**, requiring long periods of **hospitalization** (on average 36 and 30 days respectively). **Palliative or support treatment** is usually administered in the **Day Hospital** (59%), although they may also be administered in units specialized in palliative treatment (19%), hospital setting (14%) or primary care centers including home-care (8%).



DISEASE MANAGEMENT

The main treatment guidelines used as reference by most hematologists in Spain are the **PETHEMA Guidelines** (Spanish program in Hematology Treatment)⁵. Before they begin treatment, **patients must be evaluated on different factors** to assess the provability that the patient responds to treatment, is able to reach therapeutic goals in each phase, and to determine the risk of relapse. Considering the result of such evaluation and the patient's own opinion **it will be determined if the patient is fit/unfit to receive intensive induction therapy**. Patients unfit to receive intensive chemotherapy receive a **reduced intensity treatment or palliative treatment**. The most frequent options for each phase are illustrated in **Table 1**.

Table 1. Most widely used options for each treatment phase.

Treatment Phase	Most frequent alternative
Reduced intensity treatment	Hypomethylating Agents (azacitidine)
Palliative Treatment	Blood transfusions
Intensive induction therapy	3+7 (cytarabine+ idarubicin/daunorubicin)
Consolidation therapy	High doses of cytarabine (HiDAC)
Transplant	Allogenic

Main unmet needs in AML in Spain

- Lack of robust epidemiological data at a national level
- The need for new treatments and/or therapies with better results in efficacy and safety than those currently available.
- Lack of studies evaluating the results reported by patients (*Patient Reported Outcomes (PROs)*)
- Lack of standardized protocols to speed up the AML diagnosis and selection of the most appropriate treatment.
- The need for cost-benefit studies
- Lack of AML knowledge amongst health professionals involved in its diagnosis.

Proposed guidelines to address unmet needs

- Conduct epidemiological studies and establish a global registry at the national level.
- Continue with the efforts regarding investment, development, approval and timely access to new treatments.
- Include sub-studies evaluating the quality of life of patients in clinical trials.
- Promote the exchange of information between different cooperative groups and centralize the most complex diagnostic tests in certain centers, taking into consideration their geographical location.
- Quantify the total cost of treating a patient with AML in Spain to establish cost-effective parameters.
- Improve the communication between the different branches in centers, and promote training by pathology experts to all agents involved in patient management.

CONCLUSION

The study has been useful to:

- 1) Evaluate the epidemiology of AML in Spain due to the lack of published studies and consensus records.
- 2) Elucidate patient flow, impact and management of the disease in Spain, and to determine the main treatment alternatives used in each phase.
- 3) Identify the main unmet needs at the national level and propose consensual actions which contribute to the knowledge of the pathology and design guidelines to achieve the clinical objectives.

REFERENCES:

1. Gayathri B, et al. J Lab Physicians. 2011;3(1):15-20.
 2. Kantarjian H, et al. Am J Hematol. 2016;91(1):131-45.
 3. <https://www.ine.es/>
 4. Visser O, et al. Eur J Cancer. 2012;48:3257-3266.
 5. <https://www.fundacionpethema.es/>
- LX Congreso Nacional de la SEHH (del 11 al 13 de octubre del 2018)
PC-186 / SEHH - LEUCEMIAS AGUDAS