NON-INTERVENTIONAL (NI) FINAL STUDY REPORT

Study Information

Title	A retrospective, observational study on conditions of use, safety, and effectiveness of MYLOTARG® (Gemtuzumab Ozogamicin, GO) for treatment of patients with newly diagnosed CD33 positive acute myeloid leukemia (AML).
Protocol number	B1761036
Version identifier of the final study report	1.0
Date	19 December 2023
EU Post Authorization Study (PAS) register number	EUPAS44551
Active substance	GEMTUZUMAB OZOGAMICINE (L01XC05)
Medicinal product	MYLOTARG®
Research question and objectives	The objective of this study was to describe the methods of use, the effectiveness and safety of MYLOTARG® under real-life conditions, in patients not previously treated. Study objectives: • To describe the clinical and laboratory characteristics of patients with AML, at time of initiation of treatment with MYLOTARG®, • To describe the methods for prescribing of MYLOTARG®, including the administration regimen, the doses, changes to doses, the duration of treatment, total dose received, the causes and methods of discontinuation of treatment,

	• To describe safety data of specific interest, including frequency of occurrence of veno-occlusive disease (VOD), their outcome, methods of prophylaxis; prolonged thrombocytopenia and severe bleeding (hemorrhage), • To describe the parameters of effectiveness: response rate to treatment (CR MRD-, CR, CRi and CRp), overall survival (OS) causes of death, relapse-free survival (RFS), and event-free survival (EFS), • To search for prognostic factors of EFS, OS and RFS, • To describe after treatment by MYLOTARG® the care of patients with AML, and, in particular hematopoietic stem cell transplantation.
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1. ABSTRACT (STAND-ALONE DOCUMENT)

Title: A retrospective, observational study on conditions of use, safety, and effectiveness of Mylotarg® (gemtuzumab ozogamicin) for treatment of patients with newly diagnosed CD33 positive acute myeloid leukemia.

Date: 19 December 2023

Name and affiliation of the main author: Karin GOGAT MARCHANT, PhD Responsable Médical Hématologie Pfizer Oncology 23-25 Avenue du Docteur Lannelongue 75014 PARI

Keywords: Acute myeloid leukemia, gemtuzumab-ozogamicin (Mylotarg®), CD33 expression, combination induction chemotherapy.

Rationale and background:
Acute myeloid leukemia (AML) is a rare, aggressive disorder characterized by the monoclonal proliferation of immature hematopoietic cells, the myeloblasts, that invade the bone marrow and the blood, and associated with bone marrow failure. The antibody-drug conjugate, gemtuzumab-ozogamicin (Mylotarg®) that targets CD33 has been developed as part of induction chemotherapy for treating AML.

On the 03 April 2019, the French Transparency Commission registered Mylotarg® on the list of medicinal products certified for treating patients older than 15 years of age with *de novo* CD33+ AML, not previously treated, in good overall condition.

However, due to the scarcity of data, the Commission requested that further data be collected and be available within 5 years. The objective was to confirm the effectiveness and safety of Mylotarg®.

Thus, this non-interventional study was performed to collect these data to provide evidence for the safety and effectiveness of Mylotarg® in real-life clinical practice.

Research question and objectives:

- To describe the clinical and biological characteristics of patients with AML.
- To describe the methods for prescribing Mylotarg®.
- To describe the safety profile of Mylotarg®.
- To describe the effectiveness of Mylotarg®: response rate to treatment (CR MRD-, CR, CRh, and CRp), overall survival (OS) including causes of death, relapse-free survival (RFS), and event-free survival (EFS).
- To search for prognostic factors of EFS, OS, and RFS.
- To describe treatment after Mylotarg®, particularly the use of hematopoietic stem cell transplantations.

Study design: The study was designed as a multicenter, retrospective, observational study. The study did not impact the treatment of patients.

Setting: This study population included patients treated in France with Mylotarg® since December 2014. In addition to the overall population, patients have been divided into 2 different cohorts, one included all patients included in the French cohort authorization for temporary use (ATUc) and the second including all patients who received Mylotarg Post-ATUc.

Subjects and study size, including dropouts: Overall, the study enrolled 113 patients in 9 centers, that received at least one injection of Mylotarg®: 62 (54.9%) included in the ATUc and 51 (45.1%) in the Post-ATUc.

Variables and data sources: Patient and disease characteristics, use of Mylotarg®, response data, treatment after Mylotarg®, and survival data were collected from ATUc and Post-ATUc.

Results: The study included 113 patients (full analysis set [FAS]): 62/113 males (54.9%) and 51/113 females (45.1%). The median age when Mylotarg® was initiated was 63.0 years. 72/88 patients (81.8%; missing data [n=25]) had an ECOG PS of 0-1.

In the 107 patients that received first induction chemotherapy, Mylotarg® was prescribed as monotherapy in 2/107 patients (1.9%) and in association in 105/107 (98.1%). The median number of Mylotarg® doses was 3 with a median cumulative dose of 15 mg, and predominantly in 84/107 patients (78.5%) on days 1, 4, and 7.

In terms of effectiveness:

- Best response: the CR rate was 74.3% and that of CRp was 4.4%.
- Post-induction response: CR rate was 72.3%, CRp rate was 6.3%, and 52.2% were CR MRD-negative.
- Median OS was 49.8 months (95% CI: 21.8-NE).
- Median RFS was 17.5 months (95% CI: 12.6-35.6).
- Median EFS was 13.1 months (95% CI: 9.9-17.5).

After Mylotarg® treatments, in the FAS (n=113), 35/111 patients (31.5%) had HSCT (missing data [n=2]). The median time interval from the last dose of Mylotarg® to HSCT was 13.0 months (Q1-Q3: 4.8-16.4).

In terms of safety, in the FAS (n=113), 30 patients (26.5%) reported 40 treatment-related AEs: 6 patients with 10 SAEs and 24 patients with 30 treatment-related AEs not SAEs. 2 patients died of a SAE related to Mylotarg®: 1 patient for an immune system disorder (infection and septic shock) and 1 for a vascular disorder (hemorrhage). Persistent thrombocytopenia was reported in 18/113 patients (15.9%), severe hemorrhages in 6/113 (5.3%), veno-occlusive disease in 1/113 (0.9%), and infections in 3/113 (2.7%; 1 was serious).

Multivariate analyses identified older age as prognostic for shorter OS, ECOG ≥2 and adverse cytogenetic classification as prognostic for shorter RFS, and FLT3-TKD mutation and adverse cytogenetic classification as prognostic for shorter EFS.

Discussion: Mylotarg® was predominantly administered according to its indication. Compared to the pivotal ALFA0701 study, response rates to Mylotarg® were similar, median RFS and EFS were reduced, and median OS was extended: 49.8 months compared to 27.5 months in the ALFA0701 study. Overall, Mylotarg® is safe and effective added to induction therapy for treating *de novo* AML patients expressing CD33. We highlight an extended OS without any new safety signals.

Names and affiliations of principal investigators:

Name, degree(s)	**Title**	**Affiliation**
Cécile Pautas	Chair for the steering committee for this study, hematologist	Assistance Publique Hôpitaux de Paris - APHP (Hôpital Henri Mondor)
Juliette Lambert	Steering committee member for this study, hematologist	Centre Hospitalier De Versailles (André Mignot)
Emmanuel Raffoux	Steering committee member for this study, hematologist	Assistance Publique Hôpitaux de Paris - APHP (Hôpital Saint Louis)

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
ADC	Antibody-drug conjugate
AE	Adverse event
AML	Acute myeloid leukemia
ATU	Authorization for temporary use
ATUc	Authorization for temporary use cohort (ATU cohort)
ATUn	Named ATU (ATU for specifically “named” patients)
CI	Confidence interval
CR	Complete response
CRh	Complete response without hematological recovery
CRi	Complete response with incomplete blood count recovery
CRMRD-	Complete response without minimal residual disease
CRp	Complete response without platelet recovery
D	Day
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EDC	Electronic data capture
EFS	Event-free survival
ELN	European Leukemia Network
EMA	European Medicines Agency
ENCePP	European Network of Centers for Pharmacoepidemiology and Pharmacovigilance
FAB classification	French-American-British classification
FAS	Full analysis set
GPP	Good pharmacoepidemiology practices
HAS	“Haute Autorité de Santé” (French Health Ministry)
HR	Hazard ratio
HSCT	Hematopoietic stem cell transplantation
IEC	Independent Ethics Committee
IRB	Institutional Review Board

Abbreviation	Definition
IV	Intravenous
MDQOP	Monitoring Data Quality Oversight Plan
mg	Milligram
NE	Not evaluable
NR	Not reached
OS	Overall survival
PASS	Post-authorization safety study
Post-ATUc	Cohort of patients in the study that received Mylotarg® through the post-ATU system (Post-ATU cohort)
PS	Performance status
Q	Quartile
Ref	Reference value
RFS	Relapse-free survival
RTU	Recommended temporary use
SAE	Serious Adverse Event
SD	Standard deviation
SOC	System Organ Class
VOD	Veno-occlusive disease
WBC	White blood cell

3. STUDY TEAM

The names, affiliations, and contact information of the study team are shown in **List 1**.

List 1. A list of study team that performed the study

Name, degree(s)	Title	Affiliation
Delphine Berzin	Clinical Operational Responsible RWD/EAP	Pfizer, France
Yves Brault	Statistician	Pfizer, France
Karin Gogat Marchant	Medical Responsible	Pfizer, France
Jerome Krulik	Medical Director oncology Pfizer France	Pfizer, France
Barabara De Bernardi	EU Qualified Person for Pharmacovigilance	Pfizer
Cécile Pautas	Chair for the steering committee for this study, hematologist	Assistance Publique Hôpitaux de Paris - APHP (Hôpital Henri Mondor)
Juliette Lambert	Steering committee member for this study, hematologist	Centre Hospitalier De Versailles (André Mignot)
Emmanuel Raffoux	Steering committee member for this study, hematologist	Assistance Publique Hôpitaux de Paris - APHP (Hôpital Saint Louis)

4. OTHER STUDY PARTICIPANTS

The list of the other study participants are shown in **List 2**.

List 2. List of other study participants

Name and Affiliation	Role in the study
Constant Josse eXYSTAT 4, rue Ernest Renan 92240 Malakoff FRANCE	Statistician in charge of the control
Franck Lutz eXYSTAT 4, rue Ernest Renan 92240 Malakoff FRANCE	Data Manager
François Montestruc eXYSTAT 4, rue Ernest Renan 92240 Malakoff FRANCE	Statistician
Adeline Pierache eXYSTAT 4, rue Ernest Renan 92240 Malakoff FRANCE	Statistician
Marion Keraudren eXYSTAT 4, rue Ernest Renan 92240 Malakoff FRANCE	Data Manager in charge of the control
Trevor Stanbury Pro-Pens 37, rue Florian 92160 Antony FRANCE	Medical Writer

5. MILESTONES

Milestone	Planned date	Actual date	Comments
Institutional review board (IRB) submission of protocol for information The IRB submission for information date for the protocol amendment 1.1 is provided in Appendix 3.2.	NA	03 January 2022	Transmission to the Health Data Hub
Start of data collection	01 January 2022	14 April 2022	1st site opened on the 07 April 2022
End of data collection	30 November 2022	30 November 2022	
Registration in the EU PAS register	4 January 2022	4 January 2022	ENCEPP site registration
Final report of study results	31 March 2023	19 December 2023	

6. RATIONALE AND BACKGROUND

Acute myeloid leukemia (AML) is an aggressive disorder characterized by the monoclonal proliferation of immature hematopoietic cells, the myeloblasts, that invade the bone marrow and the blood. This proliferation is associated with bone marrow failure. AML is a rare disease. In 2018, in France, 3,428 new cases of AML were reported.(1) The median age of diagnosis was 69 years in males and 72 in females.(1)

Due to the heterogenous nature of the disease, the prognosis of patients varies depending on patient factors but also leukemia-related characteristics, including morphological, cytogenetic, and molecular characteristics.(2) Overall, the prognosis of adults with AML remains poor despite advances in treatment, including intensified chemotherapy, use of hematopoietic allogenic stem cell transplants, and improved supportive care.

For many years, standard treatment for AML has comprised induction therapy with anthracyclines and cytarabine, followed by consolidation chemotherapy with or without allogeneic transplants.(2) Recently, several new drugs have been assessed for treating AML, among others midostaurin (a FLT3 inhibitor), CPX-351 (a nanoscale encapsulation of cytarabine and daunorubicin [5:1 ratio] as liposomes), and cladribine (a purine analogue).(2)

In addition, the antibody-drug conjugate (ADC), gemtuzumab-ozogamicin (Mylotarg®) that comprises a monoclonal antibody gemtuzumab, that targets CD33, combined with the toxin calicheamicin has been developed for treating AML.(3) On the 19 April 2018, the European Medicines Agency granted Mylotarg® marketing authorization. Mylotarg® is approved, combined with daunorubicin and cytarabine, for treating patients aged older than 15 years with *de novo* AML, expressing CD33 antigens on the surface of their myeloblasts. Mylotarg® is not approved for treating acute promyeloid leukemia (APL) not previously treated. About 90% of AML express CD33 antigens on the surface of their myeloblast.

Mylotarg® was granted marketing authorization, based on the results from the pivotal ALFA0701 study.(4, 5) ALFA0701 was a French randomized, open-label, phase III study that assessed the benefit of adding Mylotarg® (3 mg/m^2/day on days 1, 4, and 7]) to standard 3+7 induction chemotherapy (daunorubicin [60 mg/m^2/ day on days 1-3]) combined with cytarabine (200 mg/m^2/Day on days 1-7]) for treating adults with *de novo* AML.(4, 5) Patients in remission, after induction chemotherapy, were treated with 2 courses of consolidation therapy (daunorubicin combined with cytarabine) with or without Mylotarg® (3 mg/m^2/day on day 1) according to their treatment group allocated.

The primary endpoint was event-free survival (EFS), as assessed by the investigators. EFS was defined as the time interval between randomization and the first occurrence of relapse, death from any cause, or failure to achieve complete remission (CR) or incomplete platelet recovery CRp. As of the 01 August 2011 (the reference data), 73 events (54.1%) had been observed in the Mylotarg® arm and 102 (75%) in the control group. Median EFS was significantly extended in the Mylotarg® arm, 17.3 months, compared to 9.5 months in the control arm (HR=0.562 95% CI [0.415-0.762] p=0.0002). The EFS analysis was also performed using the

blinded assessments by an independent review committee. This analysis confirmed the primary endpoint analysis with a median EFS in the Mylotarg® arm of 13.6 months compared to 8.5 months in the control arm (HR=0.66 95% CI [0.49-0.89] p=0.006).

The ALFA0701 study's secondary endpoints included the analyses of overall survival (OS) and safety. The median OS, although tending to favor the Mylotarg® arm, was not significantly different in the treatment arms: 27.5 months in the Mylotarg® arm and 21.8 months in the control arm (HR=0.807 95% CI [0.596-1.093] p=0.16). In terms of safety, no difference between the treatment arms regarding early deaths was observed. The main toxicity observed with Mylotarg® was hematological, with prolonged thrombocytopenia. There were 7 cases of veno-occlusive disease (VOD) in the Mylotarg® arm versus 2 in the control arm.

In France, Mylotarg® has been available, since 2010, within an authorization for temporary use (ATU) specifically for identified "named" patients (ATUn). On the 18 September 2014, The ANSM granted permission to open an ATU cohort (ATUc) in the following indication:

"In combination with daunorubicin and cytarabine for the treatment of patients 50 to 70 years of age with *de novo* acute myeloid leukemia, previously untreated, who have favorable or intermediate cytogenetics or an *FLT3- ITD*+ mutation".

After the marketing authorization approval, obtained on the 18 March 2018, the ATUc indication for Mylotarg® was extended to all adults. On the 19 July 2019, the early access mechanisms, i.e., the ATUn and ATUc, were terminated. After the 19 July 2018 and up until the 23 July 2019, when the reimbursement of Mylotarg® by the French social security system was officially published, Mylotarg® was available through the post-ATU system.

On the 24 June 2020, the ANSM granted Mylotarg® a recommended temporary use (RTU), for treating adults and children older than 2 years with AML expressing CD33excluding patients with promyelocytic leukemia.

Prior to this, on the 03 April 2019, the Transparency Commission agreed to register Mylotarg® on the list of medicinal products certified for use to treat "patients 15 years of age and older with *de novo* CD33+ AML, not previously treated, in good overall condition (ECOG 0 or 1) except for AML with the FLT3 gene mutation eligible for treatment with midostaurin (RYDAPT) and acute promyelocytic leukemia".

The Transparency Commission qualified Mylotarg® as having an important medical benefit and a lack of improvement of medical benefit (ASMR V). However, as the Commission was uncertain of the use and safety profile of Mylotarg® in patients aged 15 to 50 years it recommended that additional descriptive data be obtained from patients treated in France with Mylotarg®, including those treated within the post-ATU system. The objective was to determine the safety profile of Mylotarg® in real-life conditions.

The objective of this data collection was to be able:

- To describe patient and disease characteristics, as well as duration of treatment

- To assess survival outcome of patients (including those who required hematopoietic allogeneic stem cell transplantations).

- To assess the safety of Mylotarg®, and notably the real-life incidence of veno-occlusive disease (VOD) and the clinical consequences.

The Transparency Commission requested that the results of the data collection be provided within a maximum of 5 years. The Commission would then consider whether Mylotarg® should be reassessed based on the data collected. To satisfy this request from the "Haute Autorité de Santé" (HAS, the French Health Ministry), Pfizer developed a retrospective study with data collection under real-life conditions in patients with AML, expressing CD33, not previously treated, who received Mylotarg® between the 01 December 2014 (the date of the first patient treated in the ATUc) and the 31 October 2022.

This non-interventional study was designated as a Post-Authorization Safety Study (PASS) and was conducted voluntarily by Pfizer.

7. RESEARCH QUESTION AND OBJECTIVES

The objective of this study was to assess the methods of use, the effectiveness and safety of Mylotarg® under real-life conditions, in patients not previously treated, as follows:

- To describe the clinical and biological characteristics of patients with AML, when initiating Mylotarg® treatment.

- To describe the modalities of Mylotarg® prescription, including doses, dose changes, concomitant AML treatments, duration of treatment, total dose received, causes and modalities of treatment discontinuations.

- To describe the tolerance data of specific events of interest and in particular the frequency of occurrence of veno-occlusive diseases (VOD), their evolution and consequences, the modalities of prophylaxis, persistent thrombocytopenia, and severe hemorrhages.

- To describe the effectiveness parameters: including response (remission) rate (CR MRD-, CR, CRh, and CRp), overall survival (OS), and causes of death, relapse-free survival (RFS), and event-free survival (EFS).

- To search for prognostic factors of EFS, OS, and RFS.

- To describe the treatments for AML following Mylotarg® treatment, including hematopoietic stem cell transplants

8. AMENDMENTS AND UPDATES

List 3. List of protocol amendments

Amendment number	Date	Substantial or administrative amendment	Protocol section(s) changed	Summary of amendment	Reason
1.1	01 August 2022	Non substantial amendment	9.3.1 and 9.3.6	Two members of the scientific committee will carry out a double-blind interpretation of the raw biology results uploaded by the investigative teams, with the aim of determining the risk score of each patient at the time of administration of Mylotarg®	The risk score for each patient is not a piece of data that is systematically present in the source files and requires interpretation and medical expertise to extrapolate from the raw data for each patient.

9. RESEARCH METHODS

A summary of the research methods is provided in Sections 9.1 to 9.11 below, for more details refer to the protocol (**Appendix 2**) and the Statistical Analysis Plan (**Appendix 3**)

9.1. Study design

The study was designed as a multicenter, retrospective, observational study. The study did not impact the treatment of patients.

The target population concerned patients with CD33 positive AML, not previously treated, and for whom treatment with Mylotarg® was initiated between 01 December 2014 and 31 October 2022.

For each patient, data was collected from the date of initiation of treatment with Mylotarg®, up until death or the end of data collection, whichever occurred first. The data collection in the study was planned between 01 January 2022 and 30 November 2022.

9.2. Setting

This study population included patients treated in France with Mylotarg® since 01 December 2014. In addition to the overall population, patients have been divided into 2 cohorts, one

included all patients included in the French ATUc and the second including all patients who received Mylotarg post-ATU.

9.3. Subjects

9.3.1. Inclusion criteria

Patients needed to satisfy the following criteria to be eligible for the study:

1. Patient 15 years of age or older at time of initiation of Mylotarg®.
2. Patient with CD33 positive AML, as determined by the treatment centre at time of diagnosis.
3. Patient who initiated treatment with Mylotarg® between 01 December 2014 and

   31 October 2022.
4. Patient, or his/her legal guardian, who accepts collection of his/her personal clinical and laboratory data.

9.3.2. Non-inclusion criteria

Patients satisfying one of the following criteria were not eligible for the study:

1. Patient previously treated for AML (except for treatment with hydroxyurea).
2. Patient alive at time of inclusion and opposed to inclusion of his/her data or who notified his/her opposition while he/she was alive.
3. Patient deprived of his/her freedom or under conservatorship.
4. Patient who received Mylotarg® as first-line treatment in a clinical trial.

9.4. Variables

9.4.1. Characteristics of patients and of the disease at time of initiation of treatment with Mylotarg®

- Age, weight, height, and sex.
- Overall condition (ECOG performance status).
- Complete blood count (including % blasts).
- Myelogram: % blasts.
- Expression of CD33 antigen (%) (immunophenotyping).

- Cytogenetic analysis +/- FISCH.
- Molecular biology (NPM1, FLT3 [TKD or ITD] and CEBPA mutations, ASXL1, RUNX1, TP53, WT1, MLL [KMT2A], GATA2).
- Classification of the prognostic risk of the patient, according to the interpretation of the raw results made by the investigating physician center according to the ELN classification (2010 or 2017) used at the time of diagnosis.
- Relevant comorbidities present at the time of treatment with Mylotarg®.

9.4.2. Methods of treatment with Mylotarg®

- Dose units and administration regimen (monotherapy, combination, induction, consolidation).
- In cases of combination with chemotherapy: products and administration regimen (induction and consolidations).
- Dates and reasons for discontinuations of treatment with Mylotarg®.

9.4.3. Assessment of effectiveness of Mylotarg®

- Response to treatment variables

Complete response without residual disease (CR MRD-), complete response (CR), complete response with incomplete hematological recovery (CRh), complete response with incomplete platelet recovery (CRp), OS including the causes of death, RFS, and EFS, failure (primary resistance [refractory], death in aplasia, death for another cause), variables to identify prognostic factors of EFS, OS and RFS.

9.5. Data sources and measurement

The data sources and measurements for this study were primarily the data collected from the ATUc and post-ATUc. The participating centers entered this data into the study eCRF. If required, additional data were retrieved from the patients' medical files and entered in the eCRF.

9.6. Bias

No specific methods were used to limit potential bias in the study.

9.7. Study Size

The study sought to collect as much data as possible. The number of patients included was based on the potential number of eligible patients treated with Mylotarg® since December 2014. Actually, 102 patients were included in the ATUc and it was estimated that following the ATUc about 160 patients had been treated with Mylotarg ® as first-line therapy between

July 2018 and the end of planned collection of data. Based on the probability to enroll half of the AML patients treated with Mylotarg® since December 2014, the targeted number of study patients was 130. Under the assumptions of results similar to those observed in the ALFA-0701 study,(4) this sample size should allow the study to assess the effectiveness and safety with the following precision:

- Median EFS of 17.3 months with a precision of about 3.5 months.
- Percentage of expected VOD at 5% with an absolute precision around 4%.

For the EFS, 130 patients for 104 events would allow for a two-sided 95% CI with a range of 6.8 months (precision around 3.5 months), if median survival was 17.3 months with an exponential distribution and percentage of censure at 20%.

For the percentage of VOD, 130 patients would allow for a two-sided 95% CI (Clopper-Pearson exact method) with a range of 7.5% (precision around 4%) when the percentage was 5%. For other scenarios, see **Table 1**.

Table 1. Various scenarios for the estimation of the sample size required.

Sample size	Two-sided 95% confidence interval	
	Median of expected EFS of 17.3 months and 20% censure rate	**% of expected veno-occlusive disease of 5%**
75	[13.6; 22.7]	[0.1%; 9.9%]
100	[14.1; 21.8]	[0.7%; 9.3%]
125	[14.4; 21.3]	[1.2%; 8.8%]
130	[14.4; 21.2]	[1.3%; 8.7%]
150	[14.6; 20.9]	[2.1%; 9.8%]
200	[14.9; 20.3]	[2.0%; 8.0%]
250	[15.1; 20.0]	[2.3%; 7.7%]
300	[15.3; 19.7]	[2.5%; 7.5%]

9.8. Data transformation

Detailed methodology for data transformations, particularly complex transformations (e.g., many raw variables used to derive an analytic variable), are documented in the statistical analysis plan (SAP), which is dated, filed, and maintained by the sponsor (Appendix 4).

Data were collected electronically by means of the Cleanweb software (Telemedicine SA) and stored in a secure health data storage server. Only staff dedicated to the study had access to the database.

A data management plan was developed to describe all data management activities to be conducted during the study. This document includes the data validation plan which describes

all tests of consistency and lists of inconsistencies observed during the study, as well as messages requesting correction sent to participating doctors.

The use of an e-CRF made it possible to deactivate not applicable fields and to immediately perform pre-tests at data entry (tests of verification of format and limits of data). These reduced the number of data clarifications that needed to be requested.

The data manager periodically triggered tests of consistency planned on the pages recorded. The inconsistencies will be recorded online by participating doctors.

Once all patient information had been provided, all queries for clarification had been resolved, and all e-CRFs have been signed by participating doctors, the sponsor locked the database for final statistical analysis of the study.

All decisions on data management taken during the period of data collection were documented in the data management issue log.

9.9. Statistical methods

Further details concerning the statistical methods can be found in the SAP in **Appendix 3**.

9.9.1. Main summary measures

Descriptive statistics for parameters of interest are provided for the overall population and by cohorts (ATUc and post-ATUc) l. Unless otherwise specified, the following conventions were applied to all analyses:

- Mean, standard deviation (SD), median, first and third quartiles (Q1 and Q3) values are formatted to 1 more decimal place than the measured value. Minimum and maximum values were presented with the same number of decimal places as the measured value.
- Percentages are rounded to 1 decimal place. Number and percentage values are presented as xx (xx.x%).
- P-values are rounded to 4 decimal places. P-values that round to 0.0000 are presented as ‘<0.0001’ and p-values that round to 1.000 are presented as ‘>0.9999’.

Summary statistics are presented for continuous variables, by way of n, n missing (if any), mean, standard deviation (SD), median, first and third quartiles (Q1 and Q3), minimum and maximum. Qualitative/categorical parameters are presented as numbers and percentages of each modality and numbers of missing and non-missing observations. Unless otherwise stated, the percentages are calculated for the modalities provided, excluding missing data.

9.9.2. Main statistical methods

- **Analysis of time-to-event data**

Kaplan-Meier estimates (product-limit estimates) are presented together with a summary of associated statistics including the median survival time with 2-sided 95% CIs. In particular, the survival rate at 3, 6, 9 months and then every year from 1 to 7 years are estimated with

corresponding 2-sided 95% CIs. The CIs for the median were calculated according to Brookmeyer and Crowley (6) and the CIs for the survival function estimates at the time points defined above were derived using the log-log transformation according to Kalbfleisch and Prentice (7) with back transformation to a CI on the untransformed scale. The estimates of standard error were computed using Greenwood's formula. Frequency (numbers and percentages) of participants with each event type and censoring reasons are presented. The follow-up durations were also assessed using the Kaplan-Meier method, reversing the censoring and event indicators.

- **Identification of prognostic factors for OS, RFS, and EFS**

Prognostic factors were identified using Cox proportional hazard models. Initially, univariate Cox proportional hazard models were created for the potential prognostic factors. Variables that significantly impacted the outcome of interest (OS, RFS, ESF) at the 20% level were put forward into a multivariate model. A backward selection was used to remove factors from the multivariate model that were not significant at the 5% level. The covariate with the highest p-value was removed in turn until all factors had a p-value less than 0.05. Summary tables and forest plots are present.

9.9.3. Missing values

See Section 6 of the SAP (**Appendix 3**).

9.9.4. Sensitivity analyses

None.

9.9.5. Amendments to the statistical analysis plan

See Section 1 of the SAP (**Appendix 3**).

9.10. Quality control

The participating doctors were responsible for collecting and reporting of all clinical, safety, and laboratory data entered in the e-CRF and/or other forms of data collection (source documents). They were to ensure that all data were accurate, authentic, attributable to the patient, complete, consistent, legible, contemporaneous, and available if needed.

To assume the quality control of data collected, a Monitoring Data Quality Oversight Plan (MDQOP) was developed by Pfizer (**Appendix 5**).

The eCRFs included programmable edits to obtain immediate feedback if data were missing, out of range, illogical or potentially erroneous. Concurrent manual data reviews were performed according to parameters dictated by the plan. Ad hoc queries were generated using the EDC system and followed until resolution. All corrections of entries on the eCRFs needed to be explained (reason for change) and signed off (electronic signatures). Corrections of

entries were automatically recorded by the system (including date of change, identity of user changing data, old and new value, and reason for change).

Data quality was enhanced through a series of programmed data quality checks that automatically detected out of range or anomalous data.

9.11. Protection of human subjects

9.11.1. Subject information and consent

Due to the retrospective nature of the study. Informed consent depended on whether the patients were alive or not when the study was conducted.

If the patient was alive, the investigator needed to ensure that the patient or their legally representative was fully informed about the nature and objectives of the study, the sharing of data relating to the study, and the possible risks associated with the processing of the patient's personal data. This information was provided to the patients accompanied by a non-opposition letter.

With regards to patients that had died and in accordance with the application to the decision n° 2018-155 article 2.5 dated 3rd May 2018, personal data could be collected for research purpose as long as the investigator knew that the patient had died, and that the patient did not object in writing during his lifetime to the collection of their personal data.

9.11.2. Independent Ethics Committee (IEC)/Institutional Review Board (IRB)

The final protocol, any amendments, and informed consent documentation were sent for information to an IRB.

9.11.3. Ethical conduct of the study

The study was conducted in accordance with legal and regulatory requirements, as well as with scientific purpose, value and rigor and follow generally accepted research practices described in the following guidance documents:

- Guidelines for Good Pharmacoepidemiology Practices (GPP). Public Policy Committee, International Society of Pharmacoepidemiology. Pharmacoepidemiology and Drug Safety 2015; 25:2-10. https://onlinelibrary.wiley.com/doi/full/10.1002/pds.3891.
- European Medicines Agency (EMA) European Network of Centers for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology http://www.encepp.eu/standards_and_guidances/methodologicalGuide.shtml.

10. RESULTS

10.1. Participants

10.1.1. Patient enrolment

The FAS, all enrolled patients that received at least one injection of Mylotarg®, comprised 113 patients enrolled in 9 centers (see **Figure 1**). Among these, 62/113 (54.9%) were included in the ATUc and 51/113 (45.1%) in the Post-ATUc.

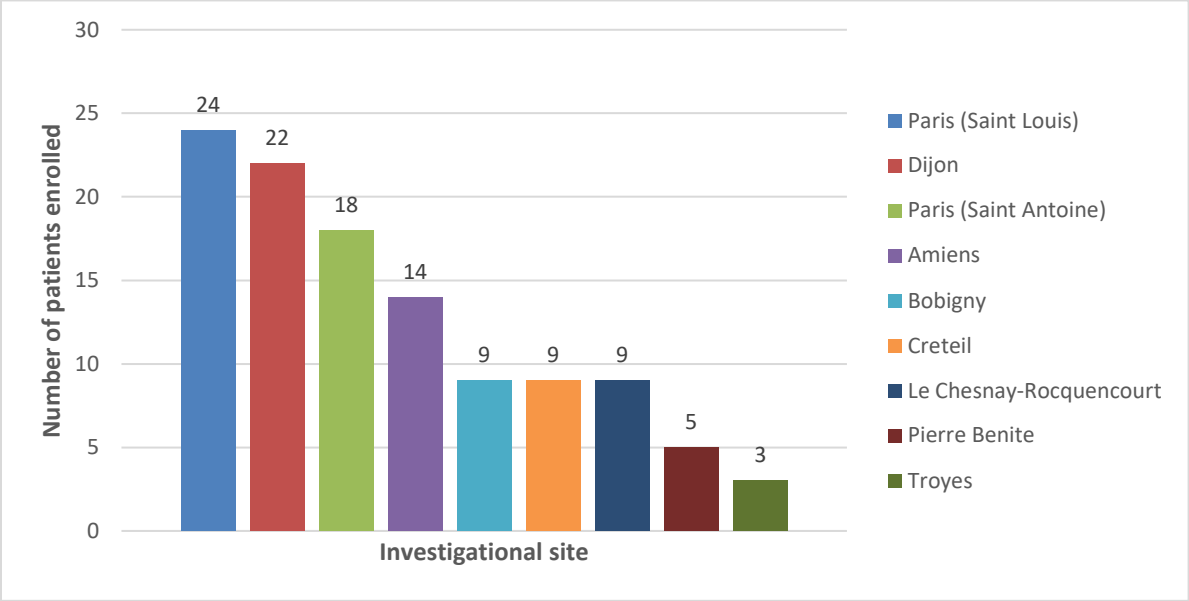


Figure 1. Patients enrolled at the investigational sites: FAS (n=113)

(Source: Table 14.1.1 TFLs_v1.0_28NOV2023)

10.1.2. Patients' baseline demographic and clinical characteristics

The study enrolled 62 males (54.9%) and 51 females (45.1%), with the ratio of males to females enrolled of 1.22. Mylotarg® was initiated at a median age of 63.0 years (Q1-Q3: 55.0-68.0). Most of the 113 patients, 72/88 patients (81.8%; missing data [n=25]) had an ECOG PS of 0-1. Further baseline demographic and clinical data are shown in **Table 2**.

Table 2. Baseline demographic and clinical data: FAS (n=113)

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Gender, n (%)			
n	62	51	113
Female	30 (48.4)	21 (41.2)	51 (45.1)
Male	32 (51.6)	30 (58.8)	62 (54.9)
Missing data	0	0	0
Age at Mylotarg® initiation (years)			
n	62	51	113
Mean (SD)	64.6 (9.5)	55.2 (15.7)	60.4 (13.5)
Median	64.0	60.0	63.0

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Q1-Q3	57.0-71.0	46.0-66.0	55.0-68.0
Range	44.0-91.0	19.0-86.0	19.0-91.0
Missing data	0	0	0
Age categories at Mylotarg® initiation, n (%)			
n	62	51	113
<50	1 (1.6)	16 (31.4)	17 (15.0)
≥50	61 (98.4)	35 (68.6)	96 (85.0)
<55	8 (12.9)	18 (35.3)	26 (23.0)
≥55	54 (87.1)	33 (64.7)	87 (77.0)
<60	22 (35.5)	24 (47.1)	46 (40.7)
≥60	40 (64.5)	27 (52.9)	67 (59.3)
<65	32 (51.6)	34 (66.7)	66 (58.4)
≥65	30 (48.4)	17 (33.3)	47 (41.6)
Height (cm)			
n	62	51	113
Mean (SD)	168.5 (8.2)	171.2 (10.0)	169.7 (9.1)
Median	168.0	170.0	170.0
Q1-Q3	163.0-175.0	164.0-178.0	163.0-176.0
Range	151.0-185.0	155.0-196.0	151.0-196.0
Missing data	0	0	0
Weight (kg)			
n	61	50	111
Mean (SD)	76.2 (17.4)	77.2 (22.1)	76.7 (19.6)
Median	75.0	74.5	75.0
Q1-Q3	63.0-85.0	65.0-81.0	64.0 - 84.0
Range	47.0-126.0	38.0-167.0	38.0-167.0
Missing data	1	1	2
Body surface area (m^2)*			
n	61	50	111
Mean (SD)	1.88 (0.22)	1.90 (0.28)	1.89 (0.25)
Median	1.89	1.89	1.89
Q1-Q3	1.70-2.04	1.75-2.02	1.71-2.03
Range	1.42-2.37	1.30-2.78	1.30-2.78
Missing data	1	1	2
ECOG PS, n (%)			
n	50	38	88
0-1	38 (76.0)	34 (89.5)	72 (81.8)
≥2	12 (24.0)	4 (10.5)	16 (18.2)
Missing data	12	13	25

AML, acute myeloid leukemia; ATU; authorization for temporary use, ECOG, Eastern Cooperative Oncology Group; PS, performance status; Q, quartile; SD, standard deviation.
*Body surface area was calculated as follows: (weight in kg x 0.425) x (height in cm x 0.725) x 71.84/10000
Source: Table 14.2.1 TFLs_v1.0_28NOV2023

10.1.3. Baseline acute myeloid leukemia (AML)-related characteristics

Concerning the baseline AML-related data, the median age at AML diagnosis was 63.0 years (Q1-Q3: 55.0-68.0). Most patients, 89 (81.7%) had CD33 positive (≥70% of their myeloblasts). According to the ELN2010 risk classification (by the scientific committee), the risk was Favorable in 51 patients (45.9%), Intermediate I in 24 (21.6%), Intermediate II in 20 (18.0%), Adverse in 7 (6.3%), and not applicable in 9 (8.1%): data was missing for 2 patients. Further details, including the risk classifications, by the scientific review committee and by the investigators, according to the ELN 2010 and 2017 are shown in **Table 3**. According to the

French-American-British AML classification: 3 (3.0%) patients were classified as M0 (with undifferentiated AML), 24 (24.0%) as M1 (AML with minimal maturation), 29 (29.0%) as M2 (AML with maturation), 16 (16.0%) as M4 (acute myelomonocytic leukemia), 13 (13.0%) as M4 eos (acute myelomonocytic leukemia with eosinophilia), and 15 (15.0%) as M5 (acute monocytic leukemia).

Table 3. Baseline AML-related data: FAS (n=113)

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Age at AML diagnosis (years)			
n	57	51	108
Mean (SD)	64.8 (9.8)	55.2 (15.7)	60.3 (13.7)
Median	64.0	60.0	63.0
Q1-Q3	57.0-71.0	46.0-66.0	55.0-68.0
Range	44.0-91.0	19.0-86.0	19.0-91.0
Missing data	5	0	5
Risk classification ELN 2010 by the scientific committee, n (%)*			
n	60	51	111
Favorable	26 (43.3)	25 (49.0)	51 (45.9)
Intermediate I	12 (20.0)	12 (23.5)	24 (21.6)
Intermediate II	13 (21.7)	7 (13.7)	20 (18.0)
Adverse	3 (5.0)	4 (7.8)	7 (6.3)
Not applicable	6 (10.0)	3 (5.9)	9 (8.1)
Missing data	2	0	2
Risk classification ELN 2017 by the scientific committee, n (%)*			
n	51	47	98
Favorable	33 (64.7)	31 (66.0)	64 (65.3)
Intermediate	6 (11.8)	4 (8.5)	10 (10.2)
Adverse	5 (9.8)	10 (21.3)	15 (15.3)
Not applicable	7 (13.7)	2 (4.3)	9 (9.2)
Missing data	11	4	15
Risk classification ELN 2010 by the investigators, , n (%)			
n	31	0	31
Favorable	7 (22.6)	0 (0.0)	7 (22.6)
Intermediate I	21 (67.7)	0 (0.0)	21 (67.7)
Intermediate II	2 (6.5)	0 (0.0)	2 (6.5)
Adverse	1 (3.2)	0 (0.0)	1 (3.2)
Not applicable	31	51	82
Risk classification ELN 2017 by the investigators, n (%)			
n	20	39	59
Favorable	10 (50.0)	20 (51.3)	30 (50.8)
Intermediate	8 (40.0)	12 (30.8)	20 (33.9)
Adverse	2 (10.0)	7 (17.9)	9 (15.3)
Not applicable	42	12	54
Cytogenetic classification by the scientific committee, n (%)			
n	62	51	113
Favorable	12 (19.4)	20 (39.2)	32 (28.3)
Intermediate	36 (58.1)	24 (47.1)	60 (53.1)
Adverse	3 (4.8)	3 (5.9)	6 (5.3)
Not applicable	11 (17.7)	4 (7.8)	15 (13.3)
Missing data	0	0	0
WBC count (10^9/L)			

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
n	62	51	113
Mean (SD)	34.2 (53.7)	44.1 (71.3)	38.6 (62.2)
Median	7.8	13.3	9.3
Q1-Q3	2.0-37.4	3.9-46.8	2.3-44.1
Range	0.37-261.4	0.6-332.7	0.37-332.7
Missing data	0	0	0
CD33 expression (positivity), n (%)			
n	61	48	109
<30	3 (4.9)	0 (0.0)	3 (2.8)
≥30	58 (95.1)	48 (100)	106 (97.3)
<70	10 (16.4)	10 (20.8)	20 (18.3)
≥70	51 (83.6)	38 (79.2)	89 (81.7)
Missing data	1	3	4
FAB classification			
n	57	43	100
M0 (undifferentiated AML)	1 (1.8)	2 (4.7)	3 (3.0)
M1 (AML with minimal maturation)	14 (24.6)	10 (23.3)	24 (24.0)
M2 (AML with maturation)	15 (26.3)	14 (32.6)	29 (29.0)
M4 (acute myelomonocytic leukemia)	10 (17.5)	6 (14.0)	16 (16.0)
M4 eos (acute myelomonocytic leukemia with eosinophilia)	4 (7.0)	9 (20.9)	13 (13.0)
M5 (acute monocytic leukemia)	13 (22.8)	2 (4.7)	15 (15.0)
Missing data	5	8	13

AML, acute myeloid leukemia; ATU; authorization for temporary use; ECOG, Eastern Cooperative Oncology Group; FAB classification, French-American-British classification; PS, performance status; Q, quartile; SD, standard deviation.
*Risk classifications were performed in patients with the required biological and molecular data available at the site.
Source: Table 14.2.1 TFLs_v1.0_28NOV2023

10.1.4. Patients' medical history at baseline

At baseline, 107/113 patients (94.7%) had at least one medical history. The medical histories that occurred in ≥10% of patients were high blood pressure in 36/113 (31.9%), hypercholesterolemia in 21/113 (18.6%), malignant tumor in 21/113 (18.6%), type 2 diabetes in 16/113 (14.2%), smoking in 36/113 (31.9%), family history of blood disease in 14/113 (12.4%), and others in 96/113 (85.0%). See **Table 4** for more details.

Table 4. Patient medical history at baseline: FAS (n=113)

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Patients with ≥1 medical history, n (%)			
n	62	51	113
No	2 (3.2)	4 (7.8)	6 (5.3)
Yes	60 (96.8)	47 (92.2)	107 (94.7)
Missing data	0	0	0
History of high blood pressure, n (%)			
n	62	51	113
No	36 (58.1)	41 (80.4)	77 (68.1)
Yes	26 (41.9)	10 (19.6)	36 (31.9)
Resolved	1 (3.8)	0 (0.0)	1 (2.8)
Ongoing	25 (96.2)	10 (100)	35 (97.2)
Missing data	0	0	0
History of hypercholesterolemia, n (%)			

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
n	62	51	113
No	46 (74.2)	46 (90.2)	92 (81.4)
Yes	16 (25.8)	5 (9.8)	21 (18.6)
Resolved	1 (6.3)	0 (0.0)	1 (4.8)
Ongoing	15 (93.8)	5 (100)	20 (95.2)
Missing data	0	0	0
History of heart failure, n (%)			
n	62	51	113
No	62 (100)	46 (90.2)	108 (95.6)
Yes	0 (0.0)	5 (9.8)	5 (4.4)
Ongoing		5 (100)	5 (100)
Missing data		0	0
History of coronary heart disease, n (%)			
n	62	51	113
No	56 (90.3)	51 (100)	107 (94.7)
Yes	6 (9.7)	0 (0.0)	6 (5.3)
Resolved	2 (33.3)		2 (33.3)
Ongoing	4 (66.7)		4 (66.7)
Missing data	0		0
History of myocardial infarction (within the prior 3 months), n (%)			
n	62	51	113
No	62 (100)	50 (98.0)	112 (99.1)
Yes	0 (0.0)	1 (2.0)	1 (0.9)
Resolved		1 (100)	1 (100)
Missing data		0	0
History of pulmonary embolism, n (%)			
n	62	51	113
No	58 (93.5)	50 (98.0)	108 (95.6)
Yes	4 (6.5)	1 (2.0)	5 (4.4)
Resolved	3 (75.0)	1 (100)	4 (80.0)
Ongoing	1 (25.0)	0 (0.0)	1 (20.0)
Missing data	0	0	0
History of deep thrombophlebitis, n (%)			
n	62	51	113
No	58 (93.5)	51 (100)	109 (96.5)
Yes	4 (6.5)	0 (0.0)	4 (3.5)
Resolved	3 (75.0)		3 (75.0)
Ongoing	1 (25.0)		1 (25.0)
Missing data	0		0
History of malignant tumor, n (%)			
n	62	51	113
No	49 (79.0)	43 (84.3)	92 (81.4)
Yes	13 (21.0)	8 (15.7)	21 (18.6)
Resolved	9 (69.2)	5 (62.5)	14 (66.7)
Ongoing	4 (30.8)	3 (37.5)	7 (33.3)
Missing data	0	0	0
History of type 2 diabetes, n (%)			
n	62	51	113
No	51 (82.3)	46 (90.2)	97 (85.8)
Yes	11 (17.7)	5 (9.8)	16 (14.2)
Ongoing	11 (100)	5 (100)	16 (100)
Missing data	0	0	0
History of chronic lung disease, n (%)			
n	62	51	113
No	57 (91.9)	49 (96.1)	106 (93.8)
Yes	5 (8.1)	2 (3.9)	7 (6.2)

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Ongoing	5 (100)	2 (100)	7 (100)
Missing data	0	0	0
History of moderate hepatic impairment (Child Pugh class B), n (%)			
n	62	51	113
No	61 (98.4)	51 (100)	112 (99.1)
Yes	1 (1.6)	0 (0.0)	1 (0.9)
Ongoing	1 (100)		1 (100)
Missing data	0		0
History of severe renal impairment (creatinine clearance <30 mL/min), n (%)			
n	62	51	113
No	60 (96.8)	51 (100)	111 (98.2)
Yes	2 (3.2)	0 (0.0)	2 (1.8)
Ongoing	2 (100)		2 (100)
Missing data	0		0
History of alcoholism, n (%)			
n	62	51	113
No	59 (95.2)	48 (94.1)	107 (94.7)
Yes	3 (4.8)	3 (5.9)	6 (5.3)
Resolved	0 (0.0)	1 (33.3)	1 (16.7)
Ongoing	3 (100)	2 (66.7)	5 (83.3)
Missing data	0	0	0
History of smoking, n (%)			
n	62	51	113
No	43 (69.4)	34 (66.7)	77 (68.1)
Yes	19 (30.6)	17 (33.3)	36 (31.9)
Resolved	12 (63.2)	11 (64.7)	23 (63.9)
Ongoing	7 (36.8)	6 (35.3)	13 (36.1)
Missing data	0	0	0
Family history of blood disease, n (%)			
n	62	51	113
No	57 (91.9)	42 (82.4)	99 (87.6)
Yes	5 (8.1)	9 (17.6)	14 (12.4)
Missing data	0	0	0
Other medical histories, n (%)			
n	62	51	113
No	10 (16.1)	7 (13.7)	17 (15.0)
Yes	52 (83.9)	44 (86.3)	96 (85.0)
Missing data	0	0	0

Source: Table 14.3.1 TFLs_v1.0_28NOV2023

10.1.5. Patients' biological and genetic characteristics at AML diagnosis

Among the 113 patients in the FAS, the median number of blasts was 22.5% (95% CI: 6.2%-45.9%) and the median number of CD33 antigens was 93.0% (95% CI: 76.0%-99.0%). Patients harboured the following mutations: NPM1 in 41/109 patients (37.6%; missing data [n=4]), FLT3-TKD in 6/64 (9.4%; missing data [n=49]), FLT3-ITD in 22/106 (20.8%; missing data [n=7]), and CEBPA in 5/77 (6.5%; missing data [n=36]). See **Table 5** for more details.

Table 5. Patient biological and genetic data at AML diagnosis: FAS (n=113)

Baseline characteristics	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Blasts (%)			
n	52	40	92
Mean (SD)	26.0 (29.1)	37.9 (30.2)	31.2 (30.0)
Median	12.4	28.7	22.5
Q1-Q3	4.0-42.2	11.5-61.5	6.2-45.9
Range	0.0-98.0	0.0- 96.0	0.0-98.0
Missing data	10	11	21
CD33 antigen (%)			
n	61	48	109
Mean (SD)	85.0 (23.7)	81.2 (18.9)	83.3 (21.7)
Median	97.0	84.5	93.0
Q1-Q3	85.0-99.0	71.0- 98.0	76.0-99.0
Range	1.00-100.0	34.6-100.0	1.0-100.0
Missing data	1	3	4
NPM1 mutation, n (%)			
n	58	51	109
Absent	31 (53.4)	37 (72.5)	68 (62.4)
Present	27 (46.6)	14 (27.5)	41 (37.6)
Missing data	4	0	4
FLT3-TKD mutation, n (%)			
n	25	39	64
Absent	24 (96.0)	34 (87.2)	58 (90.6)
Present	1 (4.0)	5 (12.8)	6 (9.4)
Missing data	37	12	49
FLT3-ITD mutation, n (%)			
n	56	50	106
Absent	46 (82.1)	38 (76.0)	84 (79.2)
Present	10 (17.9)	12 (24.0)	22 (20.8)
Missing data	6	1	7
CEBPA mutation, n (%)			
n	37	40	77
Absent	34 (91.9)	38 (95.0)	72 (93.5)
Present	3 (8.1)	2 (5.0)	5 (6.5)
Missing data	25	11	36

Q, quartile; SD, standard deviation.
Source: Table 14.4.1 TFLs_v1.0_28NOV2023

10.2. Main results

10.2.1. Modalities of Mylotarg® prescription

In the study, the data concerning the modalities of Mylotarg® prescribed as induction and consolidation courses were collected. These data are shown in **Figure 2** and described in the following sections.

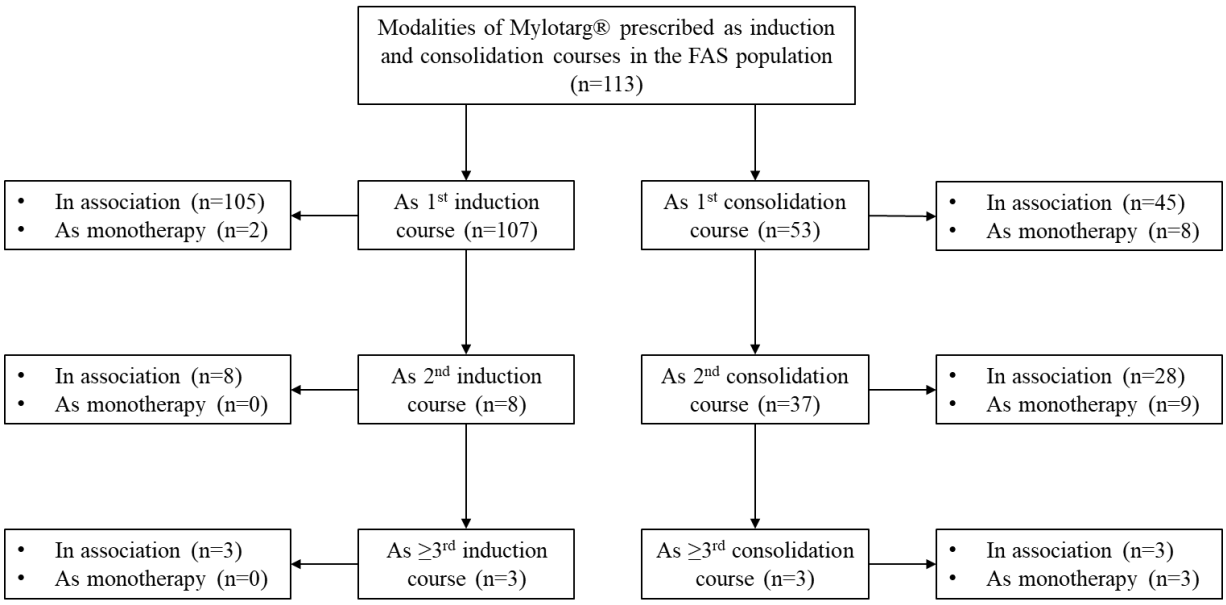


Figure 2. Modalities of Mylotarg® prescription

10.2.1.1. Mylotarg® as first induction course

During the first induction course, most patients in the FAS (n=113), 105/107 (94.7%; missing data [n=6]) received Mylotarg® in association: most frequently, 63/105 patients (60.0%), associated with cytarabine and daunorubicine. The median cumulative dose of Mylotarg® was 15.0 mg (Q1-Q3: 13.8-15.0). The median number of doses was 3.0 (Q1-Q3: 3.0-3.0): most frequently administered on D1, D4, and D7 (in 84/107 patients [78.5%]). See **Table 6** for details.

Table 6. Modalities of Mylotarg® prescribed as first induction course, FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as first induction course, n (%)			
n	62	51	113
No	2 (3.2)	4 (7.8)	6 (5.3)
Yes	60 (96.8)	47 (92.2)	107 (94.7)
Missing data	0	0	0
First induction Mylotarg® regimen, n (%)			
n	60	47	107
In association	58 (96.7)	47 (100)	105 (98.1)
Monotherapy	2 (3.3)	0 (0.0)	2 (1.9)
Missing data	2	4	6
First induction associations with Mylotarg®, n (%)			
n	58	47	105
Mylotarg® + cytarabine (bolus)	2 (3.4)	1 (2.1)	3 (2.9)
Mylotarg® + cytarabine (IV with syringe pump)	7 (12.1)	2 (4.3)	9 (8.6)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® + cytarabine (IV with syringe pump) + cytarabine (bolus) + daunorubicine + other	2 (3.4)	0 (0.0)	2 (1.9)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine	27 (46.6)	36 (76.6)	63 (60.0)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine + other	6 (10.3)	3 (6.4)	9 (8.6)
Mylotarg® + cytarabine (IV with syringe pump) + idarubicine	2 (3.4)	3 (6.4)	5 (4.8)
Mylotarg® + cytarabine (IV with syringe pump) + mitoxantrone	1 (1.7)	0 (0.0)	1 (1.0)
Mylotarg® + cytarabine (low dose)	10 (17.2)	1 (2.1)	11 (10.5)
Mylotarg® + others	1 (1.7)	1 (2.1)	2 (1.9)
Missing data	0	0	0
First induction Mylotarg® cumulative dose (mg)			
n	54	41	95
Mean (SD)	13.83 (3.06)	12.86 (3.35)	13.41 (3.21)
Median	15.00	15.00	15.00
Q1-Q3	15.00-15.00	10.00-15.00	13.80-15.00
Range	4.80-18.00	5.00-15.00	4.80-18.00
Missing data	6	6	12
Number of first induction Mylotarg® doses prescribed			
n	60	47	107
Mean (SD)	2.88 (0.45)	2.70 (0.59)	2.80 (0.52)
Median	3.00	3.00	3.00
Q1-Q3	3.00-3.00	3.00-3.00	3.00-3.00
Range	1.00-3.00	1.00-3.00	1.00-3.00
Missing data	0	0	0
First induction Mylotarg® administration scheme, n (%)			
n	60	47	107
D1	3 (5.0)	2 (4.3)	5 (4.7)
D3	0 (0.0)	1 (2.1)	1 (0.9)
D1 + D4	1 (1.7)	7 (14.9)	8 (7.5)
D1 + D4 + D7	50 (83.3)	34 (72.3)	84 (78.5)
D1 + D4 + D8	1 (1.7)	0 (0.0)	1 (0.9)
D1 + D5 + D7	1 (1.7)	0 (0.0)	1 (0.9)
D1 + D5 + D8	1 (1.7)	0 (0.0)	1 (0.9)
D2 + D5 + D8	0 (0.0)	1 (2.1)	1 (0.9)
D2 + D5 + D9	1 (1.7)	0 (0.0)	1 (0.9)
D3 + D6 + D9	1 (1.7)	1 (2.1)	2 (1.9)
D5 + D8 + D12	1 (1.7)	0 (0.0)	1 (0.9)
D7 + D10	0 (0.0)	1 (2.1)	1 (0.9)
Missing data	0	0	0
Was Mylotarg® administered as expected?, n (%)			
n	58	47	105
No	3 (5.2)	3 (6.4)	6 (5.7)
Yes	55 (94.8)	44 (93.6)	99 (94.3)
Missing data	0	0	0
Reason for dose change/discontinuation of first induction Mylotarg®, n (%)			
n	3	3	6
Other	1 (33.3)	0 (0.0)	1 (16.7)
Adverse event	2 (66.7)	3 (100)	5 (83.3)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Missing data	0	0	0

D, day; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.1.2. Mylotarg® as second induction course

In the FAS (n=113), 8/113 patients (7.1%) were administered Mylotarg® in a second induction course. All 8 (100%) were prescribed Mylotarg® in association: 4/8 patients (50.0%) associated with a low dose of cytarabine. The median cumulative dose of Mylotarg® was 12.5 mg (Q1-Q3: 5.0-15.0). The median number of doses was 2.5 (Q1-Q3: 1.0-3.0): most frequently administered on D1, D4, and D7 (in 4/8 patients [50.0%]). See **Table 7** for details.

Table 7. Modalities of Mylotarg® prescribed as second induction course: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as second induction course, n (%)			
n	62	51	113
No	57 (91.9)	48 (94.1)	105 (92.9)
Yes	5 (8.1)	3 (5.9)	8 (7.1)
Missing data	0	0	0
Second induction Mylotarg® regimen, n (%)			
n	5	3	8
In association	5 (100)	3 (100)	8 (100)
Missing data	0	0	0
Second induction associations with Mylotarg®, n (%)			
n	5	3	8
Mylotarg® + cytarabine (IV with syringe pump)	1 (20.0)	1 (33.3)	2 (25.0)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine	0 (0.0)	1 (33.3)	1 (12.5)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine + other	0 (0.0)	1 (33.3)	1 (12.5)
Mylotarg® + cytarabine (low dose)	4 (80.0)	0 (0.0)	4 (50.0)
Missing data	0	0	0
Second induction Mylotarg® cumulative dose (mg)			
n	5	3	8
Mean (SD)	9.96 (5.05)	11.67 (5.77)	10.60 (4.99)
Median	10.00	15.00	12.50
Q1-Q3	5.00-15.00	5.00-15.00	5.00-15.00
Range	4.80-15.00	5.00-15.00	4.80-15.00
Missing data	0	0	0
Number of second induction Mylotarg® doses prescribed			
n	5	3	8
Mean (SD)	2.00 (1.00)	2.33 (1.15)	2.13 (0.99)
Median	2.00	3.00	2.50
Q1-Q3	1.00-3.00	1.00-3.00	1.00-3.00
Range	1.00-3.00	1.00-3.00	1.00-3.00
Missing data	0	0	0

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Second induction Mylotarg® administration scheme, n (%)			
n	5	3	8
D1	2 (40.0)	1 (33.3)	3 (37.5)
D1 + D4	1 (20.0)	0 (0.0)	1 (12.5)
D1 + D4 + D7	2 (40.0)	2 (66.7)	4 (50.0)
Missing data	0	0	0
Was Mylotarg® administered as expected?, n (%)			
n	5	3	8
Yes	5 (100)	3 (100)	8 (100)
Missing data	0	0	0
Reason for dose change/discontinuation of second induction Mylotarg®, n (%)			
n	0	0	0
Missing data	5	3	8

D, day; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.1.3. Mylotarg® as ≥3 induction course

In the FAS (n=113), 3/113 patients (2.7%) were administered Mylotarg® in a ≥3 induction course: 1 patient received only a 3rd induction course and 2 patients received 3rd and 4th induction courses. In all the 5 ≥3rd induction courses (100%), Mylotarg® was prescribed Mylotarg® in association: in 4/5 courses (80.0%) associated with a low dose of cytarabine and in 1/5 (20.0%) associated with cytarabine and daunorubicine. The median cumulative dose of Mylotarg® was 10.0 mg (Q1-Q3: 9.0-15.0). The median number of doses was 1.0 (Q1-Q3: 1.0-1.0): most frequently administered on D1, D4, and D7 (in 4 of the 5 ≥3rd induction courses [80.0%]). See **Table 8** for details.

Table 8. Modalities of Mylotarg® prescribed as ≥3 induction course: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as ≥3 induction course, n (%)			
n	62	51	113
No	60 (96.8)	50 (98.0)	110 (97.3)
Yes	2 (3.2)	1 (2.0)	3 (2.7)
Missing data	0	0	0
≥3 induction Mylotarg® regimen, n (%)			
n	2	1	3
In association	2 (100)	1 (100)	3 (100)
Missing data	0	0	0
≥3 induction associations with Mylotarg®, n (%)			
n	4	1	5
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine	0 (0.0)	1 (100)	1 (20.0)
Mylotarg® + cytarabine (low dose)	4 (100)	0 (0.0)	4 (80.0)
Missing data	0	0	0
≥3 induction Mylotarg® cumulative dose (mg)			
n	2	1	3
Mean (SD)	9.50 (0.71)	15.00 (NA)	11.33 (3.21)
Median	9.50	15.00	10.00
Q1-Q3	9.00-10.00	15.00-15.00	9.00-15.00

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Range	9.00-10.00	15.00-15.00	9.00-15.00
Missing data	0	0	0
Number of ≥3 induction Mylotarg® doses prescribed			
n	4	1	5
Mean (SD)	1.00 (0.00)	3.00 (NA)	1.40 (0.89)
Median	1.00	3.00	1.00
Q1-Q3	1.00-1.00	3.00-3.00	1.00-1.00
Range	1.00-1.00	3.00-3.00	1.00-3.00
Missing data	0	0	0
≥3 induction Mylotarg® administration scheme, n (%)			
n	4	1	5
D1	4 (100)	0 (0.0)	4 (80.0)
D1 + D4 + D7	0 (0.0)	1 (100)	1 (20.0)
Missing data	0	0	0
Was Mylotarg® administered as expected? , n (%)			
n	4	1	5
No	2 (50.0)	0 (0.0)	2 (40.0)
Yes	2 (50.0)	1 (100)	3 (60.0)
Missing data	0	0	0
Reason for dose change/discontinuation of ≥3 induction Mylotarg®, n (%)			
n	2	0	2
Doctor's decision	2 (100)	0 (0.0)	2 (100)
Missing data	2	1	3

D, day; IV, intravenous; NA, not applicable; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.1.4. Mylotarg® as first consolidation course

In the FAS (n=113), 53/113 patients (46.9%) were administered Mylotarg® in a first consolidation course. Among the 53 patients, 45/53 (84.9%) were prescribed Mylotarg® in association: 26/45 patients (57.8%) associated with a cytarabine and daunorubicine. The median cumulative dose of Mylotarg® was 5.0 mg (Q1-Q3: 5.0-5.0). The median number of doses was 1.0 (Q1-Q3: 1.0-1.0): most frequently administered on D1 (in 50/53 patients [94.3%]). See **Table 9** for details.

Table 9. Modalities of Mylotarg® prescribed as first consolidation course: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as first consolidation course, n (%)			
n	62	51	113
No	26 (41.9)	34 (66.7)	60 (53.1)
Yes	36 (58.1)	17 (33.3)	53 (46.9)
Missing data	0	0	0
First consolidation Mylotarg® regimen, n (%)			
n	36	17	53
In association	29 (80.6)	16 (94.1)	45 (84.9)
Monotherapy	7 (19.4)	1 (5.9)	8 (15.1)
Missing data	0	0	0
First consolidation associations with Mylotarg®, n (%)			

n	29	16	45
Mylotarg® + aracytine	1 (3.4)	0 (0.00%)	1 (2.2)
Mylotarg® + cytarabine (bolus)	1 (3.4)	1 (6.3)	2 (4.4)
Mylotarg® + cytarabine (IV with syringe pump)	4 (13.8)	8 (50.0)	12 (26.7)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine	20 (69.0)	6 (37.5)	26 (57.8)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine + other	3 (10.3)	1 (6.3)	4 (8.9)
Missing data	0	0	0
First consolidation Mylotarg® cumulative dose (mg)			
n	32	14	46
Mean (SD)	4.96 (0.11)	4.92 (0.22)	4.95 (0.15)
Median	5.00	5.00	5.00
Q1-Q3	5.00-5.00	5.00-5.00	5.00-5.00
Range	4.60-5.00	4.20-5.00	4.20-5.00
Missing data	4	3	7
Number of first consolidation Mylotarg® doses prescribed			
n	36	17	53
Mean (SD)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)
Median	1.00	1.00	1.00
Q1-Q3	1.00-1.00	1.00-1.00	1.00-1.00
Range	1.00-1.00	1.00-1.00	1.00-1.00
Missing data	0	0	0
First consolidation Mylotarg® administration scheme, n (%)			
n	36	17	53
D1	34 (94.4)	16 (94.1)	50 (94.3)
D2	1 (2.8)	0 (0.0)	1 (1.9)
D4	0 (0.0)	1 (5.9)	1 (1.9)
D5	1 (2.8)	0 (0.0)	1 (1.9)
Missing data	0	0	0
Was Mylotarg® administered as expected?, n (%)			
n	29	16	45
No	0 (0.0)	0 (0.0)	0 (0.0)
Yes	29 (100.0)	16 (100.0)	45 (100.0)
Missing data	0	0	0
Reason for dose change/discontinuation of first consolidation Mylotarg®, n (%)			
n	0	0	0
Missing data	29	16	45

D, day; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.1.5. Mylotarg® as second consolidation course

In the FAS (n=113), 37/113 patients (32.7%) were administered Mylotarg® in a second induction course. Among the 37 patients, 28/37 (75.7%) were prescribed Mylotarg® in association and 9/37 (24.3%) as monotherapy. The median cumulative dose of Mylotarg® was 5.0 mg (Q1-Q3: 5.0-5.0). The median number of doses was 1.0 (Q1-Q3: 1.0-1.0): most frequently administered on D1 (in 33/37 patients [89.2%]). See **Table 10** for details.

Table 10. Modalities of Mylotarg® prescribed as second consolidation course: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as second consolidation course, n (%)			
n	62	51	113
No	30 (48.4)	46 (90.2)	76 (67.3)
Yes	32 (51.6)	5 (9.8)	37 (32.7)
Missing data	0	0	0
Second consolidation Mylotarg® regimen, n (%)			
n	32	5	37
In association	25 (78.1)	3 (60.0)	28 (75.7)
Monotherapy	7 (21.9)	2 (40.0)	9 (24.3)
Missing data	0	0	0
Second consolidation associations with Mylotarg®, n (%)			
n	25	3	28
Mylotarg® + cytarabine (IV with syringe pump)	3 (12.0)	1 (33.3)	4 (14.3)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine	21 (84.0)	2 (66.7)	23 (82.1)
Mylotarg® + cytarabine (IV with syringe pump) + daunorubicine + other	1 (4.0)	0 (0.0)	1 (3.6)
Missing data	0	0	0
Second consolidation Mylotarg® cumulative dose (mg)			
n	28	4	32
Mean (SD)	4.95 (0.13)	4.83 (0.35)	4.93 (0.17)
Median	5.00	5.00	5.00
Q1-Q3	5.00-5.00	4.65-5.00	5.00-5.00
Range	4.60-5.00	4.30-5.00	4.30-5.00
Missing data	4	1	5
Number of second consolidation Mylotarg® doses prescribed			
n	32	5	37
Mean (SD)	1.00 (0.00)	1.00 (0.00)	1.00 (0.00)
Median	1.00	1.00	1.00
Q1-Q3	1.00-1.00	1.00-1.00	1.00-1.00
Range	1.00-1.00	1.00-1.00	1.00-1.00
Missing data	0	0	0
Second consolidation Mylotarg® administration scheme, n (%)			
n	32	5	37
D1	29 (90.6)	4 (80.0)	33 (89.2)
D2	0 (0.0)	1 (20.0)	1 (2.7)
D4	1 (3.1)	0 (0.0)	1 (2.7)
D5	2 (6.3)	0 (0.0)	2 (5.4)
Missing data	0	0	0
Was Mylotarg® administered as expected?, n (%)			
n	25	3	28
No	0 (0.0)	0 (0.0)	0 (0.0)
Yes	25 (100.0)	3 (100.0)	28 (100.0)
Missing data	0	0	0
Reason for dose change/discontinuation of second consolidation Mylotarg®, n (%)			
n	0	0	0
Missing data	25	3	28

D, day; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.1.6. Mylotarg® as ≥3 consolidation course

In the FAS (n=113), 3/113 patients (2.7%) were administered Mylotarg® in a ≥3 consolidation course. All 3/3 (100%) were prescribed Mylotarg® in association with cytarabine. The median cumulative dose of Mylotarg® was 4.6 mg (Q1-Q3: 4.3-5.0). The median number of doses was 1.0 (Q1-Q3: 1.0-1.0): administered on D1 in the 3/3 patients (100.0%). See **Table 11** for details.

Table 11. Modalities of Mylotarg® prescribed as other consolidation course: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Mylotarg® administered as ≥3 consolidation course, n (%)			
n	62	51	113
No	62 (100)	48 (94.1)	110 (97.3)
Yes	0 (0.0)	3 (5.9)	3 (2.7)
Missing data	0	0	0
≥3 consolidation Mylotarg® regimen, n (%)			
n	0	3	3
In association	NA	3 (100)	3 (100)
Missing data	0	0	0
≥3 consolidation associations with Mylotarg®, n (%)			
n		3	3
Mylotarg® + cytarabine (IV with syringe pump)		3 (100)	3 (100)
Missing data		0	0
⩾3 consolidation Mylotarg® cumulative dose (mg)			
n	0	2	2
Mean (SD)		4.63 (0.53)	4.63 (0.53)
Median		4.63	4.63
Q1-Q3		4.25-5.00	4.25-5.00
Range		4.25-5.00	4.25-5.00
Missing data	0	1	1
Number of ≥3 consolidation Mylotarg® doses prescribed			
n		3	3
Mean (SD)		1.00 (0.00)	1.00 (0.00)
Median		1.00	1.00
Q1-Q3		1.00-1.00	1.00-1.00
Range		1.00-1.00	1.00-1.00
Missing data		0	0
≥3 consolidation Mylotarg® administration scheme, n (%)			
n		3	3
D1		3 (100)	3 (100)
Missing data		0	0
Was Mylotarg® administered as expected?, n (%)			
n		3	3
No		0 (0.0)	0 (0.0)
Yes		3 (100.0)	3 (100.0)
Missing data		0	0
Reason for dose change/discontinuation of ≥3 consolidation Mylotarg®, n (%)			

n	0	0
Missing data	3	3

D, day; IV, intravenous; NA, not applicable; Q, quartile; SD, standard deviation.
Source: Table 14.5.1 TFLs_v1.0_28NOV2023

10.2.2. Effectiveness of Mylotarg®

10.2.2.1. Duration of follow-up: FAS (n=113)

At analysis, the median duration of follow-up, in the FAS (n=113) was 44.6 months (95% CI: 33.8-69.3): 81.4 months (95% CI: 73.5-85.4) in the ATUc and 26.7 months (95% CI: 19.9-32.8) in the Post-ATUc. The Kaplan-Meier curves overall and in the ATUc and Post-ATUc are shown in **Figure 3** and **Figure 4**, respectively.

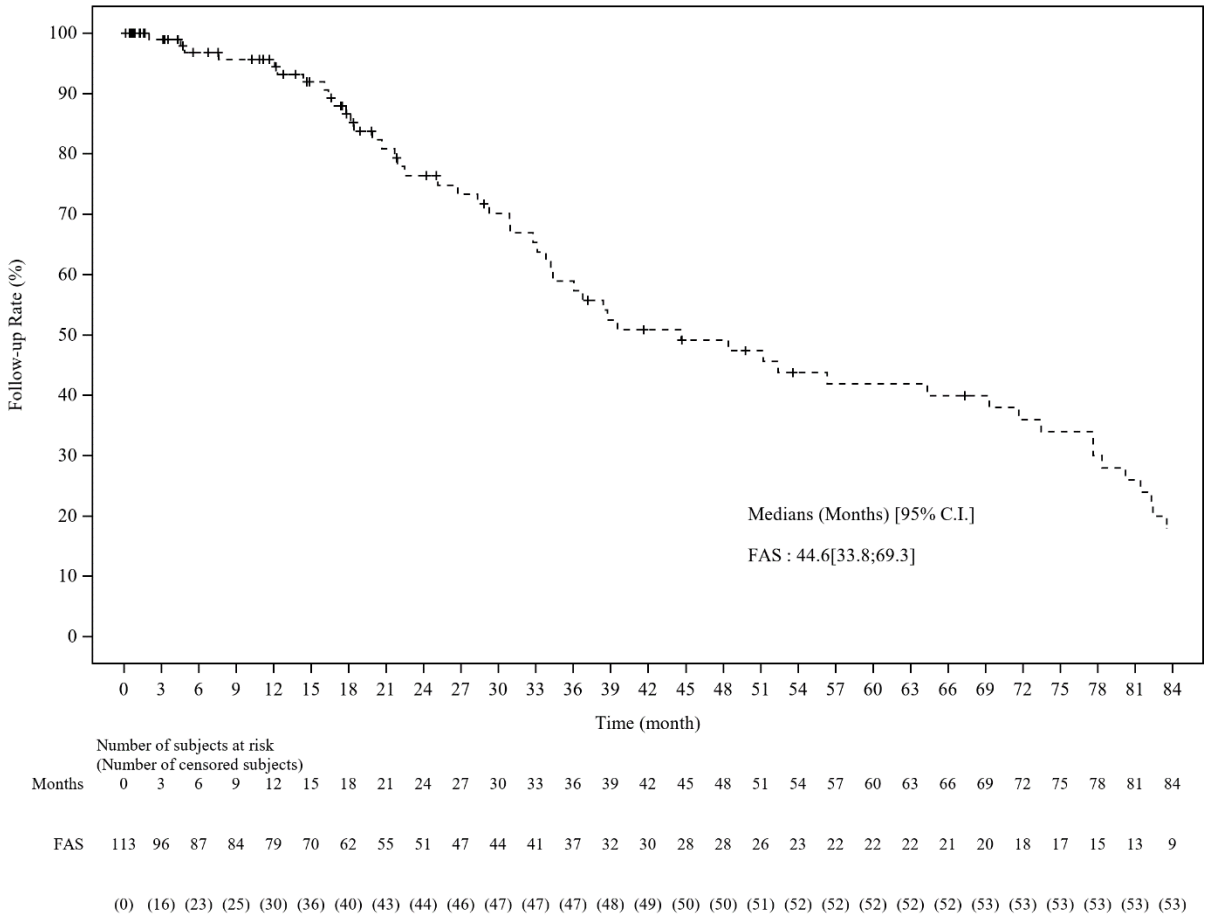


Figure 3. Kaplan-Meier curve of follow-up duration: FAS (113)

(**Source:** Figure 15.3.1 TFLs_v1.0_28NOV2023)

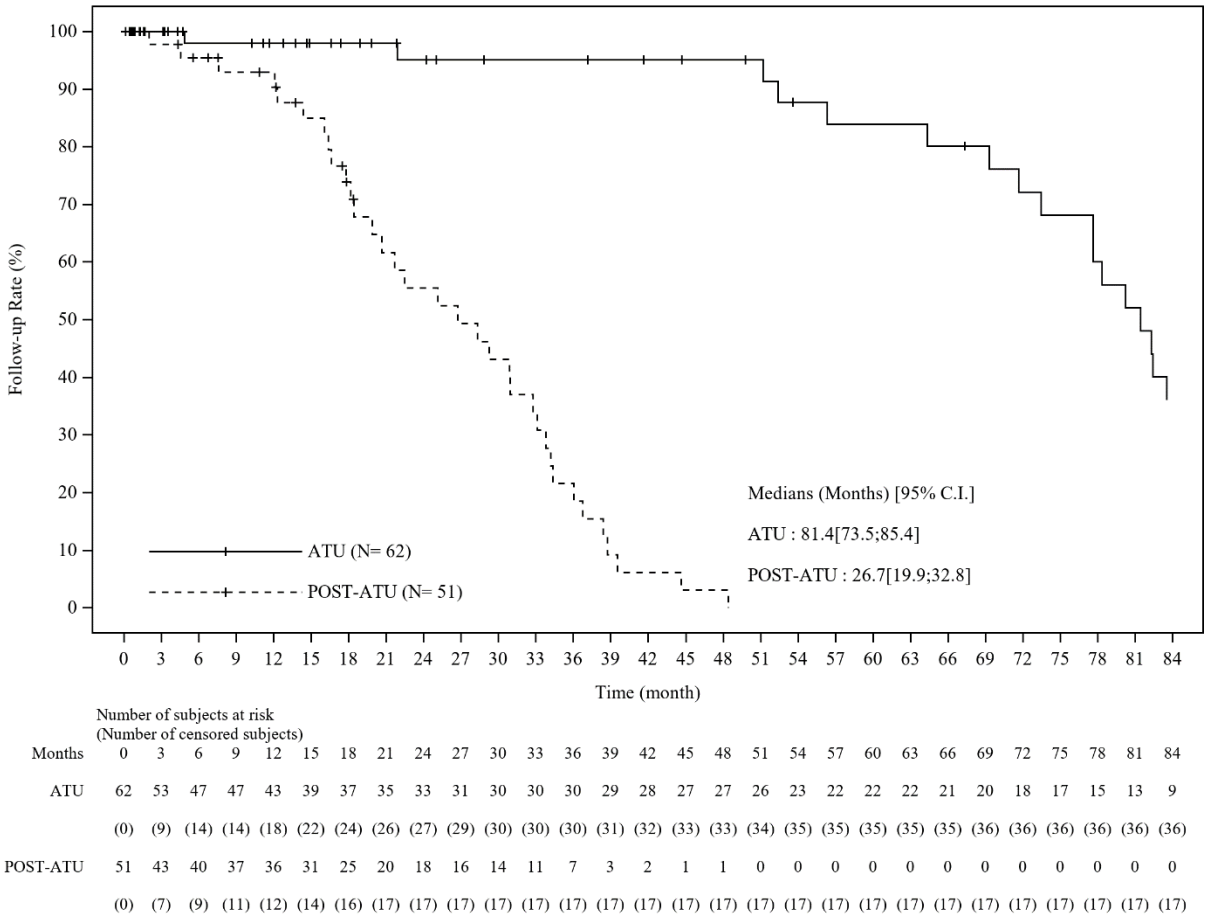


Figure 4. Kaplan-Meier curve of follow-up duration in the ATUc and Post-ATUc: FAS (113)

(Source: Figure 15.3.2 TFLs_v1.0_28NOV2023)

10.2.2.2. Analysis of best response rate during the study: FAS (n=113)

In the FAS (n=113), 89/113 patients (78.8% [95% CI: 70.1%-85.9%]) were classified as responders during the study: 84/113 (74.3%) CR and 5/113 (4.4%) CRp. See **Table 12**.

Table 12. Best response rates overall and according to cohorts: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Patients with response (CR/CRp/CRh), n (%)			
n	62	51	113
Non-responders	14 (22.6)	10 (19.6)	24 (21.2)
Responders	48 (77.4)	41 (80.4)	89 (78.8)
[95% CI]	[65.0-87.1]	[66.9-90.2]	[70.1-85.9]
Missing data	0	0	0

Type of response, n (%)			
n	62	51	113
CR	47 (75.8)	37 (72.6)	84 (74.3)
CRp	1 (1.6)	4 (7.8)	5 (4.4)
Refractory patient	6 (9.7)	5 (9.8)	11 (9.7)
Death due to aplasia	3 (4.8)	1 (2.0)	4 (3.5)
Death for other reason	3 (4.8)	2 (3.9)	5 (4.4)
Response not assessed	2 (3.2)	1 (2.0)	3 (2.7)
NA	0 (0.0)	1 (2.0)	1 (0.9)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.1 TFLs_v1.0_28NOV2023

In the 51 patients with a Favorable risk (ELN 2010), 43/51 patients (84.3% [95% CI: 71.4%-93.0%]) were classified as responders during the study: 42/51 (82.4%) CR and 1/51 (2.0%) CRp. See **Table 13** for details.

Table 13. Best response rates in patients with Favorable risk (ELN 2010) by scientific committee (n=51)

	ATU cohort (n=26)	**Post-ATU cohort (n=25)**	**Patients with favorable risk (ELN 2010) (n=51)**
Patients with response (CR/CRp/CRh), n (%)			
n	26	25	51
Non-responders	5 (19.2)	3 (12.0)	8 (15.7)
Responders	21 (80.8)	22 (87.5)	43 (84.3)
[95% CI]	[60.7-93.5]	[68.8-97.5]	[71.4-93.0]
Missing data	0	0	0
Type of response, n (%)			
n	26	24	51
CR	21 (80.8)	21 (84.0)	42 (82.4)
CRp	0 (0.0)	1 (4.0)	1 (2.0)
Refractory patient	2 (7.7)	0 (0.0)	2 (3.9)
Death due to aplasia	1 (3.9)	1 (4.0)	2 (3.9)
Death for other reason	1 (3.9)	1 (4.0)	2 (3.9)
Response not assessed	1 (3.9)	1 (4.0)	2 (3.9)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.2 TFLs_v1.0_28NOV2023

In the 24 patients with an Intermediate I risk (ELN 2010), 18/24 patients (75.0% [95% CI: 53.3%-90.2%]) were classified as responders during the study: 16/24 (66.7%) CR and 2/24 (8.3%) CRp. See **Table 14** for details.

Table 14. Best response rates in patients with Intermediate I risk (ELN 2010) by scientific committee (n=24)

	ATU cohort (n=12)	**Post-ATU cohort (n=12)**	**Patients with favorable risk**

			(ELN 2010) (n=24)
Patients with response (CR/CRp/CRh), n (%)			
n	12	12	24
Non-responders	2 (16.7)	4 (33.3)	6 (25.0)
Responders	10 (83.3)	8 (66.7)	18 (75.0)
[95% CI]	[51.6-97.9]	[34.9-90.1]	[53.3-90.2]
Missing data	0	0	0
Type of response, n (%)			
n	12	12	24
CR	10 (83.3)	6 (50.0)	16 (66.7)
CRp	0 (0.0)	2 (16.7)	2 (8.3)
Refractory patient	1 (8.3)	3 (25.0)	4 (16.7)
Death due to aplasia	1 (8.3)	0 (0.0)	1 (4.2)
NA	0 (0.0)	1 (8.3)	1 (4.2)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.3 TFLs_v1.0_28NOV2023

In the 20 patients with an Intermediate II risk (ELN 2010), 17/20 patients (85.0% [95% CI: 62.1%-96.8%]) were classified as responders during the study: 15/20 (75.0%) CR and 2/20 (10.0%) CRp. See **Table 15** for details.

Table 15. Best response rates in patients with Intermediate II risk (ELN 2010) by scientific committee (n=20)

	ATU cohort (n=13)	Post-ATU cohort (n=7)	Patients with favorable risk (ELN 2010) (n=20)
Patients with response (CR/CRp/CRh), n (%)			
n	13	7	20
Non-responders	2 (15.4)	1 (14.3)	3 (15.0)
Responders	11 (84.6)	6 (85.7)	17 (85.0)
[95% CI]	[54.6-98.1]	[42.1-99.6]	[62.1-96.8]
Missing data	0	0	0
Type of response, n (%)			
n	13	7	20
CR	10 (76.9)	5 (71.4)	15 (75.0)
CRp	1 (7.7)	1 (14.3)	2 (10.0)
Refractory patient	1 (7.7)	1 (14.3)	2 (10.0)
Death due to aplasia	1 (7.7)	0 (0.0)	1 (5.0)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.4 TFLs_v1.0_28NOV2023

In the 7 patients with an Adverse risk (ELN 2010), 4/7 patients (57.1% [95% CI: 18.4%-90.1%]) were classified as responders during the study: 4/7 (57.1%) CR. See **Table 16** for details.

Table 16. Best response rates in patients with Adverse risk (ELN 2010) by scientific committee (n=7)

	ATU cohort (n=3)	Post-ATU cohort (n=4)	Patients with favorable risk (ELN 2010) (n=7)
Patients with response (CR/CRp/CRh), n (%)			
n	3	4	7
Non-responders	2 (66.7)	1 (25.0)	3 (42.9)
Responders	1 (33.3)	3 (75.0)	4 (57.1)
[95% CI]	[0.8-90.6]	[19.4-99.4]	[18.4-90.1]
Missing data	0	0	0
Type of response, n (%)			
n	3	4	7
CR	1 (33.3)	3 (75.0)	4 (57.1)
Refractory patient	1 (33.3)	1 (25.0)	2 (28.6)
Death due to aplasia	1 (33.3)	0 (0.0)	1 (14.3)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.5 TFLs_v1.0_28NOV2023

In the 64 patients with a Favorable risk (ELN 2017), 56/64 patients (87.5% [95% CI: 76.9%-94.5%]) were classified as responders during the study: 54/64 (84.4%) CR and 2/64 (3.1%) CRp. See Erreur ! Source du renvoi introuvable. for details.

Table 17. Best response rates in patients with Favorable risk (ELN 2017) by scientific committee (n=64

	ATU cohort (n=33)	Post-ATU cohort (n=31)	Patients with favorable risk (ELN 2017) (n=64)
Patients with response (CR/CRp/CRh), n (%)			
n	33	31	64
Non-responders	5 (15.2)	3 (9.7)	8 (12.5)
Responders	28 (84.8)	28 (90.3)	56 (87.5)
[95% CI]	[68.1-94.9]	[74.3-98.0]	[76.9-94.5]
Missing data	0	0	0
Type of response, n (%)			
n	33	31	64
CR	28 (84.9)	26 (83.9)	54 (84.4)
CRp	0 (0.0)	2 (6.5)	2 (3.1)
Refractory patient	1 (3.0)	0 (0.0)	1 (1.6)
Death due to aplasia	2 (6.1)	1 (3.2)	3 (4.7)
Death for other reason	1 (3.0)	1 (3.2)	2 (3.1)
Response not assessed	1 (3.0)	1 (3.2)	2 (3.1)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.6 TFLs_v1.0_28NOV2023

In the 10 patients with an Intermediate risk (ELN 2017), 8/10 patients (80.0% [95% CI: 44.4%-97.5%]) were classified as responders during the study: 6/10 (60.0%) CR and 2/10 (20.0%) CRp. See

for details.

Table 18. Best response rates in patients with Intermediate risk (ELN 2017) by scientific committee (n=10)

	ATU cohort (n=6)	Post-ATU cohort (n=4)	Patients with favorable risk (ELN 2017) (n=10)
Patients with response (CR/CRp/CRh), n (%)			
n	6	4	10
Non-responders	0 (0.0)	2 (50.0)	2 (20.0)
Responders	6 (100)	2 (50.0)	8 (80.0)
[95% CI]	[54.1-NE]	[6.8-93.2]	[44.4-97.5]
Missing data	0	0	0
Type of response, n (%)			
n	6	4	10
CR	6 (100)	0 (0.0)	6 (60.0)
CRp	0 (0.0)	2 (50.0)	2 (20.0)
Refractory patient	0 (0.0)	1 (25.0)	1 (10.0)
NA	0 (0.0)	1 (25.0)	1 (10.0)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; NA, not applicable; NE, not evaluable.
Source: Table 15.1.7 TFLs_v1.0_28NOV2023

In the 15 patients with an Adverse risk (ELN 2017), 9/15 patients (60.0% [95% CI: 32.3%-83.7%]) were classified as responders during the study: 9/15 (60.0%) CR. See

for details.

Table 19. Best response rates in patients with Adverse risk (ELN 2017) by scientific committee (n=15)

	ATU cohort (n=5)	Post-ATU cohort (n=10)	Patients with favorable risk (ELN 2017) (n=15)
Patients with response (CR/CRp/CRh), n (%)			
n	5	10	15
Non-responders	2 (40.0)	4 (40.0)	6 (40.0)
Responders	3 (60.0)	6 (60.0)	9 (60.0)
[95% CI]	[14.7-94.7]	[26.2-87.8]	[32.3-83.7]
Missing data	0	0	0
Type of response, n (%)			
n	5	10	15
CR	3 (60.0)	6 (60.0)	9 (60.0)
Refractory patient	1 (20.0)	4 (40.0)	5 (33.3)
Death due to aplasia	1 (20.0)	0 (0.0)	1 (6.7)
Missing data	0	0	0

	ATU cohort (n=5)	Post-ATU cohort (n=10)	Patients with favorable risk (ELN 2017) (n=15)

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery.
Source: Table 15.1.8 TFLs_v1.0_28NOV2023

10.2.2.3. Analysis of post-induction response to treatment: FAS (n=113)

In the FAS (n=113), 88/112 patients (78.6% [95% CI: 69.8%-85.8%]; missing data [n=1]) were classified as responders after induction treatment: 81/112 (72.3%) CR and 7/112 (6.3%) CRp. See **Table 20**. Among the 112 patients, 24/46 (52.2%; missing data [n=67]) were CR MRD-negative.

Table 20. Post-induction response rates overall: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Patients with response (CR/CRp/CRh), n (%)			
n	62	50	112
Non-responders	14 (22.6)	10 (20.0)	24 (21.4)
Responders	48 (77.4)	40 (80.0)	88 (78.6)
[95% CI]	[65.0-87.1]	[66.3-90.0]	[69.8-85.8]
Missing data	0	1	1
Type of response, n (%)			
n	62	50	112
CR	45 (72.6)	36 (72.0)	81 (72.3)
CRp	3 (4.8)	4 (8.0)	7 (6.3)
Refractory patient	6 (9.7)	5 (10.0)	11 (9.8)
Death due to aplasia	3 (4.8)	1 (2.0)	4 (3.6)
Death for other reason	3 (4.8)	2 (4.0)	5 (4.5)
Response not assessed	2 (3.2)	1 (2.0)	3 (2.7)
NA	0 (0.0)	1 (2.0)	1 (0.9)
Missing data	0	1	1
CR MRD-negative (FAS population [n=113])			
n	22	24	46
No	9 (40.9)	13 (54.2)	22 (47.8)
Yes	13 (59.1)	11 (45.8)	24 (52.2)
Missing data	40	27	67
CR MRD-negative (in responders [n=88])			
n	22	24	46
No	9 (40.9)	13 (54.2)	22 (47.8)
Yes	13 (59.1)	11 (45.8)	24 (52.2)
Missing data	26	16	42

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.1 TFLs_v1.0_28NOV2023

In the 51 patients with a Favorable risk (ELN 2010), 42/50 patients (84.0% [95% CI: 70.9%-92.8]; missing data [n=1]) were classified as responders after induction treatment: 40/50 (80.0%) CR and 2/50 (4.0%) CRp. See **Table 21** for details.

Table 21. Post-induction response rates in patients with Favorable risk (ELN 2010) by scientific committee (n=51)

	ATU cohort (n=26)	Post-ATU cohort (n=25)	Patients with favorable risk (ELN 2010) (n=51)
Patients with response (CR/CRp/CRh), n (%)			
n	26	24	50
Non-responders	5 (19.2)	3 (12.5)	8 (16.0)
Responders	21 (80.8)	21 (87.5)	42 (84.0)
[95% CI]	[60.7-93.5]	[67.6-97.3]	[70.9-92.8]
Missing data	0	1	1
Type of response, n (%)			
n	26	24	50
CR	20 (76.9)	20 (83.3)	40 (80.0)
CRp	1 (3.8)	1 (4.2)	2 (4.0)
Refractory patient	2 (7.7)	0 (0.0)	2 (4.0)
Death due to aplasia	1 (3.8)	1 (4.2)	2 (4.0)
Death for other reason	1 (3.8)	1 (4.2)	2 (4.0)
Response not assessed	1 (3.8)	1 (4.2)	2 (4.0)
Missing data	0	1	1
CR MRD-negative (FAS [n=51])			
n	12	14	26
No	4 (33.3)	9 (64.3)	13 (50.0)
Yes	8 (66.7)	5 (35.7)	13 (50.0)
Missing data	14	11	25
CR MRD-negative (in responders [n=42])			
n	12	14	26
No	4 (33.3)	9 (64.3)	13 (50.0)
Yes	8 (66.7)	5 (35.7)	13 (50.0)
Missing data	9	7	16

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.2 TFLs_v1.0_28NOV2023

In the 24 patients with an Intermediate I risk (ELN 2010), 18/24 patients (75.0% [95% CI: 53.3%-90.2%]) were classified as responders after induction treatment: 16/24 (66.7%) CR and 2/24 (8.3%) CRp. See **Table 22** for details.

Table 22. Post-induction response rates in patients with Intermediate I risk (ELN 2010) by scientific committee (n=24)

	ATU cohort (n=12)	Post-ATU cohort (n=12)	Patients with favorable risk (ELN 2010) (n=24)
Patients with response (CR/CRp/CRh), n (%)			
n	12	12	24
Non-responders	2 (16.7)	4 (33.3)	6 (25.0)
Responders	10 (83.3)	8 (66.7)	18 (75.0)
[95% CI]	[51.6-97.9]	[34.9-90.1]	[53.3-90.2]
Missing data	0	0	0
Type of response, n (%)			
n	12	12	24
CR	10 (83.3)	6 (50.0)	16 (66.7)

CRp	0 (0.0)	2 (16.7)	2 (8.3)
Refractory patient	1 (8.3)	3 (25.0)	4 (16.7)
Death due to aplasia	1 (8.3)	0 (0.0)	1 (4.2)
NA	0 (0.0)	1 (8.3)	1 (4.2)
Missing data	0	0	0
CR MRD-negative (FAS [n=24])			
n	3	3	6
No	1 (33.3)	0 (0.0)	1 (16.7)
Yes	2 (66.7)	3 (100)	5 (83.3)
Missing data	9	9	18
CR MRD-negative (in responders [n=18])			
n	3	3	6
No	1 (33.3)	0 (0.0)	1 (16.7)
Yes	2 (66.7)	3 (100)	5 (83.3)
Missing data	7	5	12

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.3 TFLs_v1.0_28NOV2023

In the 20 patients with an Intermediate II risk (ELN 2010), 17/20 patients (85.0% [95% CI: 62.1%-96.8%]) were classified as responders after induction treatment: 14/20 (70.0%) CR and 3/20 (15.0%) CRp. See **Table 23** for details.

Table 23. Post-induction response rates in patients with Intermediate II risk (ELN 2010) by scientific committee (n=20)

	ATU cohort (n=13)	**Post-ATU cohort (n=7)**	**Patients with favorable risk (ELN 2010) (n=20)**
Patients with response (CR/CRp/CRh), n (%)			
n	13	7	20
Non-responders	2 (15.4)	1 (14.3)	3 (15.0)
Responders	11 (84.6)	6 (85.7)	17 (85.0)
[95% CI]	[54.6-98.1]	[42.1-99.6]	[62.1-96.8]
Missing data	0	0	0
Type of response, n (%)			
n	13	7	20
CR	9 (69.2)	5 (71.4)	14 (70.0)
CRp	2 (15.4)	1 (14.3)	3 (15.0)
Refractory patient	1 (7.7)	1 (14.3)	2 (10.0)
Death due to aplasia	1 (7.7)	0 (0.0)	1 (5.0)
Missing data	0	0	0
CR MRD-negative (FAS [n=20])			
n	3	3	6
No	2 (66.7)	2 (66.7)	4 (66.7)
Yes	1 (33.3)	1 (33.3)	2 (33.3)
Missing data	10	4	14
CR MRD-negative (in responders [n=17])			
n	3	3	6
No	2 (66.7)	2 (66.7)	4 (66.7)
Yes	1 (33.3)	1 (33.3)	2 (33.3)
Missing data	8	3	11

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.4 TFLs_v1.0_28NOV2023

In the 7 patients with an Adverse risk (ELN 2010), 4/7 patients (57.1% [95% CI: 18.4%-90.1%]) were classified as responders after induction treatment: 4/7 (57.1%) CR. See **Table 24** for details.

Table 24. Post-induction response rates in patients with Adverse risk (ELN 2010) by scientific committee (n=7)

	ATU cohort (n=3)	Post-ATU cohort (n=4)	Patients with favorable risk (ELN 2010) (n=7)
Patients with response (CR/CRp/CRh), n (%)			
n	3	4	7
Non-responders	2 (66.7)	1 (25.0)	3 (42.9)
Responders	1 (33.3)	3 (75.0)	4 (57.1)
[95% CI]	[0.8-90.6]	[19.4-99.4]	[18.4-90.1]
Missing data	0	0	0
Type of response, n (%)			
n	3	4	7
CR	1 (33.3)	3 (75.0)	4 (57.1)
Refractory patient	1 (33.3)	1 (25.0)	2 (28.6)
Death due to aplasia	1 (33.3)	0 (0.0)	1 (14.3)
Missing data	0	0	0
CR MRD-negative (FAS [n=7])			
N	1	3	4
No	1 (100)	1 (33.3)	2 (50.0)
Yes	0 (0.0)	2 (66.7)	2 (50.0)
Missing data	2	1	3
CR MRD-negative (in responders [n=4])			
n	1	3	4
No	1 (100)	1 (33.3)	2 (50.0)
Yes	0 (0.0)	2 (66.7)	2 (50.0)
Missing data	0	0	0

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.5 TFLs_v1.0_28NOV2023

In the 64 patients with a Favorable risk (ELN 2017), 55/63 patients (87.3% [95% CI: 76.5%-94.4%]; missing data [n=1]) were classified as responders after induction treatment: 52/63 (82.5%) CR and 3/63 (4.8%) CRp. See **Table 25** for details.

Table 25. Post-induction response rates in patients with Favorable risk (ELN 2017) by scientific committee (n=64)

	ATU cohort (n=33)	Post-ATU cohort (n=31)	Patients with favorable risk (ELN 2017) (n=64)
Patients with response (CR/CRp/CRh), n (%)			
n	33	30	63
Non-responders	5 (15.2)	3 (10.0)	8 (12.7)
Responders	28 (84.8)	27 (90.0)	55 (87.3)
[95% CI]	[68.1-94.9]	[73.5-97.9]	[76.5-94.4]

	ATU cohort (n=33)	Post-ATU cohort (n=31)	Patients with favorable risk (ELN 2017) (n=64)
Missing data	0	1	1
Type of response, n (%)			
n	33	30	63
CR	27 (81.8)	25 (83.3)	52 (82.5)
CRp	1 (3.0)	2 (6.7)	3 (4.8)
Refractory patient	1 (3.0)	0 (0.0)	1 (1.6)
Death due to aplasia	2 (6.1)	1 (3.3)	3 (4.8)
Death for other reason	1 (3.0)	1 (3.3)	2 (3.2)
Response not assessed	1 (3.0)	1 (3.3)	2 (3.2)
Missing data	0	1	1
CR MRD-negative (FAS [n=64])			
n	15	18	33
No	4 (26.7)	12 (66.7)	16 (48.5)
Yes	11 (73.3)	6 (33.3)	17 (51.5)
Missing data	18	13	31
CR MRD-negative (in responders [n=55])			
n	15	18	33
No	4 (26.7)	12 (66.7)	16 (48.5)
Yes	11 (73.3)	6 (33.3)	17 (51.5)
Missing data	13	9	22

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.6 TFLs_v1.0_28NOV2023

In the 10 patients with an Intermediate risk (ELN 2017), 8/10 patients (80.0% [95% CI: 44.4%-97.5%]) were classified as responders after induction treatment: 6/10 (60.0%) CR and 2/10 (20.0%) CRp. See **Table 26** for details.

Table 26. Post-induction response rates in patients with Intermediate risk (ELN 2017) by scientific committee (n=10)

	ATU cohort (n=6)	Post-ATU cohort (n=4)	Patients with favorable risk (ELN 2017) (n=10)
Patients with response (CR/CRp/CRh), n (%)			
n	6	4	10
Non-responders	0 (0.0)	2 (50.0)	2 (20.0)
Responders	6 (100)	2 (50.0)	8 (80.0)
[95% CI]	[54.1-NE]	[6.8-93.2]	[44.4-97.5]
Missing data	0	0	0
Type of response, n (%)			
n	6	4	10
CR	6 (100)	0 (0.0)	6 (60.0)
CRp	0 (0.0)	2 (50.0)	2 (20.0)
Refractory patient	0 (0.0)	1 (25.0)	1 (10.0)
NA	0 (0.0)	1 (25.0)	1 (10.0)
Missing data	0	0	0
CR MRD-negative (FAS [n=10])			
n	3	0	3
No	2 (66.7)	0 (0.0)	2 (66.7)
Yes	1 (33.3)	0 (0.0)	1 (33.3)

Missing data	3	4	7
CR MRD-negative (in responders [n=8])			
n	3	0	3
No	2 (66.7)	0 (0.0)	2 (66.7)
Yes	1 (33.3)	0 (0.0)	1 (33.3)
Missing data	3	2	5

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease; NA, not applicable; NE, not evaluable.
Source: Table 15.2.7 TFLs_v1.0_28NOV2023

In the 15 patients with an Adverse risk (ELN 2017), 9/15 patients (60.0% [95% CI: 32.3%-83.7%]) were classified as responders after induction treatment: 9/15 (60.0%) CR. See **Table 27** for details.

Table 27. Post-induction response rates in patients with Adverse risk (ELN 2017) by scientific committee (n=15)

	ATU cohort (n=5)	Post-ATU cohort (n=10)	Patients with favorable risk (ELN 2017) (n=15)
Patients with response (CR/CRp/CRh), n (%)			
n	5	10	15
Non-responders	2 (40.0)	4 (40.0)	6 (40.0)
Responders	3 (60.0)	6 (60.0)	9 (60.0)
[95% CI]	[14.7-94.7]	[26.3-87.8]	[32.3-83.7]
Missing data	0	0	0
Type of response, n (%)			
n	5	10	15
CR	3 (60.0)	6 (60.0)	9 (60.0)
Refractory patient	1 (20.0)	4 (40.0)	5 (33.3)
Death due to aplasia	1 (20.0)	0 (0.0)	1 (6.7)
Missing data	0	0	0
CR MRD-negative (FAS [n=15])			
n	1	5	6
No	1 (100)	1 (20.0)	2 (33.3)
Yes	0 (0.0)	4 (80.0)	4 (66.7)
Missing data	4	5	9
CR MRD-negative (in responders [n=9])			
n	1	5	6
No	1 (100)	1 (20.0)	2 (33.3)
Yes	0 (0.0)	4 (80.0)	4 (66.7)
Missing data	2	1	3

CI, confidence interval; CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; MRD, minimal residual disease.
Source: Table 15.2.8 TFLs_v1.0_28NOV2023

10.2.2.4. Analysis of overall survival (OS)

At analysis, in FAS (n=113) the median OS was 49.8 months (95% CI: 21.8-NE): 37.2 (95% CI: 16.6-NE) in the ATUc (n=62) and NE (95% CI: 18.4-NE) in the Post-ATUc (n=51). Further details and the OS rates during the study are shown in **Table 28**. The Kaplan-Meier

curves for OS, overall and in the ATUc and Post-ATUc are shown in **Figure 5** and **Figure 6**, respectively.

Table 28. Analysis of overall survival (OS), overall and in the ATUc and Post-ATUc : FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
n	62	51	113
Number of deaths	36	17	53
Number of censored patients	26	34	60
Alive at reference date	25 (96.2)	34 (100)	59 (98.3)
Lost to follow-up	1 (3.8)	0 (0.0)	1 (1.7)
Median OS, months [95% CI]	37.2 [16.6-NE]	NE [18.4-NE]	49.8 [21.8-NE]
OS rates, % [95% CI]			
3 months	85.5 [74.0-92.2]	86.3 [73.4-93.2]	85.8 [77.9-91.1]
6 months	77.4 [64.9-86.0]	82.2 [68.6-90.3]	79.55 [70.9-85.9]
9 months	77.4 [64.9-86.0]	78.1 [63.9-87.2]	77.72 [68.8-84.4]
1 year	70.8 [57.8-80.5]	76.0 [61.6-85.6]	73.10 [63.8-80.4]
2 years	56.0 [42.7-67.4]	63.6 [47.8-75.8]	59.09 [49.1-67.8]
3 years	50.9 [37.8-62.6]	63.6 [47.8-75.8]	55.54 [45.4-64.6]
4 years	45.8 [33.0-57.7]	63.6 [47.8-75.8]	50.41 [39.7-60.2]
5 years	42.3 [29.7-54.3]	NE [NE-NE]	46.52 [35.4-56.9]
6 years	40.3 [27.8-52.4]	NE [NE-NE]	44.31 [32.9-55.1]
7 years	40.3 [27.8-52.4]	NE [NE-NE]	44.31 [32.9-55.1]

CI, confidence interval; NE, not evaluable.
Source: Table 15.4.1 and 15.4.2 TFLs_v1.0_28NOV2023

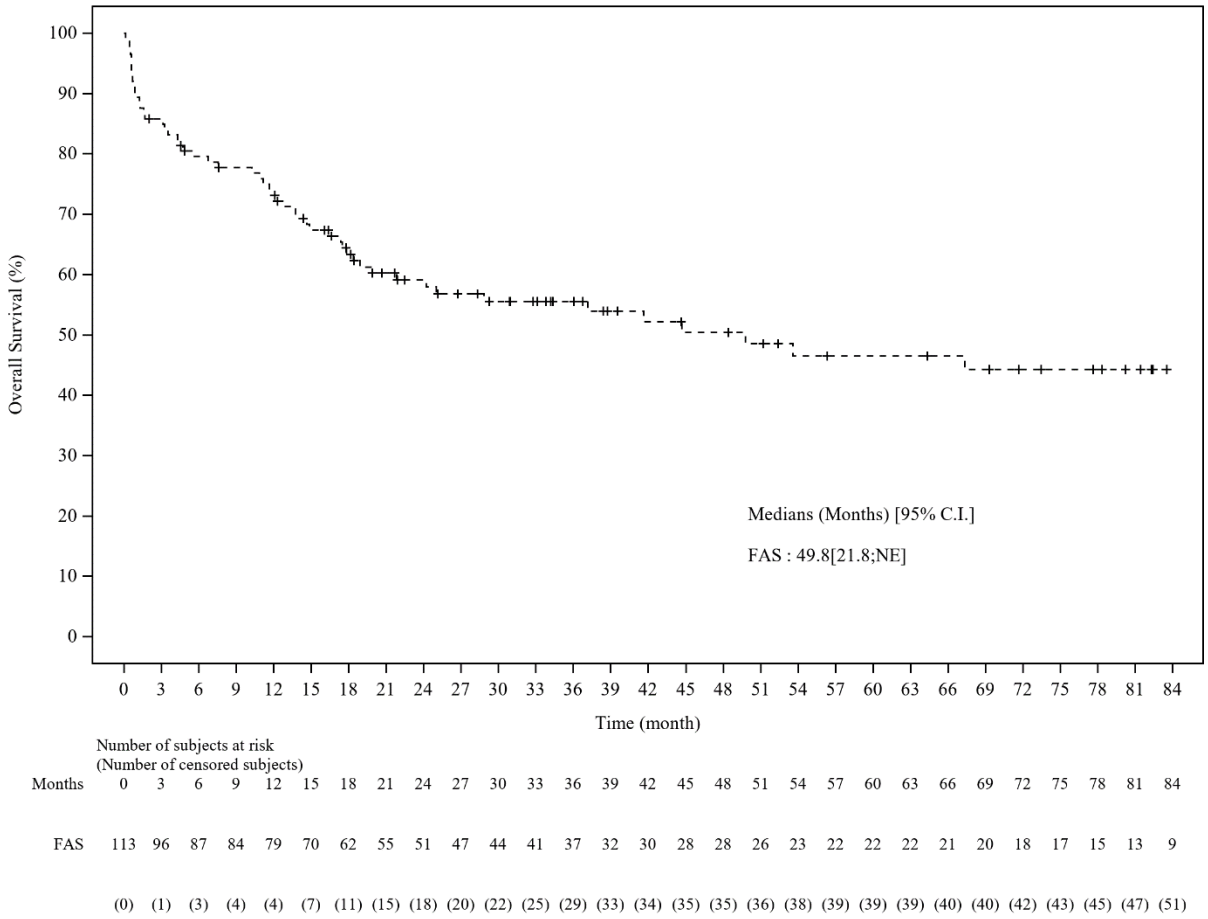


Figure 5. Kaplan-Meier curve of OS overall: FAS (n=113)

(Source: Figure 15.4.1 TFLs_v1.0_28NOV2023)

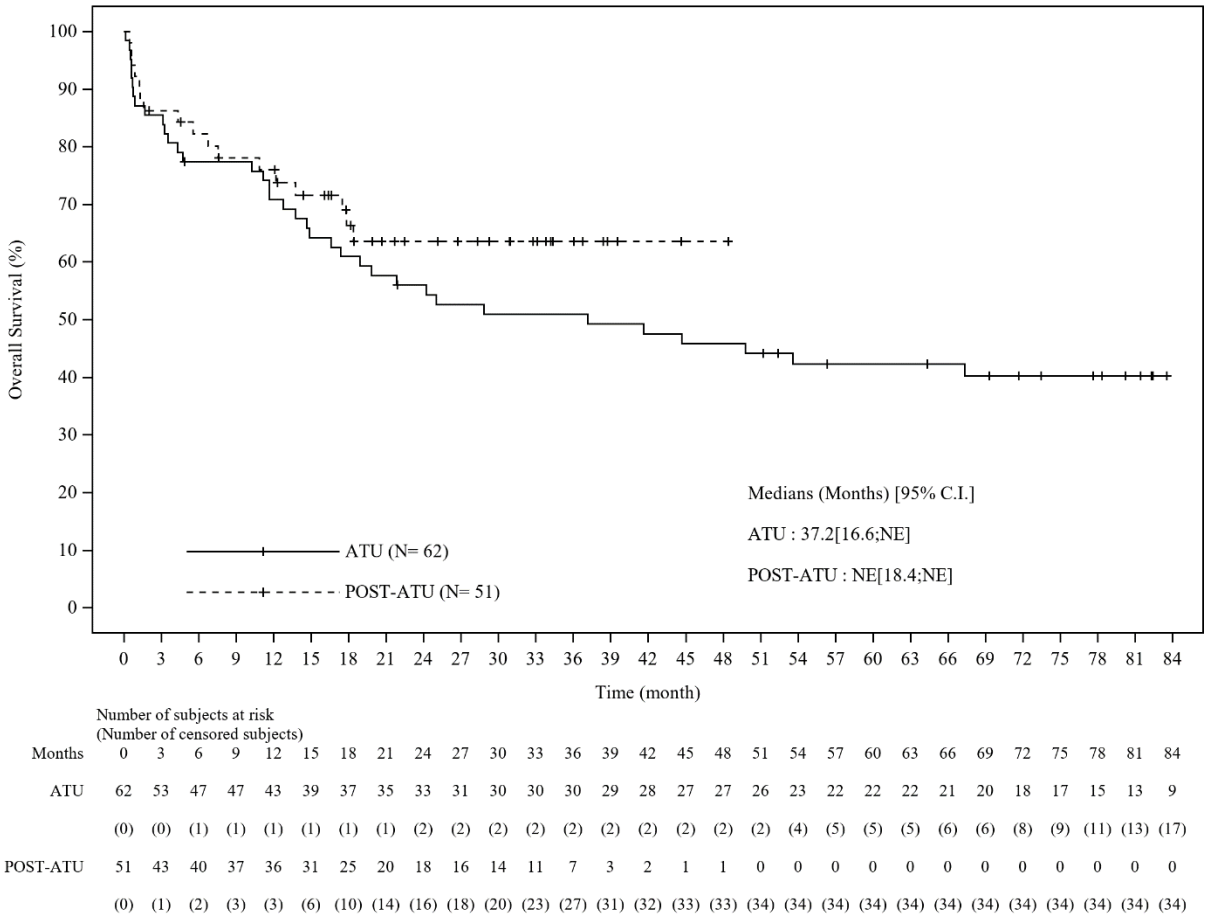


Figure 6. Kaplan-Meier curve of OS in the ATUc and Post-ATUc: FAS (n=113)

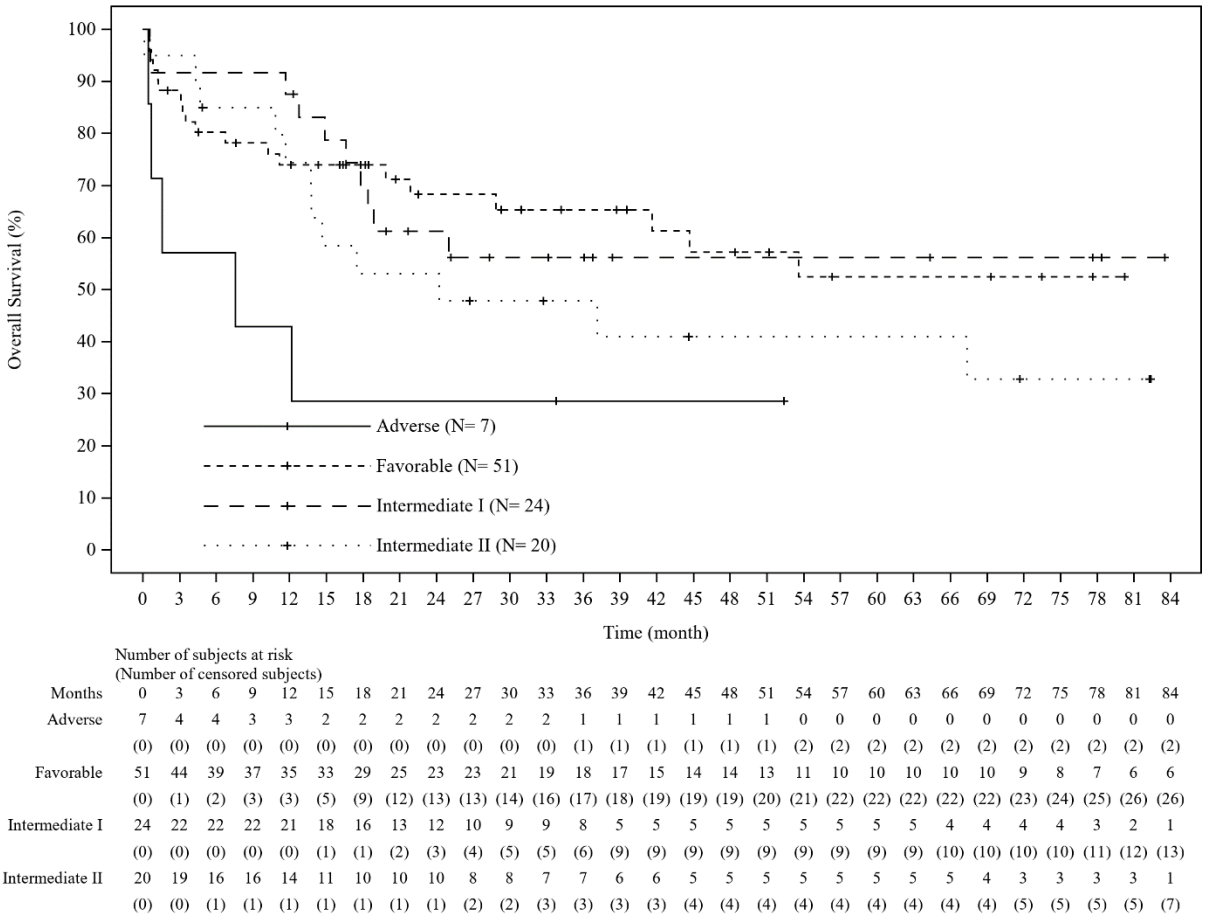
(Source: Figure 15.4.2 TFLs_v1.0_28NOV2023)

At analysis, in FAS (n=113), 102 patients had been classified according to risk factors (ELN 2010) by the scientific committee review: 51/102 (50.0%) with a Favorable risk, 24/102 (23.5%) with an Intermediate I risk, 20/102 (19.6%) with an Intermediate II risk, and 7/102 (6.9%) with an Adverse risk. The median OS, according to risk categories (ELN 2010) by scientific committee review was NE (95% CI: 28.8-NE) for patients classified as Favorable risk, NE (95% CI: 17.8-NE) for those classified as Intermediate I risk, 24.2 months (95% CI: 11.7-NE) for those classified as Intermediate II risk, and 7.6 months (95% CI: 0.4-NE) in those classified as Adverse risk. Further details and the OS rates, according to risk categories (ELN 2010) by scientific committee review during the study are shown in **Table 29**. The Kaplan-Meier curves for OS according to the risk categories (ELN 2010) by scientific committee review are shown in **Figure 7**.

Table 29. Analysis of overall survival (OS), according to risk categories (ELN 2010) by scientific committee review: FAS (n=113)

	Favorable risk (n=51)	Intermediate I risk (n=24)	Intermediate II risk (n=20)	Adverse risk (n=7)
n	51	24	20	7
Number of deaths	19	10	12	5
Number of censored patients	32	14	8	2
Alive at reference date	32 (100)	14 (100)	8 (100)	2 (100)
Median OS, months [95% CI]	NE [28.8-NE]	NE [17.8-NE]	24.2 [11.7-NE]	7.6 [0.4-NE]
OS rates, % [95% CI]				
3 months	88.2 [75.7-94.5]	91.67 [70.6-97.9]	95.0 [69.5-99.3]	57.1 [17.2-83.7]
6 months	80.2 [66.3-88.8]	91.7 [70.6-97.9]	85.0 [60.4-94.9]	57.1 [17.2-83.7]
9 months	78.2 [64.0-87.3]	91.7 [70.6-97.9]	85.0 [60.4-94.9]	42.9 [9.8-73.4]
1 year	73.9 [59.3-84.0]	87.5 [66.1-95.8]	74.4 [48.9-88.5]	42.9 [9.8-73.4]
2 years	68.4 [52.7-79.8]	61.3 [38.7-77.7]	53.1 [29.2-72.3]	28.6 [4.1-61.2]
3 years	65.4 [49.3-77.5]	56.2 [33.7-73.6]	47.8 [24.8-67.7]	28.6 [4.1-61.2]
4 years	57.2 [39.5-71.5]	56.2 [33.7-73.6]	41.0 [18.9-62.1]	28.6 [4.1-61.2]
5 years	52.4 [34.0-68.0]	56.2 [33.7-73.6]	41.0 [18.9-62.1]	NE [NE-NE]
6 years	52.4 [34.0-68.0]	56.2 [33.7-73.6]	32.8 [12.2-55.4]	NE [NE-NE]
7 years	52.4 [34.0-68.0]	56.2 [33.7-73.6]	32.8 [12.2-55.4]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.4.3 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	7	4	4	3	3	2	2	2	2	2	2	2	1	1	1	1	1	1	0	0	0	0	0	0	0	0	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)
Favorable	51	44	39	37	35	33	29	25	23	23	21	19	18	17	15	14	14	13	11	10	10	10	10	10	9	8	7	6	6
	(0)	(1)	(2)	(3)	(3)	(5)	(9)	(12)	(13)	(13)	(14)	(16)	(17)	(18)	(19)	(19)	(19)	(20)	(21)	(22)	(22)	(22)	(22)	(22)	(23)	(24)	(25)	(26)	(26)
Intermediate I	24	22	22	22	21	18	16	13	12	10	9	9	8	5	5	5	5	5	5	5	5	5	4	4	4	4	3	2	1
	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(2)	(3)	(4)	(5)	(5)	(6)	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(9)	(10)	(10)	(10)	(10)	(11)	(12)	(13)
Intermediate II	20	19	16	16	14	11	10	10	10	8	8	7	7	6	6	5	5	5	5	5	5	5	5	4	3	3	3	3	1
	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(3)	(3)	(3)	(3)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(5)	(5)	(5)	(5)	(7)

Figure 7. Kaplan-Meier curve of OS according to risk category (ELN 2010) by scientific committee review: FAS (n=113)

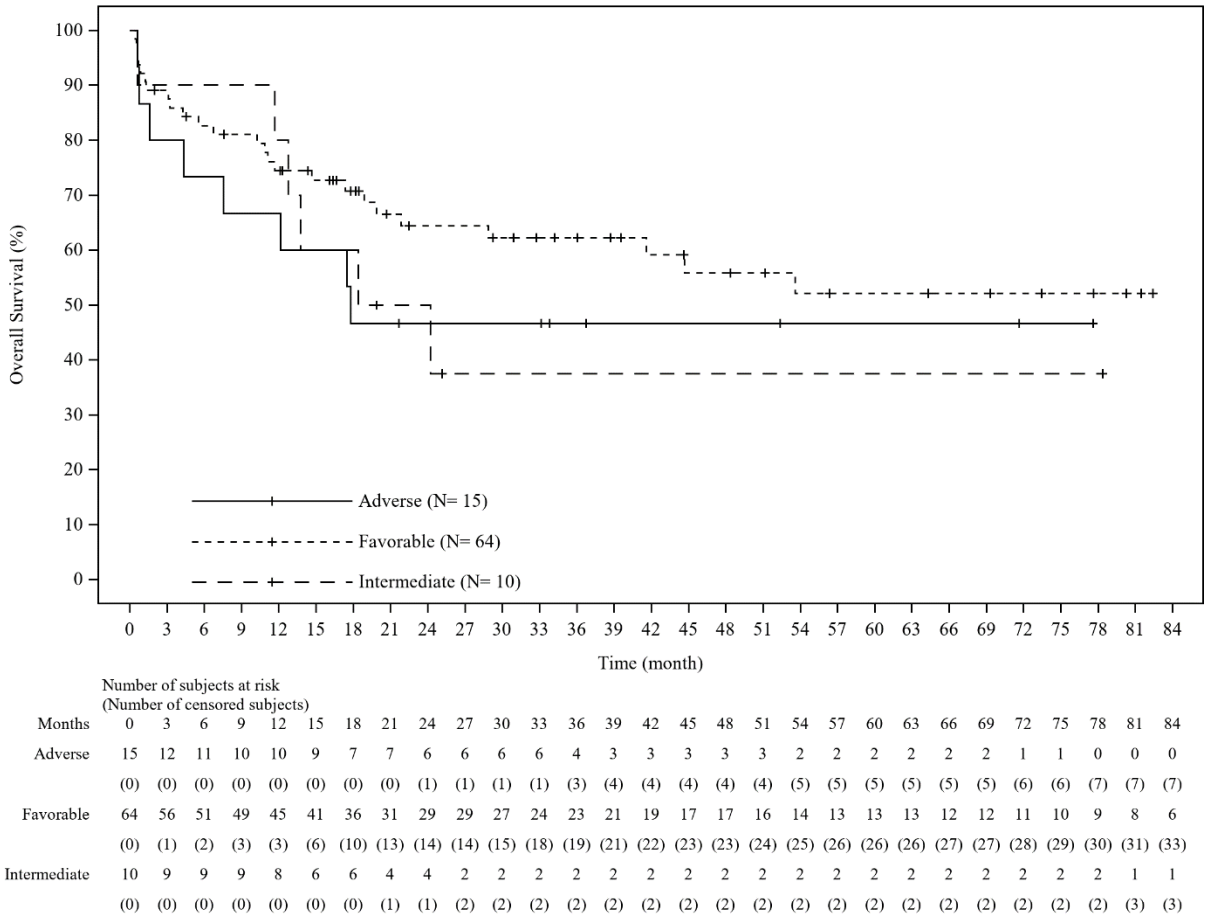
(Source: Figure 15.4.3 TFLs_v1.0_28NOV2023)

At analysis, in FAS (n=113), 89 patients had been classified according to risk factors (ELN 2017) by the scientific committee review: 64/89 (71.9%) with a Favorable risk, 10/89 (11.2%) with an Intermediate risk, and 15/89 (16.9%) with an Adverse risk. The median OS, according to risk categories (ELN 2017) by scientific committee review, was NE (95% CI: 28.8-NE) for patients classified as Favorable risk, 21.3 months (95% CI: 0.6-NE) for those classified as Intermediate risk, and 17.8 months (95% CI: 1.6-NE) in those classified as Adverse risk. Further details and the OS rates, according to risk categories (ELN 2017) by scientific committee review during the study are shown in **Table 30**. The Kaplan-Meier curves for OS according to the risk categories (ELN 2017) by scientific committee review are shown in **Figure 8.**

Table 30. Analysis of overall survival (OS), according to risk categories (ELN 2017) by scientific committee review: FAS (n=113)

	Favorable risk (n=64)	Intermediate risk (n=10)	Adverse risk (n=15)
n	64	10	15
Number of deaths	25	6	8
Number of censored patients	39	4	7
Alive at reference date	39 (100)	4 (100)	7 (100)
Median OS, months [95% CI]	NE [28.8-NE]	21.3 [0.6-NE]	17.8 [1.6-NE]
OS rates, % [95% CI]			
3 months	89.1 [78.4-94.6]	90.0 [47.3-98.5]	80.0 [50.0-93.1]
6 months	82.7 [70.9-90.0]	90.0 [47.3-98.5]	73.3 [43.6-89.1]
9 months	81.1 [69.0-88.8]	90.0 [47.3-98.5]	66.7 [37.5-84.6]
1 year	74.4 [61.7-83.5]	80.0 [40.9-94.6]	66.7 [37.5-84.6]
2 years	64.4 [50.6-75.3]	50.0 [18.4-75.3]	46.7 [21.2-68.8]
3 years	62.2 [48.1-73.5]	37.5 [10.0-65.9]	46.7 [21.2-68.8]
4 years	55.8 [40.6-68.6]	37.5 [10.0-65.9]	46.7 [21.2-68.8]
5 years	52.1 [36.3-65.8]	37.5 [10.0-65.9]	46.7 [21.2-68.8]
6 years	52.1 [36.3-65.8]	37.5 [10.0-65.9]	46.7 [21.2-68.8]
7 years	52.1 [36.3-65.8]	37.5 [10.0-65.9]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.4.4 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	15	12	11	10	10	9	7	7	6	6	6	6	4	3	3	3	3	3	2	2	2	2	2	2	1	1	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(3)	(4)	(4)	(4)	(4)	(4)	(5)	(5)	(5)	(5)	(5)	(5)	(6)	(6)	(7)	(7)	(7)
Favorable	64	56	51	49	45	41	36	31	29	29	27	24	23	21	19	17	17	16	14	13	13	13	12	12	11	10	9	8	6
	(0)	(1)	(2)	(3)	(3)	(6)	(10)	(13)	(14)	(14)	(15)	(18)	(19)	(21)	(22)	(23)	(23)	(24)	(25)	(26)	(26)	(26)	(27)	(27)	(28)	(29)	(30)	(31)	(33)
Intermediate	10	9	9	9	8	6	6	4	4	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(3)	(3)

Figure 8. Kaplan-Meier curve of OS according to risk category (ELN 2017) by scientific committee review: FAS (n=113)

(Source: Figure 15.4.4 TFLs_v1.0_28NOV2023)

10.2.2.5. Analysis of relapse-free survival (RFS)

At analysis, in FAS (n=113) 87 patients had a remission and were included in the analysis of RFS. The median RFS was 17.5 months (95% CI: 12.6-35.6): 25.1 (95% CI: 12.5-NE) in the ATUc (n=62) and 13.0 (95% CI: 8.8-NE) in the Post-ATUc (n=51). Further details and the RFS rates during the study are shown in **Table 31**. The Kaplan-Meier curves for RFS, overall and in the ATUc and Post-ATUc are shown in **Figure 9** and **Figure 10**, respectively.

Table 31. Analysis of relapse-free survival (RFS), overall and in the ATUc and Post-ATUc: FAS with remission (n=87)

	ATU cohort (n=46)	Post-ATU cohort (n=41)	FAS (n=87)
n	46	41	87

Number of events	28	22	50
Deaths	20	10	30
Relapse	23	18	41
Number of censored patients	18	19	37
Alive at reference date	18 (100)	19 (100)	37 (100)
Median RFS, months [95% CI]	25.1 [12.5-NE]	13.0 [8.8-NE]	17.5 [12.6-35.6]
RFS rates, % [95% CI]			
3 months	95.7 [83.7-98.9]	90.1 [75.8-96.2]	93.1 [85.2-96.8]
6 months	91.3 [78.4-96.6]	82.4 [66.6-91.2]	87.1 [78.0-92.7]
9 months	80.1 [65.3-89.1]	66.4 [49.3-79.0]	73.8 [63.0-81.9]
1 year	66.8 [51.0-78.5]	58.2 [41.0-72.0]	62.7 [51.4-72.2]
2 years	53.4 [38.0-66.6]	43.0 [26.6-58.4]	48.5 [37.2-58.9]
3 years	42.3 [27.8-56.1]	37.6 [20.9-54.4]	39.0 [28.0-49.9]
4 years	40.1 [25.9-53.9]	NE [NE-NE]	37.1 [26.0-48.1]
5 years	40.1 [25.9-53.9]	NE [NE-NE]	37.1 [26.0-48.1]
6 years	37.4 [23.4-51.3]	NE [NE-NE]	34.6 [23.4-46.0]
7 years	37.4 [23.4-51.3]	NE [NE-NE]	34.6 [23.4-46.0]

CI, confidence interval; NE, not evaluable.
Source: Table 15.8.2 and 15.8.3 TFLs_v1.0_28NOV2023

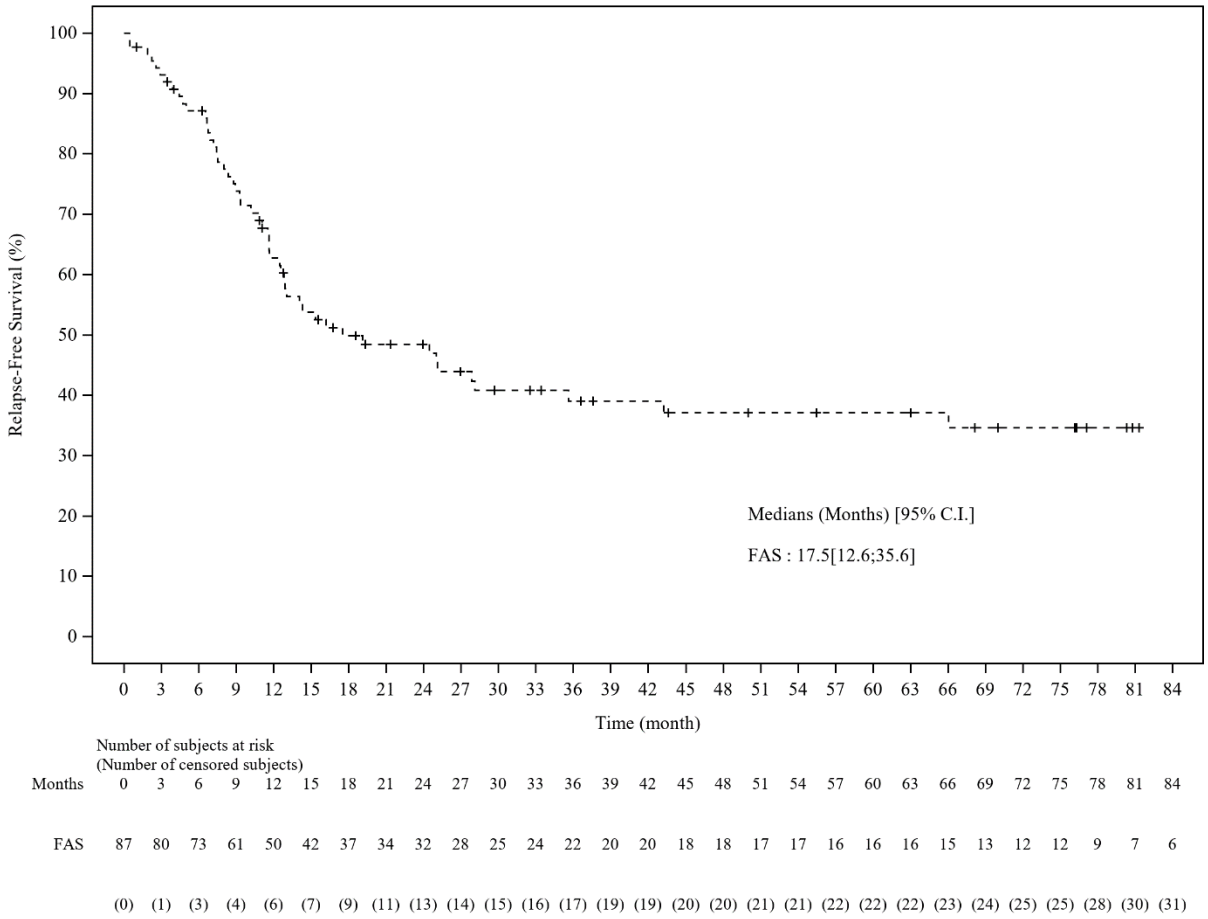
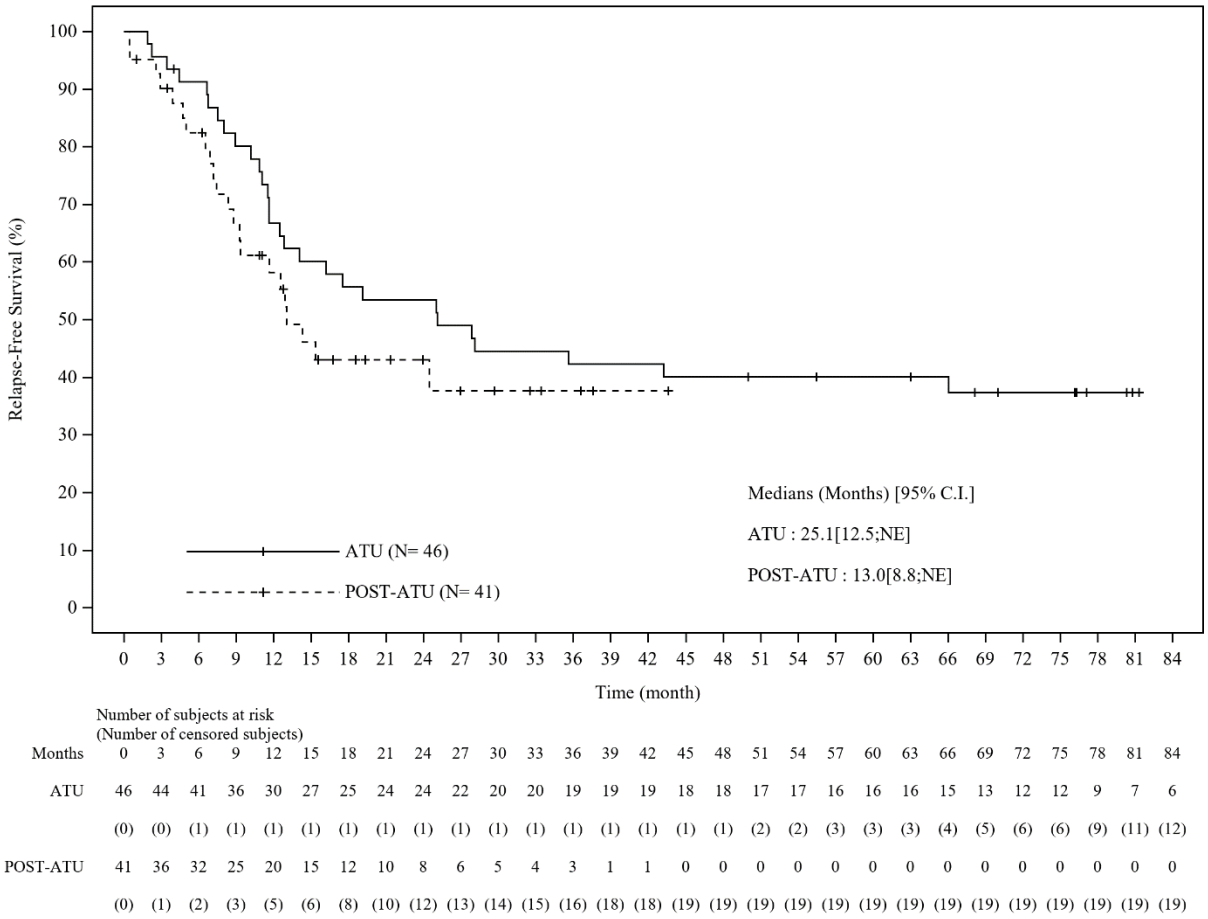


Figure 9. Kaplan-Meier curve of RFS overall: FAS with remission (n=87)

(Source: Figure 15.8.1 TFLs_v1.0_28NOV2023)



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
ATU	46	44	41	36	30	27	25	24	24	22	20	20	19	19	19	18	18	17	17	16	16	16	15	13	12	12	9	7	6
	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(3)	(3)	(3)	(4)	(5)	(6)	(6)	(9)	(11)	(12)
POST-ATU	41	36	32	25	20	15	12	10	8	6	5	4	3	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	(0)	(1)	(2)	(3)	(5)	(6)	(8)	(10)	(12)	(13)	(14)	(15)	(16)	(18)	(18)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)	(19)

Figure 10. Kaplan-Meier curve of RFS in the ATUc and Post-ATUc: FAS with remission (n=87)

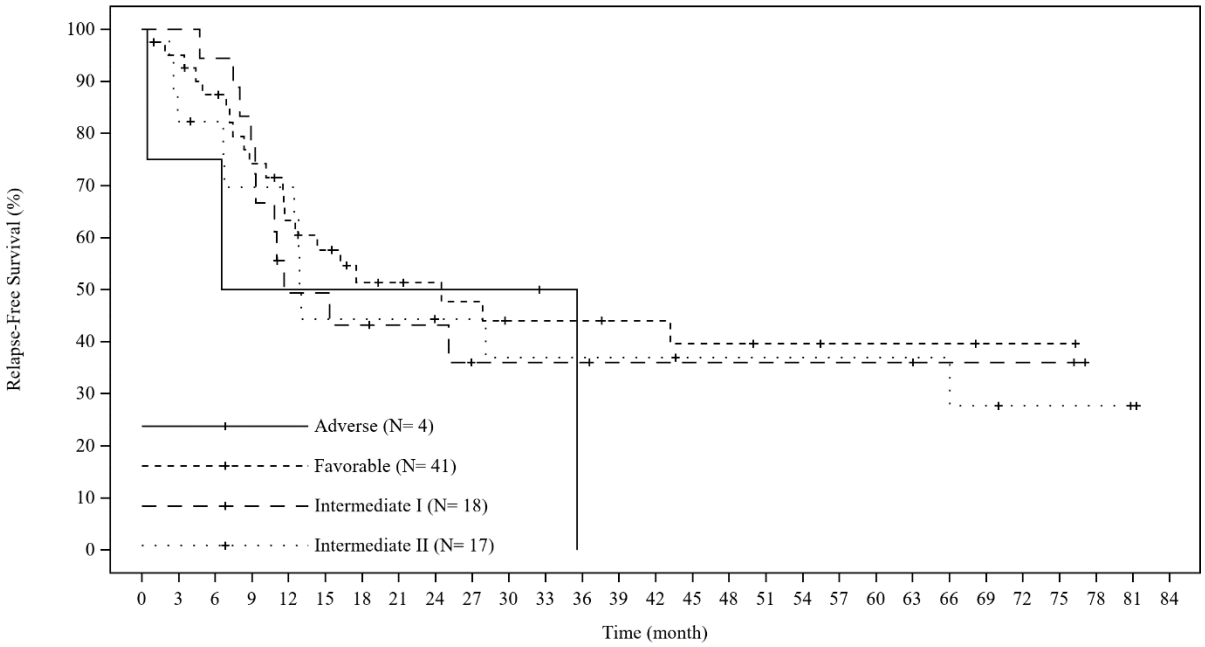
(Source: Figure 15.8.2 TFLs_v1.0_28NOV2023)

At analysis, in FAS with remission (n=87), 80 patients had been classified according to risk factors (ELN 2010) by the scientific committee review: 41/80 (51.3%) with a Favorable risk, 18/80 (22.5%) with an Intermediate I risk, 17/80 (21.3%) with an Intermediate II risk, and 4/80 (5.0%) with an Adverse risk. The median RFS, according to risk categories (ELN 2010) by scientific committee review, was 24.5 months (95% CI: 11.6-NE) for patients classified as Favorable risk, 11.6 (95% CI: 9.3-NE) for those classified as Intermediate I risk, 13.0 (95% CI: 6.6-NE) for those classified as Intermediate II risk, and 21.0 months (95% CI: 0.4-NE) in those classified as Adverse risk. Further details and the RFS rates, according to risk categories (ELN 2010) by scientific committee review during the study are shown in **Table 32**. The Kaplan-Meier curves for RFS according to the risk categories (ELN 2010) by scientific committee review are shown in **Figure 11**.

Table 32. Analysis of relapse-free survival (RFS), according to risk categories (ELN 2010) by scientific committee review: FAS with a remission (n=80)

	Favorable risk with a remission (n=41)	Intermediate I risk with a remission (n=18)	Intermediate II risk with a remission (n=17)	Adverse risk with a remission (n=4)
n	41	18	17	4
Number of events	21	11	11	3
Deaths	9	7	9	2
Relapse	16	11	9	1
Number of censored patients	20	7	6	1
Alive at reference date, n (%)	20 (100)	7 (100)	6 (100)	1 (100)
Median RFS, months [95% CI]	24.5 [11.6-NE]	11.6 [9.3-NE]	13.0 [6.6-NE]	21.0 [0.4-NE]
RFS rates, % [95% CI]				
3 months	95.1 [81.7-98.7]	100 [100-100]	82.4 [54.7-93.9]	75.0 [12.8-96.1]
6 months	87.4 [72.4-94.6]	94.4 [66.6-99.2]	82.4 [54.7-93.9]	75.0 [12.8-96.1]
9 months	74.2 [57.3-85.2]	77.8 [51.1-91.0]	69.7 [41.7-86.2]	50.0 [5.8-84.5]
1 year	63.3 [45.9-76.4]	49.4 [25.2-69.7]	69.7 [41.7-86.2]	50.0 [5.8-84.5]
2 years	51.4 [34.2-66.2]	43.21 [20.2-64.4]	44.3 [20.2-66.1]	50.0 [5.8-84.5]
3 years	44.1 [27.0-59.8]	36.01 [14.6-58.2]	37.0 [14.6-59.7]	NE [NE-NE]
4 years	39.6 [22.7-56.1]	36.0 [14.6-58.2]	37.0 [14.6-59.7]	NE [NE-NE]
5 years	39.6 [22.7-56.1]	36.0 [14.6-58.2]	37.0 [14.6-59.7]	NE [NE-NE]
6 years	39.6 [22.7-56.1]	36.0 [14.6-58.2]	27.7 [8.1-52.0]	NE [NE-NE]
7 years	39.6 [22.7-56.1]	NE [NE-NE]	NE [NE-NE]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.8.4 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	4	3	3	2	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)
Favorable	41	38	34	28	23	20	16	15	14	13	11	11	11	10	10	9	9	8	8	7	7	7	7	6	6	6	5	5	5
	(0)	(1)	(2)	(3)	(4)	(5)	(7)	(8)	(9)	(9)	(10)	(10)	(10)	(11)	(11)	(11)	(11)	(12)	(12)	(13)	(13)	(13)	(13)	(14)	(14)	(14)	(15)	(15)	(15)
Intermediate I	18	18	17	14	8	8	7	6	6	4	4	4	4	3	3	3	3	3	3	3	3	3	2	2	2	2	0	0	0
	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(2)	(2)	(3)	(3)	(3)	(3)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(5)	(5)	(5)	(5)	(7)	(7)	(7)
Intermediate II	17	14	13	11	11	7	7	7	6	6	5	5	5	5	5	4	4	4	4	4	4	4	4	3	2	2	2	1	0
	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(3)	(3)	(3)	(3)	(3)	(3)	(3)	(3)	(3)	(4)	(4)	(4)	(5)	(6)

Figure 11. Kaplan-Meier curve of RFS according to risk category (ELN 2010) by scientific committee review: FAS with a remission (n=80)

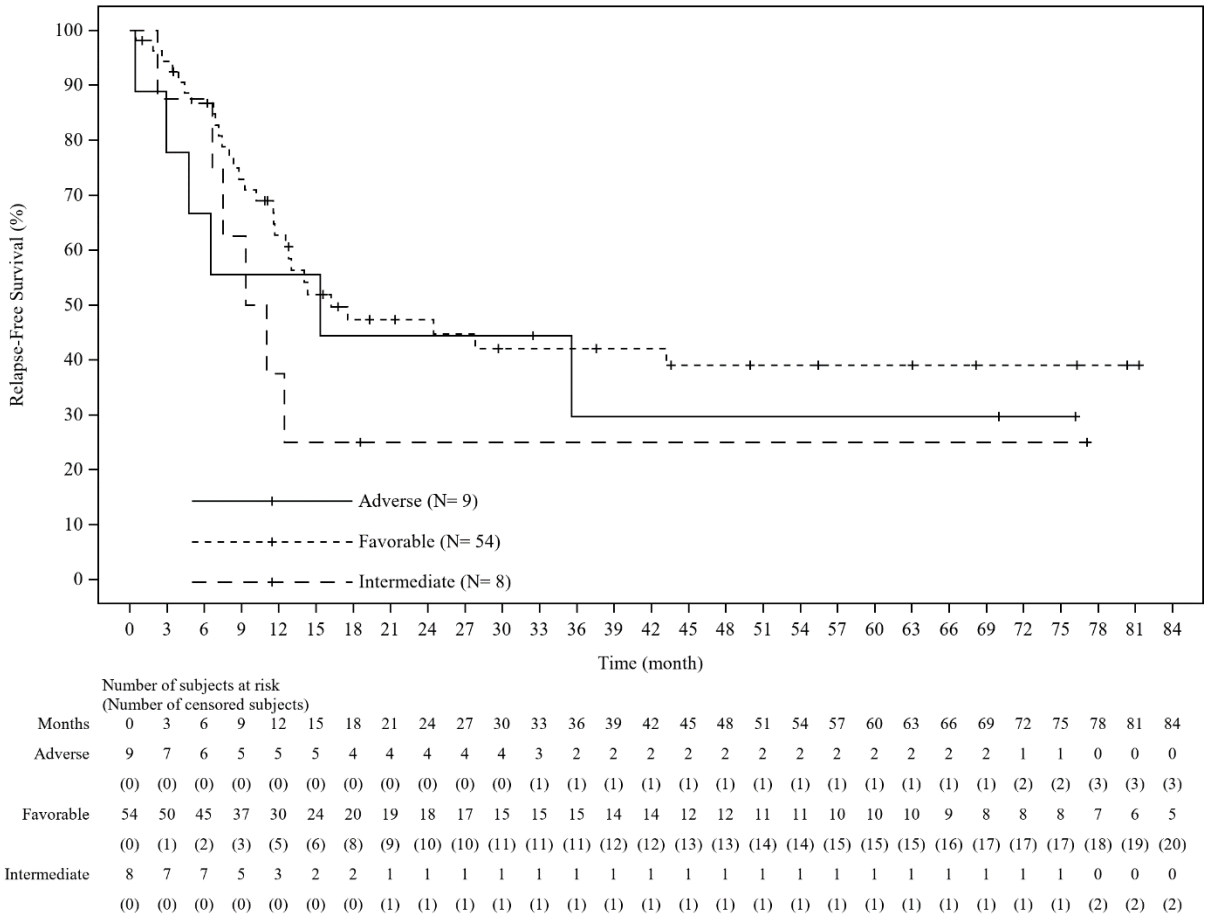
(Source: Figure 15.8.3 TFLs_v1.0_28NOV2023)

At analysis, in the FAS with remission (n=89), 71 patients had been classified according to risk factors (ELN 2017) by the scientific committee review: 54/71 (76.1%) with a Favorable risk, 8/71 (11.3%) with an Intermediate risk, and 9/71 (12.7%) with an Adverse risk. The median RFS, according to risk categories (ELN 2017) by scientific committee review, was 16.2 months (95% CI: 11.7-NE) for patients classified as Favorable risk, 10.2 (95% CI: 2.2-NE) for those classified as Intermediate risk, and 15.3 (95% CI: 0.4-NE) in those classified as Adverse risk. Further details and the RFS rates, according to risk categories (ELN 2017) by scientific committee review during the study are shown in **Table 33**. The Kaplan-Meier curves for RFS according to the risk categories (ELN 2017) by scientific committee review are shown in **Figure 12**.

Table 33. Analysis of relapse-free survival (RFS), according to risk categories (ELN 2017) by scientific committee review: FAS with a remission (n=89)

	Favorable risk (n=64)	Intermediate risk (n=10)	Adverse risk (n=15)
n	54	8	9
Number of events	29	6	6
Deaths	15	5	4
Relapse	24	6	4
Number of censored patients	25	2	3
Alive at reference date, n (%)	25 (100)	2 (100)	3 (100)
Median RFS, months [95% CI]	16.2 [11.7-NE]	10.2 [2.2-NE]	15.3 [0.4-NE]
RFS rates, % [95% CI]			
3 months	94.4 [83.6-98.2]	87.5 [38.7-98.1]	77.8 [36.5-93.9]
6 months	86.7 [74.1-93.4]	87.5 [38.7-98.1]	66.7 [28.2-87.8]
9 months	72.9 [58.6-83.0]	62.5 [22.9-86.1]	55.6 [20.4-80.5]
1 year	62.7 [47.9-74.4]	37.5 [8.7-67.4]	55.6 [20.4-80.5]
2 years	47.3 [32.8-60.6]	25.0 [3.7-55.8]	44.4 [13.6-71.9]
3 years	42.1 [27.7-55.8]	25.0 [3.7-55.8]	29.6 [5.2-60.7]
4 years	39.1 [24.8-53.1]	25.0 [3.7-55.8]	29.6 [5.2-60.7]
5 years	39.1 [24.8-53.1]	25.0 [3.7-55.8]	29.6 [5.2-60.7]
6 years	39.1 [24.8-53.1]	25.0 [3.7-55.8]	29.6 [5.2-60.7]
7 years	39.1 [24.8-53.1]	NE [NE-NE]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.8.5 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	9	7	6	5	5	5	4	4	4	4	4	3	2	2	2	2	2	2	2	2	2	2	2	1	1	0	0	0	
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(3)	(3)	(3)	
Favorable	54	50	45	37	30	24	20	19	18	17	15	15	15	14	14	12	12	11	11	10	10	10	9	8	8	8	7	6	5
	(0)	(1)	(2)	(3)	(5)	(6)	(8)	(9)	(10)	(10)	(11)	(11)	(11)	(12)	(12)	(13)	(13)	(14)	(14)	(15)	(15)	(15)	(16)	(17)	(17)	(17)	(18)	(19)	(20)
Intermediate	8	7	7	5	3	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(2)

Figure 12. Kaplan-Meier curve of RFS according to risk category (ELN 2017) by scientific committee: FAS (n=89)

(Source: Figure 15.8.4 TFLs_v1.0_28NOV2023)

10.2.2.6. Analysis of event-free survival (EFS)

At analysis, in FAS (n=113) the median EFS was 13.1 months (95% CI: 9.9-17.5): 13.9 (95% CI: 9.9-26.4) in the ATUc (n=62) and 9.9 (95% CI: 6.9-15.6) in the Post-ATUc (n=51). Further details and the EFS rates during the study are shown in **Table 34**. The Kaplan-Meier curves for EFS, overall and in the ATUc and Post-ATUc are shown in **Figure 13** and **Figure 14**, respectively.

Table 34. Analysis of event-free survival (EFS), overall and in the ATUc and Post-ATUc: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
n	62	51	113

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Number of events	44	33	77
Deaths	36	17	53
Relapse	6	7	13
Induction failures	23	18	41
Number of censored patients	18	18	36
Alive at reference date, n (%)	18 (100)	18 (100)	36 (100)
Median EFS, months [95% CI]	13.9 [9.9-26.4]	9.9 [6.9-15.6]	13.1 [9.9-17.5]
EFS rates, % [95% CI]			
3 months	79.0 [66.7-87.2]	74.5 [60.2-84.3]	77.0 [68.1-83.7]
6 months	70.9 [57.9-80.6]	66.3 [51.5-77.6]	68.9 [59.4-76.6]
9 months	66.0 [52.7-76.3]	55.8 [40.9-68.3]	61.5 [51.7-69.8]
1 year	61.0 [47.7-71.9]	47.2 [32.7-60.3]	54.9 [45.2-63.7]
2 years	41.2 [28.9-53.2]	32.7 [19.7-46.4]	37.2 [28.1-46.4]
3 years	34.6 [23.0-46.5]	28.6 [15.6-43.1]	31.5 [22.7-40.7]
4 years	31.3 [20.2-43.1]	NE [NE-NE]	28.7 [20.0-37.9]
5 years	29.6 [18.7-41.3]	NE [NE-NE]	27.1 [18.5-36.4]
6 years	27.6 [17.0-39.3]	NE [NE-NE]	25.3 [16.7-34.8]
7 years	27.6 [17.0-39.3]	NE [NE-NE]	25.3 [16.7-34.8]

CI, confidence interval; NE, not evaluable.
Source: Table 15.13.1 and 15.13.2 TFLs_v1.0_28NOV2023

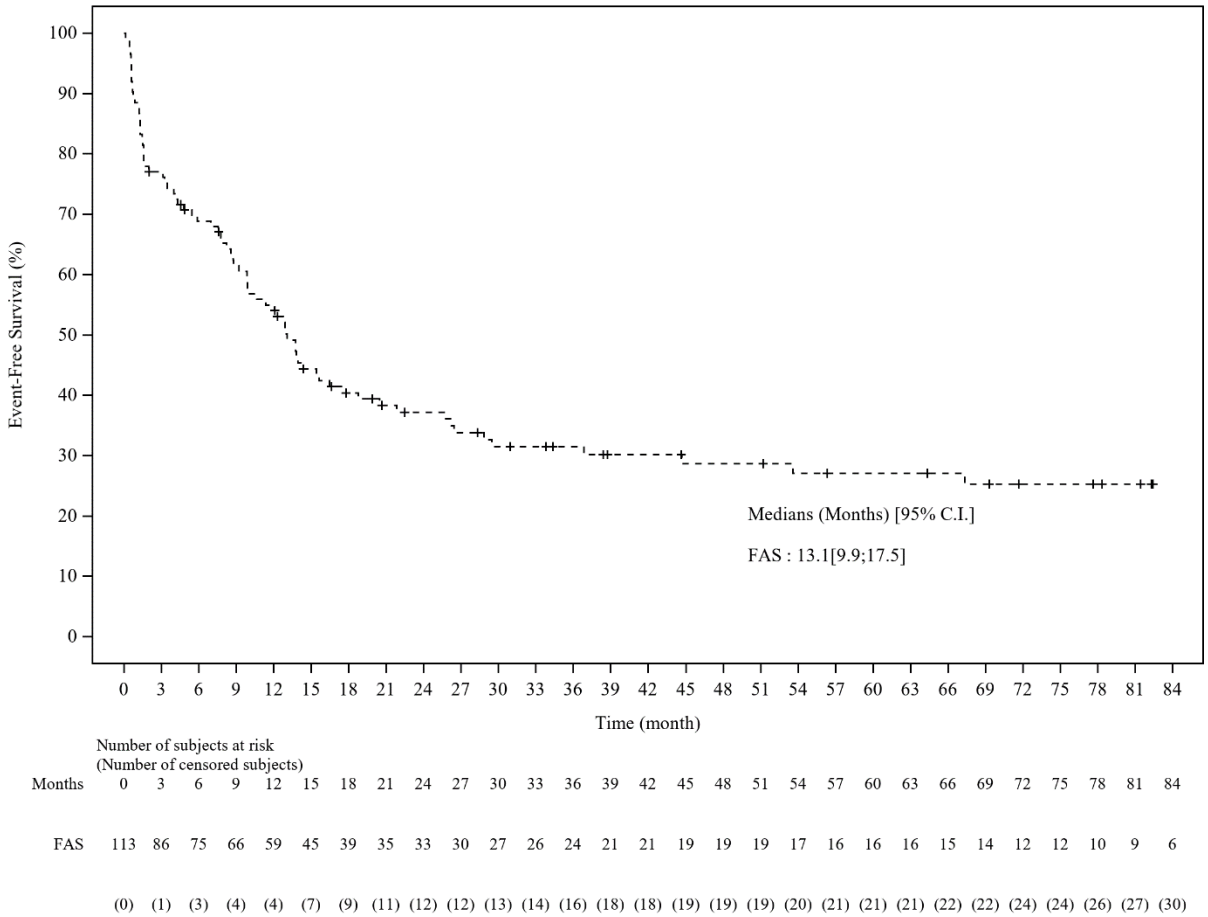


Figure 13. Kaplan-Meier curve of EFS overall: FAS (n=113)

(Source: Figure 15.13.1 TFLs_v1.0_28NOV2023)

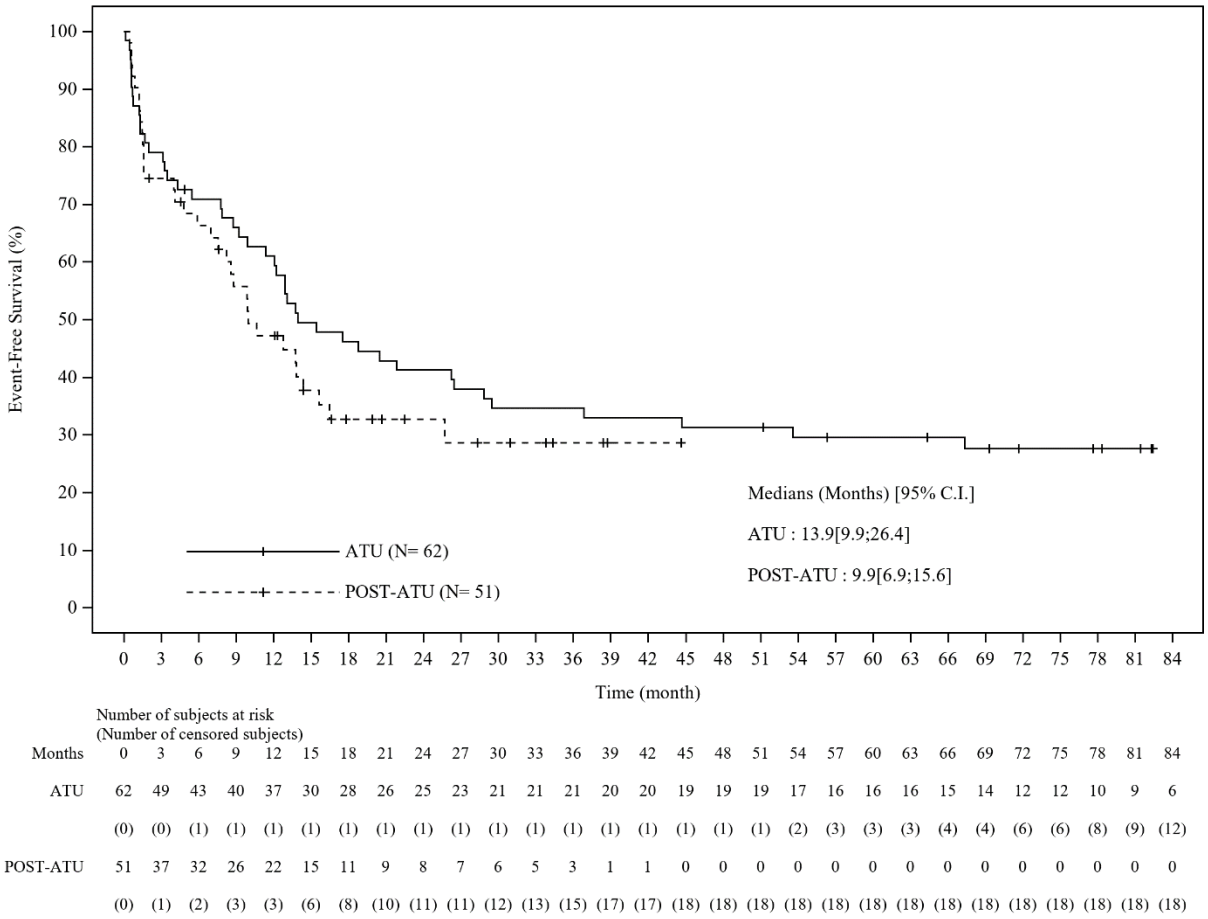


Figure 14. Kaplan-Meier curve of EFS in the ATUc and Post-ATUc: FAS (n=113)

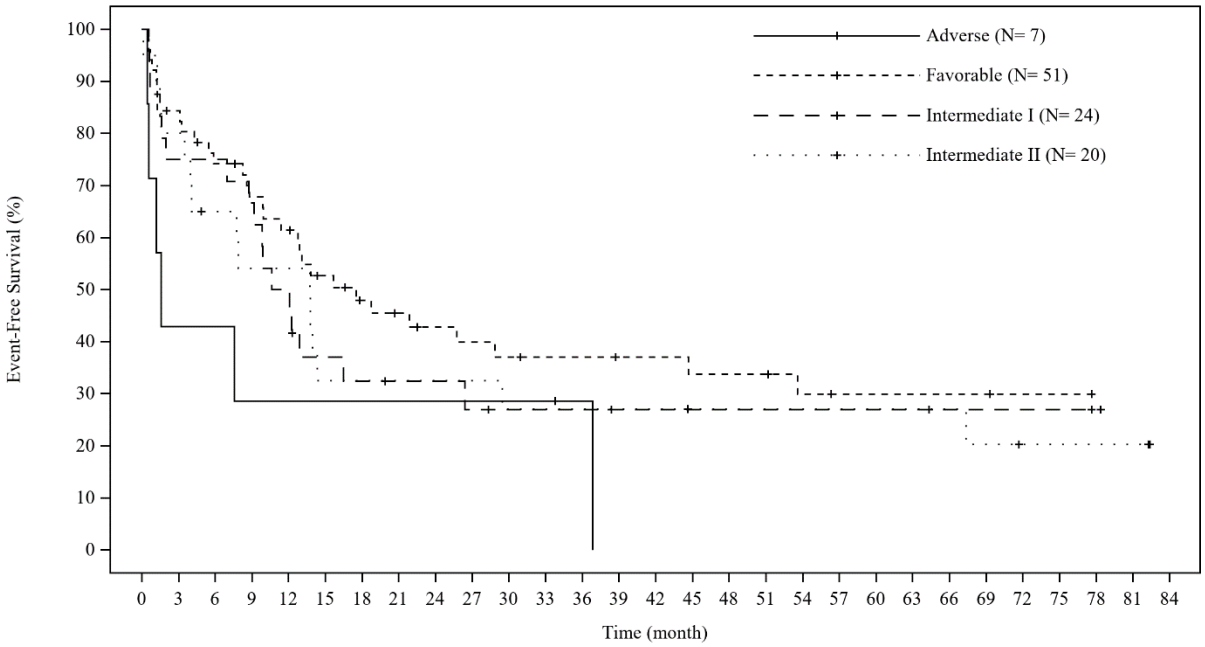
(Source: Figure 15.13.2 TFLs_v1.0_28NOV2023)

At analysis, in FAS (n=113), 102 patients had been classified according to risk factors (ELN 2010) by the scientific committee review: 51/102 (50.0%) with a Favorable risk, 24/102 (23.5%) with an Intermediate I risk, 20/102 (19.6%) with an Intermediate II risk, and 7/102 (6.9%) with an Adverse risk. The median EFS, according to risk categories (ELN 2010) by scientific committee review, was 17.5 months (95% CI: 9.9-44.7) for patients classified as Favorable risk, 11.4 (95% CI: 6.9-26.4) for those classified as Intermediate I risk, 13.7 (95% CI: 3.5-29.5) for those classified as Intermediate II risk, and 1.6 (95% CI: 0.4-NE) in those classified as Adverse risk. Further details and the EFS rates, according to risk categories (ELN 2010) by scientific committee review during the study are shown in **Table 35**. The Kaplan-Meier curves for EFS according to the risk categories (ELN 2010) by scientific committee review are shown in **Figure 15**.

Table 35. Analysis of event-free survival (EFS), according to risk categories (ELN 2010) by scientific committee: FAS (n=113)

	Favorable risk with a remission (n=51)	Intermediate I risk with a remission (n=24)	Intermediate II risk with a remission (n=20)	Adverse risk with a remission (n=7)
n	51	24	20	7
Number of events	31	17	15	6
Deaths	19	10	12	5
Induction failures	2	4	4	2
Relapse	16	11	9	1
Number of censored patients	20	7	5	1
Alive at reference date, n (%)	20 (100)	7 (100)	5 (100)	1 (100)
Median EFS, months [95% CI]	17.5 [9.9-44.7]	11.4 [6.9-26.4]	13.7 [3.5-29.5]	1.6 [0.4-NE]
EFS rates, % [95% CI]				
3 months	84.3 [71.1-91.8]	75.0 [52.6-87.9]	80.0 [55.1-92.0]	42.9 [9.8-73.4]
6 months	74.2 [59.7-84.1]	75.0 [52.6-87.9]	65.0 [40.3-81.5]	42.9 [9.8-73.4]
9 months	67.8 [52.9-78.9]	66.7 [44.3-81.7]	54.2 [30.3-73.0]	28.6 [4.1-61.2]
1 year	61.5 [46.4-73.5]	50.0 [29.1-67.8]	54.2 [30.3-73.0]	28.6 [4.1-61.2]
2 years	42.8 [28.2-56.6]	32.4 [15.0-51.3]	32.5 [13.5-53.3]	28.6 [4.1-61.2]
3 years	37.1 [22.9-51.3]	27.0 [10.9-46.1]	27.1 [10.0-47.7]	28.6 [4.1-61.2]
4 years	33.7 [19.8-48.2]	27.0 [10.9-46.1]	27.1 [10.0-47.7]	NE [NE-NE]
5 years	30.0 [16.3-44.9]	27.0 [10.9-46.1]	27.1 [10.0-47.7]	NE [NE-NE]
6 years	30.0 [16.3-44.9]	27.0 [10.9-46.1]	20.3 [5.7-41.2]	NE [NE-NE]
7 years	30.0 [16.3-44.9]	NE [NE-NE]	NE [NE-NE]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.13.3 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	7	3	3	2	2	2	2	2	2	2	2	2	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)
Favorable	51	42	36	32	29	23	19	17	15	14	13	12	12	11	11	10	10	10	8	7	7	7	7	7	6	6	5	5	5
	(0)	(1)	(2)	(3)	(3)	(5)	(7)	(8)	(9)	(9)	(9)	(10)	(10)	(11)	(11)	(11)	(11)	(11)	(12)	(13)	(13)	(13)	(13)	(13)	(14)	(14)	(15)	(15)	(15)
Intermediate I	24	18	18	16	12	8	7	6	6	5	4	4	4	3	3	3	3	3	3	3	3	3	2	2	2	2	1	0	0
	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(2)	(2)	(2)	(3)	(3)	(3)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(4)	(5)	(5)	(5)	(5)	(6)	(7)	(7)
Intermediate II	20	16	12	10	10	6	6	6	6	6	5	5	5	5	5	4	4	4	4	4	4	4	4	3	2	2	2	2	0
	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(2)	(3)	(3)	(3)	(3)	(5)

Figure 15. Kaplan-Meier curve of EFS according to risk category (ELN 2010) by scientific committee: FAS (n=102)

(Source: Figure 15.13.3 TFLs_v1.0_28NOV2023)

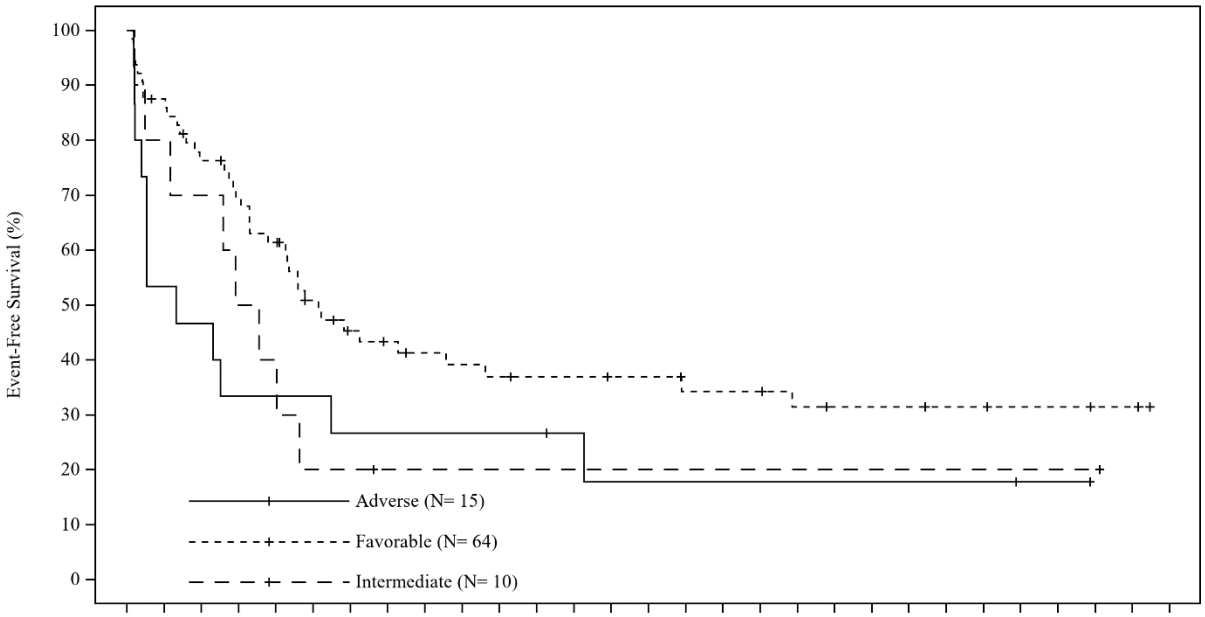
At analysis, in FAS (n=113), 89 patients had been classified according to risk factors (ELN 2017) by the scientific committee review: 64/89 (71.9%) with a Favorable risk, 10/89 (11.2%) with an Intermediate risk, and 15/89 (16.9%) with an Adverse risk. The median EFS, according to risk categories (ELN 2017) by scientific committee review, was 15.4 months (95% CI: 9.9-28.8) for patients classified as Favorable risk, 9.7 (95% CI: 0.6-13.9) for those classified as Intermediate risk, and 4.0 (95% CI: 0.7-16.5) in those classified as Adverse risk. Further details and the EFS rates, according to risk categories (ELN 2017) by scientific committee review during the study are shown in **Table 36**. The Kaplan-Meier curves for EFS according to the risk categories (ELN 2017) by scientific committee review are shown in **Figure 16**.

Table 36. Analysis of event-free survival (EFS), according to risk categories (ELN 2017) by scientific committee review: FAS (n=89)

	Favorable risk (n=64)	**Intermediate risk (n=10)**	**Adverse risk (n=15)**

n	64	10	15
Number of events	39	8	12
Deaths	25	6	8
Induction failures	2	1	5
Relapses	24	6	4
Number of censored patients	25	2	3
Alive at reference date, n (%)	25 (100)	2 (100)	3 (100)
Median EFS, months [95% CI]	15.4 [9.9-28.8]	9.7 [0.6-13.9]	4.0 [0.7-16.5]
EFS rates, % [95% CI]			
3 months	87.5 [76.6-93.5]	80.0 [40.9-94.6]	53.3 [26.3-74.4]
6 months	76.3 [63.7-85.0]	70.0 [32.9-89.2]	46.7 [21.2-68.8]
9 months	69.6 [56.6-79.5]	50.0 [18.4-75.3]	33.3 [12.2-56.4]
1 year	61.4 [48.5-72.2]	40.0 [12.3-67.0]	33.3 [12.2-56.4]
2 years	41.3 [28.5-53.6]	20.0 [3.1-47.5]	26.7 [8.3-49.6]
3 years	36.9 [24.4-49.5]	20.0 [3.1-47.5]	26.7 [8.3-49.6]
4 years	34.3 [21.9-47.1]	20.0 [3.1-47.5]	17.8 [3.4-41.4]
5 years	31.4 [19.2-44.5]	20.0 [3.1-47.5]	17.8 [3.4-41.4]
6 years	31.4 [19.2-44.5]	20.0 [3.1-47.5]	17.8 [3.4-41.4]
7 years	31.4 [19.2-44.5]	NE [NE-NE]	NE [NE-NE]

CI, confidence interval; NE, not evaluable.
Source: Table 15.13.4 TFLs_v1.0_28NOV2023



Number of subjects at risk
(Number of censored subjects)

Months	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
Adverse	15	8	7	5	5	5	4	4	4	4	4	4	3	2	2	2	2	2	2	2	2	2	2	2	1	1	0	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)	(3)	(3)	(3)
Favorable	64	55	47	42	37	28	23	21	19	18	17	16	16	15	15	13	13	13	11	10	10	10	9	9	8	8	7	7	5
	(0)	(1)	(2)	(3)	(3)	(6)	(8)	(9)	(10)	(10)	(10)	(11)	(11)	(12)	(12)	(13)	(13)	(13)	(14)	(15)	(15)	(15)	(16)	(16)	(17)	(17)	(18)	(18)	(20)
Intermediate	10	8	7	5	4	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	0
	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(1)	(2)	(2)

Figure 16. Kaplan-Meier curve of EFS according to risk category (ELN 2017) by scientific committee review: FAS (n=89)

(Source: Figure 15.13.4 TFLs_v1.0_28NOV2023)

10.2.3. Search for prognostic factors for OS, RFS, and EFS

10.2.3.1. Prognostic factors for overall survival (OS)

The multivariate analysis found age to be significantly associated with shorter OS (see **Table 37** and **Figure 17**). Therefore, older age was identified as a prognostic factor for shorter OS.

Table 37. Analysis of prognostic factors for overall survival: FAS (n=113)

Time variable: OS	Number of events	Medians (months) [95% CI]	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Age at the Mylotarg® initiation by 1			1.05 [1.02-1.07]	<.001	1.06 [1.03-1.09]	<.001
Sex				0.866		
Male (Ref)	29/62	49.8 [17.8-NE]				
Female	24/51	37.2 [17.3-NE]	0.95 [0.56-1.64]			
ECOG				0.012		
0-1 (Ref)	28/72	NR [28.8-NE]				
≥2	11/16	6.7 [4.3-NE]	2.47 [1.22-4.98]			
WBC Count by 1			1.00 [1.00-1.01]	0.177		
Blasts (%) by 1			1.00 [0.99-1.01]	0.881		
CD33 antigen				0.576		
<30 (Ref)	1/3	NR [0.9-NE]				
≥30	50/106	44.7 [19.8-NE]	1.76 [0.24-12.81]			
CD33 antigen				0.284		
<70 (Ref)	6/20	NR [14.9-NE]				
≥70	45/89	41.6 [18.4-NE]	1.59 [0.68-3.74]			
NPM1 Mutation				0.523		
Absent (Ref)	32/68	44.7 [18.4-NE]				
Present	18/41	NR [14.7-NE]	0.83 [0.46-1.48]			
FLT3TKD Mutation				0.689		
Absent (Ref)	23/58	53.6 [24.2-NE]				
Present	2/6	41.6 [4.3-NE]	1.28 [0.38-4.30]			
FLT3ITD Mutation				0.759		
Absent (Ref)	37/84	49.8 [24.2-NE]				
Present	11/22	25.0 [11.7-NE]	1.11 [0.57-2.18]			
CEBPA Mutation				0.499		
Absent (Ref)	33/72	44.7 [18.4-NE]				
Present	3/5	4.7 [1.3-NE]	1.51 [0.46-4.93]			
Risk Classification ELN 2017 as per scientific committee review				0.468		
Favorable (Ref)	25/64	NR [28.8-NE]				
Intermediate	6/10	21.3 [0.6-NE]	1.53 [0.63-3.73]			
Adverse	8/15	17.8 [1.6-NE]	1.50 [0.68-3.32]			
Risk Classification ELN 2010 as per scientific committee review				0.113		
Favorable (Ref)	19/51	NR [28.8-NE]				
Intermediate I	10/24	NR [17.8-NE]	1.03 [0.48-2.22]			
Intermediate II	12/20	24.2 [11.7-NE]	1.58 [0.76-3.25]			
Adverse	5/7	7.6 [0.4-NE]	3.09 [1.15-8.32]			

Time variable: OS	Number of events	Medians [95% CI] (months)	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Cytogenetic Classification as per scientific committee review				<.001		
Favorable (Ref)	12/32	53.6 [28.8-NE]				
Intermediate	27/60	67.4 [18.4-NE]	1.12 [0.57-2.22]			
Adverse	6/6	4.6 [0.4-NE]	5.77 [2.12-5.65]			

CI, confidence interval; HR, hazard ratio; NE, not evaluable; OS, overall survival; Ref; reference value.
Source: Table 15.5.1 TFLs_v1.0_28NOV2023

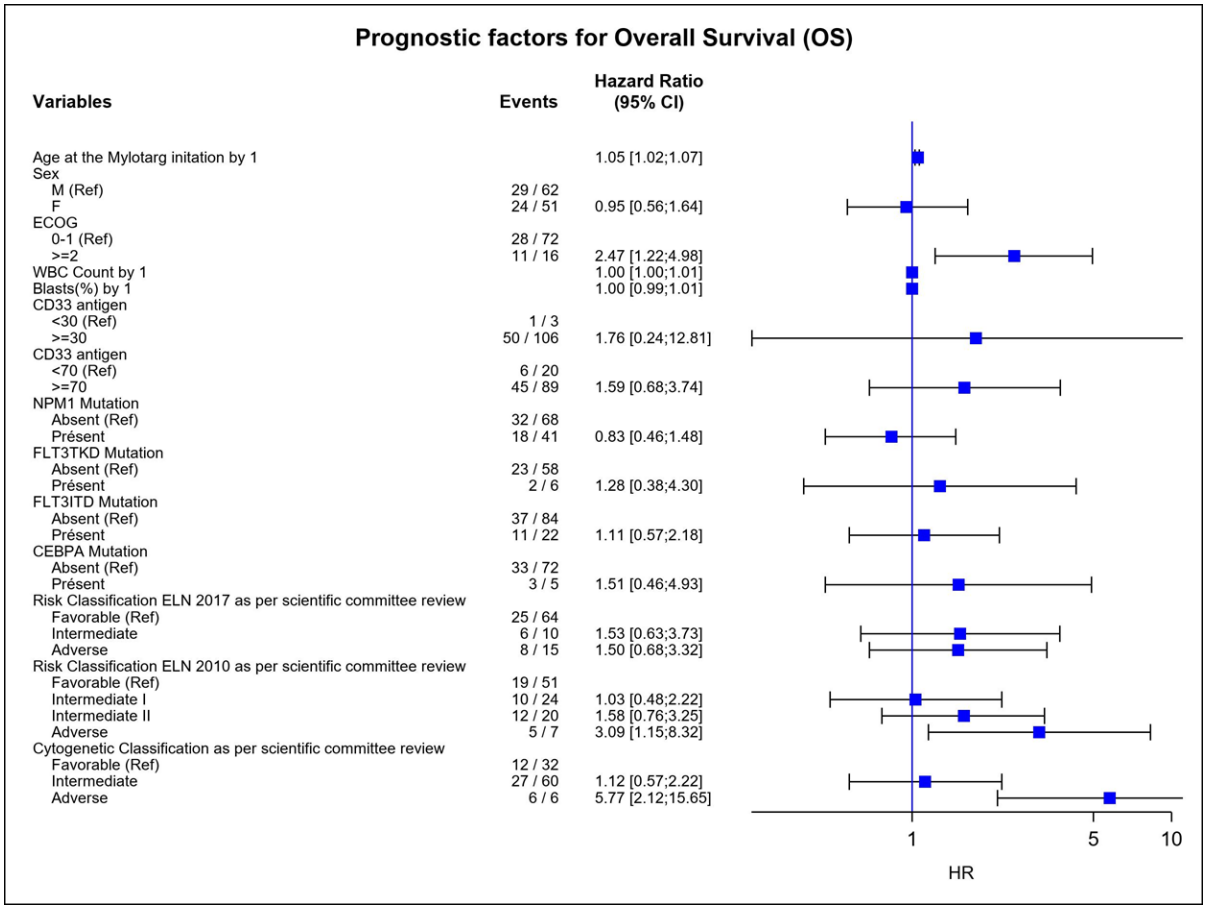


Figure 17. Forest plot of prognostic factors for overall survival (OS): FAS (n=113)

(Source: Figure 15.6.1 TFLs_v1.0_28NOV2023)

10.2.3.2. Prognostic factors for relapse-free survival (RFS)

In the multivariate analysis, ECOG ≥2 and cytogenetic classification of adverse were found to be significantly associated with shorter RFS (see **Table 38** and **Figure 18**). Therefore, ECOG ≥2 and cytogenetic classification of adverse were identified as prognostic factors for shorter RFS.

Table 38. Analysis of prognostic factors for relapse-free survival: FAS with a remission (n=87)

Time variable: RFS	Number of events	Medians (months) [95% CI]	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Age at the Mylotarg® initiation by 1			1.02 [1.00-1.05]	0.049		
Sex				0.547		
Male (Ref)	28/44	24.5 [11.6-35.6]				
Female	22/43	17.5 [11.0-NE]	0.84 [0.48-1.47]			
ECOG				0.064		0.005
0-1 (Ref)	35/61	17.5 [12.5-66.0]				
≥2	8/11	6.6 [2.9-25.1]	2.08 [0.96-4.50]		6.58 [1.77;24.48]	
WBC Count by 1			1.00 [1.00-1.01]	0.158		
Blasts (%) by 1			1.01 [1.00-1.02]	0.172		
CD33 antigen				0.986		
<30 (Ref)	0/2	NR [NE-NE]				
≥30	47/82	19.1 [12.5-43.2]				
CD33 antigen				0.799		
<70 (Ref)	8/15	27.8 [11.7-NE]				
≥70	39/69	24.5 [11.6-66.0]	1.10 [0.52-2.37]			
NPM1 Mutation				0.421		
Absent (Ref)	31/50	19.1 [11.6-35.6]				
Present	19/36	17.5 [11.0-NE]	0.79 [0.45-1.40]			
FLT3-TKD Mutation				0.004		
Absent (Ref)	24/47	25.1 [11.7-NE]				
Present	6/6	7.2 [2.9-NE]	4.03 [1.57-10.36]			
FLT3-ITD Mutation				0.603		
Absent (Ref)	38/66	19.1 [12.8-35.6]				
Present	11/19	11.0 [6.7-NE]	1.20 [0.61-2.34]			
CEBPA Mutation				0.781		
Absent (Ref)	31/56	24.5 [12.8-43.2]				
Present	2/3	12.6 [0.5-NE]	1.23 [0.29-5.16]			
Risk Classification ELN 2017 as per scientific committee review				0.407		
Favorable (Ref)	29/54	16.2 [11.7-NE]				
Intermediate	6/8	10.2 [2.2-NE]	1.77 [0.73-4.29]			
Adverse	6/9	15.3 [0.4-NE]	1.33 [0.55-3.21]			
Risk Classification ELN 2010 as per scientific committee review				0.791		
Favorable (Ref)	21/41	24.5 [11.6-NE]				
Intermediate I	11/18	11.6 [9.3-NE]	1.20 [0.58-2.50]			
Intermediate II	11/17	13.0 [6.6-NE]	1.28 [0.61-2.65]			
Adverse	3/4	21.0 [0.4-NE]	1.73 [0.51-5.81]			

Time variable: RFS	Number of events	Medians [95% CI] (months)	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Cytogenetic Classification as per scientific committee review				<.001		0.001
Favorable (Ref)	13/25	27.8 [8.8-NE]				
Intermediate	28/48	17.5 [11.6-66.0]	0.99 [0.51-1.91]		2.12 [0.76;5.87]	
Adverse	3/3	2.2 [0.4-NE]	18.41 [4.49-75.55]		72.74 [7.57;699.14]	

CI, confidence interval; HR, hazard ratio; NE, not evaluable; Ref; reference value; RFS, relapse-free survival.
Source: Table 15.9.1 TFLs_v1.0_28NOV2023

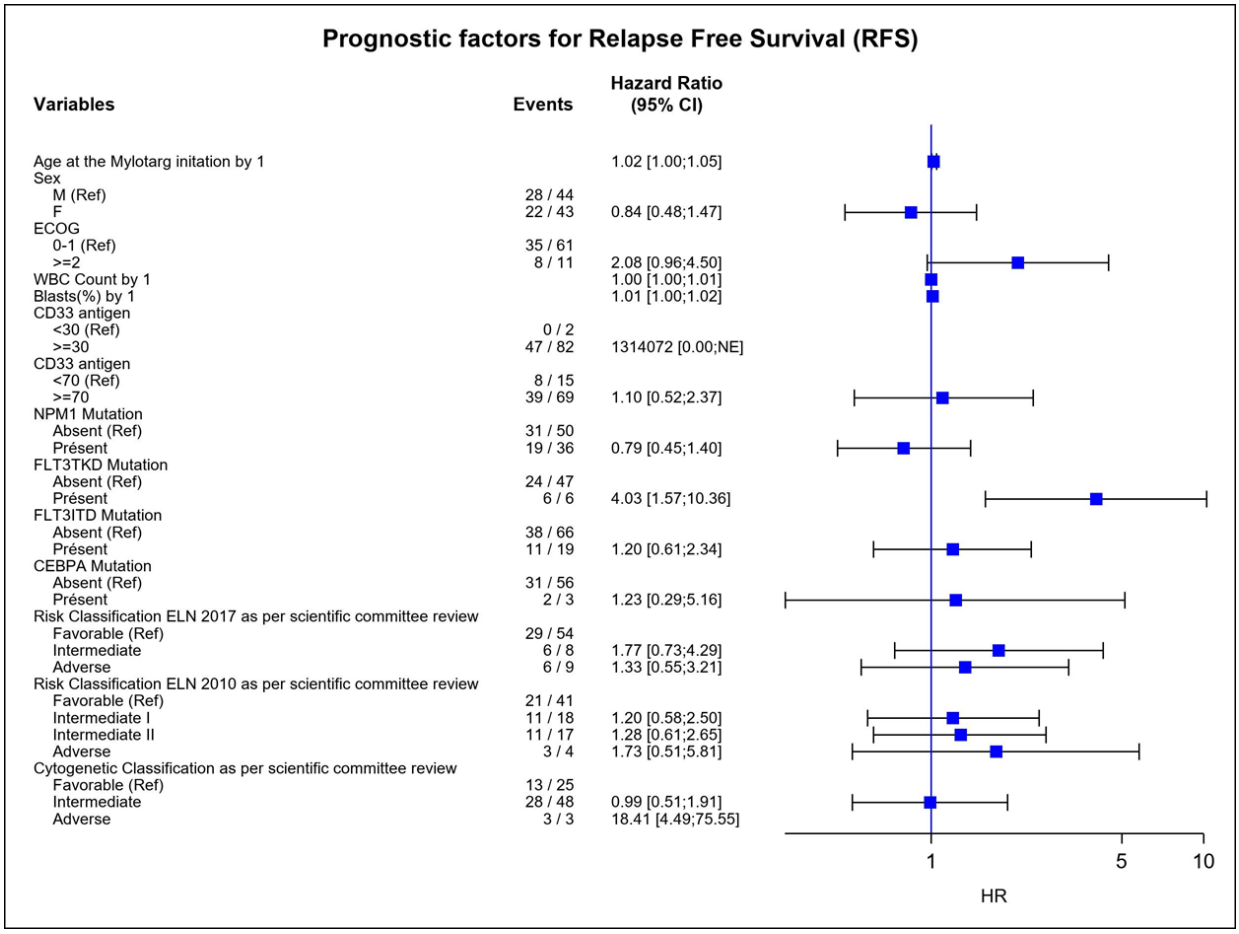


Figure 18. Forest plot of prognostic factors for relapse-free survival (RFS): FAS with a remission (n=87)

(Source: Figure 15.10.1 TFLs_v1.0_28NOV2023)

10.2.3.3. Prognostic factors for event-free survival (EFS)

The multivariate analysis found that FLT3-TKD mutation and cytogenetic classification of adverse were found to be significantly associated with shorter EFS (see **Table 39** and **Figure 19**). Therefore, FLT3-TKD mutation and cytogenetic classification of adverse were identified as prognostic factors for shorter EFS.

Table 39. Analysis of prognostic factors for event-free survival: FAS (n=113)

Time variable: EFS	Number of events	Medians (months) [95% CI]	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Age at the Mylotarg® initiation by 1			1.02 [1.00-1.04]	0.065		
Sex				0.058		
Male (Ref)	47/62	11.4 [6.9-13.8]				
Female	30/51	17.5 [9.9-53.6]	0.64 [0.41-1.02]			
ECOG				0.045		
0-1 (Ref)	46/72	13.9 [10.6-25.7]				
≥2	13/16	5.3 [1.5-21.8]	1.88 [1.01-3.50]			
WBC Count by 1			1.00 [1.00-1.01]	0.106		
Blasts (%) by 1			1.00 [1.00-1.01]	0.408		
CD33 antigen				0.303		
<30 (Ref)	1/3	NR [0.7-NE]				
≥30	72/106	13.1 [9.9-18.8]	2.83 [0.39-20.41]			
CD33 antigen				0.987		
<70 (Ref)	13/20	16.5 [1.6-36.8]				
≥70	60/89	12.9 [8.7-21.8]	1.01 [0.55-1.83]			
NPM1 Mutation				0.176		
Absent (Ref)	49/68	12.8 [8.2-17.5]				
Present	25/41	13.8 [8.7-NE]	0.72 [0.44-1.16]			
FLT3TKD Mutation				0.064		0.013
Absent (Ref)	35/58	14.4 [9.9-44.7]				
Present	6/6	8.7 [4.0-NE]	2.32 [0.95-5.64]		4.10 [1.35-12.42]	
FLT3ITD Mutation				0.654		
Absent (Ref)	56/84	13.8 [10.6-25.7]				
Present	15/22	9.5 [4.1-NE]	1.14 [0.64-2.02]			
CEBPA Mutation				0.486		
Absent (Ref)	47/72	13.8 [9.9-26.2]				
Present	4/5	1.3 [1.2-NE]	1.44 [0.52-4.02]			
Risk Classification ELN 2017 as per scientific committee review				0.099		
Favorable (Ref)	39/64	15.4 [9.9-28.8]				
Intermediate	8/10	9.7 [0.6-13.9]	1.70 [0.79-3.64]			
Adverse	12/15	4.0 [0.7-16.5]	1.88 [0.98-3.60]			
Risk Classification ELN 2010 as per scientific committee review				0.264		
Favorable (Ref)	31/51	17.5 [9.9-44.7]				
Intermediate I	17/24	11.4 [6.9-26.4]	1.31 [0.73-2.38]			
Intermediate II	15/20	13.7 [3.5-29.5]	1.33 [0.72-2.47]			

Time variable: EFS	Number of events	Medians (months) [95% CI]	Univariate HR [95% CI]	Univariate Wald p-value	Multivariate HR [95% CI]	Multivariate Wald p-value
Adverse	6/7	1.6 [0.4-NE]	2.35 [0.98-5.65]			
Cytogenetic Classification as per scientific committee review				<.001		0.015
Favorable (Ref)	20/32	17.5 [8.8-44.7]				
Intermediate	41/60	13.7 [9.2-25.7]	1.11 [0.65-1.89]		1.47 [0.66-3.29]	
Adverse	6/6	1.4 [0.4-NE]	7.16 [2.72-18.86]		13.03 [2.30-73.79]	

CI, confidence interval; EFS, event-free survival; HR, hazard ratio; NE, not evaluable; Ref; reference value.
Source: Table 15.14.1 TFLs_v1.0_28NOV2023

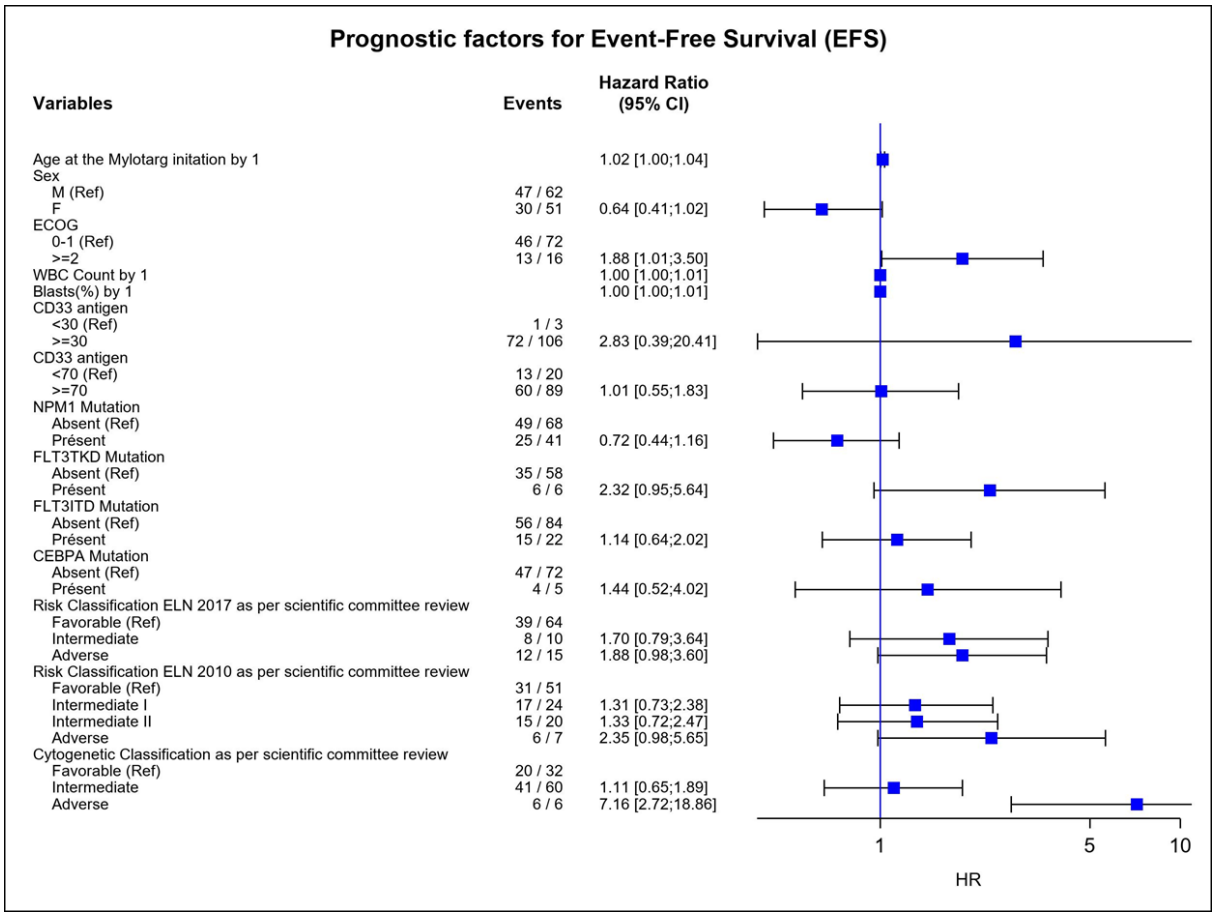


Figure 19. Forest plot of prognostic factors for event-free survival (EFS): FAS (n=113)

(Source: Figure 15.15.1 TFLs_v1.0_28NOV2023)

10.2.4. HSCT following Mylotarg® treatment

In the FAS (n=113), 35/111 patients (31.5%; missing data [n=2]) had HSCT after treatment with Mylotarg®. Among the 35 patients that received a HSCT: 15/35 (42.9%) were from related donors, 13/35 (37.1%) from unrelated donors, and for 7/35 (20.0%) the information was unknown. The median time interval from the last dose of Mylotarg® to HSCT was 13.0 months (Q1-Q3: 4.8-16.4). After HSCT, 32/35 patients (91.4%) were in remission (CR/CRp/CRh). All the 35 patients (100.0%) had HSCT ≥2 months after the last dose of Mylotarg®. See **Table 40** for details.

Table 40. (HSCT) after Mylotarg® treatment: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Hematopoietic stem cell transplantation (HSCT), n (%)			
n	60	51	111

No	48 (80.0)	28 (54.9)	76 (68.5)
Yes	12 (20.0)	23 (45.1)	35 (31.5)
Missing data	2	0	2
Type of HSCT, n (%)			
n	12	23	35
Related donor	4 (33.3)	11 (47.8)	15 (42.9)
Unrelated donor	4 (33.3)	9 (39.1)	13 (37.1)
Unknown donor	4 (33.3)	3 (13.0)	7 (20.0)
Missing data	0	0	0
Type of conditioning regimen, n (%)			
n	12	23	35
Myeloablative	8 (66.7)	13 (56.5)	21 (60.0)
Non-myeloablative	3 (25.0)	7 (30.4)	10 (28.6)
Unknown	1 (8.3)	3 (13.0)	4 (11.4)
Missing data	0	0	0
Patient's status at transplantation, n (%)			
n	12	23	35
In CR1	1 (8.3)	12 (52.2)	13 (37.1)
In CR2 or more	9 (75.0)	11 (47.8)	20 (57.1)
In relapse	1 (8.3)	0 (0.0)	1 (2.9)
Unknown	1 (8.3)	0 (0.0)	1 (2.9)
Missing data	0	0	0
Patient's status after transplantation, n (%)			
n	12	23	35
Death	0 (0.0)	1 (4.4)	1 (2.9)
Relapse	1 (8.3)	1 (4.4)	2 (5.7)
Remission (CR/CRp/CRh)	11 (91.7)	21 (91.3)	32 (91.4)
Missing data	0	0	0
Time interval between transplantation and last Mylotarg® dose (months), n (%)			
n	12	23	35
Mean (SD)	16.2 (9.5)	10.6 (7.2)	12.5 (8.4)
Median	15.8	10.9	13.0
Q1-Q3	9.1-19.8	4.5-14.8	4.8-16.4
Range	3.1-33.0	3.0-31.0	3.0-33.0
≥2 months	12 (100)	23 (100)	35 (100)
Missing data	0	0	0

CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; D, day; HSCT, hematopoietic stem cell transplantation; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 15.18.1 TFLs_v1.0_28NOV2023

In the FAS (n=113), 102 patients had data concerning HSCT and were classified according to the ELN (2010) by the scientific committee review. Among the 102 patients, 34/100 (34.0%; missing data [n=2]) had HSCT after treatment with Mylotarg®: 13/49 (26.5%; missing data [n=2]) with Favourable risk, 12/24 (50.0%) with Intermediate I risk, 7/20 (35.0%) with Intermediate II risk, and 2/7 (28.6%) with Adverse risk. Among the 34 patients that underwent HSCT, 31/34 (91.2%) were in remission (CR/CRp/CRh) after HSCT: 13/13 (100%) with Favourable risk, 10/12 (83.3%) with Intermediate I risk, 6/7 (85.7%) with Intermediate II risk, and 2/2 (100%) with Adverse risk. See **Table 41** for details.

Table 41. (HSCT) after Mylotarg® treatment by ELN 2010 as per scientific committee review: FAS (n=113)

	Favorable risk (n=51)	Intermediate I risk (n=24)	Intermediate II risk (n=20)	Adverse risk (n=7)	Total (n=102)
Hematopoietic stem cell transplantation (HSCT), n (%)					
n	49	24	20	7	100
No	36 (73.5)	12 (50.0)	13 (65.0)	5 (71.4)	66 (66.0)
Yes	13 (26.5)	12 (50.0)	7 (35.0)	2 (28.6)	34 (34.0)
Missing data	2	0	0	0	2
Type of HSCT, n (%)					
n	13	12	7	2	34
Related donor	6 (46.2)	4 (33.3)	3 (42.9)	1 (50.0)	14 (41.2)
Unrelated donor	6 (46.2)	5 (41.7)	1 (14.3)	1 (50.0)	13 (38.2)
Unknown donor	1 (7.7)	3 (25.0)	3 (42.9)	0 (0.0)	7 (20.6)
Missing data	0	0	0	0	0
Type of conditioning regimen, n (%)					
n	13	12	7	2	34
Myeloablative	11 (84.6)	3 (25.0)	5 (71.4)	1 (50.0)	20 (58.8)
Non-myeloablative	2 (15.4)	5 (41.7)	2 (28.6)	1 (50.0)	10 (29.4)
Unknown	0 (0.0)	4 (33.3)	0 (0.0)	0 (0.0)	4 (11.8)
Missing data	0	0	0	0	0
Patient's status at transplantation, n (%)					
n	13	12	7	2	34
In CR1	3 (23.1)	5 (41.7)	2 (28.6)	2 (100)	12 (35.3)
In CR2 or more	10 (76.9)	5 (41.7)	5 (71.4)	0 (0.0)	20 (58.8)
In relapse	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.9)
Unknown	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.9)
Missing data	0	0	0	0	0
Patient's status after transplantation, n (%)					
n	13	12	7	2	34
Death	0 (0.0)	1 (8.3)	0 (0.0)	0 (0.0)	1 (2.9)
Relapse	0 (0.0)	1 (8.3)	1 (14.3)	0 (0.0)	2 (5.9)
Remission (CR/CRp/CRh)	13 (100)	10 (83.3)	6 (85.7)	2 (100)	31 (91.2)
Missing data	0	0	0	0	0
Time interval between transplantation and last Mylotarg® dose (months), n (%)					
n	13	12	7	2	34
Mean (SD)	14.8 (6.9)	11.3 (8.5)	13.9 (10.8)	4.1 (1.6)	12.8 (8.4)
Median	14.7	8.8	11.5	4.1	13.5
Q1-Q3	13.0-16.3	4.6-16.1	4.5-21.0	3.0-5.2	4.8-16.4
Range	3.4-31.0	3.1-32.0	4.4-33.0	3.0-5.2	3.0-33.0
≥2 months	13 (100)	12 (100)	7 (100)	2 (100)	34 (100)
Missing data	0	0	0	0	0

CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; D, day; HSCT, hematopoietic stem cell transplantation; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 15.18.2 TFLs_v1.0_28NOV2023

In the FAS (n=113), 89 patients had received HSCT and were classified according to the ELN (2017) by the scientific committee review. Among the 89 patients (missing data [n=1]), 25/88 (28.4%) had HSCT after treatment with Mylotarg®: 15/62 (23.8%; missing data [n=1]) with Favourable risk, 5/10 (50.0%) with Intermediate risk, and 5/15 (33.3%) with Adverse risk. Among the 25 patients that underwent HSCT, 22/25 (88.0%) were in remission (CR/CRp/CRh)

after HSCT: 15/15 (100%) with Favourable risk, 3/5 (60.0%) with Intermediate risk, and 4/5 (80.0%) with Adverse risk. See **Table 42** for details.

Table 42. (HSCT) after Mylotarg® treatment by ELN 2017 as per scientific committee review: FAS (n=113)

	Favorable risk (n=64)	Intermediate risk (n=10)	Adverse risk (n=15)	Total (n=89)
Hematopoietic stem cell transplantation (HSCT), n (%)				
n	63	10	15	88
No	48 (76.2)	5 (50.0)	10 (66.7)	63 (71.6)
Yes	15 (23.8)	5 (50.0)	5 (33.3)	25 (28.4)
Missing data	1	0	0	1
Type of HSCT, n (%)				
n	15	5	5	25
Related donor	7 (46.7)	0 (0.0)	2 (40.0)	9 (36.0)
Unrelated donor	7 (46.7)	1 (20.0)	2 (40.0)	10 (40.0)
Unknown donor	1 (6.7)	4 (80.0)	1 (20.0)	6 (24.0)
Missing data	0	0	0	0
Type of conditioning regimen, n (%)				
n	15	5	5	25
Myeloablative	12 (80.0)	1 (20.0)	2 (40.0)	15 (60.0)
Non-myeloablative	3 (20.0)	3 (60.0)	1 (20.0)	7 (28.0)
Unknown	0 (0.0)	1 (20.0)	2 (40.0)	3 (12.0)
Missing data	0	0	0	0
Patient's status at transplantation, n (%)				
n	15	5	5	25
In CR1	3 (20.0)	2 (40.0)	4 (80.0)	9 (36.0)
In CR2 or more	12 (80.0)	3 (60.0)	1 (20.0)	16 (64.0)
Missing data	0	0	0	0
Patient's status after transplantation, n (%)				
n	15	5	5	25
Death	0 (0.0)	1 (20.0)	0 (0.0)	1 (4.0)
Relapse	0 (0.0)	1 (20.0)	1 (20.0)	2 (8.0)
Remission (CR/CRp/CRh)	15 (100)	3 (60.0)	4 (80.0)	22 (88.0)
Missing data	0	0	0	0
Time interval between transplantation and last Mylotarg® dose (months), n (%)				
n	15	5	5	25
Mean (SD)	15.4 (6.6)	11.1 (6.3)	6.2 (3.0)	12.7 (6.9)
Median	14.8	11.5	5.2	14.0
Q1-Q3	13.0-18.0	5.2-16.4	5.0- 6.7	5.2-16.4
Range	3.4-31.0	4.4-18.1	3.0-10.9	3.0-31.0
≥2 months	15 (100)	5 (100)	5 (100)	25 (100)
Missing data	0	0	0	0

CR, complete response; CRh, complete response without hematological recovery; CRp, complete response without platelet recovery; D, day; HSCT, hematopoietic stem cell transplantation; IV, intravenous; Q, quartile; SD, standard deviation.
Source: Table 15.18.3 TFLs_v1.0_28NOV2023

10.3. Other analyses

10.3.1. Concordance of risk classification by scientific committee and investigators

The concordance of the risk classification of patients by the scientific committee review and that of the investigators, using the ELN 2010 and 2017 classification were analyzed. The results are described in the sections below.

10.3.1.1. Risk classification by ELN 2010

Overall, the ELN 2010 risk classification concordance between investigator assessment and independent scientific committee review was 46.4%: 5/6 (83.3%) in patients were both classified with favorable risk, 7/19 (36.8%) with intermediate I risk, 1/2 (50.0%) with intermediate II risk, and 0/1 (0.0%) with adverse risk. See **Table 43** for more details.

Table 43. Concordance of risk classification (ELN 2010) between the scientific committee and investigators: FAS (n=113)

	Investigators' classifications, n (%)			
	Favorable risk (n=7)	**Intermediate I risk (n=21)**	**Intermediate II risk (n=2)**	**Adverse risk (n=1)**
Scientific committee classification, n (%)				
n	6	19	2	1
Favorable risk (n=11)	5 (83.3)	6 (31.6)	0 (0.0)	0 (0.0)
Intermediate I risk (n=9)	0 (0.0)	7 (36.8)	1 (50.0)	1 (100)
Intermediate II risk (n=8)	1 (17.7)	6 (31.6)	1 (50.0)	0 (0.0)
Adverse risk (n=0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing data (n=3)	1	2	0	0

Source: Table 15.19.2 TFLs_v1.0_28NOV2023

10.3.1.2. Risk classification by ELN 2017

The ELN 2017 risk classifications by the scientific committee review and by the investigators, of the 52 patients with data, were concordant in 41 patients (78.8%): 28/29 (96.6%) in patients classified with favorable risk, 4/14 (28.6%) with intermediate risk, and 9/9 (100%) with adverse risk. See **Table 44** for more details. The kappa coefficient was 0.74 (95% CI: 0.59-0.89).

Table 44. Concordance of risk classification (ELN2017) between the scientific committee and investigators: FAS (n=113)

	Investigators' classifications		
	Favorable risk (n=30)	**Intermediate risk (n=20)**	**Adverse risk (n=9)**
Scientific committee classification			
n	29	14	9
Favorable risk (n=35)	28 (96.6)	7 (50.0)	0 (0.0)
Intermediate risk (n=5)	1 (3.4)	4 (28.6)	0 (0.0)
Adverse risk (n=12)	0 (0.0)	3 (21.4)	9 (100)
Missing data (n=7)	1	6	0

Source: Table 15.19.1 TFLs_v1.0_28NOV2023

10.4. Safety Analyses

10.4.1. Summary of AEs of interest reported

In this retrospective study, only AEs of specific interest for Mylotarg® (related to treatment or not) have been collected, i.e.:

- VOD
- Grade ⩾3 bleeding
- Prolonged thrombocytopenia defined as all grade 3 or 4 thrombocytopenia (platelet count <50,000/mm^3) not resolved at planned date of the next course of treatment or persistent more than 45 days after D1 of the cycle of treatment with Mylotarg® in patients treated with Mylotarg® and in complete remission.
- All AEs which may have led to early permanent discontinuation of treatment with Mylotarg®.

In the FAS (n=113), 44 patients (38.9%) reported AEs of interest (see **Table 45** and **Table 46**), including 15 patients (13.3%) who reported serious AE, and 4 (3.5%) patients who reported AE leading to death. Overall, the total number of individual reported events was 67, including 40 events considered as treatment related.

Overall, the AE reported in ≥3 patients were (**Table 47**):

- Thrombocytopenia reported in 24 patients (21.2%).
- Pyrexia reported in 5 (4.4%).
- Hepatic cytolysis reported in 4 patients (3.5%).

It is noteworthy that infections occurred in 3 patients (2.7%): 2 (1.8%) with sepsis and 1 (0.9%) with a Staphylococcal infection. One of the sepsis was classified as serious.

Details concerning the non-serious AEs reported according to SOC are shown in **Table 48**.

Table 45. Overall summary of AEs of interested reported: FAS (n=113)

	Number of patients, n (%)	Number of events
Any AE of interest	44 (38.9)	67
Treatment-related AEs (any)§	30 (26.5)	40
Serious AE*	15 (13.3)	23
Treatment-related SAEs*§	6 (5.3)	10
Non-serious AE	33 (29.2)	44
Treatment-related-non-serious AEs*§	24 (21.2)	30
AE leading to death	5 (4.4)	6
Treatment-related AE leading to death§	2 (1.8)	3

*AEs with seriousness missing were imputed as “serious”.
§AEs with relationship to treatment missing were imputed as “related”.
Source: Table 16.1.1 TFLs_v1.0_28NOV2023

Table 46. Adverse events classified by system organ class (SOC) and preferred term: FAS (n=113)

System organ class Preferred term	Number of patients, n (%)	Number of events
At least one AE	44 (38.9)	67
Blood and lymphatic system disorders	25 (22.1)	25
Thrombocytopenia	24 (21.2)	24
Febrile bone marrow aplasia	1 (0.9)	1
General disorders and administration site conditions	9 (8.0)	10
Pyrexia	5 (4.4)	5
Hyperthermia	2 (1.8)	2
Aplasia	1 (0.9)	1
Drug intolerance	1 (0.9)	1
Febrile neutropenia	1 (0.9)	1
Vascular disorders	8 (7.1)	10
Pulmonary alveolar hemorrhage	2 (1.8)	2
Cerebral hemorrhage	1 (0.9)	1
Gastrointestinal hemorrhage	1 (0.9)	1
Rectal hemorrhage	1 (0.9)	1
Retinal hemorrhage	1 (0.9)	1
Shock hemorrhagic	1 (0.9)	1
Subdural hematoma	1 (0.9)	1
Thrombosis	1 (0.9)	1
Vitreous hemorrhage	1 (0.9)	1
Hepatobiliary disorders	7 (6.2)	7
Hepatic cytolysis	4 (3.5)	4
Drug-induced liver injury	1 (0.9)	1
Hemochromatosis	1 (0.9)	1
Liver disorder	1 (0.9)	1
Infections and infestations	3 (2.7)	3
Sepsis	2 (1.8)	2
Staphylococcal infection	1 (0.9)	1
Cardiac disorders	1 (0.9)	1
Cardio-respiratory arrest	1 (0.9)	1
Immune system disorders	1 (0.9)	1
Laryngeal edema	1 (0.9)	1
Injury poisoning and procedural complications	1 (0.9)	1
Toxic skin eruption	1 (0.9)	1
Metabolism and nutrition disorders	1 (0.9)	1
Diabetes mellitus inadequate control	1 (0.9)	1
Musculoskeletal and connective tissue disorders	1 (0.9)	1
Chills	1 (0.9)	1
Nervous system disorders	1 (0.9)	1
Cerebral hemorrhage	1 (0.9)	1
Renal and urinary disorders	1 (0.9)	1
Renal failure	1 (0.9)	1
Skin and subcutaneous tissue disorders	1 (0.9)	1
Rash maculo-papular	1 (0.9)	1
Not coded	2 (1.8)	4
Not coded	2 (1.8)	4

AE, adverse event.
Source: Table 16.2.1 TFLs_v1.0_28NOV2023

Table 47. Serious adverse events classified by system organ class (SOC) and preferred term: FAS (n=113)

System organ class Preferred term	Number of patients, n (%)	Number of events
At least one serious AE	15 (13.3)	23
Blood and lymphatic system disorders	5 (4.4)	5
Thrombocytopenia	5 (4.4)	5
Vascular disorders	3 (2.7)	4
Pulmonary alveolar hemorrhage	2 (1.8)	2
Cerebral hemorrhage	1 (0.9)	1
Shock hemorrhagic	1 (0.9)	1
General disorders and administration site conditions	2 (1.8)	2
Aplasia	1 (0.9)	1
Febrile neutropenia	1 (0.9)	1
Cardiac disorders	1 (0.9)	1
Cardio-respiratory arrest	1 (0.9)	1
Hepatobiliary disorders	1 (0.9)	1
Hepatic cytolysis	1 (0.9)	1
Immune system disorders	1 (0.9)	1
Laryngeal edema	1 (0.9)	1
Infections and infestations	1 (0.9)	1
Sepsis	1 (0.9)	1
Metabolism and nutrition disorders	1 (0.9)	1
Diabetes mellitus inadequate control	1 (0.9)	1
Nervous system disorders	1 (0.9)	1
Cerebral hemorrhage	1 (0.9)	1
Renal and urinary disorders	1 (0.9)	1
Renal failure	1 (0.9)	1
Skin and subcutaneous tissue disorders	1 (0.9)	1
Rash maculo-papular	1 (0.9)	1
Not coded	2 (1.8)	4
Not coded	2 (1.8)	4

AEs with seriousness missing were imputed as “serious”.
AE, adverse event.
Source: Table 16.2.1 TFLs_v1.0_28NOV2023

Table 48. Non-serious adverse events classified by system organ class (SOC) and preferred term: FAS (n=113)

System organ class Preferred term	Number of patients, n (%)	Number of events
At least one non-serious AE	33 (29.2)	44
Blood and lymphatic system disorders	20 (17.7)	20
Thrombocytopenia	19 (16.8)	19
Febrile bone marrow aplasia	1 (0.9)	1
General disorders and administration site conditions	8 (7.1)	8
Pyrexia	5 (4.4)	5
Hyperthermia	2 (1.8)	2
Drug intolerance	1 (0.9)	1
Hepatobiliary disorders	6 (5.3)	6

System organ class Preferred term	Number of patients, n (%)	Number of events
Hepatic cytolysis	3 (2.7)	3
Drug-induced liver injury	1 (0.9)	1
Hemochromatosis	1 (0.9)	1
Liver disorder	1 (0.9)	1
Vascular disorders	5 (4.4)	6
Gastrointestinal hemorrhage	1 (0.9)	1
Rectal hemorrhage	1 (0.9)	1
Retinal hemorrhage	1 (0.9)	1
Subdural hematoma	1 (0.9)	1
Thrombosis	1 (0.9)	1
Vitreous hemorrhage	1 (0.9)	1
Infections and infestations	3 (2.7)	3
Sepsis	2 (1.8)	2
Staphylococcal infection	1 (0.9)	1
Injury poisoning and procedural complications	1 (0.9)	1
Toxic skin eruption	1 (0.9)	1
Musculoskeletal and connective tissue disorders	1 (0.9)	1
Chills	1 (0.9)	1

AE, adverse event.
Source: Table 16.4.1 TFLs_v1.0_28NOV2023

10.4.1.1. Veno-occlusive disease events

In the FAS (n=113), 1 patient (0.9%) reported a VOD. The patient with VOD did not receive curative nor prophylactic treatments. In **Table 49**, the patient with VOD was classified as having a hepatic disorder (hepatic cytolysis). The data collected is described in **Table 49**.

Table 49. Veno-occlusive disease (VOD) overall and in the ATUc and Post-ATUc: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Veno-occlusive disease (VOD)			
n	62	51	113
No	61 (98.4)	51 (100)	112 (99.1)
Yes	1 (1.6)	0 (0.0)	1 (0.9)
[95% CI] for Yes	[0.4-8.7]	[NE-7.0]	[0.02-4.8]
Missing data	0	0	0

CI, confidence interval.
Source: Table 16.8.1 TFLs_v1.0_28NOV2023

10.4.1.2. Persistent thrombocytopenia and severe hemorrhages

In the FAS (n=113), 18 patients (15.9%) reported persistent thrombocytopenia (**Table 50**). Persistent thrombocytopenia was defined as all grade 3 or 4 thrombocytopenia (platelet count <50,000/mm^3) not resolved at planned date of the next course of treatment or persistent more than 45 days after D1 of the cycle of treatment with Mylotarg® in patients treated with Mylotarg® and in complete remission.

In the FAS (n=113), 6 patients (5.3%) reported severe hemorrhages. See **Table 50**.

Table 50. Persistent thrombocytopenia and severe hemorrhages events overall and in the ATUc and Post-ATUc: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Persistent thrombocytopenia			
n	62	51	113
No	51 (82.3)	44 (86.3)	95 (84.1)
Yes	11 (17.7)	7 (13.7)	18 (15.9)
[95% CI] for Yes	[9.2-29.5]	[5.7-26.3]	[9.7-24.0]
Missing data	0	0	0
Severe hemorrhages			
n	62	51	113
No	60 (96.8)	47 (92.2)	107 (94.7)
Yes	2 (3.2)	4 (7.8)	6 (5.3)
[95% CI] for Yes	[0.4-11.2]	[2.2-18.9]	[2.0-11.2]
Missing data	0	0	0

CI, confidence interval.
Source: Table 16.9.1 TFLs_v1.0_28NOV2023

10.4.1.3. AE leading to death

In the FAS (n=113), 2 patients had AEs that led to death: 1 patient had an immune system disorder (infection and septic shock) and 1 patient had a vascular disorder (hemorrhage). See **Table 51** for more details.

Table 51. Related adverse events that led to death, classified by system organ class (SOC) and preferred term: FAS (n=113)

System organ class Preferred term	Number of patients, n (%)	Number of events
At least one related AE that led to death*	2 (1.8)	3
Hepatobiliary disorders	1 (0.9)	1
Hepatic cytolysis	1 (0.9)	1
Immune system disorders	1 (0.9)	1
Laryngeal edema	1 (0.9)	1
Vascular disorders	1 (0.9)	1
Pulmonary alveolar hemorrhage	1 (0.9)	1

AEs with relationship to treatment missing were imputed as "related".
AE, adverse event.
*1 patient for an immune system disorder (infection and septic shock) and 1 for a vascular disorder (hemorrhage).
Source: Table 16.5.1 TFLs_v1.0_28NOV2023

10.4.2. Death

In the FAS (n=113), 53/113 patients (46.9%) died: 36/62 (58.1%) in the ATUc and 17/51 (33.3%). Among the 53 deaths (missing data [n=1]), 2/52 deaths (3.8%) were considered related to Mylotarg®. See **Table 52**. Of the 102 patients with an ELN 2010 risk classification, 46 (45.1%) had died: 19/51 (37.3%) with a Favorable risk, 10/24 (41.7%) with an Intermediate I risk, 12/20 (60.0%) with an Intermediate II risk, and 5/7 (71.4%) with an Adverse risk (see **Table 53**). Similarly, of the 89 patients with an ELN 2017 risk classification, 39/89 (43.8%)

had died: 25/64 (39.1%) with a Favorable risk, 6/10 (60.0%) with an Intermediate risk, and 8/15 (53.3%) with an Adverse risk (see **Table 54**).

Table 52. Deaths reported overall and in the ATUc and Post-ATUc: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Deaths overall			
n	62	51	113
Yes	36 (58.1)	17 (33.3)	53 (46.9)
No	26 (41.9)	34 (66.7)	60 (53.1)
Missing data	0	0	0
Cause of death			
n	36	17	53
Hemorrhage	2 (5.6)	2 (11.8)	4 (7.6)
Infection/septic shock	6 (16.7)	3 (17.7)	9 (17.0)
Other	7 (19.4)	4 (23.5)	11 (20.8)
Unknown	6 (16.7)	1 (5.9)	7 (13.2)
Relapse or progressive disease	15 (41.7)	7 (41.2)	22 (41.5)
Missing data	26	34	60
Deaths related to Mylotarg®			
n	35	17	52
Treatment related	1 (2.9)	1 (5.9)	2 (3.8)
Not treatment related	28 (80.0)	12 (70.6)	40 (76.9)
Unknown	6 (17.1)	4 (23.5)	10 (19.2)
Missing	1	0	1

AEs with relationship to treatment missing were imputed as "related".
Source: Table 16.6.1 TFLs_v1.0_28NOV2023

Table 53. Deaths reported according to ELN 2010 risk classification: FAS (n=102)

	ELN 2010				
	Favorable risk (n=51)	Intermediate I risk (n=24)	Intermediate II risk (n=20)	Adverse risk (n=7)	Total (n=102)
Overall death					
n	51	24	20	7	102
Yes	19 (37.3)	10 (41.7)	12 (60.0)	5 (71.4)	46 (45.1)
No	32 (62.8)	14 (58.3)	8 (40.0)	2 (28.6)	56 (54.9)
Missing data	0	0	0	0	0
Cause of death					
n	19	10	12	5	46
Hemorrhage	2 (10.5)	1 (10.0)	0 (0.0)	1 (20.0)	4 (8.7)
Infection/septic shock	2 (10.5)	2 (20.0)	2 (16.7)	2 (40.0)	8 (17.4)
Other	6 (31.6)	3 (30.0)	1 (8.3)	0 (0.0)	10 (21.7)
Unknown	4 (21.1)	2 (20.0)	0 (0.0)	0 (0.0)	6 (13.0)
Relapse or progressive disease	5 (26.3)	2 (20.0)	9 (75.0)	2 (40.0)	18 (39.1)
Missing data	32	14	8	2	56
Deaths related to Mylotarg®					
n	18	10	12	5	45
Treatment related	0 (0.0)	1 (10.0)	0 (0.0)	1 (20.0)	2 (4.4)
Nontreatment related	14 (77.8)	7 (70.0)	11 (91.7)	4 (80.0)	36 (80.0)
Unknown	4 (22.2)	2 (20.0)	1 (8.3)	0 (0.0)	7 (15.6)
Missing data	1	0	0	0	1

AEs with relationship to treatment missing were imputed as "related".
Source: Table 16.6.2 TFLs_v1.0_28NOV2023

Table 54. Deaths reported according to ELN 2017 risk classification: FAS (n=89)

	ELN 2017			
	Favorable riskIntermediate riskAdverse riskTotal (n=89) (n=64)	(n=10)	(n=15)	
Overall death				
n	64	10	15	89
Yes	25 (39.1)	6 (60.0)	8 (53.3)	39 (43.8)
No	39 (60.9)	4 (40.0)	7 (46.7)	50 (56.2)
Missing data	0	0	0	0
Cause of death				
n	25	6	8	39
Hemorrhage	2 (8.0)	0 (0.0)	1 (12.5)	3 (7.7)
Infection/septic shock	2 (8.0)	1 (16.7)	2 (25.0)	5 (12.8)
Other	6 (24.0)	3 (50.0)	0 (0.0)	9 (23.1)
Unknown	5 (20.0)	0 (0.0)	0 (0.0)	5 (12.8)
Relapse or progressive disease	10 (40.0)	2 (33.3)	5 (62.5)	17 (43.6)
Missing data	39	4	7	50
Deaths related to Mylotarg®				
n	24	6	8	38
Treatment related	0 (0.0)	0 (0.0)	2 (25.0)	2 (5.3)
Nontreatment related	19 (79.2)	6 (100)	6 (75.0)	31 (81.6)
Unknown	5 (20.8)	0 (0.0)	0 (0.0)	5 (13.2)
Missing data	1	0	0	1

Aes with relationship to treatment missing were imputed as "related".
Source: Table 16.6.3 TFLs_v1.0_28NOV2023

10.5. Longterm follow-up status

The longterm follow-up status, according to the study cohorts (ATUc and Post-ATUc) are shown in **Table 55**. Overall, in the FAS (n=113), 52 patients (46.0%) had died (1 [0.9%] died without further details, 15 [13.3%] had early deaths, 12 [10.6%] died in CR, and 24 [21.2%] died in relapse), 59 (52.2%) were alive (55 [48.7%] in CR and 4 [3.5%] in relapse), 1 (0.9%) was lost to follow up, and for 1 (0.9%) the response was not applicable. The longterm follow-up status according to the ELN 2010 and 2017 risk classifications are shown in **Table 56** and **Table 57**, respectively.

Table 55. Patient longterm follow-up status overall and in the ATUc and Post-ATUc: FAS (n=113)

	ATU cohort (n=62)	Post-ATU cohort (n=51)	FAS (n=113)
Longterm follow-up status			
n	62	51	113
Death	0 (0.0)	1 (2.0)	1 (0.9)
Early death	10 (16.1)	5 (9.8)	15 (13.3)
Death in CR	8 (12.9)	4 (7.8)	12 (10.6)
Death in relapse	17 (27.4)	7 (13.7)	24 (21.2)
Alive in CR	24 (38.7)	31 (60.8)	55 (48.7)
Alive in relapse	1 (1.6)	3 (5.9)	4 (3.5)
NA	1 (1.6)	0 (0.0)	1 (0.9)
Lost to follow-up	1 (1.6)	0 (0.0)	1 (0.9)
Missing data	0	0	0

CR, complete response; NA, not applicable.

Source: Table 16.7.1 TFLs_v1.0_28NOV2023

Table 56. Patient longterm follow-up status according to ELN 2010 risk classification: FAS (n=102)

	ELN 2010				
	Favorable risk (n=51)	Intermediate I risk (n=24)	Intermediate II risk (n=20)	Adverse risk (n=7)	Total (n=102)
Longterm follow-up status					
n	51	24	20	7	102
Death	0 (0.0)	0 (0.0)	1 (5.0)	0 (0.0)	1 (1.0)
Early death	6 (11.8)	2 (8.3)	1 (5.0)	2 (28.6)	11 (10.8)
Death in CR	7 (13.7)	1 (4.2)	2 (10.0)	2 (28.6)	12 (11.8)
Death in relapse	5 (9.8)	7 (29.2)	8 (40.0)	1 (14.3)	21 (20.6)
Alive in CR	31 (60.8)	12 (50.0)	8 (40.0)	1 (14.3)	52 (51.0)
Alive in relapse	1 (2.0)	2 (8.3)	0 (0.0)	1 (14.3)	4 (3.9)
NA	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
Missing data	0	0	0	0	0

CR, complete response; NA, not applicable.
Source: Table 16.7.2 TFLs_v1.0_28NOV2023

Table 57. Patient longterm follow-up status according to ELN 2017 risk classification: FAS (n=89)

	ELN 2017			
	Favorable risk (n=64)	Intermediate risk (n=10)	Adverse risk (n=15)	Total (n=89)
Longterm follow-up status				
n	64	10	15	89
Death	7 (10.9)	1 (10.0)	2 (13.3)	10 (11.2)
Early death	6 (9.4)	1 (10.0)	2 (13.3)	9 (10.1)
Death in CR	11 (17.2)	4 (40.0)	4 (26.7)	19 (21.4)
Death in relapse	38 (59.4)	4 (40.0)	4 (26.7)	45 (51.7)
Alive in CR	1 (1.6)	0 (0.0)	3 (20.0)	4 (4.5)
Alive in relapse	1 (1.6)	0 (0.0)	0 (0.0)	1 (1.1)
NA	0	0	0	0
Missing data	0	0	0	0

CR, complete response; NA, not applicable.
Source: Table 16.7.3 TFLs_v1.0_28NOV2023

11. DISCUSSION

11.1. Key results

In this section we indicate the key results that will be further discuss below in **Section 11.3**.

- Study population

The study included 113 patients from two cohorts: 62 from the ATUc and 51 from the Post ATUc. Among these 62 were male (54.9%) and 51 female (45.1%). The median ages when ALM was diagnosed and when Mylotarg® was initiated were 63.0 years. Most patients, 72/88

patients (81.8%; missing data [n=25]) had an ECOG PS of 0-1. Most patients, 81.7% had AML that expressed CD33 in ≥70% of their myeloblasts and 20.8% had a FLT3-ITD mutation.

- Methods of prescribing Mylotarg®

  - ✓ Overall, in the FAS (n=113), 107/113 patients (94.7%) had a Mylotarg® first induction course: 105/107 (98.1%) in association and 2/107 (1.9%) as monotherapy. Mylotarg® was mainly associated with cytarabine and daunorubicine (60.0%). Mylotarg® first induction course was administered in a median of 3 doses with a median cumulative dose of 15 mg, and predominantly in 84/107 patients (78.5%) on days 1, 4, and 7 of induction chemotherapy.

  - ✓ Following the first induction course, 8/113 patients (7.1%) received a second Mylotarg® induction course and 3/113 (2.7%) ≥3 Mylotarg® induction courses.

  - ✓ Overall, in the FAS (n=113), 53/113 patients (46.9%) received a Mylotarg® first consolidation, 37/113 (32.7%) a second Mylotarg® consolidation course, and 3/113 (2.7%) ≥3 Mylotarg® consolidation course.

- Effectiveness of Mylotarg®

  - ✓ In terms of best response during the study, the CR rate was 74.3% and that of CRp was 4.4%.

  - ✓ In terms of response, the post-induction CR rate was 72.3% and that of CRp was 6.3%. Among the 46 patients with available MRD data, 24 (52.2%) were CR MRD-negative.

  - ✓ After a median follow-up of 44.6 months (95% CI: 33.8-69.3), the median OS in our study was 49.8 months (95% CI: 21.8-NE).

  - ✓ Median RFS, in patients with remission (n=87), was 17.5 months (95% CI: 12.6-35.6): 25.1 (95% CI: 12.5-NE) in the ATUc (n=46) and 13.0 (95% CI: 8.8-NE) in the Post-ATUc (n=41)

  - ✓ Median EFS in the FAS (n=113) was 13.1 months (95% CI: 9.9-17.5): 13.9 (95% CI: 9.9-26.4) in the ATUc (n=62) and 9.9 (95% CI: 6.9-15.6) in the Post-ATUc (n=51).

After Mylotarg® treatments, in the FAS (n=113), 35/111 patients (31.5%; missing data [n=2]) had HSCT. The median time interval from the last dose of Mylotarg® to HSCT was 13.0 months (Q1-Q3: 4.8-16.4).

- Prognostic factors for OS, RFS, and EFS

  - ✓ Older age was identified as a prognostic factor for shorter OS.

- ✓ ECOG ≥2 and cytogenetic classification of adverse were identified as prognostic factors for shorter RFS.

- ✓ FLT3-TKD mutation and cytogenetic classification of adverse were identified as prognostic factors for shorter EFS.

- Safety of Mylotarg®, in the FAS (n=113):

  - ✓ 30 patients (26.5%) reported 40 treatment-related AEs: 6 patients with 10 SAEs and 24 patients with 30 treatment-related AEs not SAEs.

  - ✓ 2 patients died of a SAE related to Mylotarg®: 1 patient for an immune system disorder (infection and septic shock) and 1 for a vascular disorder (hemorrhage).

  - ✓ Concerning AE of specific interest, persistent thrombocytopenia was reported in 18/113 patients (15.9%), severe hemorrhages in 6/113 (5.3%), VOD in 1/113 patients (0.9%), and infections in 3/113 (2.7%; 1 AE of sepsis was classified as serious).

11.2. Limitations

Our study has limits, particularly those related to, and common with, other retrospective studies. However, our retrospective data were collected in the ATUc and post-ATUc, established for regulatory purposes, and with few missing data. Due to the non-interventional and retrospective study design, a centralized assessment of response to Mylotarg® was not feasible. A blinded centralized review of response would have provided a more objective analysis of EFS and RFS in our study.

11.3. Interpretation

Data concerning the use of Mylotarg® is scarce. An individual patient data meta-analysis of randomized trials concerning the addition of Mylotarg® to induction chemotherapy, published by Hill in 2014, only identified 5 randomized clinical trials with data.(8) Among these, only the French ALFA0701 study administered Mylotarg® at a dose of 3 mg/m^2/day on days 1, 4, and 7 combined with 3+7 induction chemotherapy with daunorubicin and cytarabine.(4, 5) In the other trials, Mylotarg® was administered as a single dose, either 3 or 6 mg/m^2/day, on either day 1 or 4 of induction therapy. However, there is a clear rationale for multiple doses. Indeed, van der Velden et al. reported that there was a renewed membrane expression of CD33 after the initial exposure to Mylotarg®.(9) It is noteworthy, that median OS was only extended in the ALFA0701 trial that administered multiple doses of Mylotarg® combined with induction therapy.(8) Thus, in this section we only compare our results to those obtained in the ALFA0701 study.(4)

As previously indicated (Section 6), Mylotarg® is registered as a medicinal product certified for treating patients older than 15 years of age with *de novo* CD33+ AML, not previously treated, in good overall condition (ECOG 0 or 1) except for patients with for AML with the

FLT3 gene mutation eligible for treatment with midostaurin (RYDAPT) and those with acute promyelocytic leukemia.

Our study population comprised two cohorts, the ATUc (that included 62 patients between 18 September 2014 up until the 19 July 2019), and the post ATUc (that included 51 patients since the 19 July 2019).

11.3.1. Clinical and biological characteristics of patients with AML

We enrolled 62 males (54.9%) and 51 females (45.1%) with AML, with the ratio of males to females enrolled of 1.22. The median age when Mylotarg® was initiated was 63.0 years. Among these, 17 patients (15.0%) were younger than 50 years of age. Most patients, 72 patients (81.8%) had an ECOG PS of 0-1. The median age at AML diagnosis was 63.0 years. Most patients, 81.7% had AML that expressed CD33 in ≥70% of their myeloblasts, 20.8% had a FLT3-ITD mutation, and 9.4% had a FTL3-TKD mutation. According to the French-American-British AML classification: 3 (3.0%) patients were M0 (with undifferentiated AML), 24 (24.0%) were M1(AML with minimal maturation), 29 (29.0%) were M2 (AML with maturation), 16 (16.0%) were M4 (acute myelomonocytic leukemia), 13 (13.0%) were M4 eos (acute myelomonocytic leukemia with eosinophilia), and 15 (15.0%) were M5 (acute monocytic leukemia).

11.3.2. Methods of prescribing Mylotarg®

Concerning the first induction course, 1.9% of 107 patients with data were prescribed Mylotarg® as monotherapy and 98.1% in associations. Mylotarg® was prescribed associated with cytarabine and daunorubicine (60.0%); with cytarabine alone (21.9%); with cytarabine, daunorubicine, and other treatment(s) (10.5%); with cytarabine and idarubicine (4.8%); with cytarabine and mitoxantrone (1.0%); and with other treatment(s) (1.9%). Mylotarg® first induction course was administered in a median of 3 doses with a median cumulative dose of 15 mg, and predominantly (78.5%) on days 1, 4, and 7 of induction chemotherapy. This dosage is like that used in the pivotal randomized phase III ALFA0701 study, where in the experimental arm, patients receive Mylotarg® at a dose of 3 mg/m^2/day on days 1, 4, and 7 combined with 3+7 induction chemotherapy with daunorubicin and cytarabine.(4) Only 8 patients (7.1%) received Mylotarg® as part of second induction chemotherapy, all in associations: 75.0% combined with cytarabine alone and 25.0% with cytarabine and daunorubicine. Only 3 patients (2.7%) were administered Mylotarg® as part of a ≥3 induction course.

Mylotarg® was prescribed as part of a first consolidation course in 46.9% of 113 patients, 15.1% as monotherapy and 84.9% in association: associated with cytarabine and daunorubicine (57.8%); with cytarabine alone (31.1%); with cytarabine, daunorubicine, and other treatment(s) (8.9%); and aracytine alone (2.2%). Mylotarg® first consolidation course was administered in a median of 1 dose with a median cumulative dose of 5 mg, and predominantly (94.3%) on day 1. A second consolidation course was prescribed to 37 patients (32.7%): 24.3% as monotherapy and 75.7% in associations. Mylotarg® was administered in a median of 1 dose,

with a median cumulative dose of 5 mg, and administered predominantly (89.2%) on day 1. Only 3 patients (2.7%) were administered Mylotarg® as part of a ≥3 consolidation course.

11.3.3. Effectiveness of Mylotarg®

In the ALFA0701, in patients treated with Mylotarg®, the rate of CR was 70.4% and that of CRp was 11.1%.(4) The post-induction response rates in our study are like those reported with a rate of CR of 72.3% and that of CRp of 6.3%. Among the 46 patients with data, 24 (52.2%) were CR MRD-negative.

The median OS in our study was extended with respect to that reported in the ALFA0701 study.(4) Indeed, after a median follow-up of 44.6 months, we observed a median OS of 49.8 months (95% CI: 21.8-NE). In the ATUc and post-ATUc, the median follow-ups were 81.4 months (95% CI: 73.5-85.4) and 26.7 months (95% CI: 19.9-32.8), respectively. The median OS were 37.2 months (95% CI: 16.6-NE) in the ATUc and NE (95% CI: 18.4-NE) in the Post-ATUc (n=51). These data show that compared to the median OS reported in the ALFA0701 study (27.5 months [95% CI: 21.4-45.6]), the median OS in our study is extended: overall (49.8 months), but also in the cohorts (ATUc: 37.2 months and Post-ATUc: not reached).

The median RFS, in our study, was reduced compared to that reported in the ALFA0701 study: 17.5 months (95% CI: 12.6-35.6) compared to 28.0 months.(4)

Similarly, the median EFS (by investigators' assessments) in our study was reduced compared to that report in the ALFA0701 study.(4) In the ALFA0701 study the median EFS (by the investigators' assessments) was 17.3 months, compared to 13.1 months in our study. Interestingly, the median EFS (by blinded independent central review), in the ALFA0701 study, was 13.6 months (95%: 7.5-12.0), similar to the median EFS (by investigators' assessments) of 13.1 months observed on our study.

Overall, the response to Mylotarg®, in terms of CR and CRp, is like that reported in the ALFA0701 study. While EFS and RFS were reduced compared to those reported. However, the median OS in our study, 49.8 months, is much extended compared to the 27.5 months reported in the ALFA0701 study.(4). The improvement in survival can partly be explained by a higher post-Mylotarg® allograft rate in our study than in the ALFA0701 study (31.5% versus 23.7% of patients that received an allograft). Allograft was performed in more than 50% in RC1 in the Post-ATUc cohort. Furthermore, patients with FLT3-mutation were also able to benefit from salvage treatment by targeted therapy (ALM midostaurin in 2017) to be brought to the allograft in RC2 or more.

11.3.4. Prognostic factors of OS, RFS, EFS

The multivariate analysis found age to be significantly associated with shorter OS. Therefore, older age was identified as a prognostic factor for shorter OS.

In the multivariate analysis, ECOG ≥2 and cytogenetic classification of adverse were found to be significantly associated with shorter RFS. Therefore, ECOG ≥2 and cytogenetic classification of adverse were identified as prognostic factors for shorter RFS.

The multivariate analysis found that FLT3-TKD mutation and cytogenetic classification of adverse were found to be significantly associated with shorter EFS. Therefore, FLT3-TKD mutation and cytogenetic classification of adverse were identified as prognostic factors for shorter EFS.

11.3.5. Treatments after Mylotarg®

After Mylotarg® treatments, in the FAS (n=113), 35/111 patients (31.5%; missing data [n=2]) had HSCT. The median time interval from the last dose of Mylotarg® to HSCT was 13.0 months (Q1-Q3: 4.8-16.4). After HSCT, 32/35 patients (91.4%) were in remission (CR/CRp/CRh). Similarly, in the ALFA0701 study, 23.7% in the Mylotarg® arm underwent subsequent HSCT. In our study, more patients received an allograft after having received Mylotarg®, 31.5% in our cohort vs 23.7% in the ALFA 0701 study. In the-ATUc the allograft was mainly performed in RC2 or more (75%), while in the Post-ATUc 50% of patients were allografted in RC1.

11.3.6. Safety profile Mylotarg®

During the study, 30/113 patients (26.5%) reported 40 AE considered related to Mylotarg®: 6 patients reported 10 SAEs and 24 patients reported 30 AEs not considered as serious. 2 patient died of a SAE related to Mylotarg®: 1 patient for an immune system disorder (infection and septic shock) and 1 for a vascular disorder (hemorrhage).

In our study, among the 113 patients in the FAS, persistent thrombocytopenia was reported in 18/113 patients (15.9%), severe hemorrhages in 9/113 (7.8%), VOD in 1/113 patients (0.9%), and infections in 3/113 (2.7%; 1 AE of sepsis classified as serious).

In the ALFA0701 study, among the 131 treated with Mylotarg®, 102 (77.9%) severe infections (grades ≥3), 118 (90.1%) hemorrhages of all grades (30 [22.9%] grade ≥3), and 6 (4.6%) reported VOD of all grades (5 [3.8%] grade ≥3).(4)

The incidences of AE of specific interest (thrombocytopenia, hemorrhages, and VOD) were lower than those previously reported. No new safety signals were identified during the study. In this study Mylotarg® was mainly used in fractionated doses (>90% at induction). This type of regimen considerably reduces the VOD risk compared to higher single doses. And the delay between last dose Mylotarg® and allograft was always >2 months.

11.4. Generalizability

Our non-interventional study analyzed data of patients that were included in the ATUc and Post-ATUc established to collect data concerning the use of Mylotarg® in real-life clinical

practice. Consequently, our results are representative of the use of and outcomes with Mylotarg® for treating French patients with *de novo* AML overexpressing CD33. It may also be reasonable to assume that our results are representative of the worldwide use of Mylotarg®.

12. OTHER INFORMATION

Not applicable.

13. CONCLUSIONS

Our study shows that Mylotarg® is safe and effective, added to induction therapy, for treating *de novo* AML patients expressing CD33. We highlight an extended OS, compared to that reported in the ALFA0701 study, without any new safety signals.

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15. LIST OF SOURCE TABLES AND FIGURES

Not applicable.