NON-INTERVENTIONAL (NI)/LOW-INTERVENTIONAL STUDY TYPE 1 (LIS1) STUDY REPORT

Study information

Title	GO-First: Real-world treatment patterns and effectiveness outcomes associated with gemtuzumab ozogamicin (GO) in first-line Acute Myeloid Leukaemia (AML).
Protocol number	B1761038
Version identifier of the study report	1.0
Date	16 December 2025
EU Post Authorization Study (PAS) register number	EUPAS49268
Active substance	L01XC05
Medicinal product	Gemtuzumab ozogamicin (GO) [Mylotarg®]
Research question and objectives	How is GO being used in real world clinical practice of de novo intermediate/favourable risk AML patients and what are the outcomes? **Co-Primary objectives** • To describe the patient demographics and clinical characteristics of patients treated with GO in intermediate and favourable cytogenetic risk, de novo AML. • To describe GO treatment patterns in the study population, including the number of doses of GO and the timing of GO doses in first line (1L) treatment. **Secondary objective**

	• To describe first-line (1L) treatment effectiveness outcomes for the study population, including:
	  ○ Time-to-next treatment
	  ○ Survival (event-free survival [EFS], relapse-free survival [RFS], overall survival [OS])
	
	Exploratory objective:
	
	To describe minimal residual disease status (MRD) for the study population.

Countries	Austria Belgium Germany
Author	Redacted *Adelphi Real-World* *Adelphi Mill, Grimshaw Ln, Bollington,* *Macclesfield SK10 5JB* Redacted

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1. ABSTRACT (STAND-ALONE DOCUMENT)

Title: *GO-First: Real-world treatment patterns and effectiveness outcomes associated with gemtuzumab ozogamicin (GO) in first-line Acute Myeloid Leukaemia (AML).*

Date: 16 DEC 2025

Name and affiliation of the main author:
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Keywords: Acute Myeloid Leukaemia (AML); gemtuzumab ozogamicin (GO); real-world; treatment patterns; effectiveness outcomes

Rationale and background: The survival outcomes of AML patients are poor. A population-based study in the UK estimated a 5-year overall survival (OS) of 12.9% for patients with AML.

In April 2018, GO received marketing authorisation from the EMA for the European Union, to be used in combination with daunorubicin and cytarabine chemotherapy. There is limited knowledge of its real-world use and outcomes as first line (1L) treatment with the recent licensed dosing (i.e., 3 doses during the induction cycle). This study investigated the treatment patterns and effectiveness outcomes of 1L GO use on de novo AML patients in real-word healthcare, specifically those in the favourable and intermediate risk groups.

Research question and objectives: How is GO being used in real world clinical practice of *de novo* intermediate/favourable risk AML patients and what are the outcomes?

Co-Primary objectives

- To describe the patient demographics and clinical characteristics of patients treated with GO in intermediate and favourable cytogenetic risk, de novo AML.

- To describe GO treatment patterns in the study population, including the number of doses of GO and the timing of GO doses in first line (1L) treatment.

Secondary objective

- To describe first-line (1L) treatment effectiveness outcomes for the study population, including:
  - Time-to-next treatment
  - Survival (event-free survival [EFS], relapse-free survival [RFS], overall survival [OS])

Exploratory objective

- To describe minimal residual disease status (MRD) for the study population.

Study design: A combination study design approach of a retrospective cohort study and retrospective chart review. The indexing period was 1st April 2018 – 31st May 2023. Patients were indexed on their receipt of 1L induction therapy containing GO.

Setting: The cohort study was conducted using a disease-specific dataset in Austria (AGMT). The chart review was conducted across various sites in Austria (1), Belgium (3), and Germany (1).

Subjects and study size, including dropouts: CRFs for 89 patients were collected from the five sites. Additionally, the AGMT had 26 patients that met the inclusion criteria. Patients had to have GO at induction and a minimum of 3 months follow up.

Variables and data sources: Data sources: Medical University of Vienna (CRF); Austrian Myeloid Registry (cohort); UZ Leuven (CRF); Az Sint Jan Brugge (CRF); UZ Brussels (CRF); University of Cologne (CRF)

Patient characteristics: age, sex, BMI, comorbidities, blood test results, ELN 2017 risk group, WHO specific recurrent changes, performance status.

Treatment patterns: lines of therapy, treatment regimens, treatment setting, dosing, HSCT, other treatment

Effectiveness outcomes: treatment response, time to subsequent treatment, MRD status, EFS, RFS, OS

Results: In CRF patients, 52.8% (n=47) were male and the median (IQR) patient body mass index (BMI) at baseline was 26.1 (22.8-30.1). Median (IQR) age at diagnosis of 60 (44.0-67.0). At the time of data collection, all patients were classified as favourable 37.1% (n=33) or intermediate 62.9% (n=56). According to the WHO 2016 AML subtype classification, 23.6% and 21.3% of patients had the ‘FAB M2 (with maturation)’ or ‘AML with recurrent genetic abnormalities’ classification, respectively.

All patients received GO during 1L induction in conjunction with cytarabine and an anthracycline (daunorubicin or idarubicin)); 80.9% (n=72) of patients received three doses of GO during 1L induction. The median (IQR) GO dose received during 1L induction was 5.0 mg, and in the AGMT, a median of 3.0 vials were given.

Median EFS and RFS in the CRF was 1610 days and 1732 days, respectively.

Discussion: Overall, this study indicates that label use (3 doses of 5mg fraction) of GO, has strong effectiveness in the real world, demonstrated by positive clinical outcomes, some of which surpass those observed in clinical trials.

Names and affiliations of principal investigators: Alexander Russell-Smith, MSc BA, Pfizer Inc. (NYC); Stephanie Dorman, PhD, Pfizer Inc. (NYC); Maja Strecker, PhD, Pfizer Inc. (NYC); Tom Bailey, MSc, Pfizer Inc. Adelphi Real World; Lucinda Camidge, MPH, Adelphi Real World; Alexander Ford, MBiolSci, Adelphi Real World; Teresa Taylor-Whiteley, PhD, Adelphi Real World

2. LIST OF ABBREVIATIONS

Abbreviation	Definition
AML	Acute Myeloid Leukaemia
BMI	Body Mass Index
CBF	Core Binding Factor
CI	Confidence Interval
CR	Complete Remission
CRp	Complete Remission with Incomplete Platelet Recovery
CRi	Complete Remission with Incomplete Haematologic Recovery
CRF	Case Report Form
eCRFs	Electronic Case Report Forms
ECOG	Eastern Cooperative Oncology Group
EDC	Electronica Data Capture
EFS	Event-Free Survival
ELN	European LeukemiaNet
EMA	European Medicines Agency
EMR	Electronic Medical Record
ESMO	European Society for Medical Oncology
FDA	US Food and Drug Administration
GO	Gemtuzumab Ozogamicin
GvHD	Graft vs Host Disease
HSCT	Haematopoietic Stem Cell Transplantation
ICD-10	10th International Classification of Diseases, Tenth Revision, Clinical Modification
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISCN	International System for Human Cytogenomic Nomenclature
KM	Kaplan-Meier
LDH	Lactate Dehydrogenase
LoT	Line of Therapy
MRD	Minimal Residual Disease
NIS	Non-Interventional Study
OS	Overall Survival
PAS	Post Authorization Study
PASS	Post-Authorization Safety Study
QC	Quality Control

RFS	Relapse-Free Survival
SAP	Statistical Analysis Plan
SD	Standard Deviation
SE	Standard Error
UK	United Kingdom
VOD	Veno-Occlusive Disease
WHO	World Health Organisation

3. INVESTIGATORS

Principal Investigator(s) of the Protocol

Name, degree(s)	Title	Affiliation
Alexander Russell-Smith, MSc BA	Senior Director, Health Technology Assessment, Value & Evidence Strategy	Pfizer Inc. (NYC)
Stephanie Dorman, PhD	Global Medical Strategy Director	Pfizer Inc. (NYC)
Maja Strecker, PhD	Global Medical Strategy Director	Pfizer Inc. (NYC)
Tom Bailey, MSc	Director of Observational Research	ARW
Lucinda Camidge, MPH	Associate Director of Real-World Evidence	ARW
Alexander Ford, MBiolSci	Manager Real World Evidence	ARW
Teresa Taylor-Whiteley, PhD	Senior Research Executive	ARW

Country Co-ordinating Investigators

Name, degree(s)	Title	Affiliation
Maik Scherholz	Senior Medical Advisor	Pfizer Austria
Carla AL Assaf	Medical Advisor Oncology	Pfizer Belgium

The names, affiliations, and contact information of the investigators at each study site are listed in Appendix 3.1.

Lead Investigator(s) from sites and registry

Name, degree(s)	Title	Affiliation
Professor Wolfgang Sperr, MD	Principal Investigator	Medical University of Vienna, Austria
Professor Karl-Anton Kreuzer	Principal Investigator	University Hospital Cologne, Germany
Professor Florian Kron	Principal Investigator	VITIS Healthcare Group, Cologne, Germany
Professor Johan Maertens	Principal Investigator	UZ Leuven, Belgium
Dr Ann De Becker, MD	Principal Investigator	University of Brussels, Belgium
Dr Alexander Schauwvlieghe	Principal Investigator	AZ Sint Jan Brugge, Belgium
Dr Lisa Pleyer	Principal Investigator	Austrian Myeloid Registry

4. OTHER RESPONSIBLE PARTIES

Responsible Party Name and Affiliation	Role in the study
Redacted	Data Analysis
Redacted	Data Analysis

5. MILESTONES

Milestone	Planned date	Actual date	Comments
Date of independent ethics committee (IEC) or institutional review board (IRB) approval of protocol	N/A	First approval – UoC: 23 November 2023 Last approval – UoB: 14 August 2024	Ethics approval was sought from five independent IECs. The IEC approval dates for the protocol are provided in Appendix 3.2.
Start of data collection	01 November 2023	27 February 2024	Delays in site onboarding / ethics (site communication and time taken for ethics approval processes) The protocol amendment to increase the index period and subsequentl y template updates, also caused delays.
End of data collection	30 April 2024	11 December 2024	As above.
Registration in the HMA-EMA Catalogues of RWD Studies (EUPAS49268)	N/A	01 February 2024	
Final report	06 September 2024	16 December 2025	Delays associated to delays in

Milestone	Planned date	Actual date	Comments
			data collection and analyses timelines (investigations and additional analyses of interest)

6. RATIONALE AND BACKGROUND

AML is a complex and rare cancer of the bone marrow caused by genetic alterations in stem cells (1, 2). These genetic alterations result in the accumulation of poorly differentiated myeloid cells which are important for innate immunity (2, 3). In 2013, it was estimated that the incidence of AML in Europe was 5.06 patients per 100,000 people (4). AML is more common in men and its incidence increases with older age, with the median age of diagnosis being ~70 years old (2, 5). The survival outcomes of AML patients are poor. A population-based study in the UK estimated a 5-year overall survival (OS) of 12.9% for patients with AML. This was representative of both sexes combined, although evidence suggests survival outcomes to be worse in men (4).

Suspected AML patients undergo genetic investigations to allow the classification of their cytogenetic and molecular characteristics, which helps guide treatment decisions and predict prognosis (5). The European Leukemia Net (ELN) developed recommendations (2017) which categorizes AML patients into 3 risk groups based on their cytogenetic karyotype and molecular features: favourable, intermediate, and adverse. These risk groups predict the risk of disease relapse (6).

Treatment of AML may vary between patients depending on their clinical characteristics, some of which include: a diagnosis of acute promyelocytic leukaemia (APL), a diagnosis of core binding factor (CBF) AML, white blood cell count, sign of leucostasis, cytogenetic risk groups, molecular mutations, and fitness for intensive therapy. The European Society for Medical Oncology (ESMO) have developed various treatment eligibilities and guidelines for the treatment of patients with AML (5). Types of drugs and regimens used for treatment of AML include chemotherapy and chemotherapy-free regimens (7). Initial treatment of patients who are eligible for intensive therapy typically involves induction therapy which is used to attempt to achieve a response to treatment so a patient might be able to enter a state of complete remission (CR). Following response, consolidation therapy is often required with the aim of preventing disease relapse, as residual disease may remain after induction therapy (5, 8). In patients who are eligible to receive intensive therapy, a common chemotherapy regimen used for induction is the ‘3+7’ or ‘7+3’ regimen. This includes 3 days of anthracyclines (daunorubicin) administered intravenously and 7 days of continuous infusion of cytarabine (7, 8). Consolidation therapy often involves chemotherapy or allogeneic haematopoietic stem cell transplantation (allo-HSCT) depending on patient eligibility. For example, age helps determine eligibility as elderly patients often cannot tolerate such consolidation therapy (8). In recent years, the US Food & Drug Administration (FDA) has approved the use of various regimens for the treatment of AML, including chemotherapy-free regimens, chemotherapy / non-chemotherapy drug combinations and hypomethylating chemotherapy (6). These novel agents and regimens aim to improve the survival outcomes of AML patients of all risk profiles.

Gemtuzumab ozogamicin (GO) [Mylotarg®] is an antibody-drug conjugate used for the treatment of AML patients with myeloid cells that express the CD33 receptor (9). The FDA approved GO for the treatment of newly diagnosed CD-33-positive AML in September 2017

for use alone or in combination with chemotherapy, depending on the characteristics of the patient (10). In April 2018, GO received marketing authorisation from the EMA for the European Union, to be used in combination with daunorubicin and cytarabine chemotherapy (11, 12). The ALFA-0701 multicentre Phase 3 trial results demonstrated the effectiveness of GO, which ultimately led to its approval for use in *de novo* AML patients. Patients aged 50-70 years old with newly-diagnosed de novo AML were treated with GO in combination with daunorubicin and cytarabine chemotherapy. The trial demonstrated an estimated median event-free survival (EFS) of 17.3 and 9.5 months for patients receiving GO and chemotherapy or chemotherapy alone respectively and 27.5 and 21.8 months for overall survival (OS) (10). Over the years, GO has been studied in multiple different combination regimens and different dosing schemes (12). There is limited knowledge of its real-world use and outcomes as first line (1L) treatment with the recent licensed dosing (i.e., 3 doses during the induction cycle).

Using results from a feasibility study conducted by Adelphi Real World (ARW) and contacts with data source custodians, evidence suggests that 1L treatment with GO has been used to treat AML patients in several countries. Pfizer sought to conduct a study investigating the treatment patterns and effectiveness outcomes of 1L GO use on de novo AML patients in real-word healthcare, specifically those in the favourable and intermediate risk groups. This will allow the assessment of whether GO prescription patterns are aligned with licensed dosing / guidelines and will provide novel insights into whether the observed real-world outcomes associated with these prescription patterns are effective.

This study utilized a combination of an AML-specific data source (Austrian Myeloid Registry; AGMT) and a retrospective medical chart review using a Case Report Form (CRF) to conduct a multi-country study with Austria, Belgium, and Germany. These data sources were identified during a feasibility assessment and were deemed to likely capture a sufficient sample size of patients (according to the eligibility criteria outlined in Section 9.3).

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

7. RESEARCH QUESTION AND OBJECTIVES

This study aimed to answer the following research question:

How is GO being used in real world clinical practice of *de novo* intermediate/favourable risk AML patients and what are the outcomes?

Co-Primary objectives

- To describe the patient demographics and clinical characteristics of patients treated with GO in intermediate and favourable cytogenetic risk, de novo AML.

- To describe GO treatment patterns in the study population, including the number of doses of GO and the timing of GO doses in first line (1L) treatment.

Secondary objective

- To describe first-line (1L) treatment effectiveness outcomes for the study population, including:
    - Time-to-next treatment
    - Survival (event-free survival [EFS], relapse-free survival [RFS], overall survival [OS])

Exploratory objective

- To describe minimal residual disease status (MRD) for the study population.

8. AMENDMENTS AND UPDATES

Table 1. Amendments to the Protocol

Amendment number	Date	Amendment Type (substantial or administrative)	Protocol Section(s) Changed	Summary of Amendment(s)	Reason
1	27th September 2023	Administrative	Cover Page	Updated protocol date.	Protocol date changed to reflect when the updated protocol was finalized.
	27th September	Administrative	Cover Page, 4.0 Abstract, and 8.0 Research Question and Objectives	Updated research question objectives section to include a research question.	Updated based on reviewer feedback.
	27th September 2023	Administrative	3.0 Responsible Parties	Removed study member Redacted and added member Redacted. Adjusted titles and affiliations for Redacted and Redacted to reflect current roles and for accuracy.	Change in Pfizer role titles and persons in roles.
				Removed study member Redacted and added member Redacted. Updated Redacted current role.	Change in persons in Pfizer role.
				Updated spelling mistake in Redacted name.	Updated spelling mistake.
	27th September 2023	Administrative	4.0 Abstract	Subtitle updated to include the protocol finalization date and protocol version number.	Updated to reflect the template and the updated protocol finalization date.
				Reference added in the Rationale and Background section.	Updated based on reviewer feedback.
				Updated the Research Questions and Objectives section to align with the wording listed on the cover page of the protocol.	Updated based on reviewer feedback and for alignment with research question and objectives described on the protocol cover page.

				Changed text in the Study Design section to reflect registry data is retrospective.	Updated based on reviewer feedback
				Changed text in the Population section to clarify what the meaning of 'large population' of patients refers to.	Updated based on reviewer feedback
				Updated planned study dates with latest estimates. Index date also updated accordingly (Figure 9, 9.2 Setting, and Abstract).	Delays in study caused change to timelines.
	27th September 2023	Administrative	6. Milestones	Updated planned study dates with latest estimates. Index date also updated accordingly (Figure 9 and Abstract).	Delays in study caused change to timelines.
	27th September 2023	Administrative	7. Rationale and Background	Reference added in the Rationale and Background section.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9. Research Methods, 9.4 Data Sources, and 9.5 Study Size	Cross-reference errors amended throughout.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.2 Setting	Changed text to reflect the rationale for the study inclusion/exclusion criteria.	Updated based on reviewer feedback and to reflect the protocol template.
	27th September 2023	Administrative	9.3.3.1 Baseline patient characteristics	Changed text to clarify *biological* sex is captured in the CRF.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.3.3.2 Baseline clinical characteristics	Changed text to clarify *day, month, and year* are captured in the CRF.	Updated based on reviewer feedback.
				Changed text to detail the list of comorbidities captured in the CRF.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.4 Data Sources	Updated the formatting in one paragraph.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.6 Data Management	Changed text to reflect patient identification numbers will allow to data to be	Requested from UZ Leuven site in Belgium, after

				pseudonymized, rather than pseudo-anonymized.	reviewing the protocol
				Changed text to amend a spelling mistake.	Spelling mistake updated.
				Changed text to clarify data harmonization will be detailed in the SAP.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.6.1 Case Report Forms (CRFs)	Changed text to reflect the protocol template.	Updated to reflect the protocol template.
	27th September 2023	Administrative	9.6.2 Record Retention	Changed text to reflect the protocol template.	Updated to reflect the protocol template.
	27th September 2023	Administrative	9.7 Data Analysis	Changed text to signpost reviewers to the limitations section where bias is described.	Updated based on reviewer feedback and to reflect the protocol template.
				Changed text to amend the term 'extreme levels'.	Updated based on reviewer feedback.
	27th September 2023	Administrative	9.9 Limitations of the Research Methods	Changed text to amend the term 'significantly' and amended spelling errors in this section.	Updated based on reviewer feedback.
	27th September 2023	Administrative	10.1 Patient Information	Changed text to include both paper and electronic personal data will be stored at the study site.	Updated based on reviewer feedback.
	27th September 2023	Administrative	10.2 Patient Consent and 10.3 Patient Withdrawal	Changed to text to detail the patient consent requirement in Belgium.	Updated to reflect the protocol template.
	27th September 2023	Administrative	11. Management and Reporting of Adverse Events/Adverse Reactions	Change text to update spelling mistakes and add text from the Safety Reporting template.	Updated to amend spelling mistakes and to reflect the safety reporting template.
				Edited wording in paragraph describing the reporting of adverse events related to Pfizer products to clarify that	Wording was repetitive and clarity was lacking on

				within the protocol that the sites should report via the AE Form in the appendix directly to Pfizer Safety.	process for reporting safety.
				Removed text which was template instructions around modifications and deletions.	Template instructions were accidentally left in the protocol

9. RESEARCH METHODS

9.1. Study design

All assessments described in the protocol for this study (Appendix 2.1. PROTOCOL) were performed as part of normal clinical practice or standard practice guidelines for the patient population and healthcare provider specialty in the countries where this non-interventional study was conducted.

The following study was designed to address the limited knowledge of real-world treatment patterns and effectiveness outcomes of GO treatment in AML, according to recent licensed dosing. As a result of the rarity of disease and limited patient numbers, a multicountry study was designed, to gain sufficient sample size and to assess the differences of treatment patterns in different countries. Data from the following countries were collected:

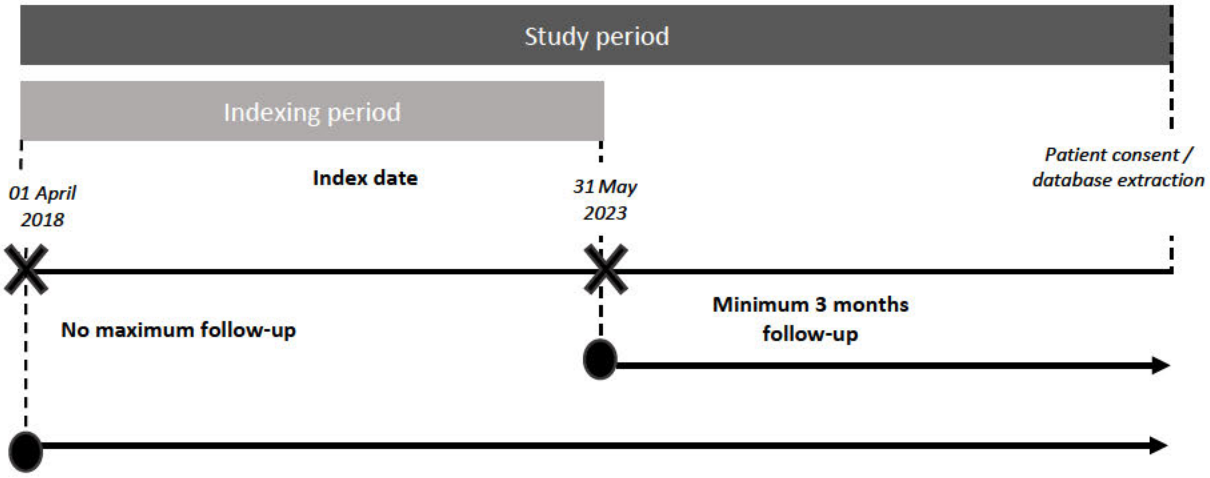
- Austria
- Belgium
- Germany

The final data sources for each country are described below. They were selected due to their associated sufficiently sized GO patient population and data availability, which was identified through previous feasibility work.

A combination study design approach of a retrospective cohort study and retrospective chart review was employed to address the study objectives described in Section 7. The cohort study was conducted using a disease-specific dataset in Austria. This source was identified during a previous feasibility assessment as a dataset with the required data variables. The chart review was conducted across various sites in Austria, Belgium, and Germany. Belgium and Germany had a high patient population, but no appropriate dataset was identified, hence the combination approach. The Austrian site and dataset together, in addition to the site-reported data captured in Belgium and Germany provided a substantial sample size to address the research objectives – see Section 9.5. for a detailed explanation of each data source.

The study aimed to assess the treatment patterns of patients treated with GO and capture their demographics and clinical characteristics, as co-primary objectives. The study also aimed to describe the clinical outcomes associated with these patients where feasible, looking at MRD as an exploratory finding. See Section 9.4 for a breakdown of the specific endpoints and variables of interest. Details of the study period are shown in Figure 1.

Figure 1. Study Schematic - eCRF and secondary data dataset design



9.2. Setting

This study aimed to look at de novo AML patients who received GO as 1L therapy in Austria, Belgium, and Germany. Some Austrian and all Belgian and German patients' data was captured via chart review; the data sources and the method of data collection for the Austrian secondary dataset is outlined in Section 9.5. Potential sites participating in the retrospective chart review were invited to complete a short feasibility questionnaire prior to site selection. The feasibility questionnaire was used to confirm suitability of sites for inclusion, confirming study critical information such as GO patient caseload and data availability. Additionally, logistical information pertaining to site contracting and IRB processes will also be assessed. Following this, eCRFs were completed by clinicians and site staff at the site for patients meeting the inclusion/exclusion criteria below.

Patients aged 18 years and above with a diagnosis of de novo AML between 01 April 2018 and 31 May 2023 (indexing period) were identified within the sites / datasets using the inclusion and exclusion criteria specified below. The indexing period allowed for a large proportion of patients treated with GO in these countries / sites to be gathered, following EMA approval in April 2018. No formal sampling was conducted in any country. Sites selected for a chart review methodology completed data collection for all eligible patients and all data collected on eligible patients captured in secondary datasets was extracted.

There were minimal inclusion / exclusion criteria (Section 9.3.1 and 9.3.2) in order to maximize the number of GO-treated patients eligible for this study. Inclusion criteria were designed to reflect the population GO is indicated for and to align with the phase III ALFA-0701 clinical trial (10) (inclusion criteria 1 – 4, exclusion criteria 1-2). Patients must have data available for a minimum of 3 months after initiation of GO-regimen to capture data relating to effectiveness outcomes (e.g., time to next treatment, survival; inclusion criteria 5). If required by country IRB, patients (or a legally acceptable representative) needed to provide a personally signed

and dated informed consent form for their data to be extracted from their medical records (inclusion criteria 6).

Each data source was expected to capture a (relatively) large proportion of GO-treated patients in that country, hence their selection. The Austrian, Belgian and German centres were selected as they met the feasibility requirements (capture the relevant data variables) and due to the sample size of GO patients that they contained. The Austrian Myeloid Registry recruits data on patients with myeloid diseases from 15 Austrian centres (excluding the Medical University of Vienna) with an estimated enrolment of 3000 patients. The eligibility criteria below were largely based upon the recommend use of GO; ensuring that the overall patient sample gathered was clinically representative of the GO treated population. The estimated and achieved sample sizes for the study are captured in Section 9.7, Table 5. Although final sample sizes fell below the estimated, likely due to application of final eligibility criteria for the study, they were not substantially low in relation to the European population of interest.

The initiation date of 1L treatment within the indexing period was defined as the index date. De novo AML diagnosis was captured within the screening questions of the eCRF and fully defined for each data source within the Statistical Analysis Plan (SAP). Baseline patient demographics and clinical characteristics were evaluated at index. Treatment patterns and effectiveness outcomes were described throughout the follow-up period. Patients had a minimum follow-up of 3 months defined as patients with 3 months of data, following the 1L treatment initiation. This allowed for assessment of treatment patterns and early effectiveness outcomes. Follow-up ended with the following endpoints: death, loss of data (e.g., transfer to a new hospital) or end of the study period. To maximise the follow-up data captured necessary to accurately assess survival outcomes (EFS, RFS and OS), follow-up extended until either the last data available for the patient (in Austrian, Belgium, and German sites), or the date of database extraction (in the Austrian Myeloid Registry). Patients who had limited follow-up data which was not sufficient for the assessment of OS and accurate EFS and RFS, were right-censored for the purpose of survival outcome specific analysis. Patients who died within the 3-month follow-up period were considered eligible for inclusion in order to evaluate EFS, RFS and OS outcomes.

9.3. Subjects

9.3.1. Inclusion Criteria

Patients had to meet all the following inclusion criteria to be eligible for inclusion in the study:

1. Patient had a clinical diagnosis of **de novo** AML.

2. Patient was aged 18 years or older.

3. Patient had a cytogenetic risk stratification of ‘favourable’ or ‘intermediate (classified according to the International System for Human Cytogenic Nomenclature criteria (13)).).

4. Patient had been treated with GO in a 1L induction setting in a combination chemotherapy treatment.

5. Patient had data points available for a minimum of 3 months data from the first GO- containing regimen (index). Patients who died within the 3 months are eligible for inclusion within the study.

6. *For patients from Belgium sites:* Evidence of a personally signed and dated informed consent document indicating that the patient (or a legally acceptable representative) had been informed of all pertinent aspects of the study[1].

9.3.2. Exclusion Criteria

Patients meeting any of the following criteria were not included in the study:

1. Patient has been exposed to any other 'non-GO' treatment regimen prior to treatment with GO for their AML (except leukoreduction with and without hydroxyurea).

2. Patient has been treated with GO only as a consolidation therapy and not as induction.

9.4. Variables

This study brought together different data sources that were harmonised to have common variables and allow for analysis of one multi-country combined dataset. The variables below and the CRF were designed using knowledge of datasets known to collect data from medical records. The CRF captured all data variables of interest therefore allowing research objectives to be addressed. The study does not include confounders or modifiers as analyses were descriptive, as well as diagnostic criteria as secondary data was used. Final variables can be found below, with further details within the SAP. Data sources were selected following feasibility assessments, whereby the presence of the variables below were assessed within the data captured.

9.4.1. Exposures

GO use

Patients were treated with GO in a 1L chemotherapy regimen for AML. GO had to be administered concomitantly with induction chemotherapy, i.e., between the start and end date of a patient's 1L therapy regimen they received GO and another chemotherapy drug between the indexing period outlined in Section 9.1.

[1] Informed consent was a legal requirement for this type of study in Belgium only. This was not required in Austria or Germany.

9.4.2. Outcomes

9.4.2.1. Treatment Patterns

The treatment landscape for GO was described for all de novo AML patients treated with the drug as a 1L therapy. The following were assessed to describe the overall treatment pathway for each patient:

Table 2. Treatments patterns

VARIABLES	DATA SET(S)	OPERATIONAL DEFINTIONS
Lines of therapy (LoT) *(continuous, binary)*	**CRF** **Registry database**	A patient is defined as changing line of therapy to 2nd line were defined by a reinduction or change in regimen after relapse. Registry only: Lines of therapy were manually assigned upon receipt of the data, using treatment intention, EoT reason and best response. Where induction intensity changed, this was considered a new line. Relapse was defined as progressive disease (PD) if partial remission (PR)/complete remission (CR) was achieved in a previous line.
Treatment regimen • 1L induction • 1L consolidation • Relapse treatment *(multiple binary)*	**CRF** **Registry database**	Regimens reported for each LoT, and categorised. Further details of definitions and categories are provided in the SAP and results.
Treatment setting pathway *(categorical, binary)*	**CRF** **Registry database**	The treatment setting by regimen (as described above) were reported as a categorical variable using the following groups: • *Induction[1]* • *Induction-Reinduction[1]* • *Induction-Reinduction-Conslidation[2]* • *Induction-Consolidation[2]* • *Induction-Consolidation-Maintenance[2]* • *Induction-Relapse[3]* • *Induction-Relapse-2L Induction[3]* • *Induction-Relapse-2L Induction-Consolidation[3]* • *Induction-Consolidation-Relapse[4]* • *Induction-Consolidation-Relapse-Consolidation[4]* Treatment setting by regimen were also reported in the following less granular groups. The superscript numbers above indicate which

		groups from the extensive list above were included in the following groups: 1. *Induction* 2. *Induction-Consolidation* 3. *Induction-Relapse* 4. *Induction-Consolidation-relapse* 'Reinduction' was defined as any subsequent induction cycle occurring after the initial (first) induction cycle.
Number of cycles *(continuous, categorical)*	**CRF** **Registry**	Number of cycles for each treatment regimen categorised as: • *0** • *1* • *2* • *3* **category only applicable to the consolidation setting*
Number of GO doses per regimen *(continuous, categorical)*	**CRF** **Registry**	The number of doses of GO (denoted by the number of vials, as one vial is equivalent to one dose in adult patients) in each first-line treatment regimen. Categorized as follows: • *0** • *1* • *2* • *3* • *4+* The number of doses for each treatment setting (induction and consolidation) was also reported. One vial was assumed to be a dose of 5mg. For the registry data, number of vials during each regimen was calculated as the ceiling of cumulative dose during each cycle divided by 5mg, summed **category only applicable to the consolidation setting*
Dosing per administration *(continuous)*	**CRF** **Registry**	The dose (mg/m^2) of GO administered reported for each cycle and total dose for each treatment setting (induction and consolidation. Calculated by the sum of the GO dosing information across the cycles for each treatment setting (induction and consolidation).
Time between dosing *(continuous)*	**CRF** **Registry database**	Time in days between the combined chemotherapy and GO initiation (and vice

		versa) for each treatment setting (where appropriate for consolidation). Time in days between GO doses (indicated by cycle dates) was also reported.
Other treatment *(multiple binary, continuous, categorical)*	**CRF** **Registry**	Whether or not patients received other treatments for their AML (as well as GO-chemotherapy induction combination therapy), categorised as: • *Stem cell transplant post-GO treatment* • *Radiation therapy (CRF only)* • *Surgery (CRF only)* • *Patient has never received any of these treatments or procedures* Number of stem cell transplants experienced per patient was also reported.

The feasibility of capturing/defining these data points were assessed upon communication with data custodians and sites. Details of variable definitions were captured in the SAP.

9.4.2.2. Effectiveness Outcomes

Table 3. Treatment effectiveness outcomes

VARIABLES	DATA SET(S)	OPERATIONAL DEFINTIONS
Cytogenetic complete remission/response *(binary, categorical)*	**CRF** **Registry database**	A patient was considered to have a cytogenetic complete response if any response is "no" (not normal) at the start of line 1, and all responses were "yes" (normal) at the initiation of next treatment.
Treatment next steps *(categorical)*	**CRF** **Registry database**	CRF only: *Induction:* • *Consolidation of 1st line treatment* • *Patient relapse and starting of therapy for relapsed/refractory disease* • *Observation – active monitoring / watchful waiting (no further treatment prescribed)* • *Best supportive care (i.e., not receiving chemotherapy, only treatment that helps relieve symptoms of AML)* • *Patient receiving treatment as part of a clinical trial* • *Patient decided to not continue treatment* • *Other* *Consolidation:*

		• *Patient began treatment for relapsed/refractory disease* • *Maintenance therapy* • *Observation – Active monitoring / watchful waiting* • *Best supportive care (i.e., not receiving chemotherapy, only treatment that helps relieve symptoms of AML)* • *Not yet decided as patient currently receiving treatment (as of the date of last assessment)* • *Patient receiving treatment as part of a clinical trial* • *Patient decided to not continue treatment* • *Other* *Relapse/refractory:* • *Proceed to transplant* • *Consolidation of relapse/refractory therapy* • *Observation - Active monitoring / watchful waiting* • *Best supportive care (i.e., not receiving chemotherapy, only treatment that helps relieve symptoms of AML)* • *Patient receiving treatment as part of a clinical trial* • *Patient decided to not continue treatment* • *Other* *Categories for registry data varied patient by patient.*
Treatment response *(categorical)*	**CRF** **Registry database**	1st line treatment only, categorised as: • *Complete remission* • *Complete remission with incomplete haematologic recovery (CRi)* • *Complete remission with incomplete platelet counts (CRp)* • *Morphologic leukaemia-free state (MLFS)* • *Partial remission* • *Stable disease* • *Progressive disease* • *Uncertain response* • *Not evaluated* *For the registry data, ELN2017 response was used.* Response to stem cell transplant was also reported (CRF only):

		• *Continued complete remission* • *Complete remission* • *Not in CR* • *Relapsed disease* • *Progressive disease* • *Unknown*
Time between 1L and response evaluation *(continuous)*	**CRF** **Registry**	Time in days between end of 1st line treatment and response evaluation, for each treatment setting (induction and consolidation).
Time to subsequent treatment *(continuous)*	**CRF** **Registry**	Time in days from initiation of one treatment regimen until the start of a subsequent treatment regimen, for each LoT. The number of days between subsequent points of interest along the patient pathway were defined in the following ways: • Start date of 1st line induction therapy to start date of 1st line consolidation therapy • Start date of 1st line consolidation therapy to start date of treatment for relapse/refractory AML • Start date of 1st line induction therapy to start date of treatment from relapse/refractory AML • Start date of 1st line induction therapy to date of stem cell transplant • Date of last Gemtuzumab ozogamicin (Mylotarg®) dose to date of stem cell transplant
Minimal residual disease (MRD) *(categorical)*	**CRF** **Registry database**	MRD status following induction and pre-transplant. CRF only: Method of MRD assessment, categorised as: • *Flow cytometry assays* • *Real-time quantitative polymerase chain reaction (RT-qPCR) assays (i.e. NPM1, CBB-MYH11, RUNX1-RUNX1T1)* • *Next generation sequencing (NGS)* • *Unspecified*
Time between 1L and MRD assessment *(continuous)*	**CRF** **Registry database**	Time in days between the start of 1st line treatment and MRD assessment, for each treatment setting (induction and consolidation).
Event-free survival (EFS) *(binary, numeric)*	**CRF** **Registry database**	Defined as the date of the start of the first line treatment for de novo AML to relapse, death from any cause, or failure to achieve any of the following: CR (including CR MRD-/+); CRp; CRi, MLFS.
Relapse-free survival (RFS) *(binary, numeric)*	**CRF**	Defined as the date of the achievement of complete remission (CR (including CR MRD-/+),

	Registry database	CRh CRi, MLFS), to relapse or death from any cause. Whether or not patients achieve relapse/refractory AML was also reported as a binary yes/no variable. Patients are considered censored at end of follow up
Overall survival (OS) *(binary, numeric)*	**CRF** **Registry database**	Defined as the date of the start of first line treatment for de novo AML, to death from any cause.
Cause of death *(categorical)*	**CRF** **Registry database**	CRF categories: • *Early death (<1 week after induction/re-induction including relapse)* • *Death in hypoplasia (> 1 week after induction/re-induction including relapse)* • *Progressive disease after refractory disease* • *Treatment-related death in complete remission* • *Death of second cause* • *Uncertain cause of death* • *Other* Registry database categories: • *Disease progression* • *Infectious complications* • *Others*
Veno-occlusive disease (VoD) *(binary, categorical)*	**CRF**	Following GO treatment and following stem cell transplant, including grade, categorised as: • *Grade 1- mild* • *Grade 2- moderate* • *Grade 3- severe* • *Grade 4-very severe* • *Grade 5- death* • *No grading undertaken*.
Graft-versus-host disease (GvHD) *(categorical)*	**CRF** **Registry database**	For patients who experience stem cell transplants, categorised as: • *Yes (acute GvHD)* • *Yes (chronic GvHD)* • *No*

Detailed methodology for identifying the effectiveness outcomes of interest was built in collaboration with the Pfizer team and aligned as closely with ELN 2017 guidelines (6) were possible, whilst recognising the limitations associated with identifying complex outcomes using routinely collected real-world data. As such, sensitivity analyses were applied where necessary, with full details to be documented in the SAP.

9.4.3. Covariates

9.4.3.1. Baseline Patient Characteristics

The following characteristics were captured at baseline.

Table 4. Baseline characteristics

VARIABLES	DATA SET(S)	OPERATIONAL DEFINTIONS
Patient's age (at diagnosis) *(continuous, categorical)*	**CRF** **Registry database**	Categorized as follows: • *≥18 years and <30 years,* • *≥30 years and <40 years,* • *≥40 years and <50 years,* • *≥50 years and <60 years,* • *≥60 years and<70 years,* • *≥70 years and <80 years* • *≥80 years* As only year of birth provided date and month will be assumed to be 2nd July. Age at diagnosis is calculated as the floor of diagnosis date – birth date in days
Patient's sex *(binary)*	**CRF** **Registry**	*Male/Female*
Body mass index (BMI) *(continuous, categorical)*		Categorised into the following mutually exclusive groups: • *Underweight (below 18.5 kg/m2)* • *Normal weight (18.5-<25.0 kg/m2)* • *Overweight (25.0-<30.0 kg/m2)* • *Obese (30.0-<35.0 kg/m2)* • *Morbidly obese (≥35 kg/m2)* BMI will be defined by BMI specific variables (registry database only) or, where the BMI is not recorded, the height and weight will be used as inputs for the following formula: $$BMI = \frac{Weight\ (kg)}{Height\ (m)^2}$$ Implausible BMI measurements will be omitted from the analysis, i.e. < 10 kg/m^2 or > 150 kg/m^2. Further outliers may be omitted on review of the distribution. Patients with weight or height recorded as 'Don't know' will be classified as missing data for BMI, for the purpose of this analysis.

		(Registry only): The BMI recored at first line will be taken.
Time from diagnosis to index *(continuous)*	**CRF** **Registry**	Time from diagnosis to index is defined as the index date – diagnosis date.
WHO AML sub-type *(categorical)*	**CRF** **Registry**	At diagnosis, categorised as*:* • *AML with minimal differentiation (FAB M0)* • *AML without maturation (FAB M1)* • *AML with maturation (FAB M2)* • *Acute myelomonocytic leukaemia (FAB M4)* • *Acute monoblastic/monocytic leukaemia (FAB M5)* • *Pure erythroid leukaemia (FAB M6)* • *Acute megakaryoblastic leukaemia (FAB M7)* The following categories reported for the CRF only: • *AML with recurrent genetic abnormalities* • *AML not otherwise categorized* • *Acute basophilic leukaemia* • *Acute panmyelosis with fibrosis*
Blast cell percentage (bone marrow) *(continuous)*	**CRF** **Registry**	N/A
Blast cell percentage (peripheral blood) *(continuous)*	**CRF** **Registry**	N/A
Hemoglobin (g/dL) *(continuous)*	**CRF** **Registry**	Where haemoglobin concentration was provided in mmol/L, this was converted to g/dL using the following formula:. *Concentration (mmol/L) X 0.018 =* ***g/dL*** Implausible values (<0 and >15 g/dl) were omitted from the data if required.
Thrombocytes (x10^9/L) *(continuous)*	**CRF** **Registry**	*N/A*
Leukocytes (x10^9/L) *(continuous)*	**CRF** **Registry**	N/A
Lactate dehydrogenase (LDH) [U/L] *(continuous)*	**CRF** **Registry**	N/A
CD33 *(continuous/binary)*	**CRF** **Registry**	Registry : CD33 positivity reported as a binary yes/no variable.

		CRF: reported as a continuous variable and CD33+ reported as a binary yes/no variable, using a CD33 result of >20 to indicate positive status.
Comorbidities (*multiple binary)*	**CRF** **Registry database** **Baseline dataset**	CRF comorbidities: • *Myocardial infarction* • *Congestive heart failure* • *Peripheral vascular disease / peripheral arterial disease* • *Stroke* • *Dementia* • *Chronic obstructive pulmonary disease (COPD)* • *Connective tissue disease* • *Peptic ulcer disease* • *Liver disease* • *Diabetes* • *Hemiplegia* • *Moderate-to-severe chronic kidney disease* • *Solid tumour* • *Lymphoma* • *Aids* • *Hepatitis B* • *Hepatitis C* • *Other* • *Unknown* • *No concomitant conditions* Registry comorbidities • *Thromboembolic* • *Renal* • *Hepatic* • *Diabetes mellitus* • *Solid tumor* • *Infection* • *Pulmonary* • *Cardiac* • *Hematologic neoplasm* • *Obesity* • *Cerebrovascular disease* • *Rheumatologic* • *Peptic ulcer* • *Inflammatory bowel disease* • *Psychiatric disturbance* • *Multiple myeloma* • *Low grade NHL* • *High grade NHL* • *MGUS* • *MBL* • *Rheumatologic disease*

		• *ITP* • *AIHA* • *PNH* • *Autoimmune hypothyroidism* • *Neutrophilic dermatosis* • *Systemic vasculitis* • *Hemochromatosis* • *Hyperthyroidism*
Hematopoietic cell transplantation (HCT) specific comobridity index (continuous, categorical)	**Registry**	Categorised as follows: - 0 - 1-2 - 3-4 - >=5
Extramedullary disease *(categorical)*	**CRF** **Registry**	At index (start of 1st line induction therapy)
Extramedullary disease location *(multipe binary)*	**CRF**	Patients meeting the above variable, categorised as: • *Skin* • *Oral* • *CNS* • *Liver* • *Spleen* • *Testes* • *Lymph nodes* • *Other*
Performance status (ECOG) *(continuous, categorical)*	**CRF** **Registry**	At index, categorized as: *0 = Fully active, able to carry out all normal activity without restriction* *1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work* *2 = Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hour* *3 = Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours* *4 = Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair*
ELN 2017 risk *(categorical)*	**CRF** **Registry**	Categorized as: • *Favourable* • *Intermediate* The number and percentage of patients in each of the following groups will also be reported for the CRF database only:

		• *Favourable: t(8;21)(q22;q22.1); RUNX1-RUNX1T1* • *Favourable: inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11* • *Favourable: Mutated NPM1 without FLT3-ITD or with FLT3-ITDlow* • *Favourable: Biallelic mutated CEBPA* • *Favourable: Classified as favourable but no genetic information available* • *Intermediate: Mutated NPM1 and FLT3-ITDhigh* • *Intermediate: Wild-type NPM1 without FLT3-ITD or with FLT3-ITDlow (without adverse-risk genetic lesions)* • *Intermediate: t(9;11)(p21.3;q23.3); MLLT3-KMT2A* • *Intermediate: Cytogenetic abnormalities not classified as favorable or adverse* • *Intermediate: Classified as intermediate but no genetic information available*
Genetic alteration *(multiple binary)*	**CRF** **Registry**	For patients with genetic information lacking for specificity in ELN 2017 risk groups, the presence of specific genetic alterations at diagnosis: • *NPM1* • *CEBPA* • *FLT3* • *ASXL1* • *JAK2* • *RUNX1* • *SRSF2* • *STAG2* • *TET2* • *BCOR* • *DNMT3A* • *IDH1/2* • *RUNX1* • *KIT* • *CBL* • *NRAS* • *PTPN11* • *WT1* • *SF3B1* • *TP53* • *Other* • *Unknown*
Cytogenetic risk group *(categorical)*	**CRF** **Registry database**	At diagnosis, categorized as: • *Favourable: t(8:21)(q22;q22)* • *Favourable: inv(16)(p13q22)/t(16;16)(p13;q22)* • *Favourable: t(15;17)(q22;q12)*

		• *Favourable: Classified as favourable but no cytogenetic information available* • *Intermediate: All karyotypes that have neither a favourable nor an unfavourable prognostic significance* • *Intermediate: Classified as intermediate but no cytogenetic information available* *Registry: cytogenetic risk will be reported as the following, and taken from the ELN 2017 risk variable:* - Favourable - Intermediate
Previous treatments for AML *(binary)*	**CRF** **Registry**	Whether the patient received treatment for their AML outside of induction treatment: • *Yes, cytarabine or hydroxyurea administered for leukoreduction only* • *No*
Living status *(binary)*	**CRF** **Registry database**	

9.5. Data sources and measurement

9.5.1. Austrian, Belgian, and German centres

For Austrian, Belgian, and German centres, an eCRF (**Appendix 5. SAMPLE CASE REPORT FORM (CRF)**) was used by physicians at study sites to abstract data for patients who met the eligibility criteria outlined in Section 9.3.1 and Section 9.3.2. Sites were selected based on the results of a site feasibility assessment.

Each eligible site was required to complete a short screener for each patient, before abstracting data from electronic medical records (EMR) into the eCRF, to confirm their eligibility for the retrospective chart review. Sites were instructed to refer to the patient's complete EMR whilst completing the eCRF and not to answer any question from memory or that is not listed within the patients' EMR.

Once the data were extracted, they were stored in a secure study database. Further details around the data management can be found in Section 9.10.

All data were abstracted by qualified physicians who received study-specific training on use of the eCRF and variable definitions to ensure consistency across sites. For quality control, each completed eCRF was reviewed by two members of the project team to check for logical and medical consistency, with discrepancies adjudicated and resolved prior to database lock. The eCRF design aligned with established clinical data standards to promote comparability across sources. Data extracted from the Austrian Myeloid Registry underwent equivalent consistency and validity checks prior to inclusion in the analysis.

9.5.2. Austrian Myeloid Registry

The Austrian Myeloid Registry aims to assess the treatment patterns, clinical outcomes and quality of life of patients with myeloid diseases from 15 Austrian sites (15). Data was extracted for patients who met the eligibility criteria outlined in Section 9.3.1 and 9.3.2, resulting in a total 26 patients. Initial feasibility investigations showed the registry extract data in a similar way to an eCRF and extract data from EMRs at multiple sites across Austria.

9.6. Bias

For the chart review, selection bias may have influenced the current sample. Site participation is influenced by willingness to take part, and may be based on workload, levels of consulting patients during the data collection period, or familiarity with the research nature of the study. It should also be noted that the sites eligible for inclusion in the study are those with whom Pfizer have existing relationships with, and those ultimately selected for inclusion may be those deemed most suitable based on the feasibility assessment stage (i.e., those sites with higher numbers of patients or who are most suited to executed non interventional data collection studies) may be chosen over those considered to be less suitable. These factors introduce a bias whereby patients from non-participating sites are not represented in the results. Nonetheless, this method of site selection is the most practical approach for a non-interventional study such as this, whereby resources and timelines, to an extent, dictate the sites that can be considered eligible for inclusion.

The need to use an ICF for Belgian sites (as mandated by the lead IRB; UZ Leuven) may have introduced selection bias. The sample population may be biased towards less severe patients who are capable and willing to provide consent to participate. To mitigate both selection biases, patient demographic and clinical characteristic data will be captured to allow for comparisons with published datasets to understand the generalizability of results. Additionally, when informed consent was required in Belgium, a legally acceptable representative was permitted to provide informed consent on behalf of the patient should they be unable to consent, reducing the bias associated with the need to obtain patient consent.

To minimise information bias, all chart reviewers used a standardised data abstraction form and underwent training to ensure consistency across sites. Data abstractors were blinded to patient outcomes to reduce observer bias. Statistical analyses include sensitivity analyses to assess the potential impact of any residual confounding.

To minimise information and observer bias, data abstraction followed a standardised process using version-controlled eCRFs, ensuring consistency and traceability of all updates. Each eCRF was independently reviewed by two members of the project team to check for logical and medical consistency, with any discrepancies adjudicated and resolved before database lock. Reviewers were blinded to study hypotheses to reduce the potential for biased interpretation of data. Automated logic and completeness checks programmed into the eCRF further ensured accuracy and minimised missing or inconsistent data. All data management

activities, including query resolution and QC procedures, were fully documented within the audit trail to allow assessment of data reliability and integrity

9.7. Study Size

This study is purely descriptive and there will be no limit on the sample size in terms of patients meeting the eligibility criteria in Section 9.3. Estimated sample sizes were presented in the study protocol and actual samples achieved are listed below (Table 5).

Table 5. Estimated and final sample sizes achieved by sites

	Site Name	Estimated Sample Size (per study protocol)	Final Sample Size (achieved)
Austria	Medical University of Vienna	50	31
	Austrian Myeloid Registry	30	26
Belgium	UZ Leuven	50	16
	Az Sint Jan Brugge	42	8
	UZ Brussels	18	10
Germany	University of Cologne	40	24
Total		230	**115**

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.

9.9. Statistical methods

This study was a descriptive study in nature and included no hypothesis testing. Further details on analysis were documented in the Statistical Analysis Plan (SAP), see Appendix 4. STATISTICAL ANALYSIS PLAN.

9.9.1. Main summary measures

For continuous (numeric) variables (excluding rate variables), the following statistics are provided:

- Sample size (counts)
- Number of missing

- Mean, standard deviation
- Median, interquartile range (IQR)
- Minimum and maximum values

Frequencies and percentages were reported for categorical variables out of those with valid data. Where applicable, all estimates are described with accompanying 95% confidence intervals (CI).

9.9.2. Main statistical methods

As indicated in Section 9.9.1, descriptive statistics were outputted for continuous and categorical variables.

For time to event survival analyses only, Kaplan-Meier (KM) curves were developed with 95% CIs of the median estimated. Kaplan-Meier analysis enables censoring to be accounted for.Where median survival is not reached as <50% of patients achieve 'survival failure', KM curves and survival functions were still reported, but the absence of median survival is flagged.

9.9.3. Missing values

All analyses were conducted on the full analysis set of patients. Where missing values were found in a particular variable, these were reported as the number of patients with a missing data point. The counts of patients with missing data for each endpoint will be summarised. In cases where there are extreme levels of missing data or where the volume of missing data was differential between important clinical/prognostic groups, no imputation was carried out and patients with such missing data were excluded from the relevant outcome analyses.

9.9.4. Sensitivity analyses

None.

9.9.5. Amendments to the statistical analysis plan

None.

9.10. Quality control

For chart review:

Data from the eCRF was stored in the study database. The database was housed and managed by ARW during the study and analysis. Any data transfers to Pfizer were carried out via a Secure File Transfer Protocol (SFTP) to ensure any international transfers are safeguarded. ARW's data server is based within the UK. Following completion of the study, the study database was archived and subsequently permanently deleted, in accordance with ARW's and Pfizer's Master Services Agreement.

Version control was used during the development of all data collection materials to ensure there is an auditable record of requested updates and changes is available.

For the chart review data collection in Austria and Belgium, each individual eCRF was reviewed by 2 members of the project team to check for logical and medical consistency. Queries were raised throughout the data management process and were closed following the satisfactory correction or explanation by each site. All queries were logged within the EDC as part of the audit trail and were also recorded within the data management plan. Following the review and sign-off of each eCRF by 2 members of the project team, the eCRF was locked and was not accessible for further data entry or changes. In Germany, where patient data must be completely anonymised (ie, no linkage document is permitted), all entered data were reviewed, but data queries were limited by the inability for sites to reidentify patients. As automated checks were programmed into the eCRF, the impact on the completeness of the data in Germany was expected to be minimal.

When all checks had been completed to the satisfaction of the project manager, the database was considered complete and the database was locked. This formally announces that there is no intention to make any further changes to the data and that data analysis can proceed. A database lock declaration form was completed by the project manager and the form was kept in the study file. The locked database was saved into a folder with restricted access. A copy of the locked database was made available to the analyst.

Secondary data analysis:

For quality control purposes, documented evidence of correct interpretation of the study protocol was achieved through development of a detailed SAP, reviewed, and approved by the Pfizer study team, and an extensive decision log maintained and updated by the ARW study team, which was shared with Pfizer throughout the course of the study. Documented evidence of correct execution of the study protocol was achieved through completion of ARW's internal quality control (QC) checklist by both the project analyst and an independent QC analyst, which, on completion, was made available to the Pfizer study team on request. The independent QC analyst was responsible for a detailed review of the project analyst's programming code and outputs prior to sign-off, ie, no code replication.

On production of study results, ARW performed QC of the outputs including, but not limited to, logic checks on base sizes, missing values and totals, consistency of output across tables, extreme/unexpected values and results, typographical errors and interpretations (where applicable). Any issues identified during this process were logged and resolved to completion with the appropriate analyst team. On receipt of any updated output, additional checks were performed in accordance with the initial data check to ensure all issues have been adequately resolved and no further issues were identified. In the event that the original issues had not been resolved or further issues had been identified, the quality control process was repeated.

9.11. Protection of human subjects

Subject information and consent

As per the ethical requirements in Belgium, written informed consent (see Appendix 6. SAMPLE STANDARD SUBJECT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT (ICD)) was obtained prior to subjects who were alive at data entry entering the study (before initiation of study protocol-specified procedures) by study personnel; the nature, purpose, and duration of the study was explained to each subject. Each subject in Belgium was informed that he/she could withdraw from the study at any time and for any reason. Each subject was given sufficient time to consider the implications of the study before deciding whether to participate. Subjects who chose to participate signed an informed consent document.

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

The final protocol, any amendments, and informed consent documentation were reviewed and approved by IEC(s) for each site participating in the study (see Appendix 3.2 List of Independent Ethics Committee (IEC) or Institutional Review Board (IRB) and Corresponding Protocol Approval Dates).

The final protocol, any amendments, and informed consent documentation were reviewed and approved by a local data protection agency for each site participating in the study.

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 followed generally accepted research practices described in:

- Guidelines for Good Pharmacoepidemiology Practices (GPP). Public Policy Committee, International Society of Pharmacoepidemiology. Pharmacoepidemiology and Drug Safety 2016; 25:2-10.
- Good Practices for Outcomes Research issued by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR)
- Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making
- International Ethical Guidelines for Epidemiological Studies issued by the Council for International Organizations of Medical Sciences (CIOMS)

- European Medicines Agency (EMA) European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology

- The ENCePP Code of Conduct for scientific independence and transparency in the conduct of pharmacoepidemiological and pharmacovigilance studies

- Food and Drug Administration (FDA) Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment

- FDA Guidance for Industry and FDA Staff: Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data

- FDA Guidance for Industry: Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims http://www.fda.gov/downloads/Drugs/Guidances/UCM193282.pdf

10. RESULTS

10.1. Participants

In total, 115 patients' data were included in the study. See Table 5 for full breakdown of patient numbers by site / data source.

10.2. Descriptive data

The total number of patients included in the study was 115. The EDC had CRFs for 89 patients collected from the five sites between the index date of 01 April 2018 and 31 May 2023 that met the inclusion criteria outlined in Section 9.3.1. The AGMT had 26 patients that met the inclusion criteria and whose data was included in this study.

10.3. Outcome data

N/A

10.4. Main results

10.4.1. Results - CRF Data

10.4.1.1. Primary Objective: Patient Demographics and Clinical Characteristics

In CRF patients, 52.8% (n=47) were male and the median (IQR) patient body mass index (BMI) at baseline was 26.1 (22.8-30.1). All patients had a physician-confirmed diagnosis of AML, with a median (IQR) age at diagnosis of 60 (44.0-67.0) (Table 6). The age at diagnosis was highest in the Belgian sample, with a median (IQR) age at diagnosis of 63 (51.0-68.0).

At the time of data collection, all patients were classified as favourable 37.1% (n=33) or intermediate 62.9% (n=56). According to the WHO 2016 AML subtype classification, 23.6% and 21.3% of patients had the 'FAB M2 (with maturation)' or 'AML with recurrent genetic abnormalities' classification, respectively. At diagnosis, the median (IQR) bone marrow blast was 53.0% (35.0-70.0) and the peripheral blood blast was 25.6% (7.0-60.0). The median (IQR) CD33+ status at diagnosis was 95.0 (87.6-98.8).

Median (IQR) follow up duration (days) was 890.0 (377.0, 1346.0).

Table 6. CRF Data: Patient demographics

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Age at diagnosis (years)						
Mean (SD)	55.9 (14.7)	54.4 (15)	56.7 (14.5)	57.4 (14.2)	59.5 (13.2)	48.7 (15.3)
Median (IQR)	60 (44.0-67.0)	61 (42.0-66.0)	59.5 (45.0- 68.0)	57 (44.0-69.0)	63 (51.0-68.0)	45.5 (35.0-63.0)

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Patient sex, n (%)						
Female	42 (47.2)	14 (42.4)	28 (50.0)	15 (48.4)	18 (52.9)	9 (37.5)
Male	47 (52.8)	19 (57.6)	28 (50.0)	16 (51.6)	16 (47.1)	15 (62.5)
BMI, n (%)						
Underweight (below 18.5 kg/m^2)	2 (2.2)	0 (0.0)	2 (3.6)	1 (3.2)	0 (0.0)	1 (4.2)
Normal weight (18.5-<25.0 kg/m^2)	36 (40.4)	15 (45.5)	21 (37.5)	14 (45.2)	15 (44.1)	7 (29.2)
Overweight (25.0-<30.0 kg/m^2)	28 (31.5)	8 (24.2)	20 (35.7)	9 (29.0)	11 (32.4)	8 (33.3)
Obese (30.0->35.0 kg/m^2)	16 (18.0)	7 (21.2)	9 (16.1)	4 (12.9)	6 (17.6)	6 (25.0)
Morbidly obese (≥35 kg/m^2)	7 (7.9)	3 (9.1)	4 (7.1)	3 (9.7)	2 (5.9)	2 (8.3)
Mean (SD)	26.8 (5)	26.8 (4.4)	26.8 (5.4)	26.7 (5.6)	26.4 (4.5)	27.5 (5.1)
Median (IQR)	26.1 (22.8-30.1)	25.3 (22.7-30.1)	26.8 (23.0-29.5)	25.2 (22.7-29.3)	25.3 (22.6-29.7)	27.1 (24.0-30.1)

Table 7. CRF Data: Clinical characteristics

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Cytogenetic risk at diagnosis (ELN 2017), n (%)						
Favourable: t(8;21)(q22;q22.1); RUNX1 RUNX1T1	9 (10.1)	9 (27.3)	0 (0.0)	3 (9.7)	6 (17.6)	0 (0.0)
Favourable: inv(16)(p13.1q22) or t(16;16)(p13.1;q22); CBFB-MYH11	9 (10.1)	9 (27.3)	0 (0.0)	3 (9.7)	3 (8.8)	3 (12.5)
Favourable: Mutated NPM1 without FLT3-ITD or with FLT3-ITDlow	27 (30.3)	10 (30.3)	17 (30.4)	9 (29.0)	12 (35.3)	6 (25.0)
Favourable: Biallelic mutated CEBPA	3 (3.4)	1 (3.0)	2 (3.6)	0 (0.0)	1 (2.9)	2 (8.3)

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Intermediate: Mutated NPM1 and FLT3-ITDhigh	12 (13.5)	3 (9.1)	9 (16.1)	0 (0.0)	6 (17.6)	6 (25.0)
Intermediate: Wild-type NPM1 without FLT3-ITD or with FLT3-ITDlow	4 (4.5)	0 (0.0)	4 (7.1)	0 (0.0)	3 (8.8)	1 (4.2)
Intermediate: t(9;11)(p21.3;q23.3) ; MLLT3-KMT2A	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	0 (0.0)	1 (4.2)
Intermediate: Cytogenetic abnormalities not classified as favorable or adverse	14 (15.7)	0 (0.0)	14 (25.0)	11 (35.5)	0 (0.0)	3 (12.5)
Intermediate: Classified as intermediate but no genetic information available	6 (6.70	1 (3.0)	5 (8.9)	3 (9.7)	1 (2.9)	2 (8.3)
AML subtype at diagnosis (WHO 2016), n (%)						
With minimal differentiation (FAB M0)	7 (7.9)	2 (6.1)	5 (8.9)	2 (6.5)	1 (2.9)	4 (16.7)
Without maturation (FAB M1)	10 (11.2)	2 (6.1)	8 (14.3)	2 (6.5)	6 (17.6)	2 (8.3)
With maturation (FAB M2)	21 (23.6)	4 (12.1)	17 (30.4)	16 (51.6)	3 (8.8)	2 (8.3)
Acute myelomonocytic leukaemia (FAB M4)	14 (15.7)	7 (21.2)	7 (12.5)	6 (19.4)	1 (2.9)	7 (29.2)
Acute monoblastic/monocytic leukaemia (FAB M5)	10 (11.2)	4 (12.1)	6 (10.7)	2 (6.5)	3 (8.8)	5 (20.8)
Pure erythoid leukaemia (FAB M6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Acute megakaryoblastic leukaemia (FAB M7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
AML with recurrent genetic abnormalities	19 (21.3)	11 (33.3)	8 (14.3)	2 (6.5)	15 (44.1)	2 (8.3)
AML not otherwise categorized	8 (9.0)	3 (9.1)	5 (8.9)	1 (3.2)	5 (14.7)	2 (8.3)

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Acute basophilic leukaemia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Acute panmyelosis with fibrosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CD33+ status at index						
Mean (SD)	86.2 (21.6)	93.4 (7.3)	82.4 (25.3)	73.0 (27.5)	94.1 (7.7)	97.4 (3.0)
Median (IQR)	95 0 (87.6-98.8)	95.0 (91.6-99.0)	95.0 (80.0-98.6)	84.0 (50.0-95.0)	96.2 (91.6-99.2)	98.5 (95.9-99.7)
Missing, n	16	8	8	0	15	1
Bone marrow blast percentage at diagnosis						
Mean (SD)	52.7 (24.6)	48.9 (25.6)	54.9 (23.9)	46.4 (20.9)	62.0 (22.7)	48.2 (28.5)
Median (IQR)	53.0 (35.0-70.0)	49.0 (27.5-66.0)	53.5 (36.7-75.0)	45.0 (30.0-65.0)	66.5 (46.5-81.2)	45.0 (26.0-66.0)
Missing, n	3	1	2	0	2	1
Peripheral blood blast percentage at index						
Mean (SD)	34.8 (30.9)	37.8 (28.9)	33.1 (32.2)	30.0 (27.1)	38.6 (33.7)	36.9 (32.9)
Median (IQR)	25.6 (7.0 - 60.0)	25.2 (9.0-60.0)	26.0 (5.0-52.0)	26.0 (7.0-52.0)	26.4 (5.5-72.2)	25.0 (7.0-69.0)
Missing, n	9	4	5	0	8	1
Haemoglobin count at index (g/dL)						
Mean (SD)	8.3 (2.3)	8.3 (2.1)	8.3 (2.4)	9.6 (2.3)	6.6 (1.8)	8.5 (1.8)
Median (IQR)	8.0 (6.6-9.5)	8.0 (6.9-9.2)	8.0 (6.5-9.6)	9.1 (8.0-11.5)	6.5 (5.5-7.6)	8.3 (7.2-9.4)
Missing, n	8	5	3	0	8	0
Thrombocytes count at index (x10^9/L)						
Mean (SD)	80.0 (79.7)	72.2 (55.4)	83.9 (89.8)	100.9 (111.7)	66.8 (27.9)	66.6 (61.4)
Median (IQR)	56.5 (34.5-83.5)	60.0 (30.0-92.0)	55.0 (35.0-83.0)	56.0 (35.0-140.0)	60.0 (49.0-82.0)	39.0 (20.0-86.0)
Missing, n	9	6	3	0	9	0
Leukocytes count at index (x10^9/L)						

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Mean (SD)	32.0 (54.6)	34.3 (51.3)	30.8 (56.7)	31.0 (57.1)	37.7 (54.9)	27.0 (52.7)
Median (IQR)	8.6 (3.4-30.4)	9.0 (5.0-45.4)	8.3 (2.0-29.1)	7.6 (2.0-28.9)	12.9 (3.8-50.0)	8.6 (3.8-18.6)
Missing, n	11	6	5	0	9	2
Lactate dehydrogenase at index						
Mean (SD)	668.4 (622.4)	698.0 (631.0)	655.0 (624.1)	508.1 (496.7)	851.4 (785.7)	693.4 (557.4)
Median (IQR)	419.0 (272.0-706.0)	419.0 (291.0-789.5)	432.0 (271.0-696.0)	377.0 (211.0-560.0)	476.0 (272.0-1263.0)	507.0 (346.0-718.5)
Missing, n	12	9	3	1	11	0
Comorbidities, n (%)						
Myocardial infarction	1 (1.1)	1 (3.0)	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)
Congestive heart failure	3 (3.4)	1 (3.0)	2 (3.6)	1 (3.2)	1 (2.9)	1 (4.2)
Peripheral vascular disease / peripheral arterial disease	4 (4.5)	2 (6.1)	2 (3.6)	0 (0.0)	4 (11.8)	0 (0.0)
Stroke	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Dementia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic obstructive pulmonary disease (COPD)	2 (2.2)	1 (3.0)	1 (1.8)	1 (3.2)	1 (2.9)	0 (0.0)
Connective tissue disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peptic ulcer disease	3 (3.4)	1 (3.0)	2 (3.6)	0 (0.0)	2 (5.9)	1 (4.2)
Liver disease	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	1 (2.9)	0 (0.0)
Diabetes	6 (6.7)	4 (12.1)	2 (3.6)	2 (6.5)	2 (5.9)	2 (8.3)
Hemiplegia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Moderate-to-severe chronic kidney disease	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	1 (2.9)	0 (0.0)
Solid tumour	5 (5.6)	3 (9.1)	2 (3.6)	0 (0.0)	4 (11.8)	1 (4.2)
Lymphoma	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
AIDS	1 (1.1)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.2)
Hepatitis B	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hepatitis C	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	32 (36.0)	5 (15.2)	27 (48.2)	19 (61.3)	13 (38.2)	0 (0.0)
No concomitant conditions	45 (50.6)	20 (60.6)	25 (44.6)	11 (35.5)	15 (44.1)	19 (79.2)

10.4.1.2. Primary Objective: GO Real-World Treatment Patterns

The time from diagnosis of AML to initiation of the index regimen (1L treatment with GO) was a median (IQR) of 7.0 (3.0-9.0 days) days. Most patients within the CRF data had induction followed by consolidation treatment or induction treatment only, 55.1% (n=49) of patients had induction and consolidation treatment and 27.0% (n=24) had induction therapy only. 85.4% (n=76) of patients received 1L treatment only, with a small proportion of patients receiving 2L+ treatment (14.6%, n=13) (Table 8).

Table 8. CRF Data: Treatment pathway

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Time from diagnosis to index (days)						
Mean (SD)	7.8 (7.3)	8.9 (9.3)	7.1 (5.8)	9.9 (6.3)	7 (7.5)	6 (7.7)
Median (IQR)	7.0 (3.0-9.0)	7.0 (4.0-9.0)	5.5 (3.0-9.0)	8.0 (5.0-13.0)	5.5 (3.0-8.0)	3.5 (2.0-7.0)
Treatment pathway, n (%)						
Induction	24 (27.0)	10 (30.3)	14 (25.0)	1 (3.2)	8 (23.5)	15 (62.5)
Induction + Consolidation	49 (55.1)	18 (54.5)	31 (55.4)	21 (67.7)	21 (61.8)	7 (29.2)
Induction + Consolidation + Maintenance	2 (2.2)	1 (3.0)	1 (1.8)	0 (0.0)	0 (0.0)	2 (8.3)
Induction + Consolidation + Relapse	1 (1.1)	0 (0.0)	1 (1.8)	1 (3.2)	0 (0.0)	0 (0.0)

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Induction + Consolidation + Relapse + Treatment for relapse/refractory	7 (7.9)	3 (9.1)	4 (7.1)	5 (16.1)	2 (5.9)	0 (0.0)
Induction + Consolidation + Relapse + Treatment for relapse/refractory + Consolidation	1 (1.1)	0 (0.0)	1 (1.8)	1 (3.2)	0 (0.0)	0 (0.0)
Induction + Relapse + Consolidation + Treatment for relapse/refractory + Consolidation	1 (1.1)	1 (3.0)	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)
Induction + Relapse + Treatment for relapse/refractory	4 (4.5)	0 (0.0)	4 (7.1)	2 (6.5)	2 (5.9)	0 (0.0)
Number of treatment lines, n (%)						
1 line	76 (85.4)	29 (87.9)	47 (83.9)	23 (74.2)	29 (85.3)	24 (100.0)
2+ lines	13 (14.6)	4 (12.1)	9 (16.1)	8 (25.8)	5 (14.7)	0 (0.0)

All patients received GO during 1L induction in conjunction with cytarabine and an anthracycline (daunorubicin or idarubicin)); 20.2% of patients received midostaurin also. Patients received a median (IQR) of 1 (1.0-2.0) treatment cycle during 1L induction therapy. 80.9% (n=72) of patients received three doses of GO during 1L induction. A small proportion of patients received less than three doses of GO during 1L induction,14.6% (n=13). The median (IQR) GO dose received during 1L induction was 5.0 mg (5.0 – 5.0; n=89). There was a median (IQR) of 3 days (3.0-3.0) between GO doses (Table 9).

Table 9. CRF Data: 1L induction treatment characteristics

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
1L induction treatment received, n (%)						

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Gemtuzumab ozogamicin	89 (100.0)	33 (100.0)	56 (100.0)	31 (100.0)	34 (100.0)	24 (100.0)
Cytarabine	89 (100.0)	33 (100.0)	56 (100.0)	31 (100.0)	34 (100.0)	24 (100.0)
Daunorubicin	81 (91.0)	32 (97.0)	49 (87.5)	31 (100.0)	26 (76.5)	24 (100.0)
Idarubicin	9 (10.1)	1 (3.0)	8 (14.3)	0 (0.0)	9 (26.5)	0 (0.0)
Midostaurin	18 (20.2)	6 (18.2)	12 (21.4)	0 (0.0)	11 (32.4)	7 (29.2)
Other	5 (5.6)	1 (3.0)	4 (7.1)	4 (12.9)	1 (2.9)	0 (0.0)
Hydroxyurea	3 (3.4)	1 (3.0)	2 (3.6)	0 (0.0)	3 (8.8)	0 (0.0)
Cladribine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number of treatment cycles during 1L induction, n (%)						
1	61 (68.5)	20 (60.6)	41 (73.2)	27 (87.1)	29 (85.3)	5 (20.8)
2	27 (30.3)	12 (36.4)	15 (26.8)	4 (12.9)	4 (11.8)	19 (79.2)
3	1 (1.1)	1 (3.0)	0 (0.0)	0 (0.0)	1 (2.9)	0 (0.0)
Mean (SD)	1.3 (0.5)	1.4 (0.6)	1.3 (0.4)	1.1 (0.3)	1.2 (0.5)	1.8 (0.4)
Median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	2.0 (2.0-2.0)
GO dose per administration during 1L induction (mg)						
Mean (SD)	5.0 (0.1)	5.0 (0.0)	5.0 (0.1)	5.0 (0.1)	5.0 (0.0)	5.0 (0.0)
Median (IQR)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (5.0-5.0)
Total GO dose during 1L induction (mg)						
Mean (SD)	14.1 (3.0)	14.7 (2.8)	13.8 (3.2)	14.6 (2.2)	13.7 (3.8)	14.2 (2.8)
Median (IQR)	15.0 (15.0-15.0)	15.0 (15.0-15.0)	15.0 (14.9-15.0)	15.0 (15.0-15.0)	15.0 (15.0-15.0)	15.0 (15.0-15.0)
Total number of doses of GO during 1L induction, n (%)						
1 only	6 (6.7)	2 (6.1)	4 (7.1)	0 (0.0)	4 (11.8)	2 (8.3)
2	7 (7.9)	0 (0.0)	7 (12.5)	4 (12.9)	3 (8.8)	0 (0.0)

Variable	Total CRF Sample (n=89)	Risk status: Favourable (n=33)	Risk status: Intermediate (n=56)	Country: Austria (n=31)	Country: Belgium (n=34)	Country: Germany (n=24)
3	72 (80.9)	29 (87.9)	43 (76.8)	25 (80.6)	25 (73.5)	22 (91.7)
4	4 (4.5)	2 (6.1)	2 (3.6)	2 (6.5)	2 (5.9)	0 (0.0)
Mean (SD)	2.8 (0.6)	2.9 (0.6)	2.8 (0.6)	2.9 (0.4)	2.7 (0.8)	2.8 (0.6)
Median (IQR)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)
Number of days between first combined chemotherapy and GO at induction						
Mean (SD)	0.2 (0.7)	0.2 (0.7)	0.2 (0.6)	0.3 (0.8)	0.2 (0.8)	0.0 (0.0)
Median (IQR)	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 (0.0-0.0)	0.0 (0.0-0.0)
Days between GO doses during induction						
n	**n=83**	**n=31**	**n=52**	**n=31**	**n=30**	**n=22**
Mean (SD)	8.3 (40.2)	16.9 (65.6)	3.3 (0.9)	3.3 (1.1)	17.5 (66.6)	3.0 (0.1)
Median (IQR)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.0)	3.0 (3.0-3.5)	3.0 (3.0-3.0)

Of the n=61 patients that received 1L consolidation therapy, the most administered treatments were cytarabine (98.4%, n=60) and GO (78.7%, n=48). Patients received a median of 2 (1.0-4.0) treatment cycles for 1L consolidation. For each dose of GO administered during 1L consolidation, the median (IQR) dose was 5.0 mg (5.0-5.0). There was a median (IQR) of 47 days (39.0-55.0) between GO doses (Table 10).

Table 10. CRF Data: 1L Consolidation treatments characteristics

Variable	Total	Risk status: Favourable	Risk status: Intermediate	Country: Austria	Country: Belgium	Country: Germany
1L consolidation treatment received, n (%)						
n	**(n=61)**	**(n=23)**	**(n=38)**	**(n=28)**	**(n=24)**	**(n=9)**
Daunorubicin	10 (16.4)	6 (26.1)	4 (10.5)	0 (0.0)	10 (41.7)	0 (0.0)
Cytarabine	60 (98.4)	22 (95.7)	38 (100.0)	28 (100.0)	23 (95.8)	9 (100.0)
Gemtuzumab ozogamicin	48 (78.7)	18 (78.3)	30 (78.9)	24 (85.7)	16 (66.7)	8 (88.9)

Variable	Total	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
Midostaurin	10 (16.4)	4 (17.4)	6 (15.8)	0 (0.0)	8 (33.3)	2 (22.2)
Idarubicin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mitoxantrone	1 (1.6)	1 (4.3)	0 (0.0)	0 (0.0)	1 (4.2)	0 (0.0)
Thioguanine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	28 (45.9)	7 (30.4)	21 (55.3)	26 (92.9)	2 (8.3)	0 (0.0)
Number of treatment cycles during 1L consolidation, n (%)						
n	**(n=61)**	**(n=23)**	**(n=38)**	**(n=28)**	**(n=24)**	**(n=9)**
1	20 (33.3)	10 (45.5)	10 (26.3)	3 (10.7)	15 (65.2)	2 (22.2)
2	13 (21.7)	2 (9.1)	11 (28.9)	6 (21.4)	6 (26.1)	1 (11.1)
3	9 (15.0)	2 (9.1)	7 (18.4)	4 (14.3)	2 (8.7)	3 (33.3)
4	18 (30.0)	8 (36.4)	10 (26.3)	15 (53.6)	0 (0.0)	3 (33.3)
Mean (SD)	2.4 (1.2)	2.4 (1.4)	2.4 (1.2)	3.1 (1.1)	1.4 (0.7)	2.8 (1.2)
Median (IQR)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	4.0 (2.0-4.0)	1.0 (1.0-2.0)	3.0 (2.0-4.0)
Missing, n	1	1	0	0	1	0
GO dose per administration during 1L consolidation (mg)						
n	**(n=48)**	**(n=18)**	**(n=30)**	**(n=24)**	**(n=16)**	**(n=8)**
Mean (SD)	4.9 (0.2)	5.0 (0.0)	4.9 (0.2)	4.9 (0.2)	4.9 (0.2)	5.0 (0)
Median (IQR)	5 (5.0-5.0)	5.0 (5.0-5.0)	5.0 (4.9-5.0)	5 (5.0-5.0)	5 (5.0-5.0)	5 (5.0-5.0)
Total GO dose during 1L consolidation (mg)						
n	**(n=48)**	**(n=18)**	**(n=30)**	**(n=24)**	**(n=16)**	**(n=8)**
Mean (SD)	7.9 (3.0)	7.5 (2.6)	8.2 (3.2)	8.2 (2.3)	7.0 (3.5)	8.8 (3.5)
Median (IQR)	8.9 (5.0-10.0)	7.5 (5.0-10.0)	8.9 (5.0-10.0)	9.9 (5.0-10.0)	5.0 (5.0-8.9)	10.0 (5.0-10.0)
Total number of doses of GO during 1L consolidation, n (%)						
n	**(n=48)**	**(n=18)**	**(n=30)**	**(n=24)**	**(n=16)**	**(n=8)**
1	21 (43.8)	8 (44.4)	13 (43.3)	8 (33.3)	10 (62.5)	3 (37.5)

Variable	Total	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
2	24 (50.0)	10 (55.6)	14 (46.7)	16 (66.7)	4 (25.0)	4 (50.0)
3	3 (6,2)	0 (0.0)	3 (10.0)	0 (0.0)	2 (12.5)	1 (12.5)
Mean (SD)	1.6 (0.6)	1.6 (0.5)	1.7 (0.7)	1.7 (0.5)	1.5 (0.7)	1.8 (0.7)
Median (IQR)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	2.0 (1.0-2.0)	1.0 (1.0-2.0)	2.0 (1.0-2.0))
Days between doses of GO during 1L consolidation						
	(n=27)	**(n=10)**	**(n=17)**	**(n=16)**	**(n=6)**	**(n=5)**
Mean (SD)	46.9 (12.3)	42.7 (11.2)	49.4 (12.5)	49.4 (11.4)	43.6 (12.6)	42.9 (15.2)
Median (IQR)	47.0 (39.0-55.0)	41.5 (35.0-51.0)	48.0 (43.0-56.0)	50.0 (42.0-55.5)	41.5 (35.0-48.0)	44.0 (30.0-49.0)

42.7% (n=38) patients received an allogeneic haematopoietic stem cell transplant (HSCT). Of these, 84.2% (n=32), received it after initiation of 1L therapy. One patient had received radiation therapy and none of the patient sample had received surgery (Table 11).

Table 11. CRF Data: Other treatments received

Variable	Total CRF Sample (n=89)	Risk status		Country		
		Favourable (n=33)	Intermediate (n=56)	Austria (n=31)	Belgium (n=34)	Germany (n=24)
Other treatments ever received, n (%)						
HSCT	38 (42.7)	13 (39.4)	25 (44.6)	12 (38.7)	15 (44.1)	11 (45.8)
HSCT following 1L therapy (% of HSCT receivers)	*32 (84.2)*	*11 (84.6)*	*21 (84.0)*	*7 (58.3)*	*14 (93.3)*	*11 (100.0)*
HSCT following 2L+ therapy (% of HSCT receivers)	*6 (15.8)*	*2 (15.4)*	*4 (16.0)*	*5 (41.7)*	*1 (6.7)*	*0 (0.0)*
Radiation therapy	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	1 (2.9)	0 (0.0)
Surgery	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
None	51 (57.3)	20 (60.6)	31 (55.4)	19 (61.3)	19 (55.9)	13 (54.2)

10.4.1.3. Secondary Objective: First-Line Treatment Effectiveness Outcomes

Within the CRF data, the majority of those with a recorded response achieved complete remission (86.6%, n=71). The median (IQR) time from end of induction to response evaluation was 26 days (20.0-32.0) (Table 12).

Table 12. CRF Data: 1L induction treatment effectiveness outcomes

		Risk status		Country		
Variable	**Total CRF Sample (n=89)**	**Favourable (n=33)**	**Intermediate (n=56)**	**Austria (n=31)**	**Belgium (n=34)**	**Germany (n=24)**
Response to 1st line induction therapy, n (%)						
Complete remission	58 (70.7)	20 (66.7)	38 (73.1)	28 (90.3)	24 (80.0)	6 (28.6)
Complete remission with incomplete haematologic recovery (CRi)	12 (14.6)	5 (16.7)	7 (13.5)	0 (0.0)	4 (13.3)	8 (38.1)
Complete remission with incomplete platelet counts (CRp)	1 (1.2)	0 (0.0)	1 (1.9)	1 (3.2)	0 (0.0)	0 (0.0)
Morphologic leukaemia-free state	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Partial remission	3 (3.7)	1 (3.3)	2 (3.8)	0 (0.0)	1 (3.3)	2 (9.5)
Stable disease	3 (3.7)	0 (0.0)	3 (5.8)	2 (6.5)	1 (3.3)	0 (0.0)
Progressive disease	1 (1.2)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	1 (4.8)
Uncertain response	4 (4.9)	4 (13.3)	0 (0.0)	0 (0.0)	0 (0.0)	4 (19.0)
Missing, n	7	3	4	0	4	3
Cytogenetic complete remission/response following induction, n (%)						
Yes	40 (90.9)	14 (82.4)	26 (96.3)	11 (100.0)	17 (81.0)	12 (100.0)
No	4 (9.1)	3 (17.6)	1 (3.7)	0 (0.0)	4 (19.0)	0 (0.0)
Missing, n	45	16	29	20	13	12
Days between end of induction treatment end response evaluation						
Mean (SD)	26.3 (11.2)	22.3 (7.6)	28.8 (12.3)	33.8 (11.4)	22.9 (7.3)	20.6 (9.7)

		Risk status		Country		
Variable	**Total CRF Sample (n=89)**	**Favourable (n=33)**	**Intermediate (n=56)**	**Austria (n=31)**	**Belgium (n=34)**	**Germany (n=24)**
Median (IQR)	26.0 (20.0-32.0)	22.0 (17.0-28.5)	28.0 (22.5-33.5)	32.0 (28.0-36.0)	22.0 (18.0-28.0)	21.0 (17.0-25.0)
Missing, n	5	1	4	0	4	1

Following 1L induction therapy, most patients went on to receive consolidation therapy (n=60, 68.2%).10.2% (n=9) of patients received a stem cell transplant after 1L induction therapy (Table 13).

Table 13. CRF Data: Treatment events after 1L induction

		Risk status		Country		
Variable	**Total CRF Sample (n=89)**	**Favourable (n=33)**	**Intermediate (n=56)**	**Austria (n=31)**	**Belgium (n=34)**	**Germany (n=24)**
Treatment events following induction, n (%)						
Consolidation of 1st line	60 (68.2)	22 (66.7)	38 (69.1)	28 (90.3)	23 (67.6)	9 (39.1)
Relapse and starting therapy for relapsed/refractory disease	5 (5.7)	1 (3.0)	4 (7.3)	2 (6.5)	3 (8.8)	0 (0.0)
Observation / active monitoring / watchful waiting	5 (5.7)	3 (9.1)	2 (3.6)	0 (0.0)	3 (8.8)	2 (8.7)
Best supportive care	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	1 (2.9)	0 (0.0)
Treatment as part of clinical trial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient decided not to continue treatment	1 (1.1)	0 (0.0)	1 (1.8)	0 (0.0)	1 (2.9)	0 (0.0)
Patient received stem cell transplant	9 (10.2)	4 (12.1)	5 (9.1)	0 (0.0)	1 (2.9)	8 (33.3)
Other	7 (8.0)	3 (9.1)	4 (7.3)	1 (3.2)	2 (5.9)	4 (17.4)
Missing, n	1	0	1	0	0	1

For patients that received consolidation therapy, the majority of patients received complete remission (67.2%, n=39). The median (IQR) time from end of consolidation to response evaluation was 38.0 days (27.0-56.0) (Table 14).

Table 14. CRF Data: 1L consolidation treatment effectiveness outcomes

Variable	Total CRF Sample	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
Response to 1st line consolidation therapy, n (%)						
n	**58**	**20**	**38**	**28**	**23**	**7**
Complete remission	39 (67.2)	16 (80.0)	23 (60.5)	16 (57.1)	18 (78.3)	5 (71.4)
Complete remission with incomplete haematologic recovery (CRi)	7 (12.1)	2 (10.0)	5 (13.2)	2 (7.1)	4 (17.4)	1 (14.3)
Complete remission with incomplete platelet counts (CRp)	10 (17.2)	1 (5.0)	9 (23.7)	10 (35.7)	0 (0.0)	0 (0.0)
Morphologic leukaemia-free state	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Partial remission	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Stable disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Progressive disease	2 (3.4)	1 (5.0)	1 (2.6)	0 (0.0)	1 (4.3)	1 (14.3)
Uncertain response	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Days between end of consolidation treatment end response evaluation						
n	**59**	**21**	**38**	**27**	**23**	**9**
Mean (SD)	48.4 (39.2)	47.6 (43.8)	48.8 (37.0)	58.3 (27.4)	34.9 (33.5)	53.0 (68.7)
Median (IQR)	38.0 (27.0-56.0)	32.0 (23.0-62.0)	43.0 (31.0-54.0)	49.0 (38.0-72.0)	30.0 (16.0-40.0)	31.0 (23.0-38.0)

Following 1L consolidation therapy, most patients were under observation / active monitoring (37.7%, n=23) or received a HSCT (n=20, 32.8%) (Table 15).

Table 15. CRF Data: Next steps after 1L consolidation

Variable	Total CRF Sample	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
Treatment next steps following consolidation, n (%)						
n	61	23	38	28	23	10
Treatment for relapsed/refractory disease	9 (14.8)	3 (13.0)	6 (15.8)	7 (25.0)	2 (8.7)	0 (0.0)
Maintenance therapy	2 (3.3)	1 (4.3)	1 (2.6)	0 (0.0)	0 0.0)	2 (20.0)
Observation / active monitoring / watchful waiting	23 (37.7)	9 (39.1)	14 (36.8)	12 (42.9)	6 (26.1)	5 (50.0)
Best supportive care	1 (1.6)	1 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)
Undecided as treatment is ongoing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Treatment as part of clinical trial	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Patient decided not to continue treatment	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	6 (9.8)	4 (17.4)	2 (5.3)	2 (7.1)	3 (13.0)	1 (10.0)
Patient received a stem cell transplant	20 (32.8)	5 (21.7)	15 (39.5)	7 (25.0)	12 (52.2)	1 (10.0)

In the whole cohort, 78% of patients achieved continued complete remission (defined as CR, CRi or CRp achieved at each line and/or setting of therapy (including HSCT), or CR at induction, where induction therapy was the only treatment received (Table 16). Overall, CR (including CRi and CRp) was achieved at 1L (including HSCT), by 92.5% of patients.

Table 16. CRF Data: Continued complete remission and best response at 1L

Variable	Total CRF Sample	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
Continued complete remission status (CR/CRi/CRp), n(%)						
n	82	30	52	31	30	21

Variable	Total CRF Sample	Risk status		Country		
		Favourable	Intermediate	Austria	Belgium	Germany
Continued complete remission	57 (69.5)	19 (63.3)	38 (73.1)	25 (80.6)	21 (70.0)	11 (52.4)
CR from induction, no further treatment	7 (8.5)	2 (6.7)	5 (9.6)	1 (3.2)	4 (13.3)	2 (9.5)
No continued complete remission	18 (22.0)	9 (30.0)	9 (17.3)	5 (16.1)	5 (16.7)	8 (38.1)
Missing, n	7	3	4	0	4	3
Best response achieved at 1L, n(%)						
n	**80**	**28**	**52**	**31**	**30**	19
Complete remission	74 (92.5)	27 (96.4)	47 (90.4)	29 (93.5)	28 (93.3)	17 (89.5)
Not in CR	5 (6.2)	1 (3.6)	4 (7.7)	2 (6.5)	2 (6.7)	1 (5.3)
Relapsed disease	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Progressive disease	1 (1.2)	0 (0.0)	1 (1.9)	0 (0.0)	0 (0.0)	1 (5.3)
Missing, n	9	5	4	0	4	5

Event-free survival (EFS) (as defined in Section 9.4.2.2) in CRF patients was evaluated (Figure 2). The median was 1610 days (4.4 years) from induction to first event. The median EFS for favourable risk patients was 1610 days (4.4 years), and the median EFS for intermediate risk patients was 1771 days (4.9 years) [Figure 3]. The EFS analyses where HSCT was considered as a censoring event, are captured in Figure 4 and Figure 5.

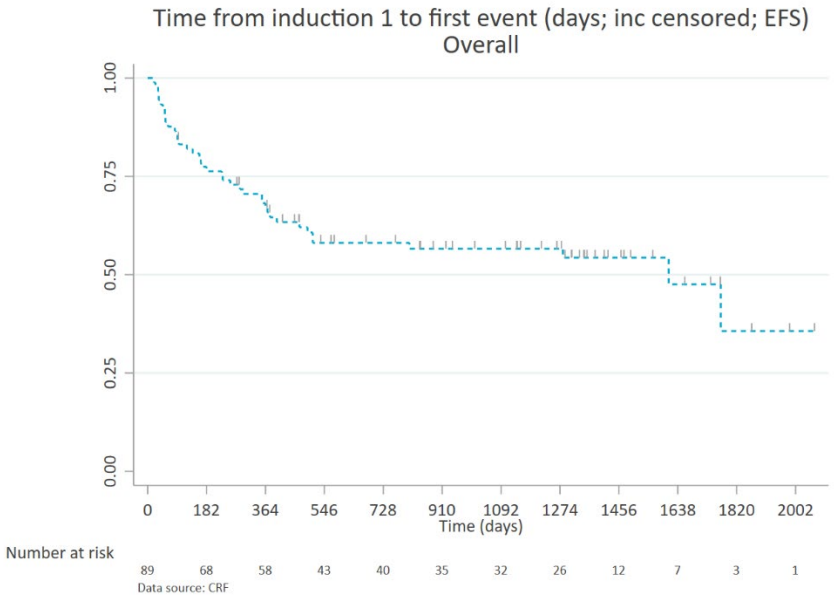


Figure 2. CRF data: Time from induction 1 to first event (days; inc censored) for all CRF sample

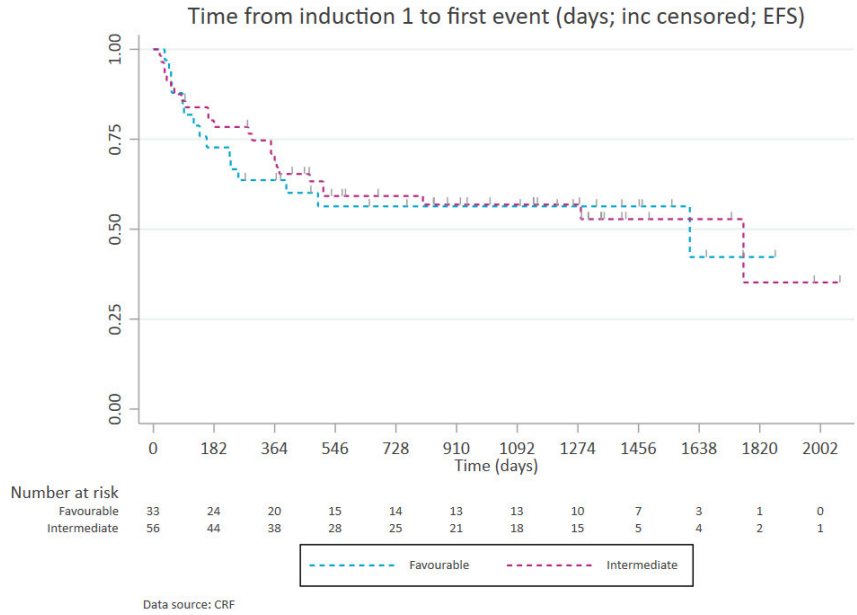


Figure 3. CRF data: Time from induction 1 to first event (days; inc censored), stratified by risk status

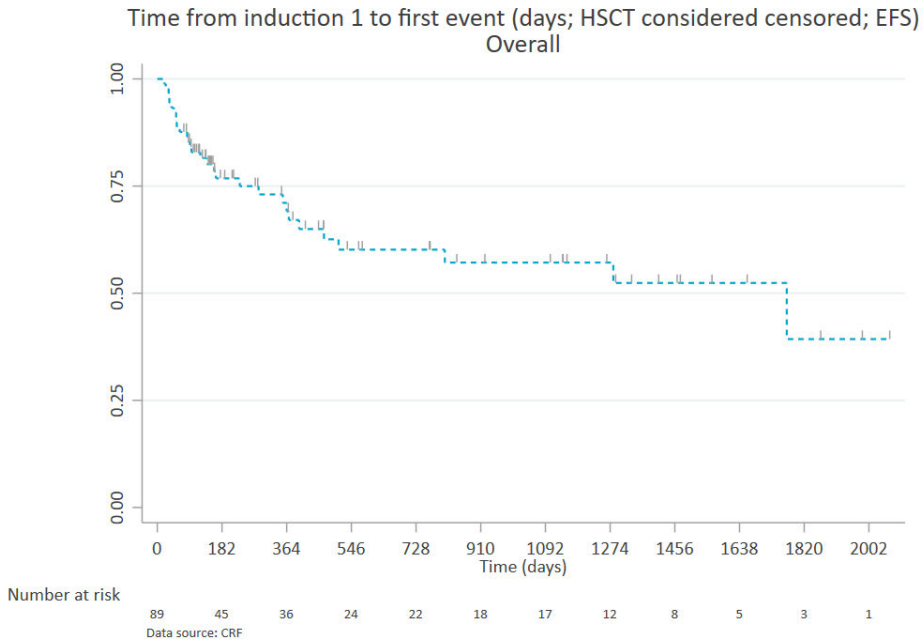


Figure 4. CRF data: Time from induction 1 to first event (days; with HSCT as a censoring event) for all CRF sample

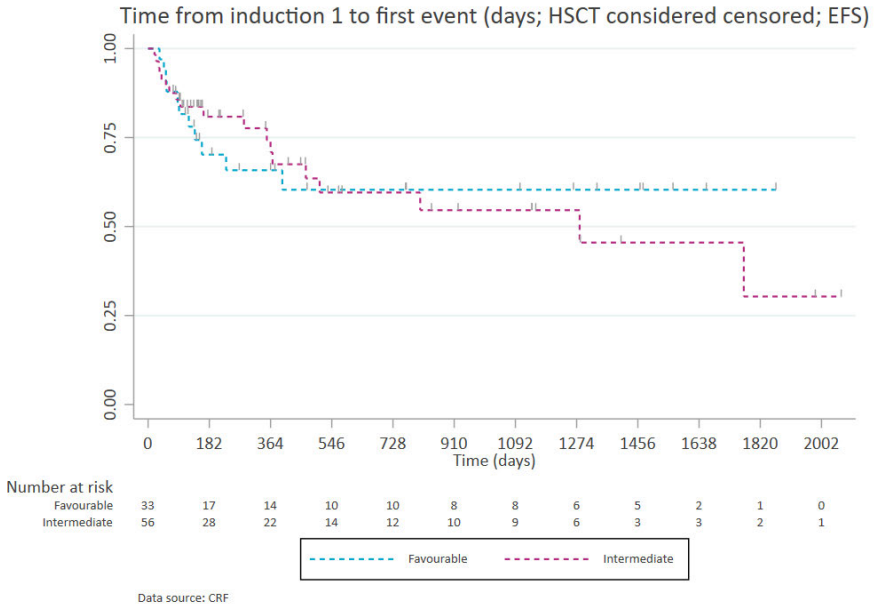


Figure 5. CRF data: Time from induction 1 to first event (days; with HSCT as a censoring event), stratified by risk status

Relapse-free survival (RFS) in CRF patients was evaluated (Figure 6). The median was 1732 days (4.7 years) from first remission to relapse / death. The RFS analyses where HSCT was considered as a censoring event, is captured in Figure 7.

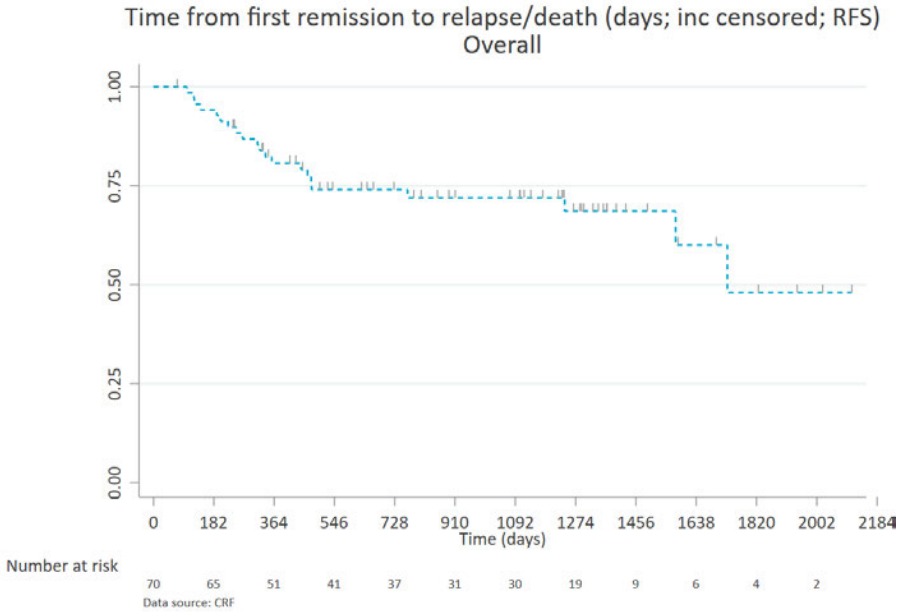


Figure 6. Time from first remission to relapse/death (days; inc censored) – CRF data

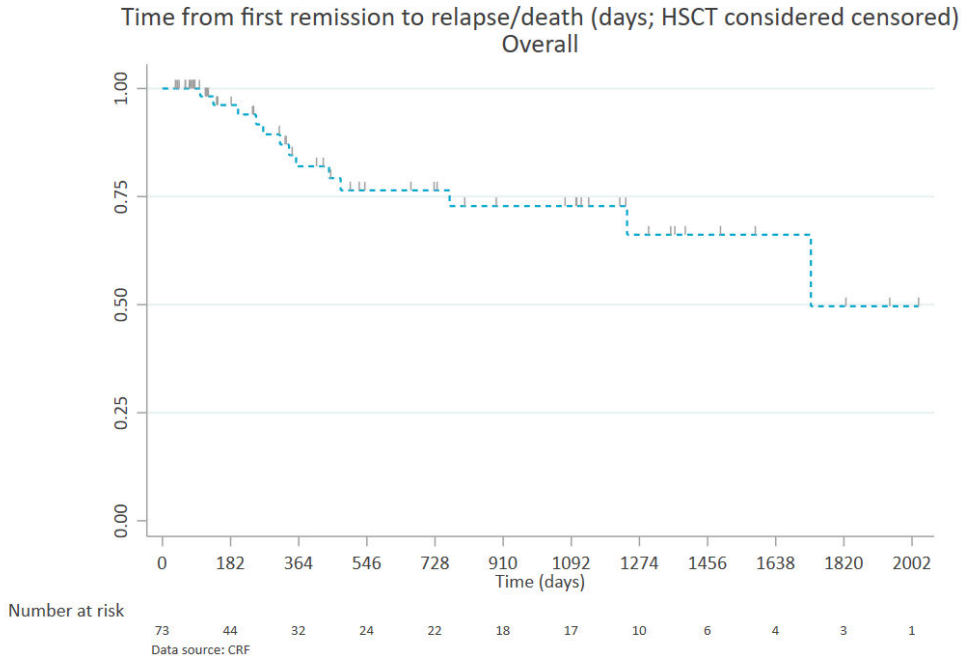


Figure 7. Time from first remission to relapse/death (days; with HSCT as a censoring event) – CRF data

Out of the total number of patients captured in the CRF, n=26 (29.2%) patients died. Progressive disease along with “other” were reported as the most common causes of death (Table 17). Of the patients that died, 3 patients (3.4%) died within 60 days of induction treatment (Table 18).

Table 17. CRF Data: Cause of death

		Risk status		Country		
Variable	**CRF Sample (n=26)**	**Favourable (n=10)**	**Intermediate (n=16)**	**Austria (n=2)**	**Belgium (n=19)**	**Germany (n=5)**
Cause of death, n (%)						
Early death (<1 week after induction/re-induction including relapse)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death in hypoplasia ('1 week after induction/re-induction including relapse)	4 (15.4)	2 (20.0)	2 (12.5)	0 (0.0)	1 (5.3)	3 (60.0)
Progressive disease after refractory disease	9 (34.6)	3 (30.0)	6 (37.5)	0 (0.0)	7 (36.8)	2 (40.0)
Treatment-related death in complete remission	3 (11.5)	2 (20.0)	1 (6.2)	0 (0.0)	3 (15.8)	0 (0.0)
Death of second cause	3 (11.5)	1 (10.0)	2 (12.5)	0 (0.0)	3 (15.8)	0 (0.0)
Uncertain cause of death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	7 (26.9)	2 (20.0)	5 (31.2)	2 (100.0)	5 (26.3)	0 (0.0)

Table 18. Number of patient deaths 30 / 60 / 1095 days following initiation of 1L treatment

		Risk status		Country		
Variable	**CRF Sample**	**Favourable**	**Intermediate**	**Austria**	**Belgium**	**Germany**
Death <= 30 days following initiation of line 1 treatment, n (%)						
n	**89**	**33**	**56**	**31**	**34**	**24**
Did not die within 30 days	87 (97.8)	33 (100.0)	54 (96.4)	31 (100.0)	32 (94.1)	24 (100.0)

Variable	CRF Sample	Risk status: Favourable	Risk status: Intermediate	Country: Austria	Country: Belgium	Country: Germany
Died within 30 days	2 (2.2)	0 (0.0)	2 (3.6)	0 (0.0)	2 (5.9)	0 (0.0)
Death <= 60 days following initiation of line 1 treatment, n (%)						
n	**89**	**33**	**56**	**31**	**34**	**24**
Did not die within 60 days	86 (96.6)	33 (100.0)	53 (94.6)	31 (100.0)	31 (91.2)	24 (100.0)
Died within 60 days	3 (3.4)	0 (0.0)	3 (5.4)	0 (0.0)	3 (8.8)	0 (0.0)
Death <= 1095 days (3 years) following initiation of line 1 treatment, n (%) *Of those who died, or with at least 1095 day follow-up*						
n	**63**	**26**	**37**	**14**	**29**	**20**
Did not die within 1095 days	41 (64.1)	18 (66.7)	23 (62.2)	13 (92.9)	12 (41.4)	15 (75.0)
Died within 1095 days	23 (35.9)	9 (33.3)	14 (37.8)	1 (7.1)	17 (58.6)	5 (25.0)

10.4.1.4. Exploratory Objective: MRD Status

MRD status post-induction therapy was recorded for n=49 patients (Table 19). Of the n=49 patients with a recorded MRD status, 53.1% (n=26) of the sample were recorded as negative. MRD status post-stem cell transplant was recorded for n=17 patients, 58.8% (n=10) of these were recorded as negative. Real-time polymerase chain reaction was the most common method to test for MRD following either induction therapy or HSCT (Table 20).

Table 19. CRF Sample: MRD status following induction or HSCT

Variable	Total	Risk status: Favourable	Risk status: Intermediate	Country: Austria	Country: Belgium	Country: Germany
MRD status following induction treatment, n (%)						
n	**49**	**23**	**26**	**15**	**21**	**13**
MRD+	23 (46.9)	14 (60.9)	9 (34.6)	12 (80.0)	10 (47.6)	1 (7.7)
MRD-	26 (53.1)	9 (39.1)	17 (65.4)	3 (20.0)	11 (52.4)	12 (92.3)
MRD status following stem cell transplant, n (%)						
n	**17**	**9**	**8**	**2**	**6**	**9**

MRD+	7 (41.2)	5 (55.6)	2 (25.5)	1 (50.0)	2 (33.3)	4 (44.4)
MRD-	10 (58.8)	4 (44.4)	6 (75.0)	1 (50.0)	4 (66.7)	5 (55.6)

Table 20. CRF Sample: Method used to test MRD following induction or HSCT

		Risk status		Country		
Variable	**Total sample**	**Favourable**	**Intermediate**	**Austria**	**Belgium**	**Germany**
Method to test MRD following induction treatment, n (%)						
n	**47**	**22**	**25**	**15**	**19**	**13**
Flow cytometry assays	3 (6.4)	1 (4.5)	2 (8.0)	0 (0.0)	3 (15.8)	0 (0.0)
Real time quantitative polymerase chain reaction	43 (91.4)	20 (90.1)	23 (92.0)	15 (100.0)	15 (78.9)	13 (100)
Next generation sequencing	1 (2.1)	1 (4.5)	0 (0.0)	0 (0.0)	1 (5.3)	0 (0.0)
Missing, n	2	1	1	0	2	0
Method to test MRD following stem cell transplant, n (%)						
n	**17**	**9**	**8**	**2**	**6**	**9**
Flow cytometry assays	1 (5.9)	0 (0.0)	1 (12.5)	0 (0.0)	1 (16.7)	0 (0.0)
Real time quantitative polymerase chain reaction	16 (94.1)	9 (100.0)	7 (87.5)	2 (100.0)	5 (83.3)	9 (100.0)
Next generation sequencing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

10.4.2. Results – Registry Sample (AGMT)

10.4.2.1. Primary Objective: Patient Demographics and Clinical Characteristics of Patients

Of the patients in the AGMT sample, 18 patients (69.2%) were female and 8 (30.8%) were male. Patient BMI at baseline was a median (IQR) 23.1 (20.0-27.4) [Table 21].

All patients had a physician-confirmed diagnosis of AML, with a median (IQR) age at diagnosis of 59.5 (35.0-66.0) [Table 21]. According to the ELN 2017 risk stratification, 57.7% (n=15) of the sample was classified as favourable and 42.3% (n=11) was classified as intermediate (Table 22). At index, the median (IQR) bone marrow blast percentage was 75 (45.0-90.0) and the peripheral blood blast percentage was 36.2 (4.0-73.0). CD33+ status at index was recorded in the dataset for 17 patients. Of these patients, their CD33+ status was positive for 41.2% (n=7) of patients. NMP1 and DNMT3A were the most common genetic alterations detected at index.

Median (IQR) follow up duration (days) was 339.5 (180.0, 574.0).

Table 21. AGMT Data: Patient Demographics

		Risk status	
Variable	**Total AGMT Sample**	**Favourable**	**Intermediate**
	(n=26)	**(n=15)**	**(n=11)**
Age at diagnosis			
Mean (SD)	51.8 (17.8)	49.0 (17.1)	55.6 (18.8)
Median (IQR)	59.5 (35.0-66.0)	47.0 (34.0-66.0)	63.0 (35.0- 73.0)
Patient sex, n (%)			
Female	18 (69.2)	10 (66.7)	8 (72.7)
Male	8 (30.8)	5 (33.3)	3 (27.3)
BMI at baseline, n (%)			
Underweight (below 18.5 kg/m^2)	2 (7.7)	1 (6.7)	1 (9.1)
Normal weight (18.5-<25.0 kg/m^2)	13 (50.0)	8 (53.3)	5 (45.5)
Overweight (25.0-<30.0 kg/m^2)	8 (30.8)	4 (26.7)	4 (36.4)
Obese (30.0->35.0 kg/m^2)	3 (11.5)	2 (13.3)	1 (9.1)
Morbidly obese (≥35 kg/m^2)	0 (0.0)	0 (0.0)	0 (0.0)

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Mean (SD)	23.8 (4.4)	23.8 (4.5)	23.8 (4.6)
Median (IQR)	23.1 (20.0-27.4)	23.5 (20.0-27.4)	22.8 (19.9-27.5)

Table 22. AGMT Data: Clinical Characteristics

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Cytogenetic risk at index (ELN 2017)			
Favourable, n (%)	15 (57.7)	15 (100.0)	0 (0.0)
Intermediate, n (%)	11 (42.3)	0 (0.0)	11 (100.0)
CD33+ status at index			
Negative, n (%)	10 (58.8)	5 (45.5)	5 (83.3)
Positive, n (%)	7 (41.2)	6 (54.5)	1 (16.7)
Missing, n	9	4	5
Bone marrow blast percentage at index			
Mean (SD)	66.8 (27.9)	67.7 (24.6)	65.6 (33.1)
Median (IQR)	75 (45.0 - 90.0)	75.0 (50.0-90.0)	85.0 (35.0-90.0)
Peripheral blood blast percentage at index			
Mean (SD)	40.5 (35.0)	45.0 (34.4)	34.2 (36.6)
Median (IQR)	36.2 (4.0 - 73.0)	43.8 (21.0-81.0)	20.0 (0.0-70.0)
Missing, n	2	1	1
Haemoglobin count at index (g/dL)			
Mean (SD)	9.4 (1.5)	9.3 (1.6)	9.6 (1.5)
Median (IQR)	9.2 (8.2 - 10.5)	9.0 (8.1-10.5)	9.2 (8.3-10.6)

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Missing, n	1	1	0
Thrombocytes count at index (x10^9/L)			
Mean (SD)	90.6 (100.0)	93.0 (93.0)	87.5 (112.9)
Median (IQR)	44 (34.0 - 105.0)	41.0 (34.0-128.0)	47.0 (34.0-69.0)
Missing, n	1	1	0
Leukocytes count at index (x10^9/L)			
Mean (SD)	17 (29.4)	9.3 (6.9)	26.8 (42.7)
Median (IQR)	6.4 (2.1 - 18.1)	7.8 (5.2-14.8)	2.4 (1.4-51.6)
Missing, n	1	1	0
Lactate dehydrogenase at index			
Mean (SD)	441.5 (579.2)	370.9 (250.3)	540.5 (864.9)
Median (IQR)	269.0 (215.5 - 405.5)	268.5 (213.0-490.0)	271.0 (218.0-383.0)
Missing, n	2	1	1

10.4.2.2. Primary Objective: Real-World GO Treatment Patterns

The time from diagnosis of AML to initiation of the index regimen (1L treatment with GO) was a median (IQR) of 6.0 (3.0-8.0) days. 80.8% (n=21) of patients received 1L treatment only, with a small proportion of patients later received 2L and 3L treatment (15.4%, n=4 receiving 2L; 3.8%, n=1 receiving 3L). The most common drugs administered in 1L induction were GO (100%, n=26), and the 3+ 7 treatment regimen (92.3%, n=24) (Table 23).

Table 23. AGMT Data: 1L Induction Treatment Characteristics

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Time from diagnosis to index (days)			
Mean (SD)	6.8 (5.2)	6.3 (6.0)	7.5 (4.2)

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Median (IQR)	6.0 (3.0-8.0)	5 (3.0-7.0)	8.0 (5.0-9.0)
Total number of lines, n (%)			
1	21 (80.8)	14 (93.3)	7 (63.6)
2	4 (15.4)	1 (6.7)	3 (27.3)
3	1 (3.8)	0 (0.0)	1 (9.1)
1L induction treatment received, n (%)			
Gemtuzumab ozogamicin	26 (100.0)	15 (100.0)	11 (100.0)
3+7 (cytarabine and anthracycline)	24 (92.3)	13 (86.7)	11 (100.0)
Midostaurin	3 (11.5)	1 (6.7)	2 (18.2)
2+5 (daunorubicin and cytarabine)	1 (3.8)	1 (6.7)	0 (0.0)
Azacitidine	1 (3.8)	0 (0.0)	1 (9.1)
CloCyt	1 (3.8)	1 (6.7)	0 (0.0)
FLAG	1 (3.8)	1 (6.7)	0 (0.0)
FLAG-IDA	1 (3.8)	0 (0.0)	1 (9.1)
HAM	1 (3.8)	1 (6.7)	0 (0.0)
Ivosidenib	1 (3.8)	0 (0.0)	1 (9.1)
Number of treatment cycles during 1L induction			
Mean (SD)	1.2 (0.6)	1.2 (0.6)	1.3 (0.6)
Median (IQR)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Cumulative GO dose during 1L induction (mg)			
Mean (SD)	11.1 (4.6)	11.0 (4.7)	11.1 (4.8)
Median (IQR)	14.1 (5.0-15.0)	13.8 (5.0-15.0)	15.0 (5.0-15.0)
Vials of GO during line 1 induction (assuming 5 mg vial)			
Mean (SD)	2.3 (0.9)	2.3 (1.0)	2.3 (0.9)

		Risk status	
Variable	**Total AGMT Sample (n=26)**	**Favourable (n=15)**	**Intermediate (n=11)**
Median (IQR)	3.0 (1.0-3.0)	3.0 (1.0-3.0)	3.0 (1.0-3.0)

Of the n=20 patients that received 1L consolidation therapy, the most commonly administered treatments were HiDAC (65.0%, n=13) and GO (50.0, n=10). Patients received a median (IQR) of 1 (1.0-1.0) treatment cycle during 1L induction (Table 23) and 3 (1.0-4.0) for 1L consolidation (Table 24). The median (IQR) cumulative GO dose during 1L induction was 14.1 mg (5.0 – 15.0), and 9.5 mg (4.8-15.0) during consolidation therapy (n=9 patients). 30.8% (n=8) patients received an allogeneic HSCT following 1L induction. Most patients with a favourable risk status did not receive a HSCT (80.0%, n=12 receiving 0 HSCTs) (Table 24).

Table 24. AGMT Data: 1L Consolidation and HSCT Treatment Characteristics

		Risk status	
Variable	**Total AGMT Sample (n=26)**	**Favourable (n=15)**	**Intermediate (n=11)**
1L consolidation treatment received, n (%)			
HiDAC	13 (65.0)	9 (75.0)	4 (50.0)
Gemtuzumab ozogamicin	10 (50.0)	7 (58.3)	3 (37.5)
FLAG	6 (30.0)	3 (25.0)	3 (37.5)
Midostaurin	4 (20.0)	1 (8.3)	3 (37.5)
MiDAC (>60 years)	3 (15.0)	2 (16.7)	1 (12.5)
3+7	2 (10.0)	0 (0.0)	2 (25.0)
Missing, n	6	3	3
Number of treatment cycles during 1L consolidation			
Mean (SD)	2.8 (1.3)	3.3 (1.2)	2.0 (1.2)
Median (IQR)	3 (1.0-4.0)	4.0 (3.0-4.0)	1.5 (1.0-3.0)
Missing, n	6	3	3
Cumulative GO dose during 1L consolidation (mg)			
n	**(n=9)**	**(n=7)**	**(n=2)**

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Mean (SD)	10.9 (5.6)	11.2 (5.7)	9.9 (7.2)
Median (IQR)	9.5 (4.8-15.0)	9.5 (4.7-15.0)	9.9 (4.8, 15.0)
Vials of GO during line 1 consolidation (assuming 5 mg vial)			
n	**(n=9)**	**(n=7)**	**(n=2)**
Mean (SD)	2.2 (1.1)	2.3 (1.1)	2.0 (1.4)
Median (IQR)	2 (1.0-3.0)	2 (1.0-3.0)	2 (1.0-3.0)
Total number of allogeneic HSCTs received			
0	18 (69.2)	12 (80.0)	6 (54.5)
1	7 (26.9)	2 (13.3)	5 (45.5)
2	1 (3.8)	1 (6.7)	0 (0.0)

10.4.2.3. Secondary Objective: First-Line Treatment Effectiveness Outcomes

The most reported response to 1L induction for AGMT patients was morphologic leukaemia-free state (34.6%), followed by CR (30.8%). The main reason for ending 1L induction treatment was CR / start of consolidation or watch and wait (76.0%). 12.0% of patients died following 1L induction. The majority of patients in the AGMT sample received consolidation treatment after 1L induction therapy (86.4%, n=19) (Table 25).

Table 25. AGMT Data: 1L induction treatment effectiveness outcomes

Variable	Total AGMT Sample (n=26)	Risk status: Favourable (n=15)	Risk status: Intermediate (n=11)
Best response to line 1 induction, n (%)			
Morphologic leukaemia-free state	9 (34.6)	8 (53.3)	1 (9.1)
Complete remission	8 (30.8)	4 (26.7)	4 (36.4)
Complete remission with incomplete platelet counts (CRp)	4 (15.4)	1 (6.7)	3 (27.3)

Variable	Total AGMT Sample (n=26)	Risk status	
		Favourable (n=15)	Intermediate (n=11)
Not evaluated	5 (19.2)	2 (13.3)	3 (27.3)
Reason for end of line 1 induction treatment, n (%)			
CR after induction / start of consolidation or watch and wait	19 (76.0)	11 (78.6)	8 (72.7)
Death	3 (12.0)	2 (14.3)	1 (9.1)
No CR after induction / start of salvage treatment	1 (4.0)	0 (0.0)	1 (9.1)
Bridging to allogeneic HSCT	1 (4.0)	1 (7.1)	0 (0.0)
Other patient reason	1 (4.0)	0 (0.0)	1 (9.1)
Missing, n	1	1	0
Treatment events following line 1 induction, n (%)			
BSC measures only	0 (0.0)	0 (0.0)	0 (0.0)
Bridging to allo-HSCT	1 (4.5)	1 (8.3)	0 (0.0)
Conditioning for allo-HSCT	1 (4.5)	0 (0.0)	1 (10.0)
Consolidation (post-remission therapy)	19 (86.4)	11 (91.7)	8 (80.0)
Cytoreduction – palliation	0 (0.0)	0 (0.0)	0 (0.0)
Maintenance	1 (4.5)	0 (0.0)	1 (10.0)
Remission induction - intensive	0 (0.0)	0 (0.0)	0 (0.0)
Remission induction - non intensive	0 (0.0)	0 (0.0)	0 (0.0)
Missing, n	4	3	1

Best reported response to 1L consolidation for AGMT patients was CR (n=10, 50.0%), followed by CRp (n=5, 25.0%). The main reason for ending 1L consolidation treatment was end of consolidation / start of maintenance (n=14, 73.7%). 46.2% (n=6) of AGMT patients received best supportive care following consolidation therapy (Table 26).

Table 26. AGMT Data: 1L consolidation treatment effectiveness outcomes

Variable	Total AGMT Sample (n=20)	Risk status: Favourable (n=12)	Risk status: Intermediate (n=9)
Best response to line 1 consolidation, n (%)			
Complete remission	10 (50.0)	8 (66.7)	2 (25.0)
Complete remission with incomplete haematologic recovery (CRi)	1 (5.0)	0 (0.0)	1 (12.5)
Complete remission with incomplete platelet counts (CRp)	5 (25.0)	2 (16.7)	3 (37.5)
Morphologic leukaemia-free state	1 (5.0)	1 (8.3)	0 (0.0)
Not evaluated	3 (15.0)	1 (8.3)	2 (25.0)
Reason for end of line 1 consolidation treatment, n (%)			
CR after induction / start of consolidation or watch and wait	1 (5.3)	1 (9.1)	0 (0.0)
Disease relapse or disease progression after induction / start of salvage treatment	1 (5.3)	0 (0.0)	1 (12.5)
End of consolidation / start of maintenance	14 (73.7)	9 (81.8)	5 (62.5)
Therapy optimization	1 (5.3)	1 (9.1)	0 (0.0)
(planned) Allogeneic HSCT	1 (5.3)	0 (0.0)	1 (12.5)
According to study protocol	1 (5.3)	0 (0.0)	1 (12.5)
Missing, n	1	1	0
Next steps following line 1 consolidation, n (%)			
BSC measures only	6 (46.2)	4 (57.1)	2 (33.3)
Bridging to allo-HSCT	1 (7.7)	1 (14.3)	0 (0.0)
Conditioning for allo-HSCT	1 (7.7)	0 (0.0)	1 (16.7)
Consolidation (post-remission therapy)	0 (0.0)	0 (0.0)	0 (0.0)
Cytoreduction – palliation	0 (0.0)	0 (0.0)	0 (0.0)
Maintenance	3 (23.1)	1 (14.3)	2 (33.3)

Variable	Total AGMT Sample (n=20)	Risk status	
		Favourable (n=12)	Intermediate (n=9)
Remission induction - intensive	1 (7.7)	1 (14.3)	0 (0.0)
Remission induction - non intensive	1 (7.7)	0 (0.0)	1 (16.7)
Missing, n	6	3	3

In the whole cohort, 52.4% of patients achieved continued complete remission (defined as CR, CRi or CRp achieved at each line and/or setting of therapy (excluding HSCT as response data not available), or CR at induction, where induction therapy was the only treatment received (Table 27). Overall, where known, CR (including CRp) or morphologic leukemia-free state was achieved at 1L by all patients, although this information was unknown for 38.5% of patients.

Table 27. AGMT Data: Continued complete remission and best response at 1L

Variable	Total AGMT Sample (n=26)	Risk status	
		Favourable (n=15)	Intermediate (n=11)
Continued complete remission status (CR/CRi/CRp), n(%)			
n	**21**	**13**	**8**
Continued complete remission	10 (47.5)	5 (38.5)	5 (62.5)
CR from induction, no further treatment	1 (4.8)	0 (0.0)	1 (12.5)
No continued complete remission	10 (47.5)	8 (61.5)	2 (25.0)
Missing, n	5	2	3
Best response achieved at 1L, n(%)			
n	**16**	**10**	**6**
Complete remission	14 (87.5)	8 (80.0)	6 (100.0)
Morphologic leukaemia-free state	2 (12.5)	2 (20.0)	0 (0.0)
Missing, n	10	5	5

For event free survival in patients within the AGMT data, it was not achieved for the overall cohort, but the median value for the intermediate risk status group was 295 days (Figure 8).

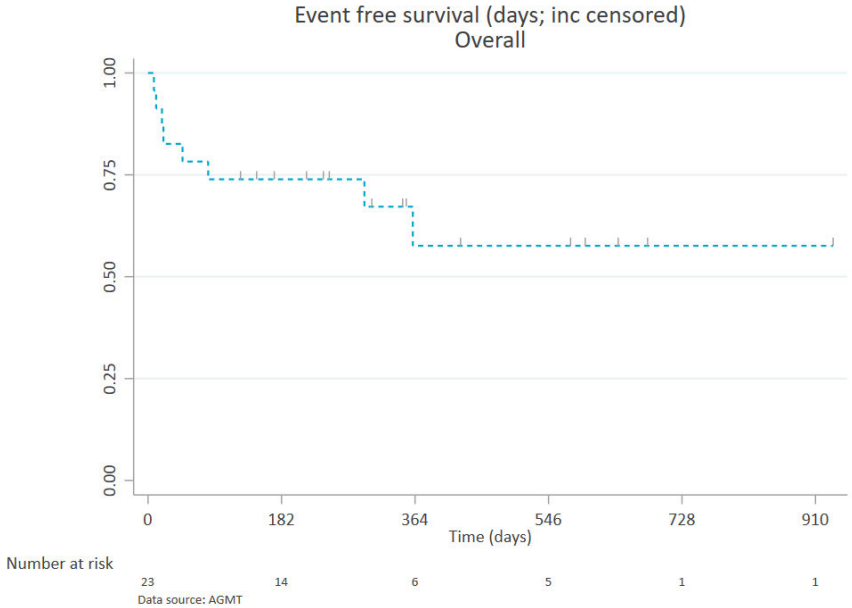


Figure 8. Event free survival (days; inc censored) - AGMT data

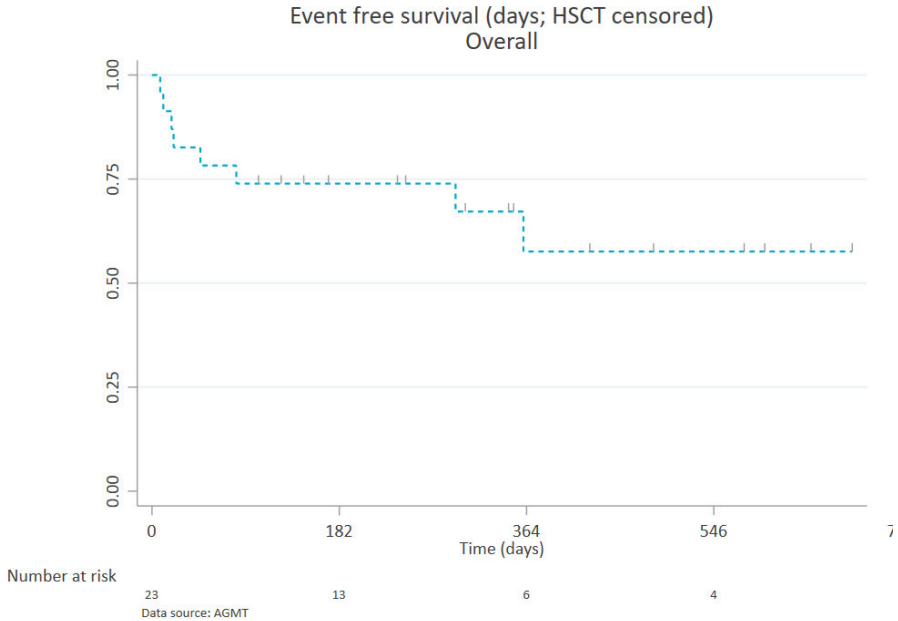


Figure 9. Event free survival (days; with HSCT as a censoring event) - AGMT data

For relapse-free survival in patients within the AGMT data, the median value was 736 days (Figure 10).

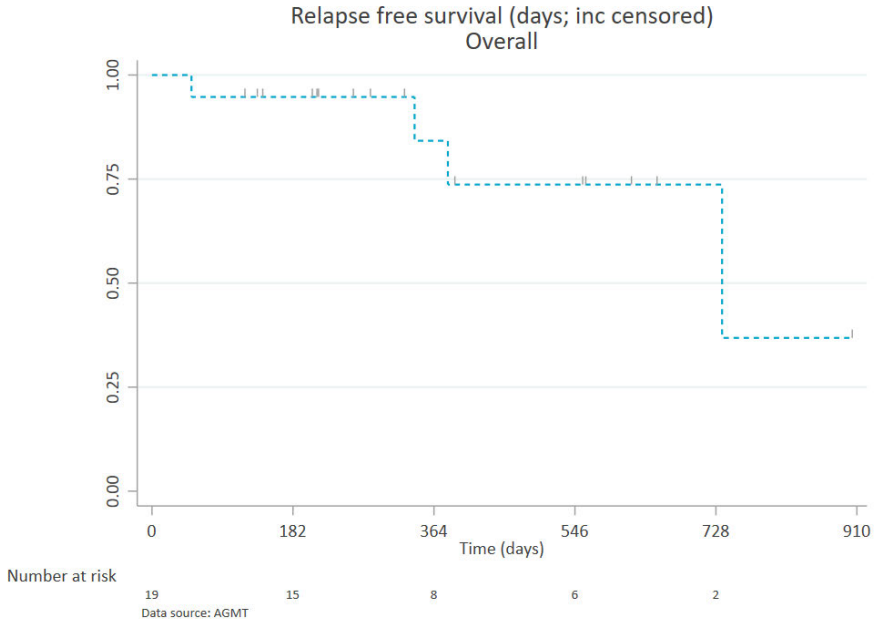


Figure 10. Relapse-free survival (days; inc censored) - AGMT data

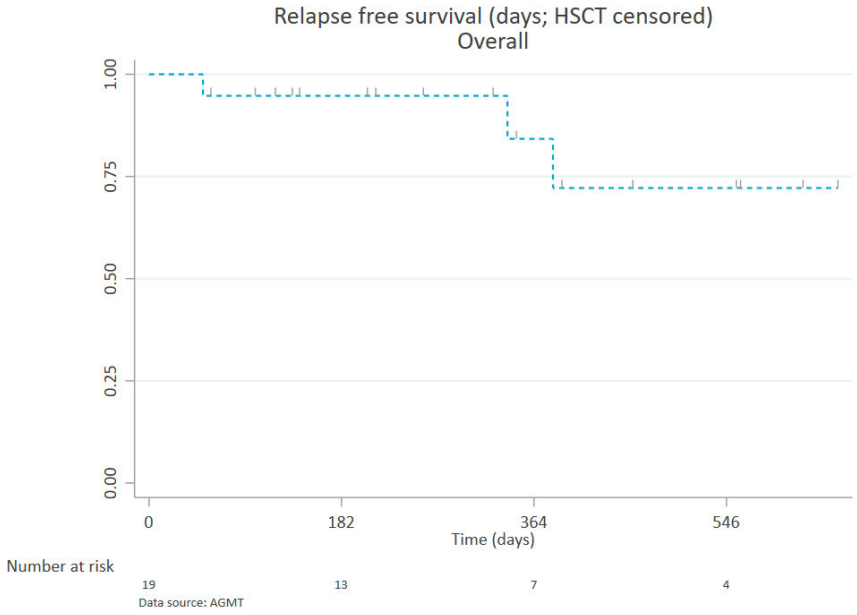


Figure 11. Relapse-free survival (days; with HSCT as a censoring event) - AGMT data

Of the n=6 patients that died in the AGMT sample, 33.3% (n=2) patients died within 30 days of 1L treatment initiartion; 50.0% (n=3) died due to disease progression (Table 28).

Table 28. AGMT Data: Cause of death

Variable	Total	Risk status: Favourable	Risk status: Intermediate
Reason for death, n (%)			
n	**6**	**3**	**3**
Disease progression	3 (50.0)	1 (33.3)	2 (66.7)
Infectious complications	1 (16.7)	1 (33.3)	0 (0.0)
Other	2 (33.3)	1 33.3)	1 (33.3)

10.5. Other analyses

All study variables collected are presented in the separate document '*Mylotarg in AML – v1.0*', containing the CRF data and AGMT data presented separately due to the differences in data collection methods. The results are presented by country (CRF data) and ELN risk group (CRF and AGMT data).

10.6. Adverse events / adverse reactions

For the CRF data, this study protocol required human review of patient-level unstructured data relating to patient medical records. The reviewer of the medical records was required to report AEs with explicit attribution to GO. The AEs of interest in this study relate to veno-occlusive disease (VOD; Table 29) and graft-versus-host disease (GvHD; Table 30) and data was collected in the EDC. One AE was reported to Pfizer PV relating to VOD with explicit attribution to GO administration. All other AEs were not attributed to GO administration; this was confirmed by the site PIs.

Table 29. CRF Data: VOD collected in the CRF

Variable	
Diagnosis of VOD, n (%)[1]	
n	**89**
VOD following GO treatment	4 (4.5)
VOD following HSCT	2 (5.3)
Severity of VOD following GO treatment, n (%)	

n	3
Grade 1 - Mild	0 (0.0)
Grade 2 - Moderate	1 (33.3)
Grade 3 - Severe	1 (33.3)
Grade 4 - Very severe	0 (0.0)
Grade 5 - Death	1 (33.3)

Severity of VOD following HSCT, n (%)

n	2
Grade 1 - Mild	0 (0.0)
Grade 2 - Moderate	0 (0.0)
Grade 3 - Severe	1 (50.0)
Grade 4 - Very severe	0 (0.0)
Grade 5 - Death	1 (50.0)

[1]One patient was recorded in the CRF as having VOD following induction therapy with GO and following HSCT.

Table 30. CRF Data: GvHD collected in the CRF

Variable	Total
Diagnosis of GvHD following stem cell transplant, n (%)	
n	**38**
Yes	23 (60.5)
No	15 (39.5)

Type of GvHD, n (%)

n	23
Acute GvHD	18 (78.3)
Chronic GvHD	9 (39.1)

From the AGMT sample, acute GvHD was recorded for n=2 patients (Table 31).

Table 31. AGMT Data: GvHD in the AGMT sample

Variable	Total
Presence of Graft vs Host disease (GvHD), n (%)	
n	**4**
No GvHD	2 (50.0)
Acute GvHD	2 (50.0)

11. DISCUSSION

11.1. Key results

For decades, patients with AML, and who are able to receive intensive therapy, have been treated using standard chemotherapies such as daunorubicin and cytarabine. The addition of GO to these regimens has demonstrated survival benefits across multiple clinical trials, including AML15, AML16, and ALFA-0701 (10, 16, 17).

In the AML15 trial, a single dose of GO (3 mg/m²) during the first and third cycles of induction therapy improved survival outcomes, with overall survival (OS) increasing to 79% compared to 51% without GO for favourable cytogenetics. Similarly, in the ALFA-0701 trial, the addition of GO (3 mg/m² on days 1, 4, and 7) to the 3+7 chemotherapy regimen significantly improved event-free survival (EFS) (40.8% vs 17.1% at two years), relapse-free survival (RFS) (50.3% vs 22.7%), and OS (53.2% vs 41.9%). The greatest benefits were observed in favourable and intermediate-risk cytogenetic groups (10).

For GO-First, data were collected from three European countries on 115 AML patients from two different data sources (AGMT registry data [26 patients] and site-based CRF data [89 patients]). All patients received GO during 1L induction as per the study inclusion criteria. In both data sources, nearly all patients received three doses of GO during 1L induction, with a median dose of 5 mg per treatment and a total median dose of 15 mg and 14.1 mg of GO for the CRF data and AGMT data, respectively. In patients that received 1L consolidation therapy in the CRF data, 78.7% (n=48) received at least one dose of GO. These results indicate that the dosing regimen in real-world clinical practice reflects the dosing of GO previously used in the ALFA-0701 trial and the current marketing authorisation for GO (10, 12). Where daunorubicin or cytarabine was administered in 1L induction, the most common dose given was 60 mg/m^2 daunorubicin and 200 mg/m^2 cytarabine, reflecting the chemotherapy dosing in the ALFA-0701 trial (10).

The results of this study indicate that GO may be effective in both favourable and intermediate-risk AML, with median EFS of 1610 days (52.9 months) and median RFS of 1732 days (56.9 months) for the overall sample from the CRF data. The EFS for the AGMT data was reported to be much lower with median EFS of 295 days (9.7 months) and median RFS of 736 days

(24.2 months). For EFS and RFS definitions, MLFS was considered as a remission event, although no patients in the CRF sample achieved this. In the ALFA-0701 trial, the EFS was reported to be 17.3 months in the GO arm vs 9.5 months in the chemotherapy alone arm. Complete remission rates in the CRF data following induction treatment were similar in the ALFA-0701 trial (CRF, 70.7% CR; ALFA-0701, 70.4%). The CR (including CRp) combined with MLFS proportion after 1L induction in the AGMT data set was 53.8%, which explains the lower EFS in this sample. The patient population in the AGMT dataset, may have had differening survival outcomes with unknown explanation, although it is important to consider that sample size and follow up time were more limited in the AGMT sample. For the CRF sample, the follow up period of this study was ample, although a median OS survival was not observed. This could suggest that the median OS is greater in the real world compared to clinical trials; an observational study in France reported a median OS of 49.8 months, in patients receiving GO at induction (18).

There are several factors that can influence outcomes (e.g. CR and EFS) in AML patients, including age, genetic abnormalities, MRD status, bone marrow involvement at diagnosis, and co-morbidities, amongst others (19, 20). Younger patients generally have better treatment outcomes, due to the increased tolerance of treatment, which could explain the reason for difference in EFS from the CRF sample compared to the ALFA-0701 trial. In the CRF sample, although the median sample of 53.0 years old is close to the median age in the ALFA-0701 trial (60 years), the CRF sample included a much wider range of ages, with a range of 20-70 years compared to 50-70 years in the ALFA-0701 trial (10). However, this does not explain the differences in EFS between the CRF and AGMT data where both data sources had similar median and range of patient ages. Due to the substantial differences in data collection methodology between the CRF and AGMT datasets, and limited sample size and follow up time in the AGMT dataset, care should be taken when comparing groups. The reason for the differences in treatment outcomes is not clear, it may be that the heterogenous nature of the disease between the populations or different definitions of treatment outcomes between populations have produced these differences, although small sample size and follow up time in the AGMT dataset, may have influenced the results also.

Larson *et al.* (2005) concluded that the best GO outcomes were observed in patients that were able to proceed with HSCT following remission (21). Patients eligible for SCT will generally be younger in age and without any significant health issues (e.g. heart, lung, or kidney disease). In the CRF sample, nearly half of the sample (42.7%) received a HSCT.Contrary to this, phase III trial results could suggest that the best GO outcomes can be observed in patients that achieve remission and do not require HSCT. Further studies could be conducted to determine the population experiencing the best GO outcomes.

In the ALFA-0701 trial, 69.6% of patients had favourable or intermediate cytogenetics, with rest of the population having either unfavourable cytogenetics or data unavailable. Previous studies have demonstrated survival benefit of GO in patients with favourable or intermediate risk cytogenetics with no evidence of benefit in those with adverse risk cytogenetics (10, 16,

22). As this CRF sample only included favourable or intermediate cytogenetic patients, this may explain the improved survival outcomes when compared to the ALFA-0701 trial.

Previous studies showed increased early mortality with higher doses of GO (6 mg/m^2, SWOG-0106 (23)) but was not observed in lower doses of GO (3 mg/m^2 (10)). Treatment-emergent AEs related to GO administration have been reported to include VOD (before and after HSCT), GvHD, and hemorrhage, among others (10, 24, 25). Safety events collected during this study and presented within this report were collected related to VOD or GvHD.

From the CRF data, n=4 (4.5%) of patients was diagnosed with VOD following GO treatment, which aligns with the proportion observed in the ALFA-0701 trial (n=6 [4.6%]) in the GO arm. VOD was diagnosed as either grade 2 moderate (n=1), grade 3 severe (n=1), or grade 5 death (n=1). VOD grading was missing for the other patient diagnosed with VOD following GO treatment. Of those that experienced VOD, n=3 (75.0%) died during follow-up from progressive disease (n=1), treatment-related death in CR (n=1), and other (n=1). The patient that did not die from VOD had a follow-up duration of 1006 days. In a previous study, patients that underwent HSCT 3.5 months or less following GO exposure were more likely to develop VOD (24). From the CRF data, the time from latest GO treatment to HSCT was a median of 719 days (23.6 months), which may explain the low number of patients experiencing VOD in this sample.

In the CRF sample, of the n=38 patients that received a HSCT, 60.5% (n=23) were diagnosed with GvHD. 78.3% (n=18) of these patients were diagnosed with acute GvHD and 39.1% (n=9) diagnosed with chronic GvHD (both acute and chronic GvHD could be selected in the CRF). In a previous study, GO exposure was associated with an increased rate of acute GvHD (25), a finding that is supported by our results.

From the CRF data, 2.2% (n=2) patients died within 30 days of initiation of 1L induction treatment, and 3.4% (n=3) patients died within 60 days of initiation of 1L treatment. Of the n=63 patients with at least 3 years follow-up (or death), 36.5% (n=23) patients died. Disease progression was cited as the most common reason for death across all data sources. In the ALFA-0701 trial, patient deaths within 30 days of treatment initiation were recorded as 2.2% (n=3) in the control sample (3+7 regimen alone) compared to 3.8% (n=5) in the GO sample (3+7 regimen + GO). The slightly lower percentage in death rates reported here may be related to the higher proportion of favourable / intermediate cytogenetic risk patients compared to ALFA-0701 as these patients generally have better prognosis (26).

Overall, this study shows that label use (3 doses of 5mg fraction) of GO, may be effective in the real world, demonstrated by positive clinical outcomes.

11.2. Limitations

Study design limitation

The overall sample size of patients (115) [89 in the CRF data and 26 in the AGMT data] limit comparisons between stratifications, such as ELN risk status (intermediate and favourable) and cytogenetic risk subgroups. However, the sample size is assumed to not be substantially low in relation to the European population of interest, given the timing (April 2018) of the marketing authorisation of GO from the EMA for the European Union (11). A higher number of patients were sought at the outset, however the final number of 115 still represents the largest known single real-world evidence study examining the front-line use of GO that the researchers are aware of; GO use is not common given the rarity of disease and prevalence of prescribing, leading to the opinion of the researchers that the final sample is could actually be considered a relatively 'large' cohort. Furthermore, this is purely a descriptive study with no statistical comparisons and so the assessment of treatment patterns and effectiveness outcomes will not be affected by the small sample sizes.

As this a multi-county multisource study, there were slight differences in data variable availability and coding practices. To mitigate this, the eCRF used for Austrian, Belgian, and German sites was designed using knowledge of datasets known to collect data from medical records. When requesting data from the AGMT, variables were requested in this same format where possible. There may have been differences in variable validity also.

GO-based treatment regimens and dosing schedules may differ through the different countries, adding to the complexity of the assessment of effectiveness outcomes. Furthermore, dosing information per regimen may not be available in the data sources. For example, a total dose of GO may be provided, without numbers and/or timings. Nevertheless, number of doses is likely to be imputable due to prescribing guidelines (11, 27).

The multiple cytogenetic risk groups included in the study cohorts, could similarly add complexity to the assessment of effectiveness outcomes. As a result, the analyses included a stratification of risk group, subject to sample sizes.

The minimum follow-up period was set to three months. Consequently, for many patients, OS and EFS were not assessable. These patients were censored for such analyses.

Information was abstracted from charts by each site and entered in the eCRF directly without any adjudication or critical analysis from those extracting the data; adjudication would have improved the validity of the data extracted and is therefore noted as a limitation in this study.

Data source related limitations:

For the chart review, selection bias may arise. Site participation is influenced by willingness to take part, and may be based on workload, levels of consulting patients during the data collection period, or familiarity with the research nature of the study. It should also be noted that the sites eligible for inclusion in the study are those with whom Pfizer have existing relationships with, and those ultimately selected for inclusion may be those deemed most suitable based on the feasibility assessment stage (i.e., those sites with higher numbers of

patients or who are most suited to executed non-interventional data collection studies) may be chosen over those considered to be less suitable. These factors introduce a bias whereby patients from non-participating sites are not represented in the results. Nonetheless, this method of site selection is the most practical approach for a non-interventional study such as this, whereby resources and timelines, to an extent, dictate the sites that can be considered eligible for inclusion. Furthermore, sites from multiple European countries were utilized and specifically those with the largest estimated sample sizes, increasing the variability of patients and medical professionals.

Further to the previous point, when informed consent is required for patient participation, the patient sample may potentially be biased towards less severe patients who are capable and willing to provide consent to participate. This could lead to more positive effectiveness outcomes observed in the study. To mitigate both selection biases, patient demographic and clinical characteristic data will be captured to allow for comparisons with published datasets to understand the generalizability of results. Additionally, when informed consent was required in Belgium, a legally acceptable representative was permitted to provide informed consent on behalf of the patient should they be unable to consent, reducing the bias associated with the need to obtain patient consent. Furthermore, patients of specific cytogenetic risk groups were included in the study, which naturally reduces bias towards patients of specific severity.

11.3. Interpretation

The addition of GO to chemotherapy regimens in favourable and intermediate-risk AML patients have shown to improve remission rates and survival outcomes in previous clinical trials, with significantly improved EFS and RFS. The results of this real-world study show that GO may be effective in these favourable and intermediate-risk AML patients due positive EFS and RFS outcomes. The treatment outcomes and highlight the role GO has in the treatment of AML.

11.4. Generalizability

The population presented within this report included patients that were diagnosed with *de novo* AML with either favourable or intermediate cytogenetics, were aged 18 or older, and received GO in a 1L treatment setting in conjunction with chemotherapy (see section 9.3 Subjects for the inclusion / exclusion criteria). The inclusion / exclusion criteria reflect the current marketing authorization for GO. Therefore, the population included in this study is likely to reflect most patients for whom GO would be prescribed (GO + chemotherapy in 1L treatment). This study did not include patients with secondary or post-myelodysplastic syndrome acute AML (same as ALFA-0701); therefore, the studied population does not reflect the wider population of patients with AML.

12. OTHER INFORMATION

Not applicable.

13. CONCLUSIONS

This multi-country real-world study indicates that GO combined with standard chemotherapy may improve survival outcomes in AML patients with favourable or intermediate cytogenetic risks. The findings for EFS and OS could indicate that three doses of GO during induction therapy is effective in the real world. Positive patient outcomes in the intermediate-risk space and low incidence of VOD, highlights GO's role in AML treatment.

14. LIST OF STANDALONE TABLES AND FIGURES

N/A

15. REFERENCES

1. Pelcovits A, Niroula R. Acute myeloid leukemia: a review. Rhode Island Medical Journal. 2020;103(3):38-40.
2. Limited TEIU. 2019.
3. Kawamoto H, Minato N. Myeloid cells. The international journal of biochemistry & cell biology. 2004;36(8):1374-9.
4. Roman E, Smith A, Appleton S, Crouch S, Kelly R, Kinsey S, et al. Myeloid malignancies in the real-world: Occurrence, progression and survival in the UK's population-based Haematological Malignancy Research Network 2004–15. Cancer epidemiology. 2016;42:186-98.
5. Heuser M, Ofran Y, Boissel N, Mauri SB, Craddock C, Janssen J, et al. Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2020;31(6):697-712.
6. Döhner H, Estey E, Grimwade D, Amadori S, Appelbaum FR, Büchner T, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood, The Journal of the American Society of Hematology. 2017;129(4):424-47.
7. Kantarjian H, Kadia T, DiNardo C, Daver N, Borthakur G, Jabbour E, et al. Acute myeloid leukemia: current progress and future directions. Blood cancer journal. 2021;11(2):1-25.
8. De Kouchkovsky I, Abdul-Hay M. Acute myeloid leukemia: a comprehensive review and 2016 update. Blood cancer journal. 2016;6(7):e441-e.
9. Appelbaum FR, Bernstein ID. Gemtuzumab ozogamicin for acute myeloid leukemia. Blood, The Journal of the American Society of Hematology. 2017;130(22):2373-6.
10. Lambert J, Pautas C, Terré C, Raffoux E, Turlure P, Caillot D, et al. Gemtuzumab ozogamicin for de novo acute myeloid leukemia: final efficacy and safety updates from the open-label, phase III ALFA-0701 trial. Haematologica. 2019;104(1):113.
11. EMA. Mylotarg 2025 [Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/mylotarg#authorisation-details.
12. Ali S, Dunmore HM, Karres D, Hay JL, Salmonsson T, Gisselbrecht C, et al. The EMA review of mylotarg (gemtuzumab ozogamicin) for the treatment of acute myeloid leukemia. The Oncologist. 2019;24(5):e171-e9.
13. International System for Human Cytogenetic Nomenclature. Guidelines for cancer cytogenetics. Mitelman F, editor. Basel, Switzerland: Karger; 1991 1991.
14. Quan H, Li B, Couris CM, Fushimi K, Graham P, Hider P, et al. Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries. American journal of epidemiology. 2011;173(6):676-82.
15. ClinicalTrials.gov. Austrian Myeloid Registry (aMYELOIDr) https://clinicaltrials.gov/ct2/show/NCT044388892020 [
16. Burnett AK, Russell NH, Hills RK, Hunter AE, Kjeldsen L, Yin J, et al. Optimization of chemotherapy for younger patients with acute myeloid leukemia: results of the medical research council AML15 trial. Journal of clinical oncology. 2013;31(27):3360-8.
17. Burnett AK, Hills RK, Hunter AE, Milligan D, Kell WJ, Wheatley K, et al. The addition of gemtuzumab ozogamicin to intensive chemotherapy in older patients with AML produces a significant improvement in overall survival: results of the UK NCRI AML16 randomized trial. Blood. 2011;118(21):582.
18. Lambert J, Raffoux E, Lebon D, Braun T, Heiblig M, Santagostino A, et al. Gemtuzumab Ozogamicin for Patients with Newly Diagnosed CD33 Positive Acute Myeloid

Leukemia: Results from a French Retrospective Observational Study. Blood. 2023;142:2893.
19. Kusurkar S, Achrekar AR, Ugale PR, Joshi S, Terse V, Shetty DL, et al. Mutational Landscape and Factors Affecting Prognosis in Acute Myeloid Leukaemia (AML) with RUNX1:: RUNX1T1. Blood. 2024;144:4290.
20. Liu H, Stanworth SJ, McPhail S, Bishton M, Rous B, Bacon A, et al. Impact of patient demographics on treatment outcomes in AML: a population-based registry in England, 2013-2020. Blood Advances. 2024;8(17):4593-605.
21. Larson RA, Sievers EL, Stadtmauer EA, Löwenberg B, Estey EH, Dombret H, et al. Final report of the efficacy and safety of gemtuzumab ozogamicin (Mylotarg) in patients with CD33‐positive acute myeloid leukemia in first recurrence. Cancer. 2005;104(7):1442-52.
22. Hills RK, Castaigne S, Appelbaum FR, Delaunay J, Petersdorf S, Othus M, et al. The addition of gemtuzumab ozogamicin to induction chemotherapy in acute myeloid leukaemia: an individualpatient data meta-analysis of randomised trials in adults. The Lancet Oncology. 2014;15(9):986.
23. Petersdorf SH, Kopecky KJ, Slovak M, Willman C, Nevill T, Brandwein J, et al. A phase 3 study of gemtuzumab ozogamicin during induction and postconsolidation therapy in younger patients with acute myeloid leukemia. Blood, The Journal of the American Society of Hematology. 2013;121(24):4854-60.
24. Wadleigh M, Richardson PG, Zahrieh D, Lee SJ, Cutler C, Ho V, et al. Prior gemtuzumab ozogamicin exposure significantly increases the risk of veno-occlusive disease in patients who undergo myeloablative allogeneic stem cell transplantation. Blood. 2003;102(5):1578-82.
25. Ho VT, Martin AS, Pérez WS, Steinert P, Zhang M-J, Chirnomas D, et al. Prior gemtuzumab ozogamicin exposure in adults with acute myeloid leukemia does not increase hepatic veno-occlusive disease risk after allogeneic hematopoietic cell transplantation: a center for international blood and marrow transplant research analysis. Biology of Blood and Marrow Transplantation. 2020;26(5):884-92.
26. Lo MY, Tsai C-H, Kuo Y-Y, Tseng M-H, Peng Y-L, Hsu C-A, et al. Prognostic Relevance of Adult Acute Myeloid Leukemia Patients According to the 2022 European Leukemianet Risk Stratification. Blood. 2022;140(Supplement 1):130-1.
27. EMA. MYLOTARG - SUMMARY OF PRODUCT CHARACTERISTICS. 2022.

Appendix 1. SIGNATURES

See standalone document

Appendix 2.1. PROTOCOL

See standalone document

Appendix 3. INVESTIGATORS AND CORRESPONDING INDEPENDENT ETHICS COMMITTEES (IECs) OR INSTITUTIONAL REVIEW BOARDS (IRBs)

Appendix 3.1 List of Investigators by Country

Name, degree(s)	Title	Affiliation
Professor Wolfgang Sperr, MD	Principal Investigator	Medical University of Vienna, Austria
Prof. Karl-Anton Kreuzer	Principal Investigator	University Hospital Cologne, Germany
Prof. Johan Maertens	Principal Investigator	UZ Leuven, Belgium
Dr Ann De Becker, MD	Principal Investigator	University of Brussels, Belgium
Dr Alexander Schauwvlieghe	Principal Investigator	AZ Sint Jan Brugge, Belgium

Appendix 3.2 List of Independent Ethics Committee (IEC) or Institutional Review Board (IRB) and Corresponding Protocol Approval Dates

IEC	PI	Date of Approval
Ethik commission Medizinische Universität Wien (Ethics Commission Medical University of Vienna)	Prof. Wolfgang Sperr, MD	2nd July 2024
Geschäftsstelle Ethikkommission, Universität zu Köln	Prof. Karl-Anton Kreuzer	23rd November 2023
Ethics Committee Research UZ/KU Leuven	Prof. Johan Maertens	12th April 2024
Commissie medische ethiek of UZ Brussel/VUB	Dr Ann De Becker, MD	14th August 2024
AZ Sint-Jan Brugge Commissee voor Ethiek	Dr Alexander Schauwvlieghe	20th November 2023

Appendix 4. STATISTICAL ANALYSIS PLAN

See standalone document

Appendix 5. SAMPLE CASE REPORT FORM (CRF)

See standalone document

Appendix 6. SAMPLE STANDARD SUBJECT INFORMATION SHEET AND INFORMED CONSENT DOCUMENT (ICD)

See standalone document

Appendix 7. LIST OF SUBJECT DATA LISTINGS

N/A

Appendix 8. ADDITIONAL DOCUMENTS

N/A

Document Approval Record

Document Name:	B1761038_Non-Interventional Study Report_V 1.0_16DEC2025
Document Title:	B1761038_Non-Interventional Study Report_V 1.0_16DEC2025

Signed By:	Date(GMT)	Signing Capacity
Redacted	Redacted	Redacted
Redacted	Redacted	Redacted