Sponsor: Sanofi **Drug substance(s):** clofarabine	**Study code:** CLO08708 (OBS12879)

Title of the study:

The Evoltra® European Registry Programme: Paediatric Leukaemia (CLO08708-OBS12879)

Study period:

Registry initiation date [date first patient in (FPI)]: 11-Aug-2010

Registry completion date [last patient completed/last patient out (LPO)]: 15-Jun-2017

Study Status: Completed

Phase of development: NA

Objectives:

The overall objective of CLO08708 was to further characterize the risk/benefit profile of clofarabine during routine clinical use for the treatment of pediatric patients (≤21 years at initial diagnosis) with acute leukemia.
The specific objectives were:

- To further document the clinical effectiveness of clofarabine as monotherapy and in combination chemotherapy in routine clinical practice.
- To further document the safety profile of clofarabine as monotherapy and in combination chemotherapy in routine clinical practice.
- To further evaluate clofarabine risk/benefit profile as monotherapy and in combination chemotherapy in routine clinical practice.

Methodology:

Data collection:
This voluntary registry consisted of a database of anonymized patients' data following treatment with clofarabine.
For all patients registered in the Evoltra® European Registry program, the following information were to be collected on the CRF: demographics and baseline characteristics, details of leukemia diagnosis and prior treatment, clofarabine treatment, blood profile (prior to each treatment cycle), concomitant medications, adverse events (AEs), minimal residual disease (MRD) status, bone marrow transplants prior to or after clofarabine, and clinical responses as documented in normal practice.
Safety variables:
Adverse Events: AEs were collected from informed consent until the end of the study as described in the protocol. AEs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) and the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03 was used to grade clinical and laboratory AEs.
All serious adverse events (SAEs) and specific AEs as detailed in the protocol were to be recorded in the CRF and transmitted to pharmacovigilance with an appropriate causality assessment.
The safety profile of clofarabine during routine clinical practice was evaluated based upon frequency of AEs and SAEs, cases with a suspected drug interaction, Grade 3 or higher renal, hepatic, or cardiac events, Grade 3 or higher events possibly related to clofarabine occurring after 3 or more cycles, and AESIs, which included suspected tumor lysis syndrome, systemic inflammatory response syndrome (SIRS), capillary leak syndrome, increased creatinine and acute renal failure, veno-occlusive disease (VOD), pregnancy, and overdose.

Efficacy variables:

Response to therapy per cycle: For each cycle of clofarabine, response to therapy was captured as CR, complete remission with incomplete platelet recovery (CRp), complete remission with incomplete neutrophil recovery (CRi), PR, relapse, or refractory.

Best response to therapy: This was the best response recorded for any cycle of therapy (but not for follow-up). If the patient had no responses to therapy during the cycles that were at least PR, best response was Treatment Failure (TF).

Date of best response to therapy: This was the date of response assessment associated with the best response. If the best response was TF, the date of TF was the latest response assessment date during a cycle with relapse or refractory responses.

Date of first remission: This was the earliest date where the cycle response assessment was CR, CRp, or CRi. It was undefined if the patient's best response was PR or TF.

Overall Survival: Overall survival (OS) was defined as the time in months from the first dose of clofarabine to the date of death (or date last known alive).

Statistical Analysis:

Analysis Population: The full analysis set is the set of all patients who received at least 1 dose of clofarabine.

As the target population was not large and the study observational in nature, only descriptive statistics are provided. Descriptive statistics included mean, standard deviation (SD), median, and minimum and maximum. Significance testing was not performed; however, 95% confidence intervals (CIs) were presented as an informal estimate of precision.

Exposure to clofarabine was summarized both overall and by cycle; the median number of cycles was also reported. Treatment-emergent AEs (TEAEs) were summarized by the number and percentage of patients with events (worst grade by patient) and were presented by system organ class (SOC) and preferred term (PT), and severity was evaluated using Common Terminology Criteria (CTC) grade.

Summary tables were created for all reported TEAEs: AEs regardless of relationship to clofarabine; AEs related to clofarabine; SAEs; related SAEs; suspected drug interaction AEs; AESIs; and renal, hepatic, cardiac and related AEs with Grade ≥3.

Summary tables for efficacy were provided for all patients, and also for the subsets of ALL and AML patients, separately. Overall survival and duration of remission (CR, CRp, and CRi patients) were summarized with time-to-event analyses number of events, percentage censored, estimated 25th and 75th percentiles, minimum and maximum, and median (with 95% CI if at least 10 deaths were reported). Kaplan-Meier curves were also created for OS by number of prior induction regimens of the patient at study entry. A summary of the number of days to death was also generated (days from last dose to death and days from transplant to death). Best response and the incidence of post-study transplant (overall and by type) were summarized with number, percentage, and 95% CI (where relevant). The patients who relapsed after achieving remission was reported based on the listing of responses by cycle. Post-treatment MRD assessments were provided in listings.

Treatment:

Clofarabine was administered as monotherapy or in combination with other cytotoxic therapy such as cyclophosphamide, etoposide, or as per local standard practice. Patients from sites in Germany were treated according to the SPC, including 1 patient with a diagnosis of biphenotypic leukemia (ALL/AML).

The recommended monotherapy dose of clofarabine was 52 mg/m2 administered by intravenous infusion over 2 hours daily for 5 consecutive days (x 5), and repeated every 2 to 6 weeks as indicated by leukemia recurrence or recovery of normal hematopoiesis and return to baseline organ function.

In combination therapy, clofarabine has been used at varying doses ranging from 20 to 40 mg/m^2 daily for 5 consecutive days depending on the combination drugs. Cyclophosphamide has been given at daily doses x 5 varying between 300 and 440 mg/m2, while etoposide doses range from 100 to 200 mg/m2 x 5. Most centers use the 440-mg dose of cyclophosphamide and the 100-mg dose of etoposide.

Summary Results:

Participants (actual):

Overall participation status:

The registry enrolled 112 patients with acute leukemia at 32 active centers in 5 countries: France (13 centers), Germany (3), Italy (6), the Netherlands (3), and Spain (7). The number of participating physicians was 52, including sites which did not enroll patients and previous participating physicians.

Participation per period of the registry:

A total of 114 pediatric leukemia patients were screened, 2 patients had screen failure, no patients were lost to follow-up, and 112 patients were analyzed. The proportion of missing data for each variable of interest was low (<2%), with the exception of disease diagnosis cellular type (missing for 14 [12.5%] ALL patients and 3 [2.7%] AML patients) and best response (missing for 13 [11.6%] of all patients).

Participant characteristics and primary analyses:
Patient disposition, demographics, and disease history:
A total of 112 patients with acute leukemia received at least 1 dose of clofarabine. The mean (SD) age was 8.4 (5.12) years and 61 patients (54.5%) were male (Table 1).
The disease diagnosis was ALL for 93 patients (83.0%), with the highest proportion with B cell ALL (73 patients, 65.2%). The disease diagnosis was AML for 9 patients (8.0%). There were 10 patients (8.9%) who fell under the Other category for disease diagnosis. Two patients under theOther category (diagnosed as PH+ ALL and Philadelphia chromosome positive ALL) were reclassified based on medical review and included in the ALL patient analysis (total of 95 ALL patients). Two patients under the Other category (diagnosed as AML) were included in the AML patient analysis (total of 11 AML patients). Analyses results for ALL only patients and AML only patients are described under the Other analyses section below.
For disease status at baseline, most patients were assessed as relapse (78 patients, 69.6%) with the remaining assessed as refractory (27 patients, 24.1%) or newly diagnosed (7 patients, 6.3%). A majority of patients had 2 prior induction regimens (73 patients, 65.2%), followed by 3 (17 patients, 15.2%) and 1 (13 patients, 11.6%) prior induction regimens. A total of 20 patients (17.9%) had prior bone marrow/stem cell transplants, including 6 (5.4%) with total body irradiation as part of conditioning.

Table 1 - Summary of Demographics, Baseline Vital Signs, and Disease Characteristics

Variable	Total (N=112)
Age[a] (years)	
n	112
Mean (SD)	8.4 (5.12)
Median	8.0
Min, Max	0, 18
Gender, n (%)	
Female	51 (45.5)
Male	61 (54.5)
Weight[b] (kg)	
n	105
Mean (SD)	34.51 (19.735)
Median	30.00
Min, Max	7.6, 85.0
Height[b] (cm)	
n	105
Mean (SD)	128.59 (30.846)
Median	133.00
Min, Max	67.0, 184.0
Body Surface Area (m^2)	
n	112
Mean (SD)	1.081 (0.4387)
Median	1.035
Min, Max	0.25, 2.08
Disease Diagnosis, n (%)	
ALL	93 (83.0)
B Cell ALL	73 (65.2)
T Cell ALL	6 (5.4)
Other	0
Missing	14 (12.5)
AML	9 (8.0)
M0	1 (0.9)
M1	0
M2	0
M3	1 (0.9)
M4	2 (1.8)
M4EOS	0
M5	2 (1.8)
M6	0
M7	0
Missing	3 (2.7)
OTHER	10 (8.9)
ALL - BIPHUNOTYPISCH	1 (0.9)
ALL: B CELL ACUTE LYMPHATIC LEUKAEMIA - MLL + PROB	1 (0.9)

AML	2 (1.8)
BIPHENOTYPIC LEUKEMIA (ALL/AML)	1 (0.9)
MIXED PHENOTYPE ACUTE LEUCEMIA	1 (0.9)
MPAL (MIXED PHENOTYPE ACUTE LEUKEMIA) T-MY	1 (0.9)
PH+ ALL	1 (0.9)
PHILADELPHIA CHROMOSOME POSITIVE ALL	1 0.9)
RAEB-T REFRACTORY ANAEMIA WITH EXCESS OF BLASTS IN TRANSFORMATION	1 (0.9)
Time from Initial Diagnosis to First Dose Date (Months)	
n	112
Mean (SD)	31.87 (29.308)
Median	21.40
Min, Max	1.4, 133.0
Disease Status, n (%)	
Newly Diagnosed [c]	7 (6.3)
Relapse	78 (69.6)
Refractory	27 (24.1)
Number of Prior Induction Regimens, n (%)	
None	4 (3.6)
1	13 (11.6)
2	73 (65.2)
3	17 (15.2)
4	3 (2.7)
5	0
6	1 (0.9)
Missing	1 (0.9)
Prior Bone Marrow / Stem Cell Transplants, n (%)	
YES	20 (17.9)
Conditioning include total body irradiation, n (%)	
No	14 (12.5)
Yes	6 (5.4)
NO	92 (82.1)
Number of Prior Bone Marrow / Stem Cell Transplants, n (%)	
0	92 (82.1)
1	18 (16.1)
2	2 (1.8)
Baseline Creatinine Clearance [d] (mL/min)	
n	101
Mean (SD)	382.108 (2395.8159)
Median	132.350
Min, Max	31.90, 24214.23

ALL=acute lymphoblastic leukemia. AML= acute myeloid leukemia, max=maximum, min=minimum, SD=standard deviation.

a Age at first dose date.

b Some patients used CRF Pre-treatment page prior to Version 3 which did not collect weight and height information, thus

have missing values for those parameters.

c "Newly diagnose" value was collected only in CRF Pre-treatment page Version 4, based on Protocol Amendments 4 and 5.

d Serum creatinine value of one patient had an incorrect laboratory unit attached to it, resulting to a high calculated creatinine clearance value of 24214.23 (maximum).

A total of 110 patients with acute leukemia received clofarabine at Cycle 1, 34 at Cycle 2, 4 at Cycle 3, and 2 at Cycle 4. The mean (SD) total exposure was 250.79 (109.161) mg/m2. A majority of patients in this registry used clofarabine as a combination therapy, with 106 patients receiving combination therapy for all cycles, 3 patients receiving monotherapy for all cycles, 2 patients switching from combination to monotherapy (one at Cycle 2 and one at Cycle 3), and 1 patient switching from monotherapy to combination therapy (at Cycle 3).

Primary analyses (all patients):

Safety:

Overall, TEAEs were reported for 91 patients (81.3%). The most common TEAEs (frequency >10%) were febrile neutropenia (26 patients, 23.2%), mucosal inflammation (20 patients, 17.9%), pyrexia (17 patients, 15.2%), anemia (12 patients, 10.7%), and thrombocytopenia (12 patients,10.7%). A total of 76 patients (67.9%) had TEAEs considered by the Investigator to be related to clofarabine, with febrile neutropenia (25 patients, 22.3%, Grade range 1-4), mucosal inflammation (15 patients, 13.4%, Grade range 1-4), anemia (12 patients, 10.7%, Grade range 2-3), and thrombocytopenia (12 patients, 10.7%, Grade range 2-4) being most frequent (>10%). Grade 3 and higher TEAEs and related Grade 3 and higher TEAEs occurred in 62.5% and 48.2% of patients, respectively.
A total of 59 (52.7%) patients reported SAEs and 41 (36.6%) patients reported SAEs considered by the Investigator to be related to clofarabine. The most common SAEs (frequency >5%) were febrile neutropenia (13 patients, 11.6%), pyrexia (10 patients, 8.9%), febrile bone marrow aplasia (6 patients, 5.4%), sepsis (6 patients, 5.4%), and pneumonia (6 patients, 5.4%). The most common SAEs (>5%) related to clofarabine were febrile neutropenia (12 patients, 10.7%, Grade range 1-4). Grade 3 and higher SAEs and related Grade 3 and higher SAEs occurred in 42.9% and 29.5% of patients, respectively.
At the end of the reporting period, 68 patients had died. The cause of death reported showed 43 deaths which were due to disease progression (including 1 relapse). Reported AEs with an outcome of death included 3 events of disease progression, 8 events under the SOC of Infections and Infestations, 2 events of multi-organ failure, and 1 event of cardiac failure. Additional causes of death not captured as AEs included 2 deaths due to multi-organ failure, 1 due to infection, 3 due to graft versus host disease, 3 were transplant-related, 1 due to cardiac failure, 1 due to toxicity of treatment, and 3 were missing a cause of death.
The summary of time from the last treatment dose to the occurrence of death showed all 68 patients deaths occurred after the last dose of clofarabine. Mortality rates were low for deaths that occurred within 30 days from the last treatment dose as well as between 30 to 60 days (4 patients, 5.9% and 5 patients, 7.4%, respectively). Fifty-nine (59) patients (86.8%) died after 60 days from the last dose. Of the 43 patients who died due to disease progression, no patients died within 30 days from the last treatment dose, 4 patients died between 30 and 60 days after last dose, and 39 patients died >60 days after the last dose. Additionally, of the 34 patients who had undergone a transplant and died, a very small number of patients died within 30 days of transplant, as well as within 30 to 60 days from transplant (2 patients, 5.9% and 5 patients, 14.7%, respectively). Twenty-seven (27) patients (79.4%) who had undergone a transplant and died had a date of death >60 days after transplant.
Suspected drug interaction events: Suspected drug interaction events were collected from Protocol Amendments 4 and 5, and therefore may be under-reported. A total of 4 patients (3.6%) had suspected drug interaction events, including 2 patients with an event of mucosal inflammation, 1 patient with events of mucosal inflammation, vomiting, periorbital hematoma, and electrolyte imbalance, and 1 patient with events of neutropenic infection, headache, neuralgia, and palmar-plantar erythrodysesthesia syndrome.
Grade 3 or higher renal events: A total of 3 patients had Grade 3 or higher TEAEs under the Renal and urinary disorders SOC, including 1 event of renal failure (Grade 4), 1 of acute kidney injury (Grade 3), and 1 of renal mass (Grade 3); all events were serious and ongoing as of the study closure, and the events of renal failure and acute kidney injury were considered by the Investigator to be related to clofarabine.
Grade 3 or higher hepatic events: A total of 12 patients had Grade 3 or higher TEAEs (all but one were Grade 3) under the Hepatobiliary disorders SOC, including 5 events of hypertransaminasemia, 3 of hepatotoxicity, 2 of hepatocellular injury, 1 of hepatic function abnormal (Grade 4), and 1 of hyperbilirubinemia; a majority were nonserious events considered by the

Investigator to be related to clofarabine and a majority resolved during continued treatment. Additionally, patients with Grade 3 or higher hepatic-related events under the Investigations SOC included: 7 events of ALT increased, 2 events of AST increased, and 1 event of blood bilirubin increased, and 1 event of transaminases increased; a majority were Grade 3, nonserious events considered by the Investigator to be related to clofarabine and a majority resolved during continued treatment.

Grade 3 or higher cardiac events: A total of 6 patients had Grade 3 or higher TEAEs under the Cardiac disorders SOC, 3 of which were not considered by the Investigator to be related to clofarabine, including: 1 patient with Grade 3 cardiac failure which had an outcome of death; 1 patient with cardiac tamponade and intracardiac mass which were both Grade 4 and ongoing; and 1 patient with Grade 4 tachycardia which was ongoing. One patient who died due to Grade 5 cardiac failure and Grade 4 myocardial infarction that was considered definitely related to clofarabine; 1 patient with cardiomyopathy and left ventricular dysfunction which were both Grade 4 events considered by the Investigator to be possibly related to clofarabine and led to treatment discontinuation but were resolved; and 1 patient with Grade 3 pericardial effusion considered by the Investigator to be related to clofarabine and which led to hospitalization but was resolved.

Grade 3 or higher events considered by the Investigator to be related to clofarabine with an onset after 3 cycles of use: Only 5 patients were treated with clofarabine for 3 or more cycles. Of those patients, 3 patients experienced Grade 3 or higher TEAEs considered by the Investigator to be related to clofarabine, including:

- 1 patient had nonserious events of ALT increased and AST increased (both Grade 3) that led to treatment interruption; both events resolved.
- 1 patient had nonserious events of hypertransaminasemia and fever (both Grade 3) and an SAE of VOD; all events resolved.
- 1 patient had SAEs of pantocytopenia, febrile neutropenia, pleurisy, pneumonia, sodium retention, pleural effusion, and pericardial effusion (all Grade 3) which led to hospitalization; all events resolved.

Adverse events of special interest: AESIs were collected from Protocol Amendments 4 and 5. The summary of patients with AESIs is presented in shows no events; however, upon inspection of the AE tables and listing, 9 AESIs did occur (prior to Protocol Amendments 4 and 5). One patient experienced a nonserious AE of tumor lysis syndrome considered by the Investigator to be a mild (Grade 1) event related to clofarabine and which resolved after 5 days. Two patients had events of capillary leak syndrome, one of which was a serious Grade 3 event considered by the Investigator to be related to clofarabine and the other a nonserious Grade 2 event considered not related to clofarabine; both events resolved. In addition to the Grade 3 or higher renal events of acute kidney injury and renal failure described above, 1 patient had an event of renal failure (nonserious Grade 2) considered by the Investigator to be related to clofarabine and which resolved. Two patients had events of VOD (1 serious Grade 3 and 1 nonserious Grade 2); both events were considered by the Investigator to be related to clofarabine and both resolved.

Efficacy:

For best response to therapy, a total of 71 patients (63.4%) had a positive response and 28 patients (25.0%) did not respond positively, with missing data for 13 patients (11.6%) (Table 2). Best response of CR was achieved by 43 patients (38.4%) and 8 patients (7.1%) had PR. In addition to the 43 patients with CR, 10 patients (8.9%) had a best response of CR with absence of total platelet recovery (CRp) and 10 patients (8.9%) had CR with absence of total neutrophil recovery (CRi). A total of 27 patients (24.1%) were refractory and 1 patient (0.9%) relapsed.

Table 2 - Summary of Best Response

Variable	Total (N=112)	95% Confidence Interval[c]
Best Response Category (per Investigator), n (%)		
Complete Response (CR)	43 (38.4)	(29.4%, 48.1%)
Complete Response / Absence Of Total Platelet Recovery (CRp)[a]	10 (8.9)	(4.4%, 15.8%)
Complete Response / Absence Of Total Neutrophil Recovery (CRi)[b]	10 (8.9)	(4.4%, 15.8%)
Partial Response (PR)	8 (7.1)	
Relapse	1 (0.9)	
Refractory	27 (24.1)	
Missing	13 (11.6)	

a CRp - Platelet counts <100 X 10^9/L.

b CRi - Absolute neutrophil counts <1.0 X 10^9/L.

c Based on Clopper-Pearson exact method.

The duration of remission (summarized in Table 3) shows a median duration of remission of 11.9 months (95% CI: 7.4 to NE) for patients with a best response of CR. Durations of remission were shorter in the CRp and CRi patients at 2.0 months (95% CI: 0.3 to 4.6) and 5.8 months (95% CI: 1.5 to 13.2), respectively. A total of 3 patients had a relapse or refractory response in Cycle 2 after achieving remission (CR, CRp, or CRi) in Cycle 1. Additionally, 3 patients had a relapse or refractory response in Cycle 2 after reporting PR in Cycle 1. No other patients were relapsed/refractory following a positive response.

Table 3 - Summary of Duration of Remission for CR, CRp, CRi Patients (Months)

		Total (N=112)
Best Response Category (per Investigator)	**Kaplan-Meier Estimates**	
Complete Response (CR)	n	43
	Median	11.9
	95% CI	(7.4, NE)
	25th%, 75th%	5.4, NE
	Min, Max	0.20, 46.25+
	% Censored	55.8
Complete Response / Absence Of Total Platelet Recovery (CRp)[a]	n	10
	Median	2.0
	95% CI	(0.3, 4.6)
	25th%, 75th%	0.9, 4.6
	Min, Max	0.30, 12.37
	% Censored	10.0
Complete Response / Absence Of Total Neutrophil Recovery (CRi)[b]	n	10
	Median	5.8
	95% CI	(1.5, 13.2)
	25th%, 75th%	4.7, 11.5
	Min, Max	1.48, 13.19
	% Censored	20.0

CI=confidence interval, min=minimum, max=maximum, NE=not estimable.

Duration of remission was calculated from the date of best response to the earliest assessment of relapsed or refractory disease, or of death. Patients without events were censored at the date of last follow-up.

a CRp - Platelet counts <100 X 10^9/L.

b CRi - Absolute neutrophil counts <1.0 X 10^9/L. Note: "+" denotes a censored observation.

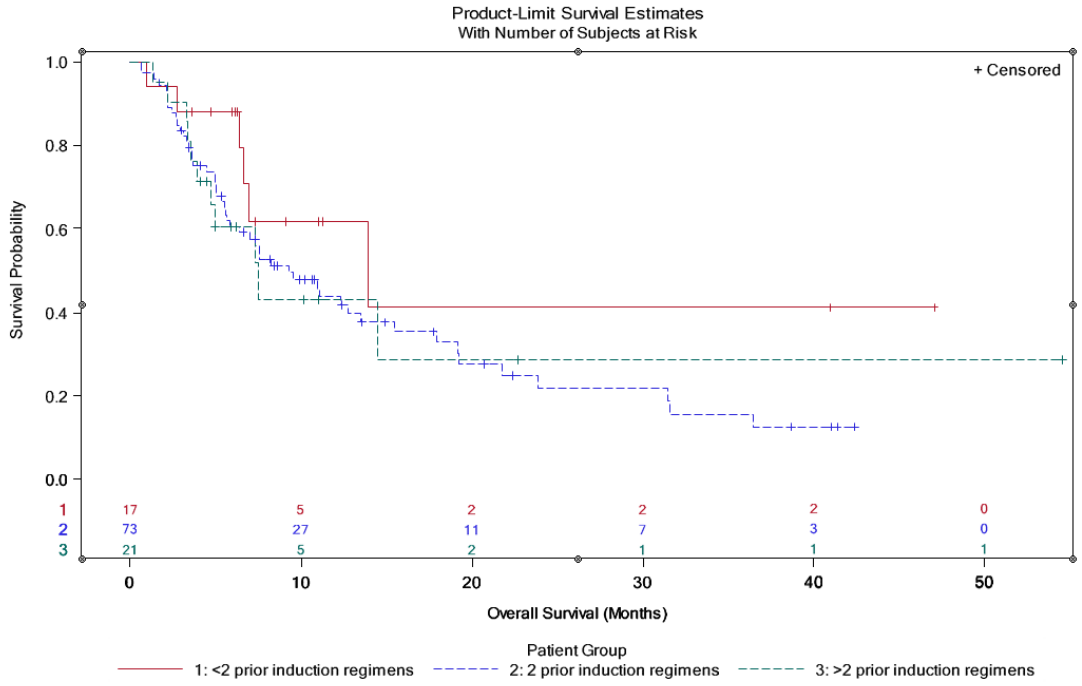
For all patients, the median OS, from first dose to date of death, was 9.5 months (95% CI: 7.0 to 13.9 months). For patients with

CR the median OS was 21.7 months (95% CI: 11.2 to NE). Median OS for CRp, CRi, and PR patients was 6.4 months (95% CI: 1.4 to 14.5), 13.5 months (95% CI: 3.7 to 36.5), and 7.6 months (95% CI: 2.8 to NE), respectively.

The Kaplan-Meier curves for OS by number of prior induction regimens at study entry are presented in Figure 1.

A majority of patients (74 patients, 66.1%) had undergone bone marrow/stem cell transplant following treatment with clofarabine. The response to transplant was CR for 48 patients (42.9%), CRp for 12 (10.7%) and CRi for 3 (2.7%).

Figure 1 - Kaplan Meier Curves for Overall Survival by Number of Prior Induction Regimens at Study Entry



Other analyses:

Subgroup efficacy analyses were conducted for ALL patients only (95 patients) and AML patients only (11 patients) and are described below.

ALL patient subgroup

For best response to therapy, 37 of the 95 ALL patients (38.9%) achieved CR and 6 patients (6.3%) achieved PR (Table 4). In addition to the 37 patients with CR, 10 patients (10.5%) had a best response of CRp and 8 patients (8.4%) had a best response of CRi. As a majority of patients in the study were ALL-diagnosed patients, best response rates within this subgroup showed similar trends as in the all-patients analysis.

Table 4 - Summary of Best Response (ALL Patients only)

Variable	Total (N=95)	95% Confidence Interval[c]
Best Response Category (per Investigator), n (%)		
Complete Response (CR)	37 (38.9)	(29.1%, 49.5%)
Complete Response / Absence Of Total Platelet Recovery	10 (10.5)	(5.2%, 18.5%) (CRp)[a]
Complete Response / Absence Of Total Neutrophil Recovery	8 (8.4)	(3.7%, 15.9%) (CRi)[b]
Partial Response (PR)	6 (6.3)	
Relapse	1 (1.1)	
Refractory	26 (27.4)	
Missing	7 (7.4)	

a CRp - Platelet counts <100 X 10^9/L.

b CRi - Absolute neutrophil counts <1.0 X 10^9/L.

c Based on Clopper-Pearson exact method.

The duration of remission is summarized in Table 5 and shows median durations of remission for CR, CRp, and CRi patients were 11.8 months (95% CI: 6.0 to NE), 2.0 months (95% CI: 0.3 to 4.6), and 5.8 months (95% CI: 1.5 to 11.5), respectively.

Table 5 - Summary of Duration of Remission for CR, CRp, CRi Patients (Months) (ALL Patients only)

Best Response Category (per Investigator)	Kaplan-Meier Estimates	Total (N=95)
Complete Response (CR)	n	37
	Median	11.8
	95% CI	(6.0, NE)
	25th%, 75th%	5.3, NE
	Min, Max	0.20, 46.25+
	% Censored	48.6
Complete Response / Absence Of Total Platelet Recovery (CRp)[a]	n	10
	Median	2.0
	95% CI	(0.3, 4.6)
	25th%, 75th%	0.9, 4.6
	Min, Max	0.30, 12.37
	% Censored	10.0
Complete Response / Absence Of Total Neutrophil Recovery (CRi)[b]	n	8
	Median	5.8
	95% CI	(1.5, 11.5)
	25th%, 75th%	4.7, 11.5
	Min, Max	1.48, 13.19
	% Censored	12.5

CI=confidence interval, min=minimum, max=maximum, NE=not estimable.

Duration of remission was calculated from the date of best response to the earliest assessment of relapsed or refractory disease, or of death.

Patients without events were censored at the date of last follow-up.

a CRp - Platelet counts <100 X 10^9/L.

b CRi - Absolute neutrophil counts <1.0 X 10^9/L.

Note: "+" denotes a censored observation.

For ALL patients, the median OS, from first dose to date of death, was 9.3 months (95% CI: 6.9 to 13.5 months), with 33.7% censored. For the best response categories of CR, PR, relapse, and refractory the median OS was 15.5, 7.6, 3.4, and 4.9 months, respectively.

A majority of ALL patients (59 patients, 62.1%) had undergone bone marrow/stem cell transplant following clofarabine treatment. The response to transplant was CR for 39 patients (41.1%), CRp for 9 patients (9.5%), and CRi for 3 patients (3.2%).

AML patient subgroup

For best response to therapy in the AML patients, 4 of the 11 patients (36.4%) achieved CR, 1 patient (9.1%) achieved CRi, 1 patient (9.1%) achieved PR, and the remaining 5 patients (45.5%) had missing data.

In the AML subgroup, the median duration of remission for AML patients with CR was not estimable, as all 4 patients had not reached any event (ie, death, relapsed, or refractory disease assessed) by study completion. The range for duration of remission for CR patients was 2.83 to 11.41 months.

The median OS was also not estimable. The OS range was 2.76 to 41.05 months; however, this only included 6 patients and 81.8% of data were censored.

All AML patients had undergone bone marrow/stem cell transplant following clofarabine treatment. For the 11 patients, the response to transplant was CR for 7 patients (63.6%), CRp for 2 patients (18.2%), and PR for 2 patients (18.2%).

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