Clinical Study Report

Version/Date: 1.0, Jul31, 2019

AN INVESTIGATOR-INITIATED STUDY TO EVALUATE ARA-C AND IDARUBICIN IN COMBINATION WITH THE SELECTIVE INHIBITOR OF NUCLEAR EXPORT (SINE) SELINEXOR (KPT-330) IN PATIENTS WITH RELAPSED OR REFRACTORY AML

Project code:	SAIL
EudraCT:	2014-000526-37
Short title:	NA
Investigational substance:	Selinexor (KPT-330) in combination with Ara-C and Idarubicin
Reference substance:	NA
Indication:	Acute Myeloid Leukemia (AML)
Study phase:	Phase II
Inclusion of first patient:	Sep10, 2014
End of treatment of last patient:	May23, 2017
Date of final report:	Jul31, 2019

Sponsor:
GSO Global Clinical Research B.V.
EBC Amsterdam
Keizersgracht 62-64
1015CS Amsterdam
The Netherlands

Head of study:
Prof. Dr. Walter Fiedler
Universitätsklinikum Hamburg-Eppendorf
II. Medizinische Klinik und Poliklinik
Martinistr. 52
20246 Hamburg
Germany

Monitoring:
GSO mbH
Mittelweg 110
20149 Hamburg
Germany

LKP:
PD Dr. Michael Heuser
Medizinische Hochschule Hannover
Hämatologie, Hämostaseologie, Onkologie und Stammzelltransplantation
Carl-Neuberg-Str. 1
30625 Hannover
Germany

Study sites:
Medizinische Hochschule Hannover, Hannover, Germany
Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany
Universitätsklinikum Frankfurt, Frankfurt a.M., Germany

GCP statement: This study was conducted in compliance with Good Clinical Practices (GCP) and the Declaration of Helsinki, and in accordance with applicable legal and regulatory requirements, including archiving of essential documents.
Confidentiality statement: The information provided in this document is strictly confidential.

Signatures

Title of the trial: **AN INVESTIGATOR-INITIATED STUDY TO EVALUATE ARA-C AND IDARUBICIN IN COMBINATION WITH THE SELECTIVE INHIBITOR OF NUCLEAR EXPORT (SINE) SELINEXOR (KPT-330) IN PATIENTS WITH RELAPSED OR REFRACTORY AML**

Trial substance: Selinexor (KPT-330) in combination with Ara-C and Idarubicin

Trial code: SAIL

The undersigned have read this clinical study report and hereby confirm that, to the best of their knowledge, it accurately describes the conduct and the results of the study.

Sponsor Representative

31.07.2019 _____
Date

_____
Dr. Anne L. Kranich

1 SYNOPSIS

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

Trial title:

An Investigator-Initiated Study To Evaluate Ara-C and Idarubicin in Combination with the Selective Inhibitor Of Nuclear Export (SINE) Selinexor (KPT-330) in Patients with Relapsed or Refractory AML

Study centres:

A total of 3 sites participated in the study. Patients were included at all sites. For a list of study sites, please refer to Appendix 3.

Trial duration:	**Phase of development:**
Inclusion of first patient: Sep10, 2014 End of treatment of last patient: May23, 2017	Phase II

Methodology:

Multicenter, open-label, non-randomized phase II trial

Trial objectives:

Primary trial objective:

- To determine the efficacy of Selinexor in combination with standard chemotherapy in patients with relapsed/ refractory AML by determination of rate of complete remission (CR) or morphologic complete remission with incomplete blood count recovery (CRi), as defined by the recommendations on diagnosis and management of AML in adults from an international expert panel, on behalf of the European LeukemiaNet

Secondary objectives:

- To determine the efficacy of Selinexor in combination with standard chemotherapy in patients with relapsed/ refractory AML by
    - Rate of partial remissions
        - Percentage of patients being transplanted after induction therapy
        - Early death rate
        - Overall survival (OS)
    - Event-free survival
- To evaluate overall safety and tolerability of Selinexor characterized by type, frequency, severity (graded using the National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] Version 4.03), timing and relatedness of adverse events (AEs) and laboratory abnormalities observed during the treatment within this study.

Exploratory objective:

- To identify the Pharmacokinetics and Pharmacodynamics of Selinexor in patients with relapsed/refractory AML

Name of the sponsor:	*Individual study table*	*(For National Authority use only)*
GSO Global Clinical Research B.V.	*Referring to part of the dossier:*	
Name of the finished product		
NA	*Volume: N/A*	
Name of the active substances:		
Selinexor (KPT-330)	*Page: N/A*	

Number of patients: 43 (one was a screening failure)

Included in the final evaluation:

Number of patients	**Total**
Recruited	43
Evaluable regarding toxicity	42
Evaluable regarding efficacy	42

Diagnosis and key inclusion and exclusion criteria:

Inclusion criteria:

To be eligible for this trial, patients had to meet the following criteria:

1. Cytological or histological diagnosis of AML with the exception of promyelocytic leukemia (AML M3)
2. Patients had to have relapsed/refractory disease (relapse after stem cell transplantation was permitted) as defined as:
   a. patients with <PR after first cycle of induction chemotherapy, or
   b. patients with <CR(i) after second cycle of induction chemotherapy, or
   c. patients who relapsed after conventional chemotherapy or
   d. patients who had undergone a single stem cell transplantation and who had relapse of their AML.
3. Men and women aged ≥18 years and eligible for standard dose of chemotherapy (7+3);
4. A period of at least 3 weeks needed to have elapsed since last treatment (with the exception of hydroxyurea) before participating in this study. Hydroxyurea induction therapy to reduce peripheral blast counts was permitted prior to initiation of treatment on protocol. Treatment might begin in <3 weeks from last treatment if deemed in the best interest of the patient after discussion with the PI of the study;
5. ECOG performance status ≤ 2;
6. Serum biochemical values with the following limits unless considered due to leukemia: creatinine ≤2 mg/dl; total bilirubin ≤2 x ULN, unless increase was due to hemolysis or congenital disorder; transaminases (SGPT or SGOT) ≤2.5 x ULN.
7. Ability to swallow and retain oral medication
8. Ability to understand and provide signed informed consent;
9. Cardiac ejection fraction had to be ≥50% (by echocardiography).
10. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures.

Exclusion criteria:

Patients with any of the following were not eligible for participation:

1. Treatment with any investigational agent within four weeks.
2. Cumulative anthracycline dose (daunorubicin or equivalent) >360 mg/m^2
3. HIV infection

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

4. Presence of any medical or psychiatric condition which might limit full compliance with the study, including but not limited to:
5. Presence of CNS leukemia
6. Unresolved toxicity from previous anti-cancer therapy or incomplete recovery from surgery.
7. For patients after SCT as part of prior treatment:

a. Necessity of immunosuppressive drugs
b. GvHD > grade 1

8. Any of the following within the 12 months prior to study drug administration: myocardial infarction, severe/unstable angina, coronary/peripheral artery bypass graft, symptomatic congestive heart failure, cerebrovascular accident or transient ischemic attack, pulmonary embolism, deep vein thrombosis, or other thromboembolic event.
9. Ongoing cardiac dysrhythmias of NCI CTCAE Grade $\geq$ 2.
10. Other severe acute or chronic medical or psychiatric condition, or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, and in the judgment of the investigator would make the patient inappropriate for entry into this study.
11. Clinically significant bleeding within 1 month

Treatment duration:

All enrolled patients were to be treated with one induction cycle which had a duration of 4 weeks.

If a bone marrow CR or CRi was achieved, the patient was to be recommended for stem cell transplantation, have his/her end of treatment, and followed for event-free and overall survival.

If a patient had achieved a partial remission, an additional induction cycle (4 weeks) was to be initiated. If a CR was achieved, the patient was to be recommended for stem cell transplantation and was to be followed for event-free and overall survival.

In patients achieving CR or CRi after 1 or 2 4-weeks cycles who were not eligible for stem cell transplantation, but, in the opinion of the investigator, were benefiting from Selinexor, then oral Selinexor dosed twice weekly might be continued parallel to consolidation therapy with Ara-C until relapse or toxicity developed. Consolidation with Ara-C was to consist of 3 4-week cycles. Selinexor twice weekly might continue until relapse or for maximally 1 year of treatment.

Patients who achieved a > 50% blast reduction after the end of 2 induction cycles, were not candidates for SCT, and in the opinion of the investigator, were benefiting from Selinexor, oral Selinexor dosed twice weekly might be continued until PD or for maximally 1 year of treatment.

Treatment should continue until progression of disease (PD) or unacceptable toxicity, withdrawal of consent by the patients, or non-compliance by the patient with protocol requirements.

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

Patients for whom none of the above mentioned was achieved after two 4-week induction cycles should have had their end of treatment and were to be followed for overall survival.

Trial medication, dose and method of administration:

All enrolled patients were to be treated with Ara-C at a dose of 100 mg/m^2 continuous infusion (day 1-7) and idarubicin at a dose of 10 mg/m^2 iv (day 1,3,5) every 4 weeks and Selinexor. If a second cycle was applied, idarubicin was only given on day 1 and 3.

In the first 25 patients, Selinexor was to be administered at a dose of 40 mg/m² twice weekly orally (total of 8 doses per 4-week induction cycle).

After an amendment, 15 further patients were to be included. In these patients, Selinexor was to be administered at a flat dose of 60 mg twice weekly orally during weeks 1-3 of a 4-week cycle (day 2,4,9,11,16,18; total of 6 doses per induction cycle).

If patients were to be treated with consolidation therapy, the dose of Ara-C was 3 g/m^2 iv for 2 hours every 12 hours at 3 consecutive days for patients with a good performance status and younger than 60 years. (in total 6 doses). If patients were older than 60 years, the dose was 1 g/m^2 iv for 2 hours every 12 hours at 3 consecutive days. During consolidation, Selinexor dosing (40 mg/m² and 60 mg, respectively) was to start on days 2 and continue twice weekly (for the first 25 patients: 8 doses per 4-week cycle, for the 15 further patients only in weeks 1-3 of a 4-week cycle, thus a total of 6 doses per cycle).

If oral Selinexor was continued until relapse or up to maximally one year of treatment, drug administration was to occur twice weekly with ~48 hours between two consecutive doses at a dose of 40 mg/m² and 60 mg, respectively. One cycle was 4 weeks with 8 doses of Selinexor per cycle and 6 doses of Selinexor during weeks 1-3, respectively (e.g. on Monday and Wednesday or on Tuesday and Thursday or on Wednesday and Friday).

All enrolled patients might participate in an optional baseline translational research study. Patients were to receive a single dose of Selinexor (40 mg/m² and 60 mg, respectively) after registration and before the first induction cycle. Bone marrow aspirate samples were to be collected pre-dose and 24 hours post dose.

Evaluation criteria:

Primary endpoint:

Percentage of patients achieving a complete response (CR) or CRi (complete remission without normalization of peripheral blood counts)

Secondary endpoints:

- Partial response rate
- Percentage of patients undergoing subsequent allogeneic stem cell transplant

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

- Early death rate
- Overall survival (OS)
- Event-free survival (Events were defined as Death, not achieving a CR or CRi, Relapse after CR or CRi)
- Toxicity (acc. to NCI CTC AE v4.03)

<u>Exploratory endpoints (optional studies):</u>

- Limited pharmacokinetics to measure plasma concentration of Selinexor
- Selinexor-induced changes in mRNA levels of XPO1 and tumor suppressor markers
- Selinexor-induced changes in plasma cytokine levels
- Selinexor-induced changes in gene expression profiling of leukemic blasts isolated from patients
- Expansion of leukemic blasts in mice for therapeutic studies

Statistical methods:

All statistical analyses were performed and all summary tables and data listings were prepared using with Statistical Analysis System® (SAS) v9.3 for Windows (SAS Institute Inc., Cary, NC, USA). For continuous variables, summary statistics (mean, standard deviation, median, minimum and maximum values) were tabulated. For discrete variables, the frequency distribution was tabulated. Statistical tests were of descriptive nature only except for the analysis of the responder rate.

The primary efficacy measure was the rate of complete responders (CR). To determine the efficacy of Selinexor in combination with standard chemotherapy, the best response after Selinexor treatment was analysed, thus the best response after the induction cycle.

The secondary efficacy measures were the rate of partial remissions, percentage of patients being transplanted after induction therapy, and early death rates were analysed as rates.

Overall survival (OS), event free-survival (EFS) and relapse-free survival (RFS) were analysed applying the Kaplan-Meier method (KM) and described by median survival time and respective 95%-confidence intervals.

In the statistical analysis a p-value less than 0.05 was considered as statistically significant. If not stated otherwise, all tests were performed as two-sided tests and two-sided 95% confidence intervals (CIs) were produced for all treatment differences. No adjustments for p-values were made.

For safety evaluation, the number of patients developing adverse experiences was tabulated according to NCI CTCAE Version 4.03. The CTC v4.03 also was the basis for grading the laboratory changes. Additionally, the subset of adverse experiences considered treatment-related was summarized and listings of adverse experiences leading to treatment discontinuation and those identified as 'severe' or of 'maximal' severity were displayed.

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

Summary:

Demographic data and baseline data:
A total of 43 patients were registered in the clinical trial at 3 sites. One patient was a screening-failure. Of the remaining 42 patients, the first 27 patients were treated in cohort 1 (Selinexor dosed by body surface area [BSA] 40 mg/m² per dose) and the other 15 patients were treated in cohort 2 (flat dose of Selinexor of 60 mg).
Twenty-five patients (59.5%) were men, 17 patients (40.5%) were women. The median age was 59.5 years with a range of 22-78 years.
Thirty-one patients (73.8%) had de-novo AML, 2 patients (4.8%) therapy-induced AML, and 9 patients (21.4%) secondary AML after MDS/MPN. Of the 2 patients with therapy-induced AML, 1 patient had a prior radio-/chemotherapy for a preceding neoplastic disease, and 1 patient had been treated with azathioprine for Crohn's disease.
Seventeen patients (40.5%) had received prior allogeneic SCT. All patients either had refractory AML (11 patients, 26.2%), or had relapsed after a prior chemotherapy for their AML. Of the latter, 13 patients (31.0%) had an early relapse within 12 months of their previous CR, and 18 patients (42.9%) had a late relapse at least 12 months after a previous CR.

Efficacy results:

Primary endpoint: Rate of CR/CRi
Of the 42 patients, 21 patients achieved an objective response: 9 patients (21.4%) a CR, 11 patients (26.2%) a CRi and one patient a MLFS, resulting in an overall response rate (ORR) of 50.0% (CI: 37.7 – 62.3%). The ORR was 55.6% for cohort 1 (CI: 40.0 – 70.1%) and 40.0% for cohort 2 (CI: 22.3 – 60.7%). Four patients in cohort 2 were not evaluable for response due to early death and were considered as non-responding patients.
Thus, the primary hypothesis that the observed response rate is equal or more than the predefined limit of 30% has been reached for both the total population and cohort 1. For cohort 2, the results were slightly above the limit of statistical significance.

Secondary endpoints:

- Rate of partial remission

No patients had a partial remission after the first induction cycle.

- Percentage of patients being transplanted after induction therapy

The intention of the salvage therapy was to bring the patients to a first or second SCT. In the ITT population, SCT was performed in 15 of 42 (35.7%) patients (11 in cohort 1 and 4 in cohort 2). Twelve of these 15 patients received a first and 3 patients received a second SCT after a SCT prior to enrolment into the study.

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

Of the 15 patients with SCT, 8 patients had achieved a CR/CRi after the first induction cycle. The other seven transplanted patients had either stable disease (SD) (5 patients) or progressive disease (PD) (2 patients) prior to SCT.
In addition, 2 previously transplanted patients received donor lymphocyte infusions (DLIs) as consolidation, in one case combined with azacytidine according to local standards.

- Early death rate

Early death was defined as death before the end of the first induction cycle. In the ITT population, 4 patients (9.5%) died during this period, all of them of cohort 2 (26.7% of patients in cohort 2).

- Survival

The median follow-up for the whole group was 8.2 months ranging from 0.5 to 38.4 months:
12.6 months for cohort 1, range: 1.1 - 38.4 months
8.0 months for cohort 2, range: 0.5 - 16.1 months

Overall survival (OS): The median OS was 8.2 months (12.6 months for cohort 1 and 8.0 months for cohort 2). The difference between the groups was not statistically significant (p = 0.47).
Relapse-free survival (RFS): The median RFS was 17.7 months for the whole group and 10.9 months for cohort 1. For cohort 2, the median RFS was not reached as only 2 events in 6 patients occurred (p = 0.28)
Event-free survival (EFS): The median EFS was 4.9 months in the whole group, 5.6 months in cohort 1 and 4.3 months in cohort 2 (p = 0.87).

Toxicity:
All 42 patients who had taken at least one dose of study medication experienced at least one adverse event (AE).
Twenty-six out of 27 patients in cohort 1 (96.3%) and 14/15 patients in cohort 2 (93.3%) experienced at least one AE of grade 3 or higher (total: 40/42 patients, 95.2%).
In all 27 patients in cohort 1 (100.0%) and in 13/15 patients in cohort 2 (86.7%) at least one AE was assessed as related to selinexor. The same percentages were observed for the relationship of AEs to cytarabine and idarubicine.
In 26/27 patients in cohort 1 (96.3%) and in 14/15 patients in cohort 2 (93.3%), at least one AE was not resolved at the end of treatment visit.

The pre-dominant clinical AEs were nausea (85.7% of patients), diarrhea (83.3%), vomiting (73.8%), anorexia (71.4%), febrile neutropenia (66.7%), and fatigue (64.3%). The most frequently observed AEs related to laboratory values were neutropenia and thrombocytopenia (61.9% each), and anemia (59.5%).

Name of the sponsor: GSO Global Clinical Research B.V.	*Individual study table* *Referring to part of the dossier:*	*(For National Authority use only)*
Name of the finished product NA	*Volume: N/A*	
Name of the active substances: Selinexor (KPT-330)	*Page: N/A*	

The majority of AEs was of mild to moderate intensity (grade 1-2). However, in the initial cohort 1 we observed a high occurrence of gastrointestinal side effects, especially grade ≥3 diarrhea (55.6%) and febrile neutropenia (85.2%). Due to those side effects, the selinexor dose was reduced during the study by an amendment from 40 mg/m² twice weekly for 4 weeks (cohort 1) to 60 mg flat dose for 3 weeks out of 4 weeks (cohort 2). This resulted in a reduction of vomiting (all grades) from 81.5% to 60.0% and grade ≥3 diarrhea from 55.6% to 40.0%.
We also compared the recovery times of neutrophils above 1,000/µl and of thrombocytes above 100 000/µl: For cohort 1 compared to cohort 2, the median recovery time was 40 days vs. 30 days for neutrophils and 42 days vs. 35 days for the thrombocytes. The earlier recovery of neutrophils translated to a decrease of febrile neutropenia (all grades) from 85.2% in cohort 1 to 33.3% in cohort 2.

In total, 16 patients of cohort 1 (59.3%) and 9 patients of cohort 2 (60.0%) died (total number of patients: 25, 59.5%).
Early death defined as death before the end of the first 4-weeks induction cycle occurred in 4 patients (9.5%), all of them of cohort 2 (26.7%). The causes of death were asystole (patient 01-032), sepsis (patient 01-035), lung infection (patient 01-037) and haemophagecytosis syndrome (haemophagocytic lymphohistiocytosis/HLH, patient 03-036). All four deaths were unexpected. During the follow-up period, 21 additional patients died. The causes of death were progressive leukemia (12 patients), infectious complications (4 patients), graft-versus-host-disease (GvHD) (2 patients), multiple brain infarcts (1 patient), systemic inflammatory response syndrome (SIRS) (1 patient), and multi-organ failure (1 patient).

A total of 12 patients in cohort 1 (44.4%) and 8 patients in cohort 2 (53.3%) experienced at least one SAE (total number of patients with SAE: 20, 47.6%). In total, the sponsor received 30 SAE reports.
The majority of SAEs reported were infections that affected 19.0% of patients. SAEs concerning the blood and lymphatic system affected 9.5% of patients, and gastrointestinal disorders and general disorders were reported as SAEs in 7.1% of patients each.

Date of report: Jul31, 2019

Appendix 1: Changes in the conduct of the study or planned analysis

During the course of the study, three protocol amendments were submitted and approved:

Amendment 1 (protocol version 1.2, Sep01, 2014):

The full ophthalmological examination at baseline and if clinically indicated during treatment has been implemented into the protocol as part of the safety assessments for patients included in the trial in order to help determine if Selinexor is contributing any visual changes. In phase I clinical trials, a baseline full ophthalmological examination had been implemented since November 2012, because there had been few reports of “blurred vision” and other visual changes during two phase I trials with Selinexor (KCP-330-001 and KCP-330-002). The baseline ophthalmological examination was accidently omitted in the initially submitted protocol.

The change of the address of the pharmaceutical entrepreneur, Karyopharm Therapeutics, Inc, was included in the amendment additionally.

Amendment 2 (protocol version 2.0, Aug24, 2015):

The findings of the study showed that very good response was achieved with treatment with Ara-C and idarubicin in combination with Selinexor. The most frequent non-hematologic AEs observed had included vomiting, diarrhea, nausea, fatigue, anorexia and neutropenic fever. Taking into account the promising results, 15 more patients were planned to be recruited reaching a total of approximately 40 patients for the trial.

The sample size calculation, statistical considerations, the anticipated enrolment period, and the planned duration of the study had been updated accordingly.

The new cohort of patients was to receive selinexor at a flat dose of 60 mg twice weekly in weeks 1-3 of a 4-week cycle. The objective of the new dose regimen was to improve management of most common AEs and further investigating the response to the treatment. Dose modification levels had been adapted accordingly.

Furthermore, several sections in section 6 (Treatment) of the protocol were updated according to the updated Investigator’s Brochure version 5.0.

Amendment 3 (protocol version 3.1, Jan13, 2017):

The protocol was updated following the regular update of the Reference Safety Information (Investigator’s Brochure Selinexor). Furthermore, finishing Source Data Verification and collecting data for final study results revealed the necessity of additional data to interpret the safety and efficacy.

Additional data were to be collected regarding hematological recovery (platelets and neutrophils) to define the recovery times for platelets and neutrophils more detailed. Platelet recovery was

defined as platelets ≥ 50x 10^9/L and ≥ 100x 10^9/L, ANC recovery was defined as ANC ≥ 0.5x 10^9/L and ≥1.0x 10^9/L.

The primary objective “remission status after induction” was to be classified according to Döhner et al.: the recommendations from the European LeukemiaNet, and not according to Cheson et al.

An Independent DMC consisting of 2-3 AML specialists with high international reputation was implemented to make recommendations regarding the interpretation of the safety and efficacy results.

The protocol was updated accordingly to the Investigator’s Brochure version 6.0 (Nov14, 2016). Subsequent to the IB update, all cases of cerebellar toxicity ≥ Grade 3 were added as AESIs and were to be reported as SAEs.

An addendum to patient’s information (version 3.0, Dec14, 2016) for patients still in maintenance and follow-up had been updated according to the amended protocol and IB and was approved by the Ethics Committee.

Appendix 2: IMP Identification and batch numbers

Selinexor (KPT-330) for oral administration was supplied as 10 mg tablets. Bottles of 50 tablets per bottle were supplied. Each bottle of Selinexor tablets was labelled in accordance with current ICH GCP and specific national requirements.

	Investigational product
INN:	Selinexor
Company's Drug ID:	KPT-330
Drug Supply:	Karyopharm Therapeutics, Inc, 85 Wells Ave, Newton MA 02459, USA
Mode of administration:	Oral
Batch no.:	F140204-001, F141021-001
Expiry date:	Nov07, 2015, Feb07, 2016, Feb07, 2017 (F140204-001), Oct21, 2017 (F141021-001)
Storage instructions:	Selinexor tablets were to be stored at ambient temperatures between 5 –30 °C in a locked and secured area with restricted access to study staff. The tablets should not be stored at freezer temperatures or allowed to freeze. Tablets were supplied in white high density polyethylene (HDPE) bottles.

Appendix 3: List of study sites

Site	Address
01	Medizinische Hochschule Hannover Hämatologie, Hämostaseologie, Onkologie und Stammzelltransplantation Carl-Neuberg-Str. 1 30625 Hannover
02	Universitätsklinikum Hamburg-Eppendorf II. Medizinische Klinik und Poliklinik Martinistr. 52 20246 Hamburg
03	Universitätsklinikum Frankfurt Medizinische Klinik II Hämatologie, Onkologie, Rheumatologie, Infektiologie Theodor-Stern-Kai 7 60590 Frankfurt am Main