Cover Page

Official Title: An Investigator-sponsored, Phase 1/2 Trial of the Oral XPO1 Inhibitor Selinexor (KPT-330) Monotherapy and in Combination With Docetaxel for Previously Treated, Advanced KRAS Mutant Non-small Cell Lung Cancer (NSCLC)

NCT03095612

Document Date: 01/30/2023

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research:	An Investigator-Sponsored Phase 1/2 trial of the oral XPO1 inhibitor selinexor (KPT-330) monotherapy and in combination with docetaxel for previously treated, advanced KRAS mutant non-small cell lung cancer (NSCLC)
Sponsor:	UT Southwestern Medical Center
Sponsor-Investigator:	David E. Gerber, MD
Drug Supplier/Funding Provider:	Karyopharm Therapeutics Inc.

You may call the study doctors or research personnel during regular office hours at 214-648-4180. At other times, you may call them at 214-645-4673.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to evaluate the safety of the investigational study drug, selinexor alone or when given with docetaxel to patients who have been previously treated for advanced KRAS mutant lung cancer.

Why is this considered research?
This is a research study because selinexor is investigational and has not been approved by the U.S. Food and Drug Administration (FDA) for the treatment of non-small cell lung cancer.
Docetaxel is an approved FDA drug for the treatment of advanced stage non-small cell lung cancer.

The following definitions may help you understand this study:

- Standard medical care means the regular care you would receive from your personal doctor if you choose not to participate in this research.
- Researchers means the study doctor and research personnel at the University of Texas Southwestern Medical Center at Dallas and its affiliated hospitals.
- Pharmacodynamics (PD) control the effects the study drug will have on your body.
- Treatment cycle for this study is **21 days**
- Dose Escalation – increase in the amount of study drug you will receive
- Dose Expansion – continuation of drug use at a specific dose

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you have non-small cell lung cancer that may have a mutation (defect) in the KRAS gene in the tumor.

If you agree to participate in this study, you may be foregoing your opportunity to receive FDA approved therapies for your type of cancer. Some of the therapies have demonstrated clinical benefit compared to the monotherapy docetaxel including PD-1/L1 inhibitors. For more information about alternative treatments, please ask your study doctor.

Do I have to take part in this research study?
No. You have the right to choose whether you want to take part in this research study. If you decide to participate and later change your mind, you are free to stop participation at any time.

If you decide not to take part in this research study it will not change your legal rights or the quality of health care that you receive at this center.

How many people will take part in this study?
About 30 people will take part in this study at UT Southwestern. This study also is taking place at a number of other medical facilities around the country. There will be about 71-86 people participating in this research study throughout the United States.

Dose escalation phase – Between 9 and 24 patients will be enrolled for this part.

Dose expansion phase will have 3 cohorts:

- Approximately 35 patients will be enrolled for the combination docetaxel plus selixenor cohort.
- Approximately 34 patients will be enrolled into one of two selinexor monotherapy cohorts(once weekly or twice weekly dosing).

Patients will be enrolled to one of these 3 cohorts. Initial enrollment will be open to the dose expansion combination cohort for treatment with docetaxel plus selinexor. After

this combination cohort is completed, patients will be randomly assigned to either selinexor monotherapy cohorts of once or twice weekly dosing. If you choose to participate, your physician or study member will confirm to which cohort you have been assigned.

What is involved in the study?
If you volunteer to take part in this research study, you will be asked to sign this consent form and will have the following tests and procedures. Some of the procedures may be part of your standard medical care, but others are being done solely for the purpose of this study.

Screening Procedures *(Performed within -4 weeks prior to start of study therapy)*

To help decide if you qualify to be in this study, the researchers will ask you questions about your health, including medications you take and any surgical procedures you have had.

You may also have to fill out certain forms or have the following exams, tests or procedures:

- We will confirm that you have KRAS mutant Lung Cancer.
- Your medical history and demographic data (this includes information about your gender, age, and race/ethnicity) will be recorded.
- You will be asked about any medications you are currently taking or have taken during the past 2 weeks and any symptoms you might be having.
- A Physical examination will be done which will include body weight, height, body surface area (BSA) measurement and vital signs (heart rate, blood pressure, temperature)
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- A urine sample will be taken for routine tests.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), and how well your organs are functioning including your thyroid.
- A blood sample will be taken to check for hepatitis
- An electrocardiogram (EKG) which records the electrical activity of your heart will be performed twice.
- If you are a woman who is able to become pregnant, a blood sample will be collected to test if you are pregnant.
- A measurement of your tumor will be done by computed tomography scan (CT scan) or a magnetic resonance scan (MRI) of your chest and abdomen if you have not had one in the last 28 days.

- A brain MRI will be performed if needed **OR**
- Chest x-ray
- Nutrition counseling to discuss food recommendations and strategies to lessen potential side effects
- Archival tumor tissue (tissue which has already been collected) will be obtained for biomarker testing

If you are eligible (you are able to take part in the study), and agree to receive the study drug, you will need to come to the study site at various times to have procedures done as described below.

Study Medication/Intervention
This study consists of a 21-day treatment cycle of treatment.

Docetaxel
If you are enrolled to the combination cohort, you will receive docetaxel intravenously (through an IV) for 1 hour on the first day of each 21-day cycle (every 3 weeks) at the dose of either 60 or 75 mg/m^2 throughout your study participation. However, if you experience bad effects and the researchers believe it may be related to docetaxel your dose may be lowered to 55 mg/m2 or you may be taken off the study.

Selinexor (KPT-330)
The study drug selinexor is provided in 20 mg tablets in blister packs of 12 tablets, which is to be taken orally (by mouth) once a week for the combination cohort or weekly monotherapy cohort and twice weekly for the twice weekly monotherapy cohort. The tablet should be taken with or within 30 minutes of a meal.

In the combination cohort, the selinexor will be taken starting 1 week before your first docetaxel infusion. Selinexor (KPT-330) should be swallowed whole and should be taken with or within 30 minutes of a meal. You will be instructed to take a specific number of tablets on certain days. You will be asked to keep a diary to write down the date and time each time you take the selinexor. You will also be asked to keep all of your blister packs of study drug (including the empty ones). Bring your blister pack(s) and your daily diary to the clinic so that 'accountability' can be done (a check to see whether you have taken your study drug as instructed).

You will receive the same dose of selinexor throughout your participation in this study unless your dose is reduced because you are experiencing side effects.

Below is a table of the dose levels that may be administered during this study. The amount of selinexor that will be given to you will be based on the time at which you are enrolled and which cohort is available for study participation. Your study doctor will tell you which dose you will receive before it is given to you.

Combination Selinexor and Docetaxel dose levels:

Dose Level	Dose of Selinexor (mg oral)	Dose of Docetaxel (mg/m^2 IV), every 3 weeks
1[a]	60 once weekly	75
2[a]	80 once weekly	75
3	100 once weekly	75
-1	40 once weekly	75
-2	40 once weekly	60

Selinexor monotherapy cohort dose levels—weekly dosing:

Dose Level	Dose of Selinexor (mg oral)
1	80 once weekly
-1	60 once weekly
-2	40 once weekly

Selinexor monotherapy cohort dose levels—twice weekly dosing:

Dose Level	Dose of Selinexor (mg oral)
1	60 twice weekly
-1	40 mg twice weekly
-2	60 mg once weekly

*If you take acetaminophen (such as Tylenol) while you are on this study, you must not take more than 1 gram on the days you take the selinexor. Ask a study team member if you have any questions about the use of acetaminophen.

Procedures and Evaluations during the Research

If your study doctor decides you can be in the study, you can start treatment. You will have the following tests and evaluations during the study. For each cycle, the following will take place on the days indicated:

Combination Selinexor and Docetaxel cohort

Cycle 1 Day -7 (selinexor administration)

This visit will be completed for Cycle 1 only.

- Limited physical examination including body weight,and vital signs (heart rate, blood pressure, temperature)
- If you are a woman who is able to become pregnant, a blood sample will be collected to test if you are pregnant. If you have had a pregnancy test within 3 days before this visit, it may not need to be repeated.

- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- If your lab values are acceptable and your doctor feels you are ready to start treatment, the selinexor will be dispensed and you will take your first dose in clinic.
- About 2.5 tablespoons of blood will be drawn for Pharmacodynamic (PD) testing before your take the selinexor in clinic, and 4 hours after you take the selinexor.
- Provide study drug dosing diary

Cycle 1 Day 1 (docetaxel administration)

- Limited physical examination including body weight, height, body surface area (BSA) measurement and vital signs (heart rate, blood pressure, temperature)
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
    - You will take the selinexor in clinic.
    - If your lab values are acceptable and your doctor feels you are ready to start treatment with docetaxel, docetaxel will be administered through IV
- About 2.5 tablespoons of blood will be drawn for Pharmacodynamic (PD) testing before your take the selinexor in clinic, and 4 hours after you take the selinexor.
    - Drug accountability: review of pill diary and count all pills that are returned

Cycle 1 Day 3 (contact)

- A member of the study team will contact (via telephone) you to see how you are feeling and to see if you have had any changes in medication.

Cycle 1 Day 8 (±1 day)

- Limited physical examination including body weight, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking

- You will be asked about how you are feeling and if you are having any side effects
- Drug accountability: review of pill diary and count all pills that are returned

Cycle 1 Day 15 (±1 day)

- Limited physical examination including body weight, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- Drug accountability: review of pill diary and count all pills that are returned

Cycles 2 and Subsequent Cycles Day 1 (docetaxel administration) ± 3 days

- Physical examination including body weight, height, body surface area (BSA) measurement and vital signs (heart rate, blood pressure, temperature)
- If you are a woman who is able to become pregnant, a blood sample will be collected to test if you are pregnant. If you have had a pregnancy test within 3 days before this visit, it may not need to be repeated.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), and how well your organs are functioning. Urine will be collected
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- You will take your dose of selinexor in clinic
- Cycle 2 only - About 2.5 tablespoons of blood will be drawn for Pharmacodynamic (PD) testing before your take the selinexor in clinic, and 4 hours after you take the selinexor.
- Drug accountability: review of pill diary and count all pills that are returned
- Provide new study drug dosing diary

After 7 weeks for first 2 cycles then every 6 weeks

After 7 weeks for first 2 cycles then every 2 cycles you will have a CT or MRI scan of your chest and abdomen to how your disease is responding to treatment. If necessary, you may also be asked to have a MRI of your Brain.

End-of-Treatment Visit (≥ 30 Days after Last Dose)

Study procedures will be performed at 30 days (+/- 7 days) after the last dose of study medication for all patients, including early termination patients, as summarized below.

- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- A Physical examination will be done which will include body weight, and vital signs (heart rate, blood pressure, temperature)
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), and how well your organs are functioning including your thyroid.
- An electrocardiogram (EKG) which records the electrical activity of your heart will be performed twice.
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- You will have blood collected (about 2.5 tablespoons) for biomarker (pharmacodynamic) testing.

After Treatment - Biopsy

If your doctor decides that you need an additional biopsy after you finish treatment on this study, we would like to collect a sample of the tissue. We are not requesting an additional biopsy to this one, only a sample of the archived tissue from this biopsy. The additional tumor sample analyses will help with further knowledge and understanding of the study treatment.

<u>Selinexor monotherapy cohorts (weekly and twice weekly dosing)</u>

Cycle 1 Day 1 (selinexor administration)

- Limited physical examination including body weight, height, body surface area (BSA) measurement and vital signs (heart rate, blood pressure, temperature)
- If you are a woman who is able to become pregnant, a blood sample will be collected to test if you are pregnant. If you have had a pregnancy test within 3 days before this visit, it may not need to be repeated.
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- If your lab values are acceptable and your doctor feels you are ready to start treatment, the selinexor will be dispensed and you will take your first dose in clinic.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries

(elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- You will take the selinexor in clinic.
- Provide study drug dosing diary
- About 2.5 tablespoons of blood will be drawn for Pharmacodynamic (PD) testing before your take the selinexor in clinic, and 4 hours after you take the selinexor.

Cycle 1 Day 3 (±1 day)
- A member of the study team will contact (via telephone) you to see how you are feeling and to see if you have had any changes in medication.
- You will take the selinexor dose (for monotherapy twice weekly cohort only)

Cycle 1 Day 8 (±1 day)
- Limited physical examination including body weight, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- You will take the selinexor in clinic
- Drug accountability: review of pill diary and count all pills that are returned

Cycle 1 Day 10 (±1 day; for monotherapy twice weekly cohort only)
- You will take the selinexor dose (for monotherapy twice weekly cohort only)

Cycle 1 Day 15 (±1 day)
- Limited physical examination including body weight, and vital signs (heart rate, blood pressure, temperature)
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), and how well your organs are functioning.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- You will take the selinexor in clinic
- Drug accountability: review of pill diary and count all pills that are returned

Cycle 1 Day 17 (±1 day; for monotherapy twice weekly cohort only)
- You will take the selinexor dose

Cycles 2 and Subsequent Cycles Day 1 (selinexor administration) ± 3 days

- Physical examination including body weight, height, body surface area (BSA) measurement and vital signs (heart rate, blood pressure, temperature)
- If you are a woman who is able to become pregnant, a blood sample will be collected to test if you are pregnant. If you have had a pregnancy test within 3 days before this visit, it may not need to be repeated.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), and how well your organs are functioning. Urine will be collected
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- You will take your dose of selinexor in clinic
- Cycle 2 only - About 2.5 tablespoons of blood will be drawn for Pharmacodynamic (PD) testing before your take the selinexor in clinic, and 4 hours after you take the selinexor.
- Drug accountability: review of pill diary and count all pills that are returned
- Provide new study drug dosing diary

Cycles 2 and Subsequent Cycles Day 3 (±3 days; for monotherapy twice weekly cohort only)

- You will take the selinexor dose

Cycles 2 and Subsequent Cycles Day 8 (±3 days)

- You will take the selinexor dose

Cycles 2 and Subsequent Cycles Day 10 (±3 day; for monotherapy twice weekly cohort only)

- You will take the selinexor dose

Cycles 2 and Subsequent Cycles Day 15 (±3 days)

- You will take the selinexor dose

Cycles 2 and Subsequent Cycles Day 17 (±3 days; for monotherapy twice weekly cohort only)

- You will take the selinexor dose

After 7 weeks for first 2 cycles then every 6 weeks

After 7 weeks for first 2 cycles then every 2 cycles you will have a CT or MRI scan of your chest and abdomen to how your disease is responding to treatment. If necessary, you may also be asked to have a MRI of your brain.

End-of-Treatment Visit (≥ 30 Days after Last Dose)

Study procedures will be performed at 30 days (+/- 7 days) after the last dose of study medication for all patients, including early termination patients, as summarized below.

- You will be asked about any medications you are currently taking
- You will be asked about how you are feeling and if you are having any side effects
- A Physical examination will be done which will include body weight, and vital signs (heart rate, blood pressure, temperature)
- A performance assessment (your ability to do your daily activities) will also be completed using the Eastern Cooperative Oncology Group (ECOG) Performance Status Scale.
- Blood samples (about 2 tablespoons) will be taken for routine tests to check your blood counts (numbers of different types of cells in your blood), chemistries (elements and minerals in your body), coagulation (how well your blood clots), and how well your organs are functioning including your thyroid.
- An electrocardiogram (EKG) which records the electrical activity of your heart will be performed twice.
- You will have blood collected (about 2.5 tablespoons) for biomarker (pharmacodynamic) testing.

After Treatment - Biopsy
If your doctor decides that you need an additional biopsy after you finish treatment on this study, we would like to collect a sample of the tissue. We are not requesting an additional biopsy to this one, only a sample of the archived tissue from this biopsy. The additional tumor sample analyses will help with further knowledge and understanding of the study treatment.

For all cohorts: If you miss a dose, please contact your primary research personnel for this study or your study doctor to determine when next to resume dosing.

If you are taken off study due to progression but are receiving clinical benefit, your doctor will let you know if you have the option to continue treatment.

If you agree to have this additional tumor tissue collected for additional testing, please check the box next to <u>Yes</u> below.

- ☐ **Yes, I agree to the collection of these additional samples for additional testing.**

Initial: _____ Date:_____

If you do not agree, please check the box next to <u>No</u> below:

- ☐ **No, I do not agree to the collection of these additional samples for additional testing.**

Initial: _____ Date:_____

Follow-Up
After you stop treatment, a study team member will call you or your family every 3 months to see how you are doing and see if you have received any other treatment.

How long can I expect to be in this study?
The study is estimated to continue for 3 years. This is not the length of time you will stay in the study. The length of time you will stay in the study will be affected by several factors such as your response to treatment, whether you develop any clinically important side effects, or if you decide to withdraw consent.

You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests. Your authorization to use your health information will not expire and any data or samples collected before your withdrawal will continue to be used as necessary to preserve the integrity of the study, however no additional information or samples will be collected after you withdraw your authorization.

What are the risks of the study?
It is possible for any drug to cause side effects. You need to know and understand about side effects that could occur in this study before you agree to be a study participant. In addition to the risks listed below, there may be risks that are currently unknown. If significant new risks develop during the course of study that might affect your willingness to participate, information will be reported to you as soon as possible.

Side Effects of Selinexor (KPT-330)

Selinexor may cause one or more of the side effects listed below. In addition, there may be side effects that are not yet known that may occur. As of March 2022, Selinexor has been administered in over 4,475 patients. This information is based on data from cancer patients in other clinical trials with selinexor. You should tell your doctor or nurse right away about any possible side effects that you experience.

Very common side effects (≥10%):
In 100 people receiving selinexor more than 10 people may have:

- Nausea
- Fatigue
- Decreased appetite
- Thrombocytopenia – decrease in platelets, which help your blood clot
- Anemia – decrease in red blood cells
- Vomiting
- Diarrhea
- Hyponatremia – low sodium
- Constipation
- Dyspnea- shortness of breath
- Neutropenia – decrease in neutrophils – a specific type of white blood cell that helps fight infections
- Weight loss
- Dizziness
- Dysgeusia – change in taste
- Blurred vision
- Leucopenia – decrease in white blood cells
- Dehydration
- Asthenia- loss of energy; weakness
- Fever
- Cough
- Abdominal pain
- Swelling
- Hypokalemia – low potassium
- Hyperglycemia – elevated glucose (sugar) levels
- Headache

- Back pain
- Insomnia (difficulty sleeping)
- Pneumonia
- Blood electrolyte imbalance (that may increase risk of seizure)
- Cramps
- Increased blood pressure
- Creatinine Increased – increase of creatinine in the blood due to a reduction in kidney function, often related to dehydration

Common side effects (≥1-10%)**:**
In 100 people receiving selinexor about 1 to 10 people may have:

- Confusion
- Febrile neutropenia – Fever in the absence of a normal white blood cell response that may mean you have an infection
- Sepsis- potentially life-threatening complication of an infection
- Dry mouth
- Swelling and sores in the mouth
- Syncope – fainting
- Cognitive disorder
- Urinary Tract Infection
- Bronchitis (infection of the tubes that car air to and from the lungs)
- Eye disorders (cataracts, visual disturbances and dry eye)

Uncommon side effects (>0.1-1%):
In 1,000 people receiving selinexor about 1 to 10 people may have:

- Altered behavior
- Tumor lysis syndrome – potentially a life-threatening side effect caused by the rapid breakdown of tumor cells and may cause irregular heartbeat, kidney failure or abnormal blood test results which included elevated uric acid level, elevated serum potassium and phosphorus levels, and a decreased calcium level.
- Nose bleeds

Rare side effects (>0.01-0.1%):
In 10,000 people receiving selinexor about 1 to 10 people may have:

- Acute cerebellar syndrome – symptoms can include a sudden loss of coordination, balance, or slurred speech

Serious adverse effects (≥ 3 cases reported as related by the principal investigator)

- Acute kidney injury
- Aspartate aminotransferase increased – elevated liver enzyme level
- Bacteremia – bacterial infection in the blood

- Delirium – state of acute confusion
- Encephalopathy – brain disease, damage, or malfunction, which can present different symptoms that range from mild, such as some memory loss or subtle personality changes, to severe, such as dementia, seizures, or coma.
- General physical health deterioration
- Hyperglycemia – elevated blood sugar level
- Hypotension – low blood pressure
- Pulmonary embolism – pulmonary embolism occurs when a clump of material, most often a blood clot, gets wedged into an artery in your lungs.
- Pyrexia – fever
- Septic shock
- Upper respiratory tract infection

Side effects of selinexor (KPT-330) in COVID-19 patients (20 mg selinexor)

- In patients with severe disease, age ≥75 years and pre-existing illness, deaths were higher in the selinexor group compared to the placebo group. Treating doctors indicated that the deaths were due to COVID-19 and not related to study treatment. In patients with less severe disease and who were younger than 75 years of age, the deaths were comparable in patients who received selinexor or placebo.
- Other side effect such as i.e. nausea, vomiting, constipation, low sodium etc. were similar to what was observed in other patients treated with selinexor.

Side Effects of Docetaxel

Although not all of these side effects may occur, if they do occur they may need medical attention.

Check with your doctor immediately if any of the following side effects occur:

- **Very common side effects (>10%):** Burning, numbness, tingling, or pain in the arms, hands, legs, or feet
- swelling of the stomach, face, fingers, hands, feet, or lower legs
- unusual tiredness or weakness
- weight gain

Uncommon side effects (>0.1-1%):

- Black, tarry stools
- blood in the urine or stools
- cough or hoarseness (accompanied by fever or chills)
- difficult or labored breathing

- difficult or painful urination (accompanied by fever or chills)
- difficulty with swallowing
- dizziness
- fast heartbeat
- fever or chills
- hives or skin rash
- itching, puffiness, face, lips, or tongue
- lower back or side pain (accompanied by fever or chills)
- noisy, rattling breathing
- pinpoint red spots on the skin
- red, scaly, swollen, or peeling areas of the skin (severe)
- tightness in the chest
- troubled breathing while at rest
- unusual bleeding or bruising

Rare side effects (>0.01-0.1%):
- Chest pain or discomfort
- decreased blood pressure
- fast or irregular heartbeat
- increased blood pressure

Risks of Neutropenia Associated with Selinexor and Docetaxel
Some patients have experienced a decrease of a specific type of white blood cell called neutrophils (which help the body fight infections) after receiving selinexor + docetaxel. To help avoid this, you may be given a medication known as a myeloid growth factor. This decreases the possibility of infection by increasing the number of neutrophils in the blood. Your physician or healthcare provider will let you know if this is needed for your care.

Study Procedure/Intervention
Because of your participation in this study, you are at risk for the following side effects. You should discuss these with the researchers and your regular health care provider.

Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality
Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Risks to Sperm, Embryo, Fetus or Breast-fed Infant
Males: Being in this research may damage your sperm, which could cause harm to a child that you may father while on this study. If you take part in this study and are

sexually active, you must agree to use two forms of medically-acceptable birth control during the study and for **3 months** following the last dose of study treatment.

Medically-acceptable forms of birth control include:
(1) surgical sterilization (vasectomy), or
(2) a condom used with a spermicide (a substance that kills sperm).

Females: If you are part of this study while pregnant or breast-feeding an infant, it is possible that you may expose the unborn child or infant to risks. For that reason, pregnant and breast-feeding females cannot participate in the study. If you can become pregnant, a blood pregnancy test will be done (using 1 teaspoon of blood drawn from a vein by needle-stick), and it must be negative before you participate in this study. If you take part in this study and you are sexually active, you and any person that you have sex with must use two forms of medically-acceptable birth control (contraceptives) during the study and for **3 months** following the last dose of study treatment.

Medically-acceptable birth control (contraceptives) includes:
(1) surgical sterilization (such as hysterectomy or "tubes tied"),
(2) approved hormonal contraceptives (such as birth control pills, patch or ring; Depo-Provera, Implanon),
(3) barrier methods (such as condom or diaphragm) used with a spermicide (a substance that kills sperm), or
(4) an intrauterine device (IUD).
If you do become pregnant during this study, you must tell the researchers immediately.

Radiation exposure to a woman's reproductive organs may harm an embryo or fetus. Also, if radioactive materials are used for certain types of scans, harm may come to an embryo, fetus, or an infant who is breast feeding.

Pregnancy tests performed during the early stages of pregnancy do not always reveal pregnancy. Therefore, radiation exposure that includes the reproductive organs will be limited to the first ten days after a woman who can become pregnant has begun her most recent menstrual period. This is standard policy in clinics and hospitals within UT Southwestern. This policy applies unless there is an important medical reason requiring radiation outside this time frame

<u>Risks of Radiation – Diagnostic Test</u>
The radiation dose that you will get from diagnostic tests is medically indicated for your condition and it is the same that you would get if you were not involved in this research study.

<u>Risks of Computed Tomography (CT) Imaging:</u>
CT imaging is a painless procedure that is safe for most people. During the imaging, you will lie flat with your body in a long metal cylinder. Some people who fear closed spaces may be frightened during the procedure. You will be observed by the

operator(s) at all times during the procedure and can be assisted if necessary. If you request, you can be moved out of the machine. A small proportion of people develop short-lived reactions during the dye administration, including nausea, headache, hot flashes, and heart palpitations. These symptoms usually resolve on their own within minutes. A smaller group of people are actually allergic to the dye and may develop a rash, hives, difficulty breathing and in extreme cases, the person may stop breathing, the heart may stop, and the person may die. You will be closely monitored during the procedure and if any allergic reaction develops, you will be treated immediately.

Risk of MRI:

The imager makes a loud, banging noise while it is taking pictures. Patients may experience nervousness from confinement in a tight space (claustrophobia). Patients may feel uneasy or experience some discomfort and fatigue from lying still on a moving table for a long period of time. There is the possibility that patients may have a rare or previously unknown complication. There are no known effects from exposure to magnetic fields.

MRI may not be appropriate if patients have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:

- heart pacemaker, heart valve replacement, or aortic clips
- metal fragments in your eyes, skin, or elsewhere in your body
- brain clips or pieces of metal used in aneurysm surgery or intercranial bypass
- venous umbrella
- pieces of metal in the body resulting from work as a sheet-metal worker or welder
- clips placed in an internal organ
- prosthetic devices, such as middle ear, eye, joint, or penile implants
- joint replacement.
- hearing aid that cannot be removed
- neurostimulator
- insulin pump
- intrauterine device (IUD)
- shunts or stents
- metal mesh or coil implants
- metal plate, pin, screws, or wires, or any other metal implants

If you have a history of an implanted device or clips in your pelvis (involving your uterus or fallopian tubes) or under your skin, action as a contraceptive to prevent pregnancy, the MRI technologist will obtain specific information about the make and model of your implanted device to determine if it is safe for you to receive the MRI examination.

The contrast agent you will receive is FDA-approved and used routinely for MRI exams. It contains a material called Gadolinium (dye used to highlight organs or tissues during imaging). The injection of Gadolinium may cause discomfort like headache, nausea, strange taste, or coldness at site of injection. These symptoms occur in less than 1 out of 20 patients receiving Gadolinium and go away quickly. There is a small risk of a severe allergic reaction that can cause breathing difficulties and/or low blood

pressure; these symptoms are extremely rare (approximately 1 in 10,000 to 1 in 100,000 administrations). In the unlikely event you experience these symptoms, a physician and nursing staff will be available to evaluate and, if necessary, provide treatment.

People with severe kidney failure who receive Gadolinium (dye used to highlight organs or tissues during imaging) are at risk of developing a disorder called Nephrogenic Systemic Fibrosis (NSF). This disease can cause wide spread tissue scarring or hardening (fibrosis). In rare cases NSF can lead to lung and heart problems and cause death. If you have severe kidney failure and receive gadolinium, the risk of developing NSF is 1-5%. We may perform a blood test 30 days before your MRI to check how well your kidneys are working before you receive the Gadolinium. This test may be repeated closer to your MRI appointment if your medical condition has changed. If your kidneys are working at levels known to be at risk for NSF, you will not receive Gadolinium. You will not receive Gadolinium for research purposes if you have sickle cell disease (a disease of the blood cells).

Risks of Chest X-rays
The x-ray will provide information about the status of your lungs, heart and chest wall.

As part of this study you may have X-rays which involve exposure to radiation. The amount of radiation exposure you may receive from these standard diagnostic tests is considered small and will not adversely affect the treatment of your disease.

Risks of Blood Drawing
Risks associated with drawing blood from your arm include minimal discomfort and/or bruising. Infection, excess bleeding, clotting, and/or fainting also are possible, although unlikely.

You will have about 3 tablespoons of blood drawn at each visit because you are on this research study. The total amount of blood collected during the study depends on your length of participation.

Other Risks
There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

How will risks be minimized or prevented?
Prior to being treated on this study, your medical history and current medical conditions will be reviewed. You will be closely monitored at each cycle with blood tests and other physical assessments to ensure that any side effects are being monitored and treated appropriately. Medication may be given to reduce side effects. Dose levels may be minimized for safety.

What will my responsibilities be during the study?
While you are part of this study, the researchers will follow you closely to determine

whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' instructions.
- Let the researchers know if your telephone number or address changes.
- Store study materials and study drug in a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell your regular doctor about your participation in this study.
- Carry information about selinexor in your purse or wallet.
- Record the date and time on your study drug diary as directed by the study team
- Report to the researchers any injury or illnesses while you are on study even if you do not think it is related.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
Yes. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your health or safety.

What should I do if I think I am having problems?
If you have unusual symptoms, pain, or any other problems while you are in the study, you should report them to the researchers right away. Telephone numbers where they can be reached are listed on the first page of this consent form.

If you have a sudden, serious problem, like difficulty breathing or severe pain, go to the nearest hospital emergency room, or call 911 (or the correct emergency telephone number in your area). Tell emergency personnel about any medications you are taking, including any medications you are taking for this study.

What are the possible benefits of this study?
If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research.

We hope the information learned from this study will benefit others with non-small cell lung cancer in the future. Information gained from this research could lead to better treatment.

What options are available if I decide not to take part in this research study?
You do not have to participate in this research to receive care for your medical problem. Instead of being in this study, you have the following options:

- Other type of treatment, either in a different study or without a study

- Supportive care without chemotherapy
- Palliative care (meant to sooth symptoms without curing)

Please talk to the researchers or your personal doctor about these options.

Will I be paid if I take part in this research study?

There are no funds available to pay for parking expenses, transportation to and from the research center, lost time away from work and other activities, lost wages, or child care expenses. You will not be paid for taking part in this research study. Data obtained from this study may be used for commercial purposes. It is the policy of Karyopharm Therapeutics, the drug provider, not to provide financial compensation to you should this occur.

Will my insurance provider or I be charged for the costs of any part of this research study?

No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

Selinexor will be provided free of charge while you are participating in this study.

However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care. You will be charged in the standard manner for the procedures and doctor visits, standard or care medications, chemotherapy infusions, routine laboratory blood work and draws, MRI, CT-Scans, pregnancy tests; urinalysis, and tumor biopsy.

What will happen if I am harmed as a result of taking part in this study?

It is important that you report any illness or injury to the research team listed at the top of this form immediately.

Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas or Karyopharm Therapeutics Inc.

You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?

Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time.

If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

Your doctor is a research investigator in this study. S/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

If I agree to take part in this research study, can I be removed from the study without my consent?

Yes. The researchers may decide to take you off this study if:

- Your medical problem remains unchanged or becomes worse.
- The researchers believe that participation in the research is no longer safe for you.
- The researchers believe that other treatment may be more helpful.
- The sponsor-investigator, drug supplier or the FDA stops the research for the safety of the participants.
- The sponsor-investigator cancels the research.
- You are unable to keep appointments or to follow the researcher's instructions.

Will my information be kept confidential?

Medical information collected during this study and the results of any test or procedure that may affect your medical care may be included in your medical record. The information included in your medical record will be available to health care providers and authorized persons including your insurance company.

You should know that certain organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Karyopharm Therapeutics Inc.and its representatives.
- Simmons Comprehensive Cancer Center Biomarker Research Core Laboratory:
- Simmons Comprehensive Cancer Center Phase 1 Disease Oriented Team and Data and Safety Monitoring Committee
- The UT Southwestern Institutional Review Board.
- Representative of government agencies, like the U.S. Food and Drug Administration, involved in keeping research safe for people.
- Representatives of domestic and foreign governmental and regulatory agencies.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you.

At most, the Web site will include a summary of the results. You can search this Web site at any time.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Are there procedures I should follow after stopping participation in this research?
Yes. If you, the researchers, or the sponsor-investigator stops your participation in the research, you may be asked to do the following:

- Let the researchers know immediately that you wish to withdraw from the research.
- Return to the research center for tests that may be needed for your safety.
- Return any unused study materials, including empty containers.
- Discuss your future medical care, if any, with the researchers and/or your personal doctor.

Whom do I call if I have questions or problems?
For questions about the study, contact Dr. David Gerber at 214-648-4180 during regular business hours and at 214-645-4673 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Medical Center Human Research Protection Program (HRPP) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.
- You understand that a copy of this signed consent document, information about this study, and the results of any test or procedure that may affect your medical care, may be included in your medical record. Information in your medical record will be available to health care providers and authorized persons including your insurance company.

_____
Name of Participant (Printed)

_____ _____ _____ AM / PM
Signature of Participant Date Time

_____
Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM
Signature of Person Obtaining Consent Date Time

Witness:

I attest that the information in the consent form was accurately explained to, and apparently understood by the patient or the patient's legal authorized representative, and that informed consent was freely given by the patient or the patient's legal authorized representative.

_____	_____	_____AM / PM
Name of Witness (Printed)	Date	Time
_____	_____	_____AM / PM
Signature of Witness	Date	Time