Lesson Summary:

Students complete a webquest to learn about clinical trials as homework the night before the lesson. In class students will explore the relationships between patients, doctors, medical researchers, drug companies, and the IRB in a role-play as an individual with relapsed leukemia entering a clinical trial. Students will then perform a close read of a recent article on the effectiveness of clinical trials. As a final formative assessment students will practice designing their own clinical trials using a guided student worksheet.

Student Learning Objectives:

The student will be able to...
1. Differentiate between the four phases of a clinical trial
2. Design a scientific experiment
3. Recognize the importance of placebos and control groups in a scientific experiment

Standards:

| SC.912.L.16.8 | SC.912.N.1.3 | SC.912.N.2.4 |
| SC.912.L.16.10 | SC.912.N.1.4 | SC.912.N.2.5 |
| SC.912.N.1.1  | SC.912.N.1.6 | SC.912.N.4.1 |
| SC.912.N.1.2  | SC.912.N.1.7 |

Materials:

- Computers with internet access
- Copies of student webquest (1 copy per student)
- Copies of New York Times Article: Do Clinical Trials Work? (1 copy per student)
- Copies of Student Page: Close Reading Guide for Do Clinical Trials Work? (1 copy per student)
- Copies of Student Page: Clinical Trial Design (1 copy per student)
- Clinical Trials Web Cards
- Ball of string
Background Information:

Clinical trials are research studies that involve humans to test new ways to prevent, detect, diagnose, or treat cancer and other diseases. Clinical trials are conducted in phases. The trials at each phase have a different purpose and help scientists answer different questions:

In Phase I trials, researchers test an experimental drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.

In Phase II trials, the experimental study drug or treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety.

In Phase III trials, the experimental study drug or treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely.

In Phase IV trials, post marketing studies delineate additional information including the drug’s risks, benefits, and optimal use.

Every clinical trial has a protocol that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. National and international regulations and policies have been developed to protect the rights, safety, and well being of people who take part in clinical trials and to ensure that trials are conducted according to strict scientific and ethical principles. Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, or whether to continue participating in it. Many states require that insurance companies cover the costs of routine care for people taking part in a clinical trial. In other states, voluntary agreements between the states and insurance companies include such a provision. However, coverage varies by state, by health insurance plan, and by type of clinical trial. From http://www.cancer.gov/cancertopics/factsheet/Information/clinical-trials

Advance Preparation:

- Teacher should read through the entire lesson, student pages, and familiarize himself with the clinicaltrials.gov site.
- Read the article New York Times article Do Clinical Trials Work? and be prepared to address any student questions/misconceptions about the piece.
- Make copies of webquest, close reading guide and clinical trial design student pages for each student.
- Prepare Clinical Trials Web cards by printing them on colored paper, cutting between the “speaker paragraphs” and possibly laminating for future use.

Procedure and Discussion Questions with Time Estimates:

1. Assign the clinical trials webquest as homework the night before the lesson. Alternatively, if using the Webquest during class, allow approximately 30 minutes for completion.
2. (8-10 min) Instruct students to stand/sit in a circle. Pass out the Clinical Trials Web cards randomly to students, ensuring the cards are equally distributed amongst the circle of students (not all clumped at one end of the circle, for example), and that the three “John” cards go to the same student. Students must determine the order of events and in the process will see how all the people involved are interconnected. The web should start and end with John.
a. To begin the activity, students who have the cards should simply read the title, so all the students in the class know who the “players” in the Clinical Trial Web are.
b. As indicated the web should begin with John I, who will hold the end of the ball of string while he reads his card.
c. The class can then decide who the next likely person in the story should be.
d. The ball of yarn should be passed from “John”, to the next card holder (“John” keeps the end of the string, the next student will hold the piece of the continuous string in front of them and so on, creating the visual web)
e. See the teacher page for the suggested order. The students may come up with a different order, which is fine, just debrief with them at the end.

3. **(5 min)** Review student answers to the homework questions in the webquest. Make sure students understand the difference between a blind and double blind trial, as well as the purpose of a placebo.

4. **(15-20 min)** Students will complete a close read of article Do Clinical Trials Work? following the guided student page. **Instructor Note:** There are various “styles” of close reading; we have chosen to include a simple guide for close reading often used in the science classroom as a support activity for English and reading instruction.
   a. Pass out the Student Page: Do Clinical Trials Work? and a copy of the article to each student. Instruct students to follow the guided process on the handout, answering questions as needed.
   b. After the students complete the second read of the article answer invite them to share the questions they generated about the article, annotated as the ?, also allow students to share their “surprise you” ! annotates as well, if time permits. Allow group discussion, so the students can attempt to answer each other’s questions, correcting misconceptions where necessary. **Instructor Note:** Depending on your students’ reading level a group read of the article may be beneficial prior to students completing the reflective writing portion of the assignment.
   c. Instruct students to complete the reflective writing portion of the Student Page, using support from the text, as well as factual information from the webquest, in their answer.

5. **(15 min)** Students will practice designing scientific experiments from given scenarios.
   a. Divide the class into four groups and have each group design one phase of the clinical trial, as indicated on the Student Page: Clinical Trials Design.
   b. Discuss the answers as a whole class. Make sure to highlight the goal of each phase of the trial
   c. Lastly, instruct students to complete the remaining two design questions in class, or as homework, for additional practice and to demonstrate mastery.

**Assessment Suggestions:**

- Teachers could collect the webquest worksheet to assess student knowledge of clinical trials.
- Instruct students to create a concept map showing the relationship between the individuals portrayed in the Clinical Trials Web activity.
- Teachers should collect the experimental design worksheet to assess student’s understanding of placebos, control groups and the importance of well-designed experiments.

**Resources**

- [www.clinicaltrials.gov](http://www.clinicaltrials.gov)
- [www.cancer.gov](http://www.cancer.gov)
Notes:

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Clinical Trials Webquest

Go to http://www.cancer.gov/cancertopics/factsheet/Information/clinical-trials and answer the following questions:

1. Fill out the table below describing what happens in each phase of a clinical trial.

<table>
<thead>
<tr>
<th>PHASE</th>
<th>DESCRIPTION OF WHAT HAPPENS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Clinical</td>
<td>• Lab and animal studies</td>
</tr>
<tr>
<td>Phase I</td>
<td></td>
</tr>
<tr>
<td>Phase II</td>
<td></td>
</tr>
<tr>
<td>Phase III</td>
<td></td>
</tr>
<tr>
<td>Phase IV</td>
<td></td>
</tr>
</tbody>
</table>

2. List and describe the five most common types of clinical trials.

3. What are eligibility criteria and why are they important?

4. Describe the role of an Institutional Review Board (IRB) in a clinical trial. Who makes up the Institutional Review Board?
5. What is informed consent? What happens if you want to leave a clinical trial before the end of the study?

6. Describe the risks and benefits of participating in a clinical trial.

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>RISKS</th>
</tr>
</thead>
</table>

7. Explain randomization and why it is important in clinical trials?

8. Who is responsible for the costs associated with clinical trials?

9. Go to [http://clinicaltrials.gov/ct2/info/glossary](http://clinicaltrials.gov/ct2/info/glossary) and define the following terms

Randomized Trial:

Blind:

Double Blind:

Placebo:
Clinical Trials Webquest

Go to http://www.cancer.gov/cancertopics/factsheet/Information/clinical-trials and answer the following questions:

1. Fill out the table below describing what happens in each phase of a clinical trial.

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<td>Phase I</td>
<td>• Safety study</td>
</tr>
<tr>
<td></td>
<td>• 20-80 people</td>
</tr>
<tr>
<td>Phase II</td>
<td>• Safety study</td>
</tr>
<tr>
<td></td>
<td>• Identify side effects</td>
</tr>
<tr>
<td></td>
<td>• Measure effectiveness</td>
</tr>
<tr>
<td></td>
<td>• 100-200 people</td>
</tr>
<tr>
<td>Phase III</td>
<td>• Measure effectiveness</td>
</tr>
<tr>
<td></td>
<td>• Monitor side effects</td>
</tr>
<tr>
<td></td>
<td>• 1,000-3,000 people</td>
</tr>
<tr>
<td>Phase IV</td>
<td>• Monitor long-term side effects</td>
</tr>
</tbody>
</table>

2. List and describe the five most common types of clinical trials.

**Teacher note: There are different types of trials for other diseases.**

**Treatment:** These trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer.

**Prevention:** These trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer.

**Screening:** These trials test new ways of finding cancer early.

**Diagnostic:** These trials study new tests or procedures that may help identify, or diagnose, cancer more accurately.

**Quality of life or supportive care:** These trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials.

3. What are eligibility criteria and why are they important?

Eligibility criteria are guidelines for who can and cannot participate in the trial. Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested (the independent variable) and not to other factors.

4. Describe the role of an Institutional Review Board (IRB) in a clinical trial. Who makes up the Institutional Review Board?

The IRB reviews all aspects of a clinical trial to make sure that the rights, safety, and well-being of trial participants will be protected. An IRB must have at least five members, including one scientist, one person who is not a scientist, and one person who is not affiliated with the institution where the trial is taking place and who is not an immediate family member of someone who is affiliated with that institution.
5. What is informed consent? What happens if you want to leave a clinical trial before the end of the study?

_Informed consent is a process through which people 1) learn the important facts about a clinical trial to help them decide whether or not to take part in it, and 2) continue to learn new information about the trial that helps them decide whether or not to continue participating in it. Anyone can choose to leave a trial at any time._

6. Describe the risks and benefits of participating in a clinical trial.

<table>
<thead>
<tr>
<th>BENEFITS</th>
<th>RISKS</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Access to promising new interventions that are generally not available outside of a clinical trial.</td>
<td>• The new intervention being studied may not be better than standard therapy, or it may have harmful side effects.</td>
</tr>
<tr>
<td>• The intervention being studied may be more effective than standard therapy.</td>
<td>• Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.</td>
</tr>
<tr>
<td>• Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.</td>
<td>• Health insurance may not cover all patient care costs in a trial.</td>
</tr>
<tr>
<td>• The results of the trial may help other people who need cancer treatment in the future.</td>
<td></td>
</tr>
<tr>
<td>• Trial participants are helping scientists learn more about cancer</td>
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</tr>
</tbody>
</table>

7. Explain randomization and why it is important in clinical trials?

_The trial participants are assigned to their individual groups by random assignment, or randomization. Randomization helps ensure that the groups have similar characteristics. This balance is necessary so the researchers can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups._

8. Who is responsible for the costs associated with clinical trials?

_The costs of care for people participating in a clinical trial fall into two general categories: 1) routine care costs and 2) research costs. Routine care costs are costs associated with treating a person’s cancer whether or not they are in a trial. These costs are usually covered by health insurance, but requirements vary by state and type of health plan. Research costs are costs associated with conducting a clinical trial; these costs may include the costs of extra doctor visits, extra tests, and procedures that are required for the trial but would not be part of routine care. Research costs are usually covered by the organization that sponsors the trial. The National Institute of Health (NIH) funds many research trials, particularly in the early phases before drug companies invest in the project._

9. Go to [http://clinicaltrials.gov/ct2/info/glossary](http://clinicaltrials.gov/ct2/info/glossary) and define the following terms

Randomized Trial: A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial. Occasionally placebos are utilized

Blind: A randomized trial is “Blind” if the participant is not told which arm of the trial he is on. A clinical trial is “Blind” if participants are unaware of whether they are in the experimental or control arm of the study; also called masked.

Double Blind: A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study.

Placebo: A placebo is an inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment’s effectiveness.
Clinical Trials Web Activity

Teacher Instructions: See procedure above. Salary amounts have been included for most positions to encourage science career discussion. The intended order for the cards is listed below:

John Part I • Primary Care Physician • Oncologist • University of Florida Principal Investigator • Drug Company CEO • Clinical Trial Nurse • John Part II • IRB Member • Lab Tech • John Part III

<table>
<thead>
<tr>
<th>John Part I ($45,000 Manager of a Locally Owned Hardware Store)</th>
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</thead>
<tbody>
<tr>
<td>I was diagnosed in August 2011 with AML. It didn’t fit into a subtype according to my doctors and I was only one of three people known in the world to have these particular chromosomal changes. I underwent intense chemotherapy and a bone marrow transplant. I was in remission successfully by October 2012 and finished chemo in December 2012. Ever since I entered remission, I've been getting stronger and stronger. My health has been better than I ever remember and I even started going to the gym. The past few weeks though I’ve noticed changes, I've been bruising easily, I've been out of breath walking the shortest distance and I’m tired way more than usual. Am I just imagining these symptoms or could they point to a relapse? I keep trying to tell myself that they are just phantom symptoms because it's coming up to my one-year remission anniversary next week.</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>John Part II</th>
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<tbody>
<tr>
<td>I received the results of my bone marrow biopsy and my AML is back. A nurse who works in the oncologist's office told me about a clinical trial that I qualify for. I’m a nervous because this is a Phase I clinical trial and there could be negative side effects, but at this point it's my only option. Even if this new drug doesn't help me, at least I will be helping people in the future and contributing to scientists' knowledge of AML.</td>
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</table>

<table>
<thead>
<tr>
<th>John Part III</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have been part of the clinical trial for 3 months now and so far things look good. My blood cell counts are returning to normal. There is no guarantee that the drug will continue to work and I might relapse again, but I remain optimistic.</td>
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</table>

<table>
<thead>
<tr>
<th>Primary Care Physician ($180,000)</th>
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</thead>
<tbody>
<tr>
<td>John came into my office complaining of shortness of breath and bruising. I first saw John in August of 2011 when he came in complaining of the same symptoms. As John has only been in remission from AML since October of 2012, I immediately suspected the worst...John’s AML was back. I recommended he see an AML expert again.</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Lab Tech ($32,000)</th>
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<tbody>
<tr>
<td>My job is to process patient samples and measure patient's complete blood count (CBC). I sometimes have to work late or come in on weekends, because samples arrive at various times and must be processed immediately. I report the results to the principal investigator. Even though I never see the patient, I still hope that what I am doing makes a difference. I am excited because the patients' blood cell counts in this trial seem to be returning to normal.</td>
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</tbody>
</table>
Oncologist ($295,000)
AML is the most common type of acute leukemia. More than 11,900 new cases occur in the United States each year, mostly in older adults. The average age of a person with AML is 65 years. The symptoms of AML are caused by low numbers of healthy blood cells and high numbers of leukemia cells. White blood cells fight infection. Low numbers can lead to fever and frequent infections. Red blood cells carry oxygen throughout the body. Low numbers can lead to anemia — feeling tired or weak, being short of breath and looking pale. Platelets control bleeding. Low numbers can lead to easy bleeding or bruising and tiny red spots under the skin (petechiae). High numbers of leukemia cells may cause pain in the bones or joints.

I was very concerned when John came back to my office. Five-year survival varies from 15–70%, and relapse rate varies from 33–78%, depending on the subtype of AML. Patients with relapsed AML post bone marrow transplant, may be offered treatment in a clinical trial, as conventional treatment options are limited. I’m going to see if there are any clinical trials that John will qualify for.

University of Florida Primary Investigator (MD-PhD) ($165,000)
I have been working on AML for the last 10 years. I recently read an article about pazopanib. VEGF is a chemical signal produced by cells that stimulates the growth of new blood vessels. When VEGF is overexpressed, it can contribute to disease. Solid cancers need an adequate blood supply or they will not be able to grow. Hence, cancers that can express VEGF are able to grow and metastasize. Pazopanib has already been approved to treat renal cancer and I wondered if it could be used to treat AML. I began tests on in vitro AML cell lines and then moved into experiments with mice. I have obtained some very promising results and am now looking for funding to start a phase I clinical trial.

Sanofi (drug company) CFO Chris Viehbacher (Salary $4.71 million)
The uncertainties…Can you get a drug approved? What's it going to pay? “Research and development is either a huge waste of money or too, too valuable. It's not really anything in between. The reality is the best people who have great ideas in science don't want to work for a big company…. So, in other words, if you want to work with the best people, you’re going to have go outside your own company and work with those people …I’ve decided that our company should start working with more outside companies, startup biotechs, with universities.” I just read a paper about a researcher at the University of Florida who might have a promising new treatment for AML.

Institutional Review Board (IRB) Member (salary is NOT paid from clinical trial money to prevent bias)
I have been asked to serve as an IRB member for a clinical trial testing the effect of a new drug on AML patients. I will make sure that all the informed consent forms are written and filled out properly. Before, during and after the trial I will be reviewing all protocols and make sure they are implemented correctly to ensure patient safety and produce valid results.

Clinical Trial Nurse (CTN) ($57,000)
My job is to help identify qualified patients for clinical trials. I explain the protocols to patients and make sure they understand all potential risks and benefits. During the trial, I work to identify trends in side effects and work with the principal investigator to develop and evaluate patient management strategies. I also work with caregivers, primary care physicians and other hospital staff to ensure the best patient care and produce reliable results.
Close Reading Guide for “Do Clinical Trials Work?”

How to Close Read:
1. **First Reading**: Read the article in completion, to determine the gist of the article.
2. **Second Reading**: Carefully re-read the article writing a 2-3 word summary to the left of each paragraph and annotating other details to the right of each paragraph, using the following guide:

   ![Close Reading Guide]

   **A Note to Students about Annotating:**
   You might not find it necessary to complete every one of the suggested annotations on the guide for each paragraph.

   Remember, you are using the annotations to draw out the key points of the article, as well as focus on your interests and possible areas of confusion, which you will discuss with your teacher and your classmates before your final reflection on the article.

3. **Reflective Writing**: Consider the following quote from the article you just read:

   “Listen, it’s not lost on anybody that about 95 percent of drugs that enter clinical testing fail to ever get approved,” says Dr. Barron. “It’s not hard to imagine that at least some of those might have failed because they work very, very well in a small group. We can’t continue to have failures due to a lack of appreciation of this heterogeneity in diseases.”

   Using evidence from the article and your knowledge of how clinical trials are run from the webquest you completed, respond to the following prompt, using formal paragraph structure:

   **Why is it necessary to have regulations and strict controls in clinical trials? What are some weaknesses in the current clinical trial model that lead to the failure of 95% of the drugs that undergo clinical testing? Do you think the current clinical trial model should be changed? Why or why not?**
Clinical Trial Design

Combrestatin was discovered in the 1970s from the South African Bush Wallow. Combrestatin breaks down microtubules and prevents spindle formation.

1. What would be the effect of combrestatin on acute myeloid leukemia (AML) cells?

2. Design Phase I, II, III and IV double blind clinical trials to test the effects of combrestatin on in vitro AML cells. In your experiment be sure to include the following:

   Independent Variable: ____________________________

   Dependent Variable: ____________________________

   Experimental Group (Arm): ____________________________

   Control Group (Arm): ____________________________

Clearly state the goal for each phase of the clinical trial:

Phase I:

Phase II:

Phase III:

Phase IV:
Use the in class model and your knowledge of experimental design to complete the following clinical trial proposals:

Pazopanib is used to treat advanced renal cell carcinoma (RCC, a type of cancer that begins in the cells of the kidneys) in adults. Pazopanib is in a class of medications called tyrosine kinase inhibitors. It works by slowing or stopping the spread of cancer cells. Researchers want to see if pazopanib is also effective on AML cells. Design an experiment to test the effects of pazopanib on in vitro AML cells.

Scientists are studying the effects of bevacizumab (an angiogenesis inhibitor) on colon cancer. They want to determine if adding bevacizumab to chemotherapy is more effective than chemotherapy alone. Design a Phase III clinical trial to determine which treatment method is more effective. Would this study be more effective as a double blind study? Why or why not?
Clinical Trial Design

Combrestatin was discovered in the 1970s from the South African Bush Wallow. Combrestatin breaks down microtubules and prevents spindle formation.

1. What would be the effect of combrestatin on acute myeloid leukemia (AML) cells?

*Chromosomes would no longer be able to separate into sister chromatids, thus no viable cells would be produced from the cycles of cellular division under Combrestatin conditions.*

2. Design Phase I, II, III and IV double blind clinical trials to test the effects of combrestatin on in vitro AML cells. In your experiment be sure to include the following:

- **Independent Variable:** combrestatin
- **Dependent Variable:** CBC count (number of leukemia cells)
- **Experimental Group (Arm):** Group that receives combrestatin (or group that receives combrestatin and standard care)
- **Control Group (Arm):** Group that receives the standard care

Clearly state the goal for each phase of the clinical trial.

**Phase I:** Twenty patients would be enrolled in the Phase I trial. In the experimental group, ten of the patients would receive combrestatin and standard AML therapy. In the control group the other ten patients would receive only standard AML therapy. In order to make this a blind trial, the nurses would not know which patients were in each group or what medication they were administering (combrestatin or the placebo). The number of leukemia cells in a blood sample would be counted before the trial began and then each week for every patient for six months. In this trial patients would receive low doses of combrestatin because the purpose of a phase I trial is to determine if the drug is safe for human use. In order to control as many variables as possible (and make sure any differences between the two groups were due to the combrestatin and not any other factors) the patients in the two groups would have approximately the same age, gender and race distribution.

**Phase II:** If the drug was found to be safe in the Phase I trial, then a phase II trial would be conducted. Two Hundred patients would be enrolled in the Phase II trial. In the experimental group, 100 of the patients would receive combrestatin and standard AML therapy. In the control group the other 100 patients would receive only standard AML therapy. In order to make this a blind trial, the nurses would not know which patients were in each group or what medication they were administering (combrestatin or the placebo). The number of leukemia cells in a blood sample would be counted before the trial began and then each week for every patient for six months. This trial would increase the dose of combrestatin to determine its efficacy and side effects. In order to control as many variables as possible (and make sure any differences between the two groups were due to the combrestatin and not any other factors) the patients in the two groups would have approximately the same age, gender and race distribution.

**Phase III:** If the drug was found to be safe, effective, and did not produce severe side effects in the Phase II trial, then a phase III trial would be conducted. One thousand patients would be enrolled in the Phase III trial. In the experimental group, 500 of the patients would receive combrestatin and standard AML therapy. In the control group the other 500 patients would receive only standard AML therapy. In order to make this a blind trial, the nurses would not know which patients were in each group or what medication they were administering (combrestatin or the placebo). The number of leukemia cells in a blood sample would be counted before the trial began and then each week for every patient for six months. This trial continues to determine its efficacy and side effects of combrestatin. In order to control as many variables as possible (and make sure any differences between the two groups were due to the combrestatin and not any other factors) the patients in the two groups would have approximately the same age, gender and race distribution.
Phase IV: If the drug was approved by the FDA and on the market, the drug company might conduct a phase IV trial. An even greater number of patients would be enrolled in the Phase IV trial. The purpose of the phase IV trial would be to gain additional information about the drugs side effects, benefits and optimal uses. There would be no control arm.

Use the in class model and your knowledge of experimental design to complete the following clinical trial proposals:

Pazopanib is used to treat advanced renal cell carcinoma (RCC, a type of cancer that begins in the cells of the kidneys) in adults. Pazopanib is in a class of medications called tyrosine kinase inhibitors. It works by slowing or stopping the spread of cancer cells. Researchers want to see if pazopanib is also effective on AML cells. Design an experiment to test the effects of pazopanib on in vitro AML cells.

Independent Variable: pazopanib
Dependent Variable: number of cells that die (or conversely the number of living cells at the end of the experiment)
Experimental Group (Arm) cells that receives pazopanib
Control Group (Arm) cells that receive more media
Constants: cells grown in same media, cells incubated at the same temperature, cells grown in the same type of containers, receive the same amount of light

In this phase III trial four cell cultures each containing 4 million cells/ml (the same amount of cells) will be prepared. The cultures will contain the same media, incubated at the same temperature, be the same size and receive the same amount of light. Two of the cell cultures will be given 2µL of pazopanib everyday for one week and the two other cultures will be given 2 µL of media. At the end of the week the number of cells alive in each culture will be measured using the appropriate assay.

Scientists are studying the effects of bevacizumab (and angiogenesis inhibitor) on colon cancer. They want to determine if adding bevacizumab to chemotherapy is more effective than chemotherapy alone. Design a Phase III clinical trial to determine which treatment method is more effective. Would this study be more effective as a double blind study? Why or why not?

Independent Variable: bevacizumab
Dependent Variable: amount of cancer cells in biopsy sample
Experimental Group (Arm) Patients that receives bevacizumab and chemotherapy
Control Group (Arm) Patients that receive only chemotherapy
Constants: Patients would all have the same stage of colon cancer, be between the ages of 35-55 and approximately 50% of the subjects in each group would be female and 50% would be male.

One thousand patients would be enrolled in the Phase III trial. In the experimental group, 500 of the patients would receive bevacizumab and chemotherapy. In the control group the other 500 patients would receive only chemotherapy. The number of cancer cells in biopsy would be counted before the trial began and then each week for every patient for six months. In order to control as many variables as possible (and make sure any differences between the two groups were due to the combrestatin and not any other factors) the patients in the two groups would have approximately the same age, gender and race distribution.

I would know if the bevacizumab and chemotherapy were more effective then chemotherapy alone if the patients in the experimental group had a more significant reduction in the % of cancer cells in their biopsy samples than those patients in the control group who just received chemotherapy.

This study would be more effective as a double blind study, because it would eliminates bias and produces more objective results, since the expectations of the doctors, nurses and the patients about the experimental drug do not affect the outcome.
Notes: