Cancer Biomarkers

1. A biomarker is a biological molecule that is found in blood, other body fluids, or tissues indicating a normal or abnormal process, or a condition or disease.

Questions answered by biomarkers

2. Diagnostic : These help diagnose conditions, as in the case of identifying early stage cancers.
3. Prognostic: To forecast how aggrieve a condition is, as in the case of determining a patient's ability to fare in the absence of treatment.
4. Predictive: To predict how well a patient will respond to treatment
5. Pharmacodynamics: Whats the optimal dose for my body
6. Recurrence: Will the cancer return.

Use of Biomarkers in Cancer research

1. Identifying cancer drug targets
2. Studying the effects of drugs/

treatment(finding endpoints- measurable signs whether a treatment or drug is working)

Identifying Drug Targets

1. For instance in 1960s, researchers discovered that the majority of the patients with CML have a particular genetic abnormality called Philadelphia chromosome (BCR ABL)
2. In such patients, this abnormality drives leukemia(excess WBCs)
3. Pharmaceutical companies ere eventually able to develop imatinib, a powerful drug that effectively inhibited this protein and significantly decreases the production of cells containing BCR-ABL.

Finding Endpoints

1. Endpoint biomarkers help find the effects of a drug on cancer progression and patient survival.

Examples:
circulating tumor cells (CTCs)
circulating tumor DNA (CtDNA)
These are proportional to the number of tumor cells present in the blood, affected by drug
These also provide an idea of tumor progression and metastasis, affected by drug

Are all cancers equally deadly?

1. If the symptoms of cancer appear early in the natural course of the disease, it's generally curable. First, if the cancer is detected before it has escaped the reach of a surgeons knife it can be removed. Second, even if it cant be cut out(most blood cancers) if cancer only had a few years to accumulate mutations, it is less likely to have acquired mutations that will make it unresponsive to therapy.
2. If you don't feel sick until very late in the process, as in pancreatic cancer, it is likely to have acquired mutations, and no matter what treatment you try, you are unlikely to be cured of the disease. The result, in pancreatic cancer, there is a 7% 5-year relative

survival rate.

Why are solid cancers generally more lethal than blood cancers of immune cells?

1. There are more checks in our cells in place to prevent solid cancers than there are to prevent cancers of the immune system.
2. You typically feel sick early with blood/immune cell cancers when the cells have fewer faults. Therefore, when a patient presents with leukemia or lymphoma, there are a fewer faults in their cells, so there is a higher chance that the cancer will respond to the treatment.
3. In contrast, for solid cancers, too many mutations have to happen before making the patient feel sick. Solid cancers, in general, are often diagnosed late in the course of the disease.
4. For tumors with fewer faults we have a

better chance of cure through therapy. However, we need to consider how to ensure that tumors with many faults respond to drugs, as more faults can make cells insensitive to treatments. Of course, if the tumor hasn't metastasized, surgery can effectively avoid this problem.

What treatment is effective for a faulty tumor?

1. Highly faulty tumors have more abnormalities to be detected by the immune system and get cleared. Immunotherapy activates patient's own immune system with drugs. Hence, faulty tumors respond better to immunotherapy.

How can skin cancers be so common, yet highly survivable?

1. This is because basal and squamous cell carcinomas of the skin are so

common, they are often excluded from studies and cancer registries, such as the database to produce most of table.

2. Approximately 5.4 million skin cancers(other than melanoma) are diagnosed cancers. However, only about 2K Americans die from them each year because the vast majority are detected before they metastasize and can e removed.

Why is melanoma so highly survivable?

1. Melanoma is the fourth most survivable cancer.
2. It is one of the most mutated of all cancers. Those mutations are legacy of UV light and smoking.
3. Melanoma metastasises fast and, unlike most cancers, can spread anywhere in the body.
4. However because melanomas are visible on the skin, we can often see them in the mirror and catch them early. The result is that 84% of

melanomas are diagnosed before they metastasize and can be cured surgically, with a 98% 5 year relative survival rate.

Why do patients with hormone-dependent cancer survive longer?

1. Although hormones help cells grow/ divide, it is very slow. Some cancers are so slow- growing that we can live them without killing us- they are indolent(not wanting to work/ lazy). This is famously true for bth prostate cancer and thyroid cancer.
2. In USA, autopsy studies have replaced that 80% of the mean over the age of 70 have some cancer hanging out in their prostates, but few of them will die from this. These are extensive screening programs for both breast and prostate cancer.
3. Small nodules of cancer in thyroid are so common that they are considered normal. Autopsy studies have found

minute nodules of thyroid cancer in 8% of the general population, however, it rarely discovers a way to generate blood vessels to feed itself, so it never gets enough food to grow large to harm us.

What is the inherent bias of cancer screening programs?

1. They prefrentially find the slowest growing tumors because those are the ones that have been hanging around for years, making them available to be detected.
2. In contrast, fast growing tumors can develop and make us sick before we even have a chance to detect them through regular screening. This implies that many of the cancers we detect, would never cause us harm even if they were left untreated. The survival statistics in the table are inflated by indolence.

What are the statistics about cancer in young people?

1. Testicular cancer, Hodgkin lymphoma and the childhood cancers are all detected at young ages. These cancer get less time to grow and have lesser faults. Because success of many treatments depends on the extent of genetic faults in cancer cells, these are often curable.

Are childhood cancers different from adult cancers?

1. Most adult cancers are linked to environmental factors or lifestyle choices that lead to the development of faulty cells. However, childhood cancers are rarely caused by external factors, except for exposure to radiation and infectious agents earlier in life(during development in the

mother's womb).
2. Childhood cancers are also associated with inherited mutations or genetic conditions, which are less common in adult cancers. The causes of many childhood cancers are unknown.

Cancer clinical trial

1. Clinical trials are also done to test ways to prevent cancer, diagnose cancers, improve the quality of life of cancer patients and assess the risk of developing cancers from inherited mutations.

Important considerations of clinical trials

1. Patient selection (inclusion and exclusion criteria)
2. Patient consent and ethical guideline compliance
3. Maintainice of strict confidentiality
4. Randomized design

Steps of Clinical Trials

PHASE	PURPOSE	TIME
PRE-CLINICAL	Assess safety and biological activity in the laboratory and in animal models	3.8 YEARS
PHASE 1	Determine what dosage is safe and how treatment should be given	10.4 YEARS
PHASE 2	Evaluate effectiveness and look for side effect	
PHASE 3	Determine whether the new treatment is a better alternative to the current standard	
POST-CLINICAL TRIALS	Follow individuals taking the drug to look for side effects and adverse events	1.5 YEARS