

Dissertation Presentation:

“Study on disease overview and market dynamics of therapy area oncology in the U.S.”

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INTRODUCTION

- Oncology is a branch of medicine that deals with the prevention, diagnosis and treatment of cancer
- Cancer is the second leading cause of deaths in the U.S and some of the common cancers include bladder cancer, liver cancer, leukemia, breast cancer, lung cancer etc
- Due to advancement in science & technology, diagnosis is possible at a quite early stage
- With the increase in number of cases of cancer, market of oncology is also expanding at a faster pace
- Increased knowledge about the disease is also helping in the development of new types of drugs
- Big companies are launching new drugs with better efficacy and many small players are also entering the market and thus the market for the cancers is expanding at a rapid pace

RATIONALE OF STUDY

- Therapy Area Overview (TAO) provides the comprehensive view of a disease, its etiopathogenesis, treatment and market available for it. This information is used in internal decision making to help ZS identify its prospective clients. TAO also aids in forecasting for a disease by assessing the opportunity areas and competitive landscape for that disease. It could also be leveraged to provide business solutions to various pharmaceutical companies thereby helping them plan the launch of their drugs in the market
- Oncology has remained the interest area for various pharmaceutical companies as cancer is the second leading cause of deaths in the U.S. In recent decades, tremendous progress has been made in the fight against cancer. Advances in molecular and genomic research have revealed underlying complexities and provided insights into cancer. Currently, more than 800 medicines and vaccines are in clinical testing for cancer. Despite these advancements, huge unmet need still exists in this therapy area making it an attractive market for the pharmaceutical companies.

- Some of the common cancer includes Hepatocellular carcinoma which is the third leading cause of cancer deaths worldwide; Bladder cancer which is the 9th leading cause of cancer worldwide and occurs mainly due to tobacco; Liver metastases which account for 95% of all hepatic malignancies in the U.S and Acute lymphocytic leukemia which accounts for 0.3% of all diagnosed cancers

Research Question

- What is the disease overview and current market dynamics for primary & metastatic liver cancer, bladder cancer and acute lymphocytic leukemia in the U.S?

STUDY OBJECTIVES:

- To create Therapy Area Overview (TAO) of primary & metastatic liver cancer, bladder cancer and acute lymphocytic leukemia which includes their clinical overview, epidemiology and disease management
- To study the market dynamics of these cancers in the U.S

Methodology

- **Study design:** Systematic review and secondary desk research for primary & metastatic liver cancer, bladder cancer & acute lymphocytic leukaemia based on the following parameters: clinical overview, diagnosis, treatment, epidemiology and market dynamics
- **Data sources:** Various research papers and articles on primary & metastatic liver cancer, bladder cancer and leukemia and publically available secondary research data source like Medscape, Epocrates, WebMD, SEER (Surveillance, Epidemiology and End Result), American Cancer Society, NCCN guidelines (National Comprehensive Cancer Network), obroncology; ZS specific data sources*
- **Data analysis:** Data for market dynamics is analyzed using pivot tables and charts

A. CLINICAL OVERVIEW

I. Hepatocellular carcinoma (HCC)

- HCC is a primary malignancy of the liver and occurs predominantly in patients with underlying chronic liver disease and cirrhosis

Etiology & Risk factors

Causes are not completely understood but risk factors include:

- Hepatitis B or Hepatitis C
- Cirrhosis
- Heavy drinking
- Obesity & Diabetes
- Iron storage diseases
- Foods with aflatoxin*

Sign & Symptoms

- Pain in the upper right part of belly
- A lump or feeling of heaviness in upper belly
- Bloating or swelling in belly
- Yellow skin and eyes
- Pale, chalky bowel movements and dark urine
- Loss of appetite, Weight loss, weakness

II. Metastatic Liver Cancer

- These are the tumors that have spread to the liver from other areas of the body
- Most common types of cancer that spread to the liver are: Colorectal, Lung, Breast, Pancreatic, Stomach, Melanoma, Neuroendocrine
- After the lymph nodes, liver is the most common site of metastatic spread

Etiology

- For cancers that occur in the gastrointestinal tract ,frequency of metastasis to liver is high due to the venous drainage of the gastrointestinal organs via the hepatic-portal system to the liver
- Other extra-abdominal tumors such as lung cancer, breast cancer and malignant melanoma, may also spread to the liver via haematogenous dissemination

Symptoms

- Loss of appetite. Nausea, fever
- Fatigue & weight loss
- Jaundice, itchy skin
- Discomfort or pain in the abdomen
- Swelling of the abdomen caused by a buildup of fluid
- Swelling of the ankles

III. Bladder Cancer

Bladder cancer is a common urologic cancer generally originating in the urothelium, which is a 3- to 7-cell mucosal layer within the muscular bladder

Etiology

- Bladder inflammation
- Smoking and other chemical exposure
- Consumption of nitrates in smoked and cured meats
- Chemotherapy
- Use of the herb *Aristolochia fangchi*: Generally used for weight loss
- Genetic and familial disorders

Symptoms

- Blood in the urine(Hematuria): First sign of bladder cancer
- Changes in bladder habits: Frequent urination, pain or burning during urination, feeling to go right away, even when the bladder is not full, weak urine stream
- Advancer bladder cancer has following symptoms: Being unable to urinate, lower back pain on one side, loss of appetite and weight loss, feeling tired or weak, swelling in the feet, bone pain

IV. Acute Lymphocytic Leukaemia

ALL is a malignant (clonal) disease of the bone marrow in which early lymphoid precursors proliferate and replace the normal hematopoietic cells of the marrow

Risk Factors

- Previous cancer treatment
- Exposure to radiation
- Genetic disorders
- Having a brother or sister with ALL

Symptoms

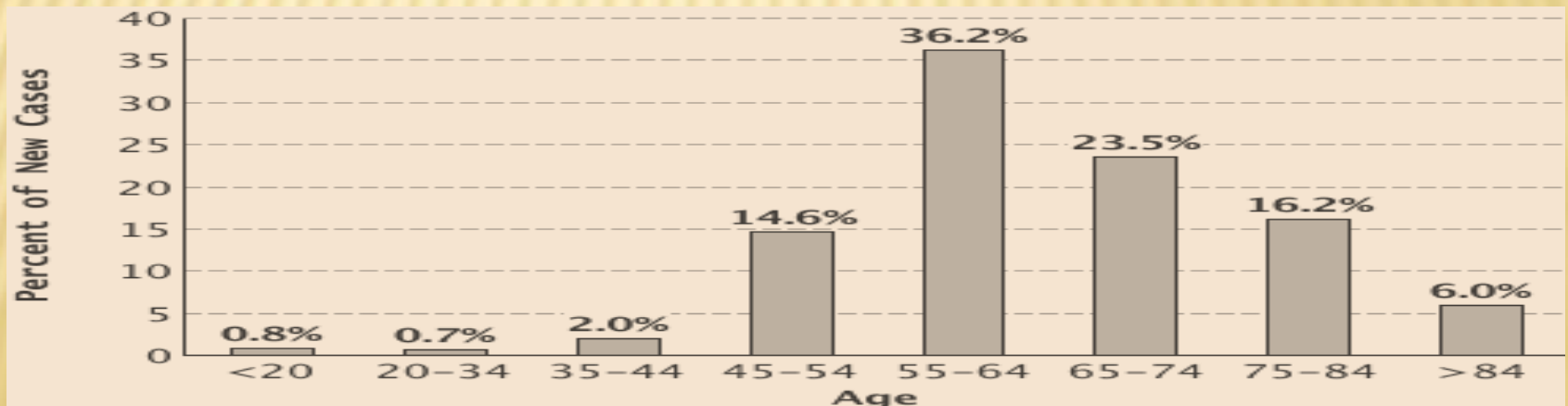
- Bleeding from the gums
- Bone pain, Fever
- Frequent infections or severe nosebleeds
- Lumps caused by swollen lymph nodes in and around the neck, underarm, abdomen or groin
- Pale skin
- Shortness of breath
- Weakness, fatigue or a general decrease in energy
- In children, joint or extremity pain may be the only presenting symptom

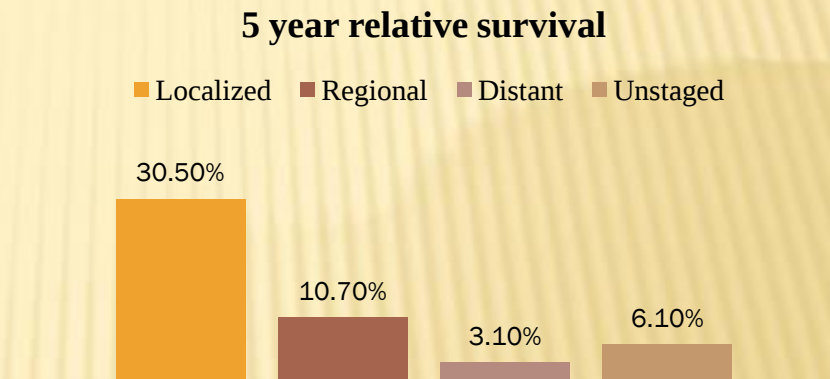
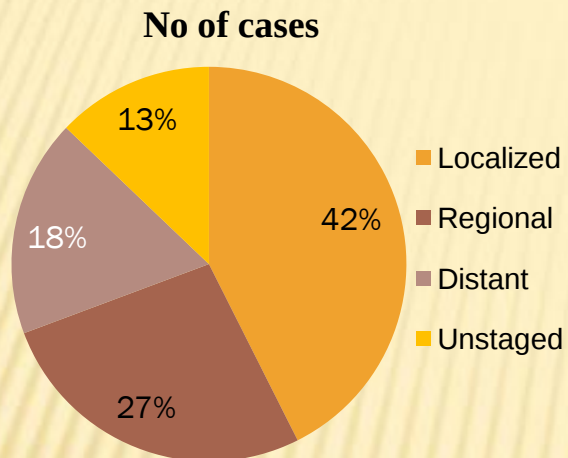
B. EPIDEMIOLOGY

I. HCC

- Liver cancer represents 2.2% of all new cancer cases in the U.S

Parameters	
Incidence	35,660 patients (2015)
Mortality	24,550 patients (2015)
Prevalence (as of 2012)	75,176 patients
Median age at diagnosis (2008-2012)	63 years
Median age at death (2008-2012)	67 years
Overall 5 year relative survival (2005-2011)	17.2 %





High unmet need exists in metastatic patients where 5 year survival rate is the lowest & currently sorafenib is the only treatment option available

II. Metastatic Liver Cancer

- In the U.S & Europe secondary liver cancer is more common than the primary liver cancer
- Primary liver cancer(HCC) varies in incidence from 30 per 100,000 population per year in high-risk regions, such as Asia and Africa, to less than 3 per 100,000 population per year in low-risk regions, such as northern Europe and North America
- Secondary liver cancers are much more common and represent the most common malignant tumor of the liver. The relative proportion of primary to secondary neoplasms is estimated to be 1:20
- Colorectal cancer (CRC) is the most common cancer metastasizing to the liver. It is expected that as many as 25% of patients with CRC will have liver metastases at presentation and 50% will have liver metastases developed metachronously

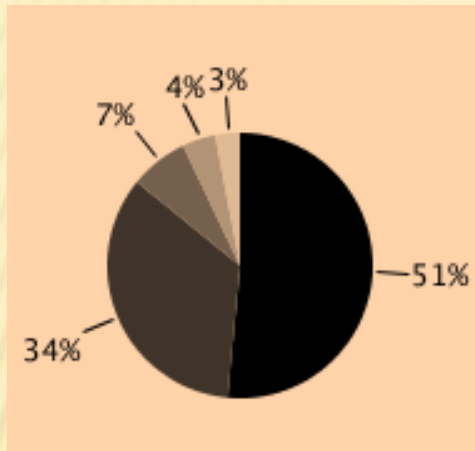
III. Bladder Cancer

- Bladder cancer represents 4.5% of all new cancer cases in the U.S

Parameters	
Incidence (E) (2016)	76,960 (about 58,950 in men and 18,010 in women)
Mortality (E) (2016)	16,390 (about 11,820 in men and 4,570 in women)
Prevalence (as of 2010)	577,403 patients
Median age at diagnosis (2008-2012)	73 years
Median age at death (2008-2012)	79 years
Overall 5 year relative survival (2005-2011)	77.4 %

Variation among cohorts

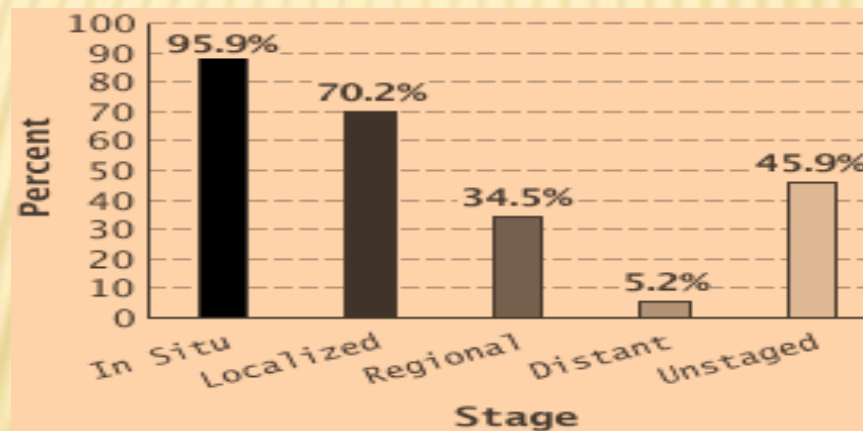
- **Age:** The likelihood of being diagnosed with bladder cancer increases with age. More than 70% of people with bladder cancer are older than 65 years old.
- **Gender:** Men are three to four times more likely to develop bladder cancer than women, but women are more likely to die from bladder cancer than men. Before smoking rates for women increased, men were five to six times more likely to develop bladder cancer than women.
- **Race:** Caucasians are more than twice as likely to be diagnosed with bladder cancer as black people, but black people are twice as likely to die from the disease



Percent of Cases by Stage

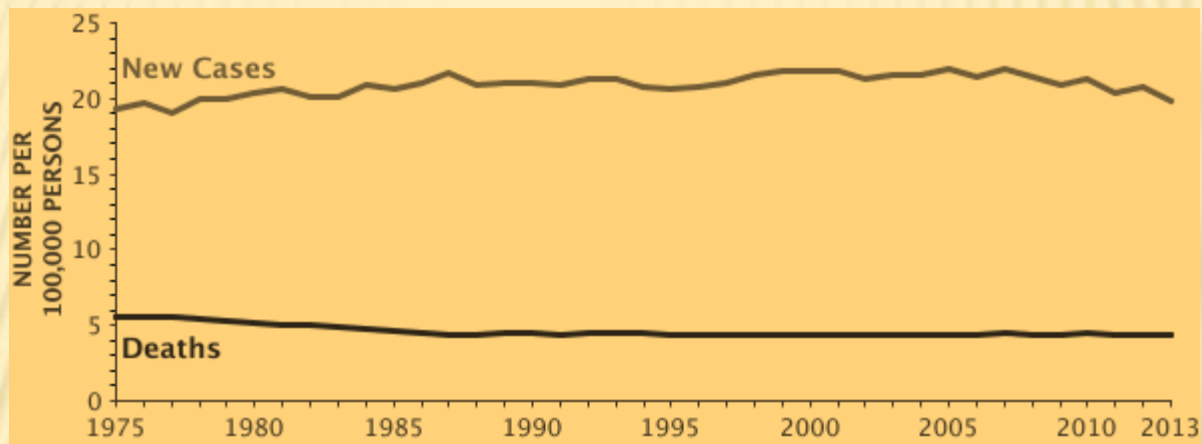
- **In Situ (51%)**
Only in Originating Layer of Cells
- **Localized (34%)**
Confined to Primary Site
- **Regional (7%)**
Spread to Regional Lymph Nodes
- **Distant (4%)**
Cancer Has Metastasized
- **Unknown (3%)**
Unstaged

5 year relative survival



Opportunity area lies in metastatic cases which though are rare but have the least 5 year relative survival rate and thus provides scope of better treatment

Trends in new cases, deaths and 5 year relative survival rates

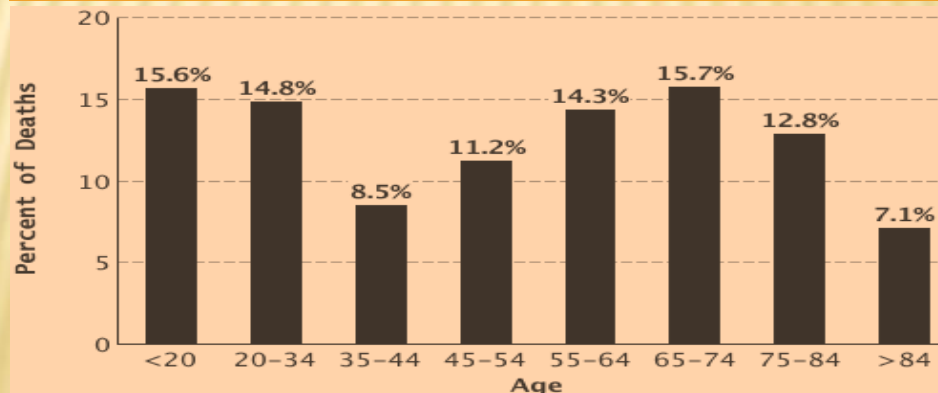


Year	1975	1980	1985	1990	1995	2000	2004	2008
5-Year Relative Survival	71.5%	73.8%	76.0%	79.7%	81.1%	80.3%	80.0%	77.5%

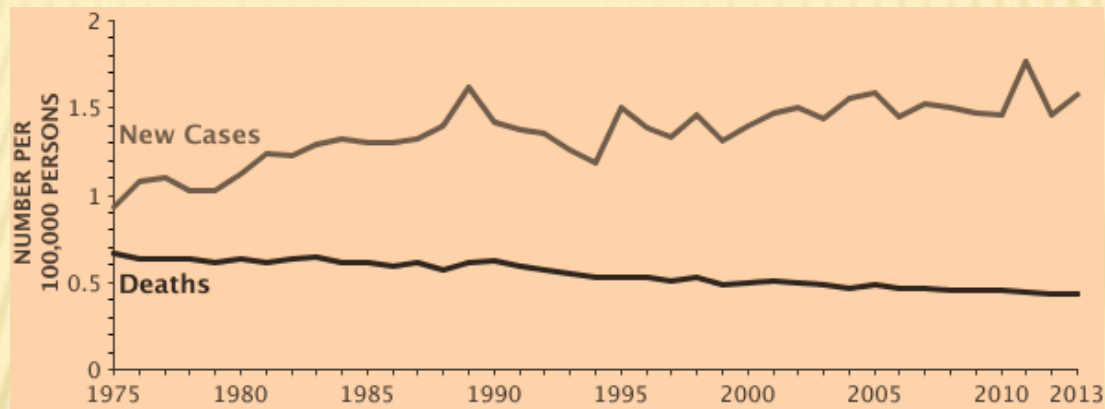
IV. ALL

Parameters	
Incidence (E)	About 6,590 (3,590 in males and 3,000 in females) (2016)
Mortality(E)	About 1,430 (800 in males and 630 in females) (2016)
Prevalence (as of 2012)	75,176patients
Median age at diagnosis(2008-2012)	14 years
Median age at death(2008-2012)	54 years
Overall 5 year relative survival(2005-2011)	67.5 %

Percent of Deaths by Age Group: Acute Lymphocytic Leukemia



New Cases, Deaths and 5-Year Relative Survival



Year	1975	1980	1985	1990	1995	2000	2004	2008
5-Year Relative Survival	31.0%	49.0%	56.0%	55.8%	61.7%	62.6%	67.5%	71.7%

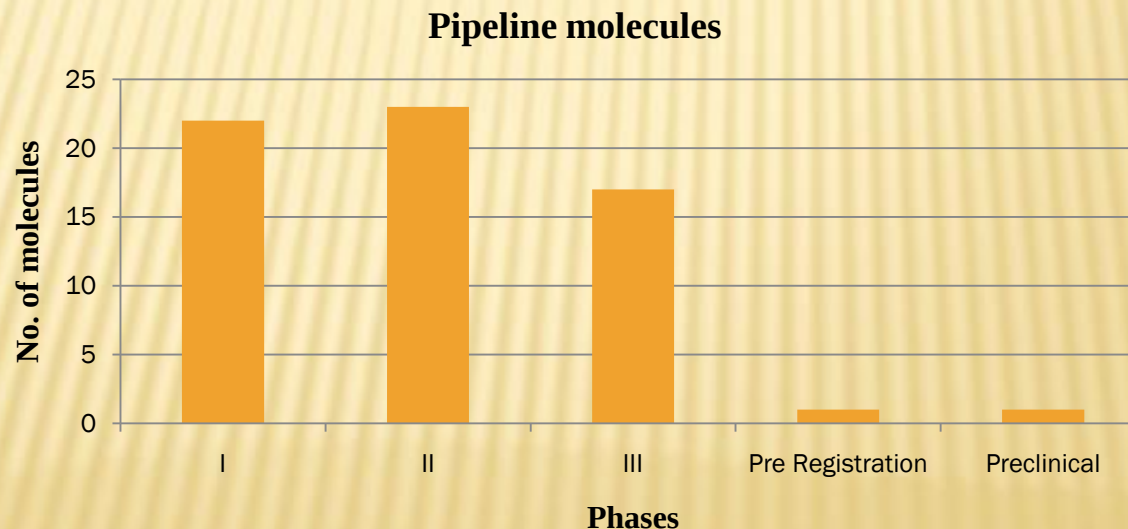
C. DISEASE MANAGEMENT

Parameter	HCC	Metastatic liver cancer	Bladder cancer	ALL
Diagnosis	Primarily done by the use of various imaging techniques like ultrasound, CT, MRI	Majorly involves tumor marker tests, biopsy & various imaging techniques like CT, angiography	Urinalysis, Cystoscopy and biopsy (transurethral resection of bladder tumor)	Based on the presence of $\geq 20\%$ of bone marrow lymphoblasts upon the examination of bone marrow aspirate or biopsy
Treatment	First line of treatment is: Resectable- surgical resection or transplant Unresectable- Systemic therapy with Sorafenib and other systemic therapy with or without radiotherapy Locoregional therapy	Management is based on the primary source of tumor origin. <u>Radiofrequency ablation:</u> Uses electrical currents to create heat that destroys cancer cells <u>Cryotherapy:</u> Uses extreme cold to freeze and destroy abnormal and cancerous cells or tissue <u>Chemotherapy & targeted therapy</u> eg: sorafenib, avastin	Chemotherapy (mitomycin) remains the mainstay of primary treatment with BCG therapy being the most commonly used adjuvant therapy, Targeted therapies are expected to enter soon in the market	Tyrosine kinase inhibitors are widely used as treatment options for Ph+ ALL cases along with hematopoietic cell transplant in suitable patients

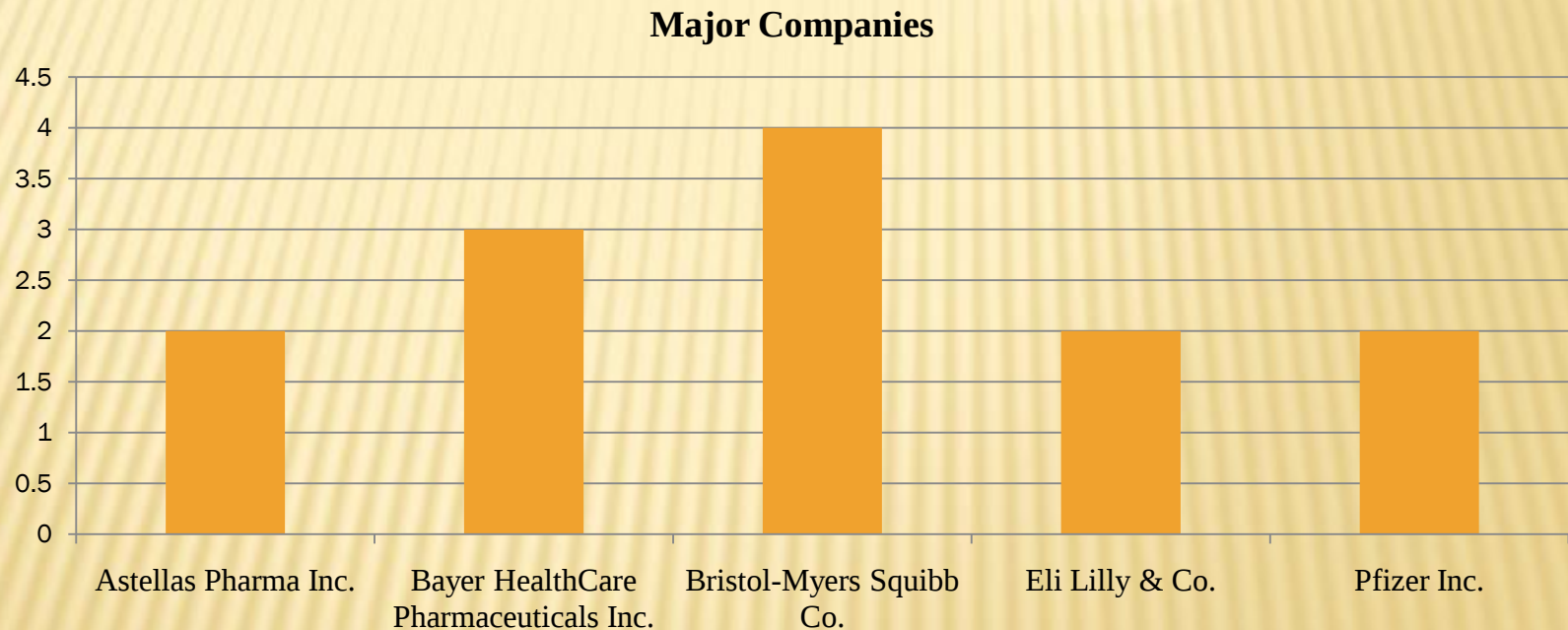
D. MARKET DYNAMICS

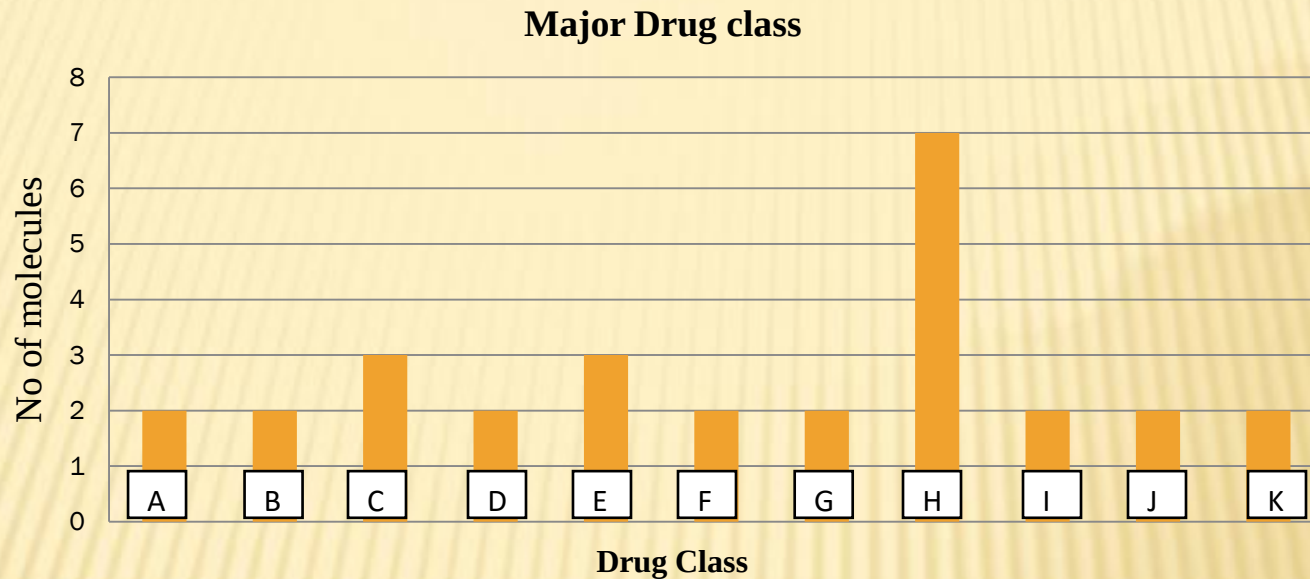
I.HCC

- Currently, there is only one product approved for use in HCC that is Nexavar (sorafenib) but its sales are going to decline steeply after its patent expiry in 2020
- The value of the HCC market is set to grow by 172% and hit \$1.4bn by 2019
- Currently, there are 17 molecules in Phase III, 23 molecules in Phase II and 22 molecules in Phase I for HCC



- Major companies having their drugs in pipeline are Bristol-Myers Squibb Co. with 4 molecules, Bayer Healthcare with 3 molecules; Pfizer, Eli Lilly, Astellas with 2 molecules





- A: anti-IGF monoclonal antibody
- B: chimeric monoclonal antibody (inhibits CD105 - humanized)
- C: c-met kinase inhibitor
- D: doxorubicin enhanced with lysolipid thermally sensitive liposomes (LTSL)
- E: HDAC inhibitor
- F: Immunotherapy
- G: Kinase inhibitor
- H: Multiple tyrosine kinase inhibitor
- I: Oncolytic virus
- J: VEGFR-2 inhibitor
- K: p53 activator

II. Metastatic liver cancer

- Melphalan drug delivery system - Delcath Systems is the only approved drug in market
- Currently, only one drug (Stivagra) is in Phase III , one drug in Phase II and two drugs in Phase I for secondary liver cancer
- There is a huge unmet need in this area offering opportunity for pharmaceutical companies
- Targeted therapies are expected to rule the market in near future

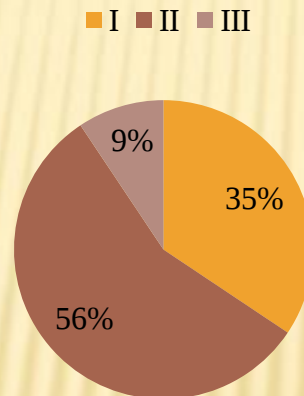
III. Bladder Cancer



*Sales figures have been sanitized as the data is confidential and cannot be shared as per the company's policy

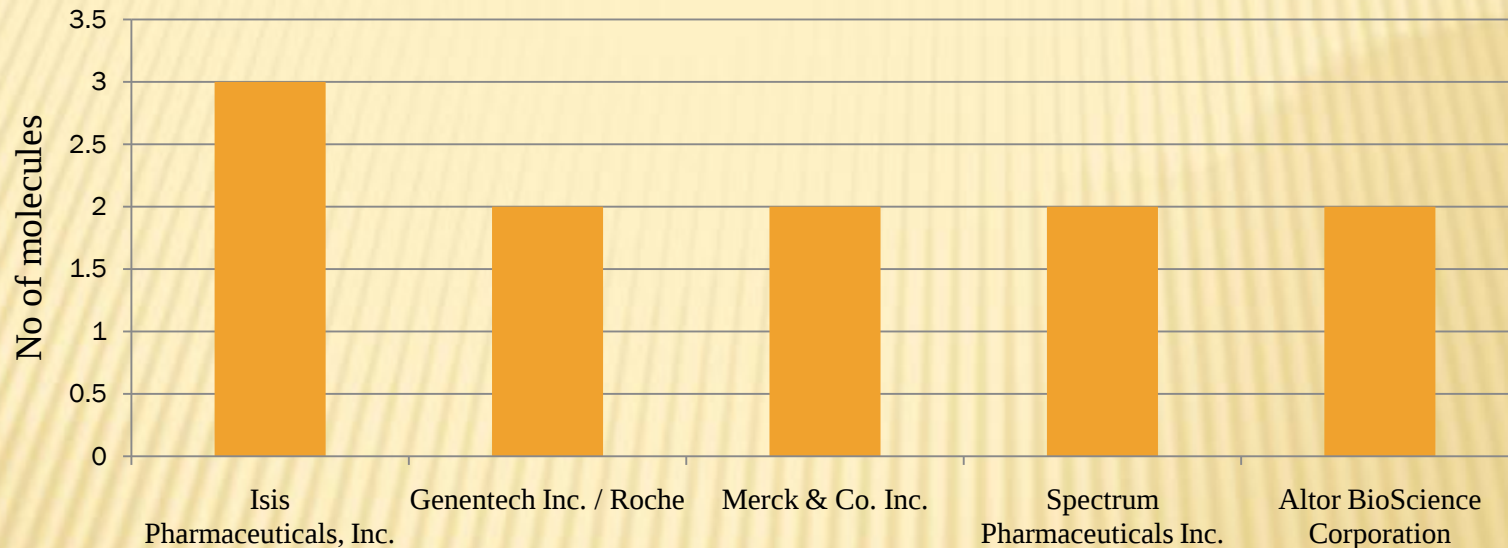
- Market for bladder cancer is expected to rise significantly 2016 onwards with the introduction of new drugs
- Atezolizumab is expected to emerge as the market leader in near future

Molecules in pipeline



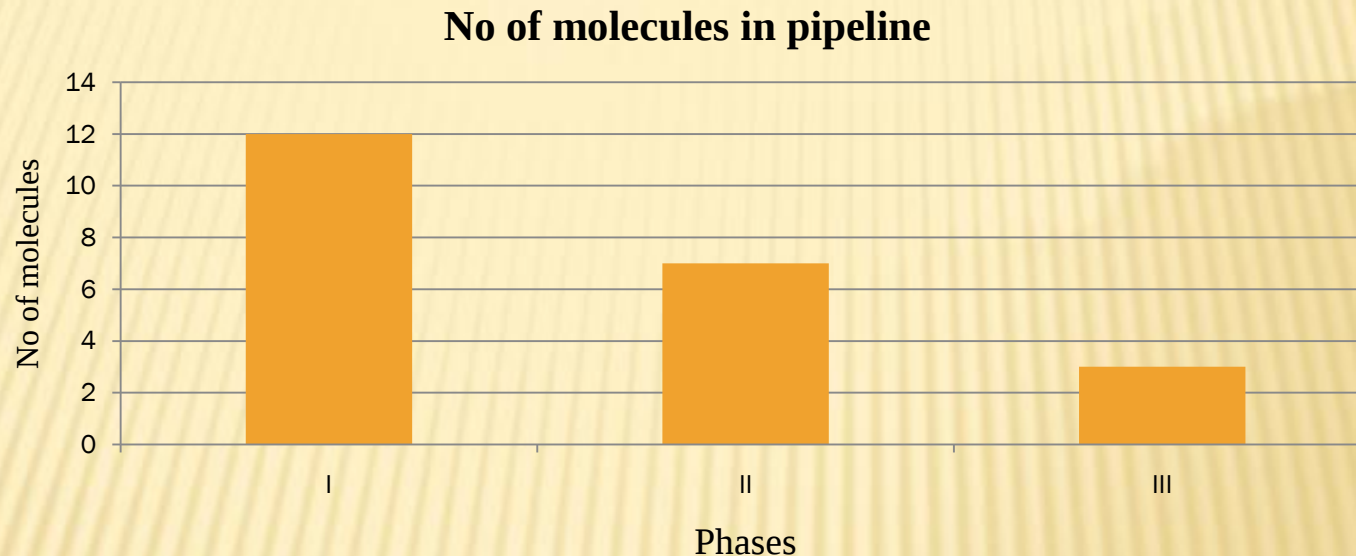
➤ Currently, 56% molecules are in Phase II and 35% in Phase I which shows the market for bladder cancer is expected to grow widely in the near future

Major Companies with molecules in pipeline



- Major company with 3 molecules in pipeline is Isis Pharma followed by Genentech, Merck & Co, Spectrum pharma and Altor Bioscience with 2 molecules in pipeline
- Major drug classes with 4 molecules in pipeline are Hsp27(heat shock proteins) inhibitors and monoclonal antibodies

IV. ALL



- Market of ALL is buzzing with new drugs with 12 molecules in Phase I and 3 molecules ready for the launch
- Around 22 companies are competing for the ALL market which include major companies like Novartis, Pfizer, Sanofi, Merck & co.
- TKIs have been the dominant players since many years but in the near future anti-CD 19 monoclonal antibodies are expected to rule over the market
- 6 new molecules are in pipeline under this drug class

BUSINESS IMPLICATIONS

General implications: TAO: Onboarding process; repository; assess opportunity area; plan new drug launch

Specific implications: Clinical overview & Disease management – onboarding process

Epidemiology – target population, assess unmet needs, trends in epidemiological patterns

Market dynamics – recent developments, competitive landscape, plan the launch using information regarding patent expiry & first launch



THANK YOU