PharmaACE

Market Assessment of Immunotherapy for Treatment of NSCLC in China: Present And Outlook

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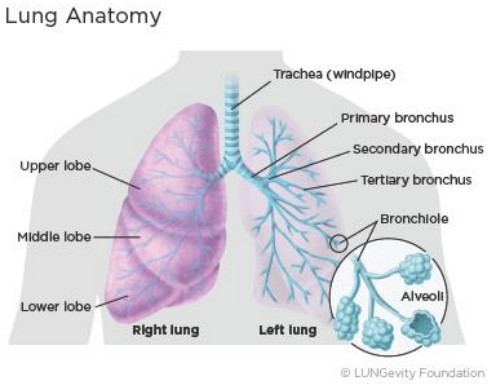
INTRODUCTION: 1. LUNG CANCER OVERVIEW

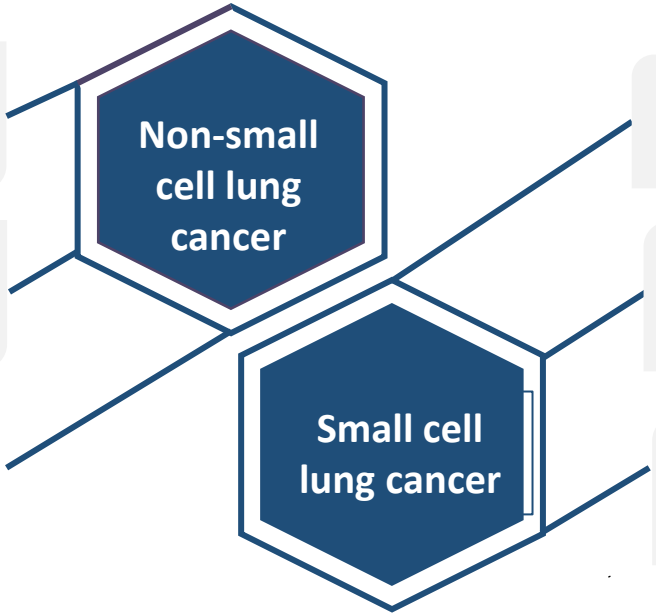


- The second most common cancer, accounting for about 1 out of 5 malignancies in men and 1 out of 9 in women.
- The incidence of lung cancer has gradually declined in men, it has been rising alarmingly in women.
- Active and passive Smoking, air pollution, chronic lung disease, radiations, family history are some common risk factors for lung cancer.
- Sign symptoms are persistent cough, blood in sputum, changes in voice, chest pain, recurrent pneumonia, difficulty swallowing, etc.

Lung adenocarcinoma-
- Starts in glandular cells.
- Develop in smaller airways, such as alveoli.

Squamous cell lung cancer-
Starts in the squamous cells.
Cells appear like fish scales and are thin and flat

Large cell lung cancer-
Larger size cells
It is more often found in the periphery.



Also called small cell carcinoma or oat cell cancer.

Cells are round, oval, or spindle-shaped and smaller than healthy cells and the cells of NSCLC.

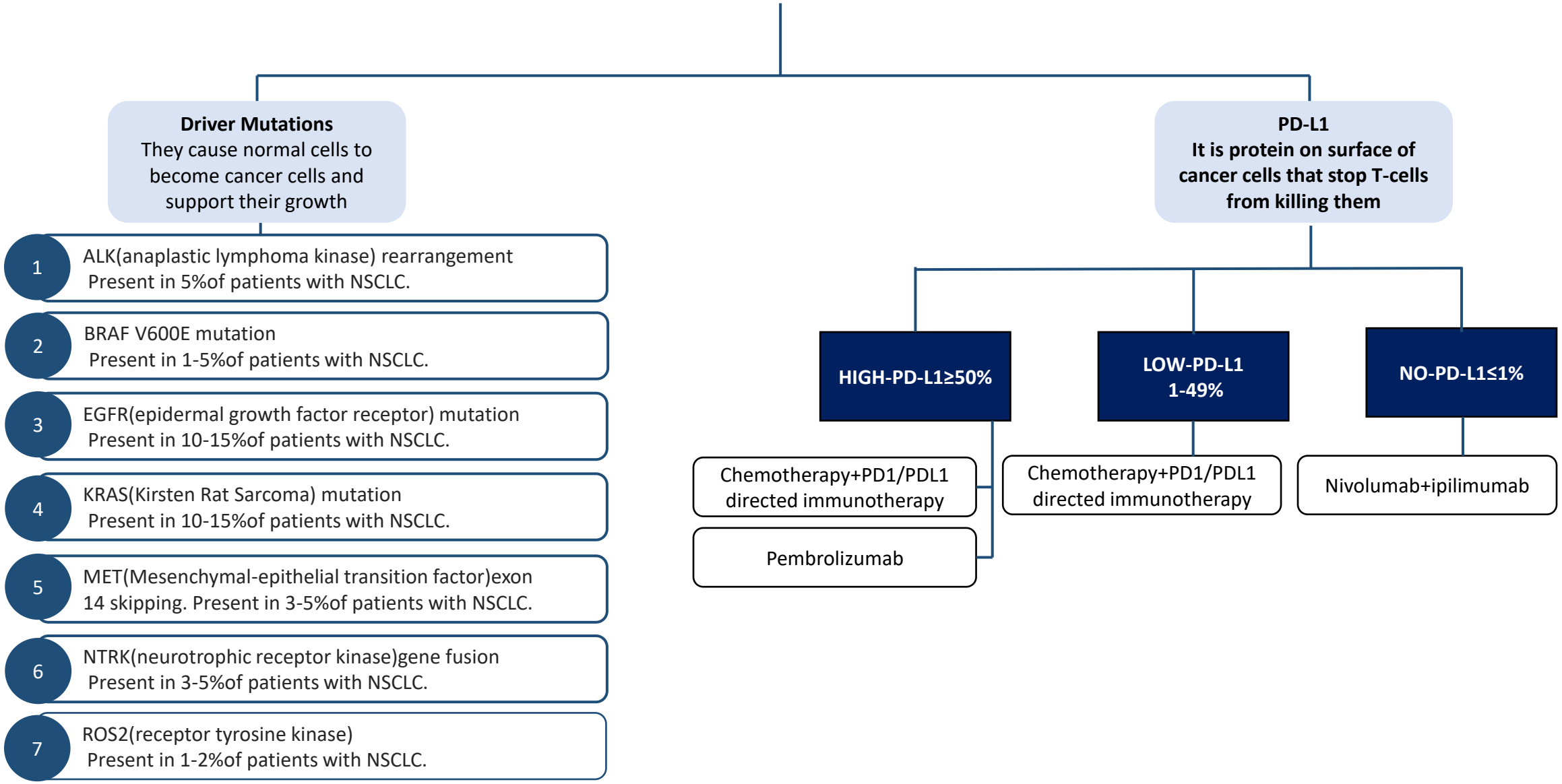
Begins from bronchi and is found most often in people with a smoking history.

2.NSCLC STAGING

3.STANDARD OF CARE

STAGE 0	This is called in situ disease, meaning the cancer is “in place” and has not grown into nearby normal lung tissues or spread outside the lung.	Segmentectomy or wedge resection (removal of part of the lobe of the lung)
STAGE 1	Tumor has not spread to any lymph nodes. • Stage IA tumors are 3 centimeters (cm) or less in size, further divided into IA1, IA2, or IA3 based on the size of the tumor. • Stage IB tumors are more than 3 cm but 4 cm or less in size.	Radical surgery(lobectomy, sleeve resection, segmentectomy, or wedge resection).
STAGE 2	• Stage IIA-Tumor > 4 cm but ≤5 cm size that has not spread to the nearby lymph nodes. • Stage IIB- Tumor ≤5 cm that has spread to the lymph nodes within the lung, called the N1 lymph nodes.	Adjuvant cisplatin-based for completely resected NSCLC tumors. Additionally, radiotherapy for patients with N2 lymph nodes.
STAGE 3	Classified as either stage IIIA, IIIB, or IIIC. The stage is based on the size of the tumor and which lymph nodes the cancer has spread to. Most commonly the cancer has spread to the lymph nodes in the mediastinum (the area in the chest between the lungs)	4 cycles of cisplatin-based chemotherapy plus a 3rd generation cytotoxic agent or a cytostatic (anti-EGFR, anti-VEGFR) drug
STAGE 4	• Stage IVA cancer has spread within the chest and/or has spread to 1 area outside of the chest. • Stage IVB has spread outside of the chest to more than 1 place in 1 organ or to more than 1 organ	

4.BIOMARKERS



5.NSCLC TREATMENT

Surgery

- Lobectomy
- Wedge resection
- Pneumonectomy
- Sleeve resection

Radiation therapy

- External-beam radiation therapy, radiations are aimed at cancer from
- Internal radiation therapy, radioactive substance is placed close to cancer and delivered via needle, wires, seeds, or catheters.

Chemotherapy

- Carboplatin
- Cisplatin,
- Docetaxel,
- Gemcitabine,
- Etoposide,
- Paclitaxel,
- Pemetrexed

Targeted Therapy

- EGFR inhibitors- Afatinib, Dacomitinib, Entrectinib, Erlotinib, Gefitinib, Osimertinib
- Anaplastic lymphoma kinase (ALK) inhibitors- Alectinib, Brigatinib, Ceritinib, Crizotini, Lorlatinib
- ROS1 fusion-Critotinib,Ceritinib, Loratinib and Enterctinib
- KRAS G12 mutation- Sotorasib.
- NTRK mutation- Loratectinib and enrecitinib.
- BRAF V600E mutation- Dabrafetinib and Trametinib
- MET exon 14 Skipping- Capmatinib and Tepotinib.
- RET inhibitors-Pralsetinib and Selpercatinib.

Immunotherapy

- PD-1/PD-L1 inhibitors-Pembrolizumab and Nivolumab are PD-1 inhibitors, Atezolizumab and durvalumab are PD-L1 inhibitors.
- CTLA-4 inhibitors-Ipilimumab

RESEARCH QUESTION

1. What is the current market scenario of PD-1 and PD-L1 inhibitors for treatment of NSCLC in China?
2. What would the PD-1 and PD-L1 inhibitor market would look like in coming years?

OBJECTIVES

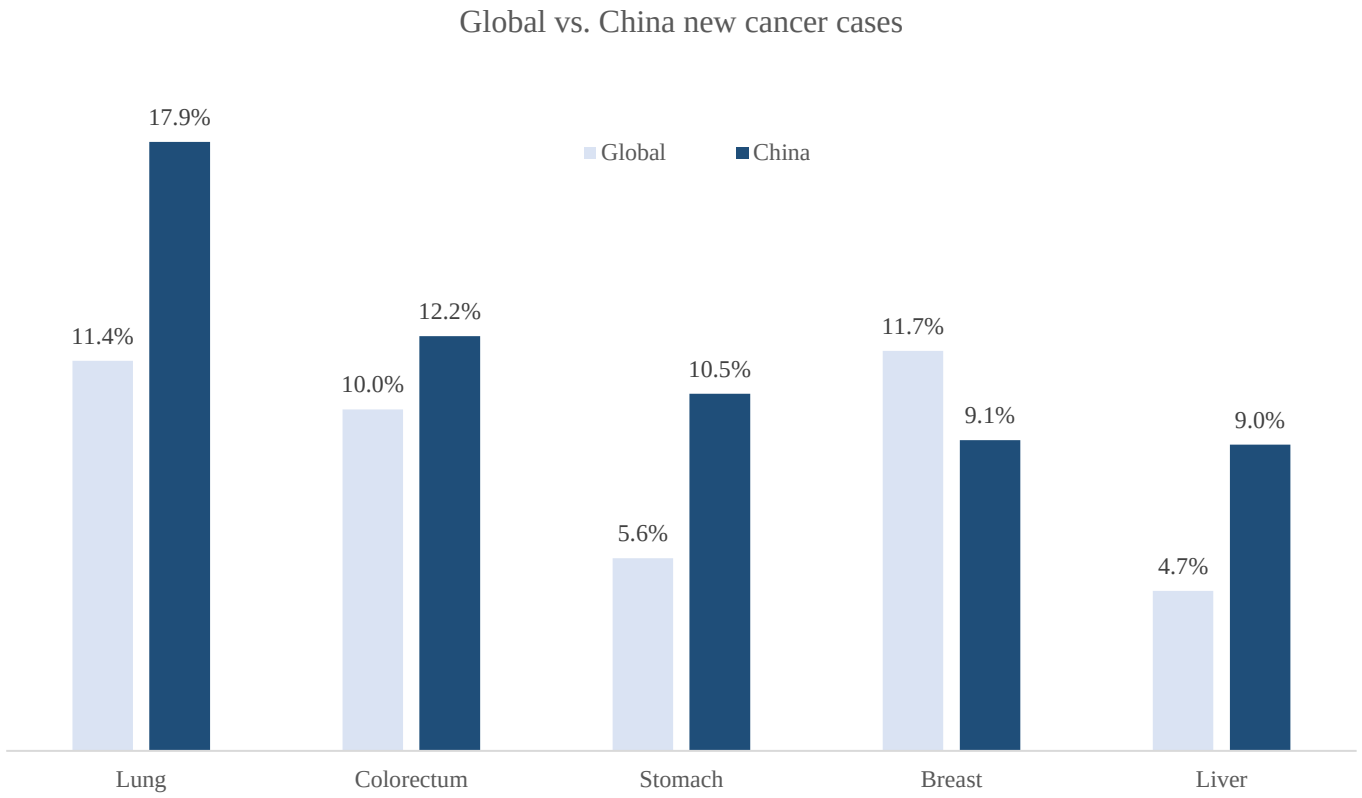
1. To study population demographics of China and disease burden
2. To study multi-tiered healthcare system of China
3. To identify the number of prevalent cases of NSCLC in China
4. To study competitor landscape of Immunotherapy.
5. To understand outlook of PD-1and PD-L1 inhibitors therapy .

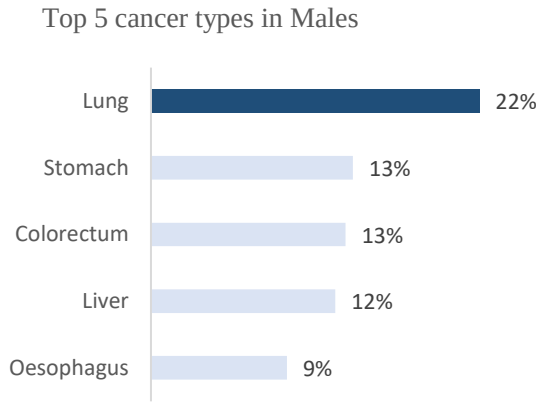
RESEARCH METHODOLOGY

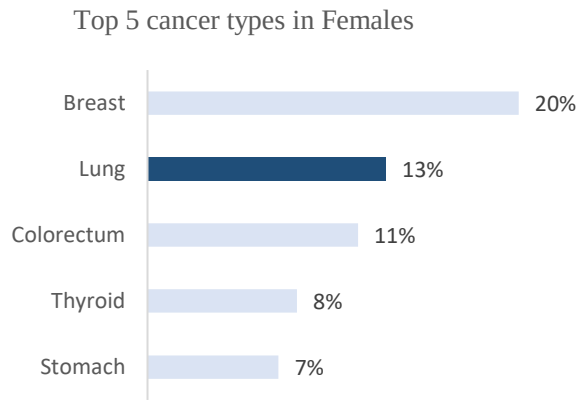
Study area	The study is based on entire China market with the therapy of interest being Immunotherapy for Non-small cell lung cancer.
Study design	Descriptive and analytical study to evaluate and assess current market of Immunotherapy in China.
Study duration	The study was carried out for 3 months from 21 March 2022 to 19 June 2022
Data collection method	Secondary search using open sources like PubMed, Globocan, Cancer today, WHO cancer observatory, Sage journals etc
Plan of Analysis	The plan of analysis intends to determine the demographic trends and lung cancer burden in China. Patient funnel for NSCLC will be made, starting with lung cancer cases in China, and applying cuts like % of NSCLC cases, Biomarker testing rate and positivity rate. Followed by studying brand profiles and making future inferences

RESULTS: 1. CANCER BURDEN IN CHINA

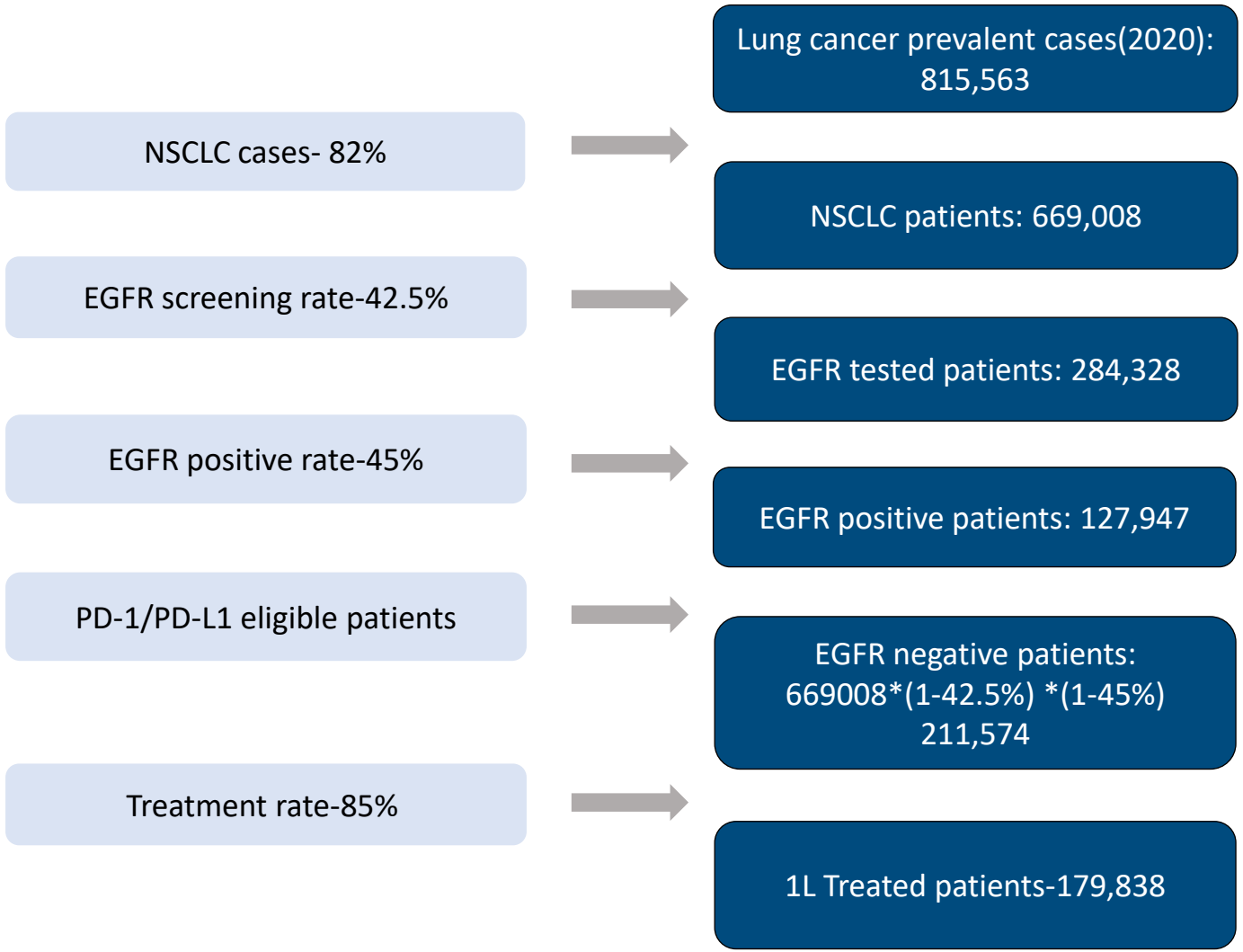
In 2020, Lung cancer cases Globally and in China were estimated to be 2,206,771 and 815,563 respectively.







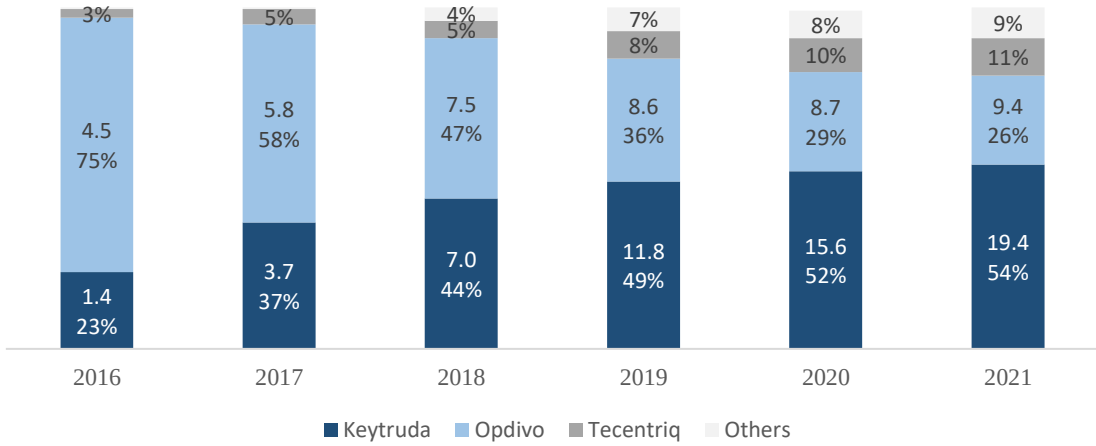
2. NSCLC PATIENT FUNNEL



3. MARKET OVERVIEW OF PD-1/PD-L1 INHIBITORS

- The global PD-1 and PD-L1 inhibitors market is set to record market value of US$ 43.7 Bn in the year 2022 with a CAGR of 10.7% for period of 2022-2030.
- NSCLC segment will lead the market and is projected to account for 37.0% of the total market revenue share in 2022.
- Major brands in global markets are — Keytruda, Opdivo, Tecentriq, Imfinzi, Bavencio, Libtayo, and Jemperli.
- 80% of market is captured by Opdivo and Keytruda together. Tecentriq holds sizeable market share of about 11%, whereas all other brands have limited share of 9% combined. This also includes three domestically approved ones in China-— Tyvyt, Baizean, Tuoyi.

Global PD-1 sales (in $ Bn)& contribution by Brands



4.COMPETITOR's LANDSCAPE

Brand(API)	Company	China launch date	Approved Indication in china	NRDL entry	Annual cost
Keytruda (Pembrolizumab)	Merck	2018	3 approvals- 1L non-squamous and squamous NSCLC, 1L monotherapy metastatic NSCLC	No	160,000
Opdivo (Nivolumab)	BMS	2018	1 approval: Locally advanced or metastatic NSCLC	No	479,500
Tecentriq (Atezolizumab)	Roche	2020	3 approvals: Adjuvant NSCLC, 1L metastatic NSCLC and 1L non-squmous NSCLC	No	-
Imfinzi (Durvalumab)	AstraZeneca	2019	1 approval: Unresectable NSCLC	No	-
Daboshu (Sintilimb)	Innovent biologics and Eli Lily	2018	2 approvals: 1L non-squamous and squamous NSCLC	Yes	266,500
Tuoyi (Toripalimab)	Junshi Biosciences	2018	1L NSCLC approval application submitted	Yes	187,200
Airuika Camrelizumab)	Jiangsu Hengrui Medicine	2018	2 approvals: 1L non-squamous and squamous NSCLC	Yes	118,000
Baizean (Tislelizumab)	Beigene Ltd.	2019	3 approvals: 1L non-squamous and squamous NSCLC and 2L/3L advanced NSCLC	Yes	-

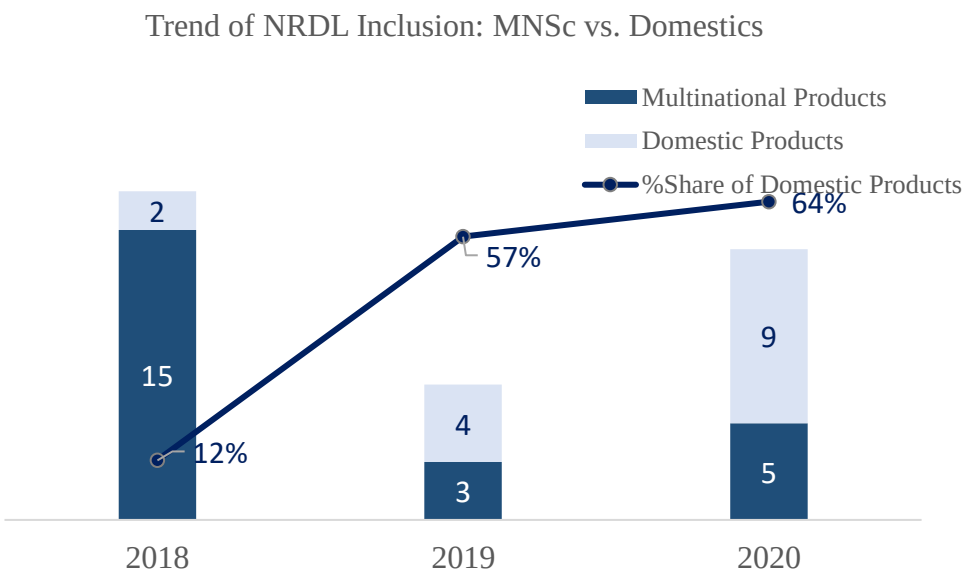
5.FUTURE OUTLOOK

- **Increasing Healthcare spending will contribute to growth of PD-1 and PD-L1 market**

The health expenditure in China has raised from 500 billion yuan in 2000 to higher than 6.5 trillion in 2019. The drivers for this growth are increasing living standard and aging population. The share of population being covered by basic health insurance has also grown in last decade. Number of people covered in BHSI surpassed 1 billion in 2017 and as of 2019 more than 96% of population got covered.

- **Current regulatory framework to be in favor of domestic firms, Challenge for MNCs**

Over the past few years, the ratio of domestic oncology brands getting listed in NRDL is being constantly increasing in comparison with MNCs. Securing position into NRDL list will help brands like Baizean, Daboshu, AiRuiKa and Tuoyi to penetrated deeper into marketplace. However, as none of the MNCs are yet into NRDL, there market share might be taken over by these emerging domestic brands.



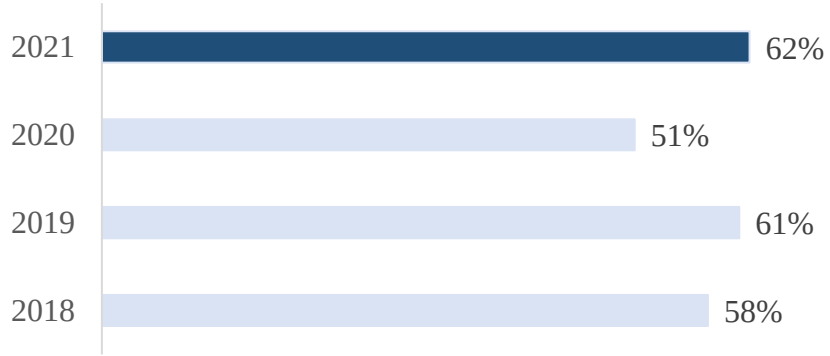
- **Fragmentation of marketplace: Opportunity for late-comers**

The market is getting increasing crowded with brands aiming to get market share. But as brands like Keytruda, Opdivo, Baizean are deeply entrenched, thus will be able to hold dominant position in coming years as well. Late-comers might face fragmentation that will drive them to smaller market segment

- **Impact of NRDL listing on market shares**

For getting included into NRDL list, brands are required to bear heavy price cuts, brands like BaiZean, AiRuika and Tuoyi have slashed their prices by almost 80% to win their places. However, 80% discounts is too much for brands like Keytruda and Opdivo as they were already launched with almost half the price as in U.S. This lack of inclusion is likely to affect their market share in future.

Figure 8: Average NRDL price cut



CONCLUSION

- Lung cancer has the **highest incidence and mortality** among all cancer types, and is divided into two subtypes, NSCLC and SCLC, account for about 85% and 15% of lung cancer cases in China respectively.
- Main predictive biomarker for these cancer types is **PD-1 and PD-L1** protein expression in tumor cells.
- As per treatment is concerned, **Immune checkpoint inhibitors** have become the latest treatment modalities and it is benefitting Chinese population significantly.
- The MNC brands that have established strong foot in China market are **Keytruda, Opdivo, Tecentriq and Imfinzi**. In recent year, a lot of domestic companies like **Daboshu, BaiZean, Tuoyi and AiRuika** are also entering into PD-1 drug categories.
- Current regulatory framework of China seems to be **in favor of domestic firms** as they are being preferred to be included in National drug reimbursements list, while MNCs still struggling for it.
- The future seems bright for PD-1 inhibitors due to changing **population demographics, increasing prevalence of lung cancer and entry of new comers**.

Thank You

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