

A MARKET INVESTIGATION OF NSCLC DRUGS IN INDIA

Dissertation Submitted to



The IIHMR University, Jaipur

For the partial fulfillment for the award of the degree of Master of Business
Administration (MBA)

in

Pharmaceutical Management

by

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Under the Supervision and Guidance of

Dr Saurabh Kumar Banerjee

2022

DECLARATION BY STUDENT

I hereby declare that this dissertation titled **A Market Investigation of NSCLC Drugs in India** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

A handwritten signature in black ink, appearing to read 'Mohd Moonis', is written over a light gray rectangular background.

Name of Student: Mohd Moonis

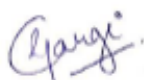
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TO WHOMSOEVER IT MAY CONCERN

This is to certify that, **Mohd. Moonis**, student of IIHMR University, Jaipur has completed his internship with **PharmaACE Analytics LLP** during the period of **March 22, 2022 to June 19, 2022**. During his internship he worked with the Forecasting department and has successfully worked on the project; **A Market Investigation of NSCLC Drugs in India**.

We wish him every success in life.



Gargi Agrawal
Executive – Corporate Communications
PharmaACE

CERTIFICATE

This is to certify that dissertation titled A MARKET INVESTIGATION OF NSCLC DRUGS IN INDIA is a record of the research work undertaken by (Name of Student) in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management)/MBA (Pharmaceutical Management)/MBA (Rural Management) from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

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School Dean

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This secondary research boiled down to thorough reading of therapies associated with lung cancer, a subject that was made easy given my pharmacy background. However, conducting research requires proper methodology and concentration of efforts, a feat made entirely possible by the direct and sometimes indirect efforts of those surrounding me. I would like to put out a word of gratitude to my college mentor Dr Saurabh Kumar Banerjee who helped envision the idea and PharmaACE reporting managers Srinivas Kaushik and Surabhi Labde, who helped me by directing my attention towards fruitful data sources. My company project work on lung cancer medicines also helped me understand the NSCLC market.

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Market Investigation of NSCLC Oncology Drugs in India

1 Introduction

1.1 Research Question

What are the prices of top NSCLC drugs in the Indian market across brands? Which manufacturers or generic companies offer cheaper oncology drugs and whose products are dearer? What is the current landscape of NSCLC therapies in India?

1.2 Objectives

The primary objective of this report is to analyse the Indian NSCLC market, conduct a cost analysis, and review the status of pricing of select NSCLC drugs in India.

1.3 Background

Cancer, also called carcinoma, malignancy, neoplasms, or tumour is one of the most notorious diseases around. WHO defines cancer as ‘a large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably, go beyond their usual boundaries to invade adjoining parts of the body and/or spread to other organs’. Cancer is the second biggest reason of death globally, causing an estimated 9.6 million deaths, or one in six deaths, in 2018.¹

These staggering numbers underline the already massive relevance of the oncology drugs market. The global oncology drugs market size was valued at \$135,494.17 million in 2020, and is projected to reach \$274,400.63 million by 2030, registering a CAGR of 7.5% from 2021 to 2030.² In India, Oncology Market In India to grow at a CAGR of 13.02% by 2025.³ The key players in Indian market are- AstraZeneca Plc, Bristol-Myers Squibb Co., Cadila Healthcare Ltd., Cipla Inc., F. Hoffmann-La Roche Ltd., Merck and Co. Inc., NATCO Pharma Ltd.⁴ Some top oncology drugs available in the global market space right now are

Revlimid (Celgene), Opdivo (Bristol-Myers Squibb; Ono Pharmaceutical), Imbruvica (AbbVie (Pharmacyclics); Johnson & Johnson), Keytruda (Merck & Co), and Ibrance (Pfizer).⁵

These drugs cover different therapies and are sold under various brand names in India. Prices vary according to the brand. It is important that an assessment of these prices is conducted, which may further help us develop oncology market insights in the Indian market. This report intends to utilise secondary data to find out and analyse pricing data of top NSCLC oncology drugs available in India. Finally, the report summarizes the data and comments on the pricing range of NSCLC oncology drugs in India. Price variation percentage for a particular drug among varied brands have also been summarized.

1.4 Cancer

There are over 100 types of cancers that affect humans.⁶ It has been known to exist for almost the entirety of human history.⁷ The most common in 2020 (in terms of new cases of cancer) were:

- breast (2.26 million cases);
- lung (2.21 million cases);
- colon and rectum (1.93 million cases);
- prostate (1.41 million cases);
- skin (non-melanoma) (1.20 million cases); and
- stomach (1.09 million cases)⁸

90-95% of cancers are due to genetic mutations from environmental and lifestyle factors. The rest 5-10% are caused due to inherited genetics.⁹ There were an estimated 18.1 million cancer cases around the world in 2020. Of these, 9.3 million cases were in men and 8.8 million in women.¹⁰ The projected incidence of patients with cancer in India among males was 679,421 (94.1 per 100,000) and among females 712,758 (103.6 per 100,000) for the year 2020.¹¹

1.5 Lung Cancer

Simply put, cancer that originates in the lungs is called lung cancer. It may also be referred to as lung carcinoma. There are two types of lung cancer: non-small cell lung cancer and small cell lung cancer. Most lung cancers are caused by smoking, but nonsmokers can also develop lung cancer.¹²

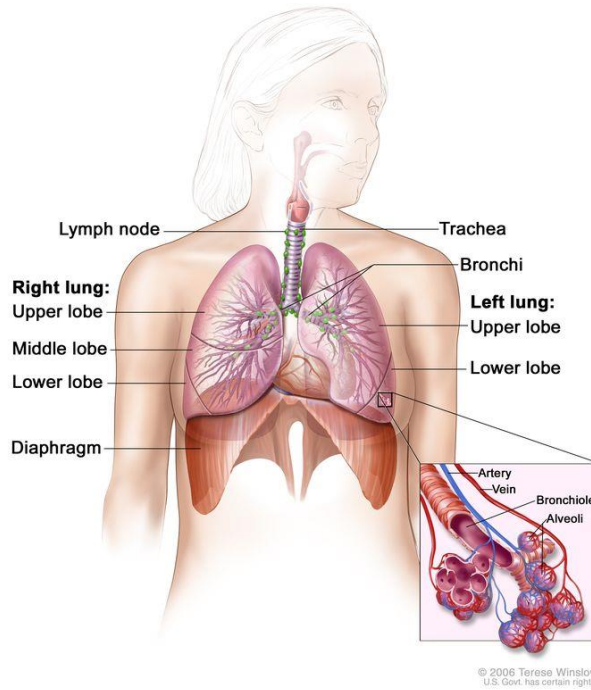


Figure 1.1: Inhaled oxygen enters the lungs and travels through the thin membranes of the alveoli into the bloodstream.
(Source: <https://www.cancer.gov/types/lung/patient/small-cell-lung-treatment-pdq>)

The following are risk factors for lung cancer:

- Currently or previously smoking cigarettes, pipes, or cigars. The most significant risk factor for lung cancer. The earlier in life a person begins smoking, the more frequently and for how long a person smokes, the greater the risk of lung cancer.
- Exposure to secondhand smoke.
- Workplace exposure to asbestos, arsenic, chromium, beryllium, nickel, soot, or tar.
- Exposure to radiation from any of the following sources:
 - Breast or chest radiation therapy
 - Radon levels in the home or workplace
 - CT scans are examples of imaging tests.

- Radiation from an atomic bomb
- Living in an area where there is air pollution.
- Having a lung cancer family history.
- Having a human immunodeficiency virus infection (HIV).
- Taking beta carotene supplements and smoking heavily.¹³

Lung cancer may be divided into two subtypes: Small cell lung carcinoma (SCLC) and Non-small cell lung carcinoma (NSCLC).

SCLC

- Because of their clinical and biologic characteristics, small cell lung cancer (SCLC), formerly known as oat cell carcinoma, is distinguished from other types of lung cancer known as non–small cell lung cancers (NSCLCs).¹⁴

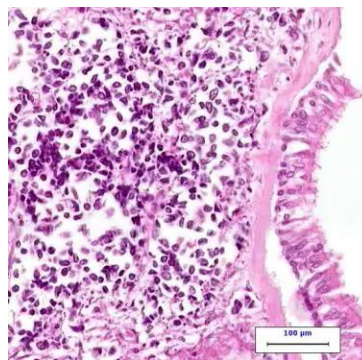


Figure 1.2:: Photo with high resolution: On the left is a micrograph of small cell carcinoma, and on the right is a micrograph of normal ciliated respiratory epithelium. (Source: <https://emedicine.medscape.com/article/280104-overview>)

Small cell lung cancer is classified into two types. Many different types of cells are included in these two categories. Each type of cancer cell grows and spreads in a unique way. Small cell lung cancer types are named after the types of cells found in the cancer and how the cells appear under a microscope:

- Small cell carcinoma (oat cell cancer).
- Combined small cell carcinoma.

NSCLC

NSCLC refers to any epithelial lung cancer that is not small cell lung cancer (SCLC). Squamous cell carcinoma, large cell carcinoma, and adenocarcinoma are the most common types of NSCLC, but there are several other types that occur less frequently, and all types

can have unusual histologic variants. Although NSCLCs are linked to cigarette smoking, adenocarcinomas can occur in people who have never smoked.

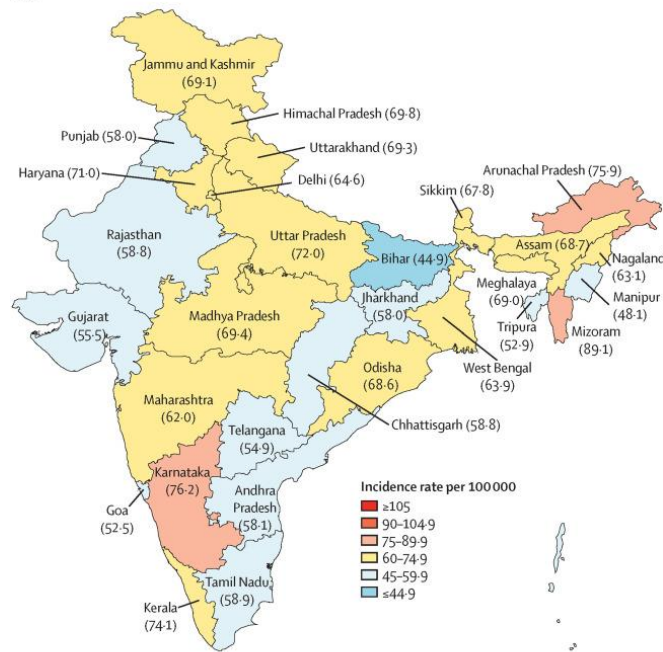
In general, NSCLC is less sensitive to chemotherapy and radiation therapy than SCLC. Surgery or surgery followed by chemotherapy can cure patients with resectable disease. Local control with radiation therapy can be achieved in a large number of patients with unresectable disease, but cure is only seen in a small number of patients. Patients with locally advanced unresectable cancer may benefit from radiation therapy combined with chemotherapy for long-term survival. Chemotherapy, targeted agents, and other supportive measures may improve survival and symptoms in patients with advanced metastatic disease.¹⁵

- The risk factors of NSCLC are like SCLC.
- Diagnosis: Patients with suspected NSCLC are investigated to confirm the diagnosis and determine the extent of the disease. Patients' treatment options are determined by histology, stage, general health, and comorbidities. The procedures used to determine the presence of cancer include the following:
 - History.
 - Physical examination.
 - Routine laboratory evaluations.
 - Chest x-ray.
 - Chest CT scan with infusion of contrast material.
 - Biopsy.

1.6 India and Cancer

India is a large country located in South Asia. It is the second largest country in the world in terms of population, and the 7th largest in the world in terms of area. As mentioned above, India had a projected incidence of patients with cancer in India among males at 679,421 (94.1 per 100,000) and among females at 712,758 (103.6 per 100,000) for the year 2020.¹⁶

1990



2016

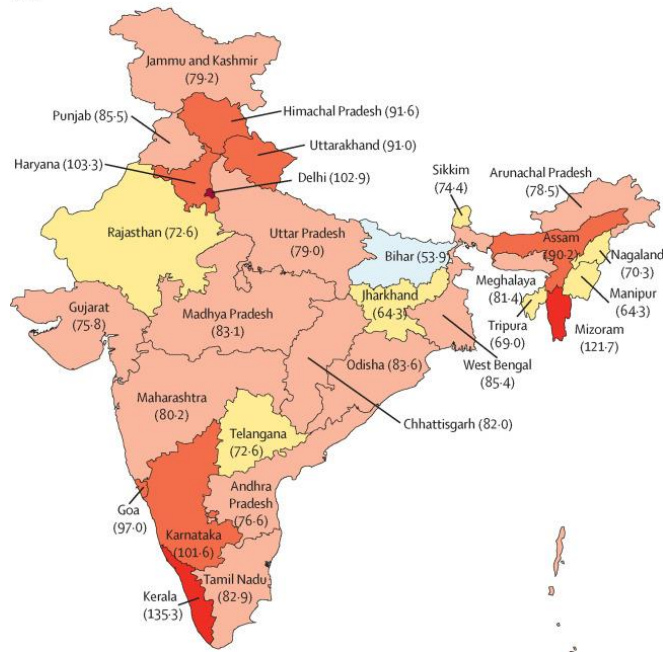


Figure 1.3: Map showing the burden of cancer in Indian states in 1990 and 2016. Source: [http://dx.doi.org/10.1016/S1470-2045\(18\)30447-9](http://dx.doi.org/10.1016/S1470-2045(18)30447-9)

1.7 NSCLC: India Outlook

Lung cancer is the most common type of cancer and the leading cause of cancer deaths worldwide. Lung cancer accounts for 5.9 percent of all cancers and 8.1 percent of cancer-related deaths in India. The prevalence of smoking in lung cancer patients is nearly 80%.¹⁷

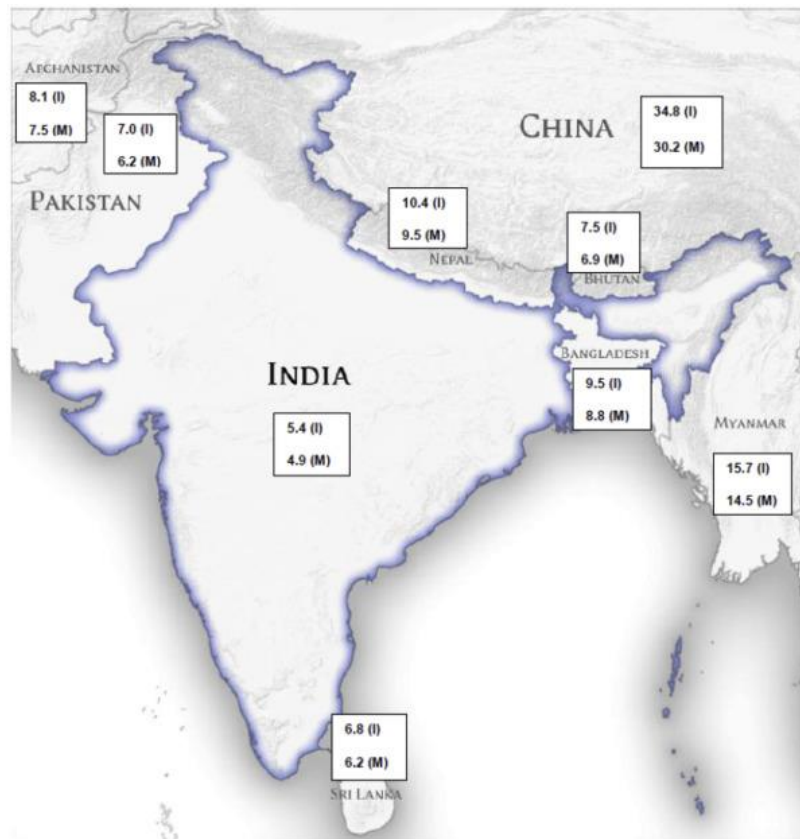


Figure 1.4: Age-standardized incidence and mortality rates of lung cancer in India as compared with neighboring countries. Data Source: GLOBOCAN 2020 (<https://gco.iarc.fr/today/fact-sheets-populations>)



Figure 1.5: Leading cancer sites in Population Based Registries in India 1995-96 (Source: MOHFW)

Table 1.1: Lung cancer demographics from various parts of India, various sources (1990-2020)

Author/Reference	Place/Year	Patient Number	Male: Female	Mean Age (y)	Smokers (%)	SqCC (%)	ADC (%)	SqCC: ADC	SCLC (%)
Jindal and Behera ^{S3}	Chandigarh, 1990	1009	4.5:1	51	63.0	34.3	25.9	1.3	25.9
Gupta et al. ^{S4}	Rajasthan, 1998	279	6.1:1	57	81.6	42.0	20.0	2.1	14.0
Prasad et al. ^{S5}	Lucknow, 2004	400	4.3:1	57	71.0	46.5	18.5	2.5	18.2
Khan et al. ^{S6}	Kashmir, 2006	321	11.3:1	—	88.4	77.3	5.3	14.6	17.1
Prasad et al. ^{S7}	Lucknow, 2009	799	4.8:1	—	80.4	47.3	18.2	2.6	13.7
Rawat et al. ^{S8}	Uttarakhand, 2009	203	8.2:1	56.4	81.8	44.8	19.4	2.3	16.8
Sheikh et al. ^{S9}	Kashmir, 2010	783	7.0:1	57.8	68.1	71.3	2.6	27.4	20.8
Singh et al. ⁴	Chandigarh, 2012	654	5.0:1	58.2	76.9	38.1	27.5	1.4	20.5
Dey et al. ^{S10}	Kolkata, 2012	607	4.1:1	57.9	67.2	35.1	30.8	1.1	16.5
Noronha et al. ^{S11}	Mumbai, 2012	489	3.5:1	56	52.0	26.2	43.8	0.6	8.0
Krishnamurthy et al. ^{S12}	Tamil Nadu, 2012	258	3.5:1	56	60.5	15.8	42.6	0.4	13.2
Sharma et al. ^{S13}	Himachal Pradesh, 2012	105	10.6:1	62.7	89.5	37.1	36.2	1.0	—
Malik et al. ^{S14}	New Delhi, 2013	434	4.6:1	55	67.9	32.1	37.1	0.9	14.7
Mandal et al. ^{S15}	Manipur, 2013	466	1.1:1	58.5	73.0	49.1	30.8	1.6	14.8
Baburao et al. ^{S16}	Bangalore, 2015	96	3.0:1	—	69.7	47.9	28.1	1.7	—
Mohan et al. ^{S17}	New Delhi, 2016	397	7.4:1	57.8	79.0	25.1	24.1	1.0	14.6
Murali et al. ¹⁸	Chennai, 2017	678	3.2:1	—	53.4	16.1	51.2	0.3	9.0
Kaur et al. ⁵	Chandigarh, 2017	1301	4.6:1	58.6	76.9	36.4	36.4	1.0	19.2
Mohan et al. ²	Delhi, 2020	1862	4.9:1	58	76.2	28.6	34.0	0.8	16.1

Based on a quick look at the table, one can make a quick conclusion that there is an 80-20 split between NSCLC and SCLC patients in almost any given region, which is in line with the global NSCLC/SCLC split. Thus, NSCLC poses the lion's share of threat when talking about lung cancer in India and elsewhere.

1.8 Oncology/Anti-Cancer Drugs

Drugs which are used to treat or manage cancer are called oncology drugs, antineoplastic agents, or anti-cancer drugs. There exists a wide variety of oncology drugs used for different types of cancer. The pharmacological classification, historically, consists of the following drug classes:

- Alkylating Agents
- Antimetabolites
- Natural Products
- Hormones and Antagonists
- Miscellaneous

When talking about drugs used to treat NSCLC (or any other cancer), classification becomes a bit more complicated than simply segregating on the basis of chemical agents as there are various different types of therapies used to treat cancer, and multiple lines of therapies. Some

therapies incorporated to treat cancer are chemotherapy, immunotherapy, targeted therapy, adjuvant, and neoadjuvant therapies etc.

In recent years, the miscellaneous group has grown to include some of the most important anticancer agents.¹⁸ With the advent of cancer research and anticancer drug discovery in recent years, more than 100 anticancer drugs have been approved by FDA.¹⁹ Anticancer drugs are usually more expensive than most other therapies and are responsible for increasing patient expenditure manifold.¹⁹

India follows a system of out-of-pocket medical expenditure, in contrast to the system of medical insurance in place in many developed countries. Thus, the high prices of anticancer drugs present a bigger problem in India. The high cost of these drugs is often responsible for decreasing compliance in patients.²⁰

1.9 Key Players in the Indian Oncology Market

AstraZeneca Plc, Bristol-Myers Squibb Co., Cadila Healthcare Ltd., Cipla Inc., F. Hoffmann-La Roche Ltd., Merck and Co. Inc., NATCO Pharma Ltd, Poly Medicure Ltd. And Siemens Healthineers AG are the key players in the Indian oncology market, as of 2022, according to *MarketWatch*.⁴

This study aims to identify and quote prices of oncology brands marketed by these companies and, wherever possible, look to compare prices of the same drug across brands. In addition to this, this study aims to establish price ranges of these drugs based on the availability of pricing data across public domain.

2 Review of Literature

Table 2.1: Literature Review

Sr no.	Publication	Author	Details	Derivation
1	Perspective of Oncology Patients During COVID-19 Pandemic: A Prospective Observational Study From India, JCO Global Oncology 2020 :6, 844-851	Joydeep Ghosh, Sandip Ganguly, Debapriya Mondal, Prashant Pandey, Deepak Dabkara, and Bivas Biswas	Total of 302 patients (median age, 56 years; range, 21-77 years)	This research found out that in total of 302 patients (median age, 56 years; range, 21-77 years) most common sites of cancer were breast (n = 114), lung (n = 44), ovary (n = 34), and colon (n = 20).
2	Cancer Statistics, 2020, Report From National Cancer Registry Programme, India, JCO Global Oncology 2020	Report From National Cancer Registry Programme, India	On behalf of ICMR-NCDIR-NCRP Investigator Group	It reports that the projected number of patients with cancer in India is 1,392,179 for the year 2020, and the common 5 leading sites are breast, lung, mouth, cervix uteri, and tongue.
3	Oncology Market in India by End-user, Type, and Geography - Forecast and	-	Published: Oct 2021, SKU: IRTNTR7 1137	The oncology market growth will increase by \$734.18 million during 2020-2025.

	Analysis 2021-2025			
4	3 cancer drug studies to watch at next month's ASCO meeting, <i>BioPharma Dive</i>	Ben Fidler and Ned Pagliarulo	Published May 26, 2022	Enhertu, an antibody drug from Daiichi Sankyo and AstraZeneca, has become a go-to treatment option for breast cancer patients whose tumors overexpress a protein known as HER2. This highlights the continued efforts of AstraZeneca in oncology research.
5	AstraZeneca a Key Player in the Small Cell Lung Cancer Drugs Market, GlobalData Plc	Global Data	May 31, 2022 11:20 ET	There are three leading marketed drugs for the treatment of SCLC. AstraZeneca is a key player in the disease space.
6	Bristol-Myers Squibb to acquire cancer drugmaker Turning Point for \$4.1bn, <i>Financial Times</i>	Jamie Smyth	Published 05/04/2022	Bristol-Myers Squibb has agreed to acquire Turning Point Therapeutics for \$4.1bn in the latest in a series of bolt-on acquisitions by pharmaceutical companies looking to bolster their drug pipelines. This cements BMS' status as a leader in the global oncology landscape.
7	Article by Businesswire	-	Published June 02, 2022	Bristol Myers Squibb has announced topline results showing treatment with Orencia (abatacept) improved survival in people hospitalized with COVID-19.

8	Article by <i>Businesswire</i>	-	Published on May 19, 2022	It reports that Bristol Myers Squibb Data at ASCO and EHA 2022 highlighted progress in transforming treatment for patients with cancer and blood disorders.
9	The top 10 cancer drug makers of 2024, <i>Fierce Pharma</i>	Carly Helfand	Published Nov 12, 2018	Roche, Celgene and Bristol-Myers Squibb—which took the top three spots last year—are projected by EvaluatePharma to rank 1-2-3 six years from now, too. This highlights Roche and BMS’s sustained strong position in the global oncology market.
10	Business Standard Article	-	Published May 24, 2021	Cadila Healthcare has announced the launch of Trastuzumab Emtansine, the first Antibody Drug Conjugate (ADC) biosimilar for treating both early and advanced HER2 positive breast cancer.
11	New drug combination lengthened survival for some with lung cancer	Peer-Reviewed Publication SWOG CANCER RESEARCH NETWORK	NEWS RELEASE 3-JUN-2022	Ramucirumab plus pembrolizumab combination reduced risk of death by 31 percent compared to standard of care in patients with advanced non-small cell lung cancer that had progressed on prior immunotherapy. S1800A was funded by the NIH/NCI through grants CA180888, CA180819, and CA180821, and in part by the

				Foundation for the National Institutes of Health, Eli Lilly and Company, and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc.
12	Merck KGaA nabs another baton in protein degradation race with \$554M Proxygen deal, <i>Fierce Biotech</i>	Max Bayer	Published Jun 2, 2022	Merck KGaA has decided it needs more than one baton in the metaphorical clinical relay race, inking a \$554 million deal with Austrian biotech Proxygen.
13	Lung cancer: Prevalent trends & emerging concepts	Prabhat Singh Malik and Vinod Raina	Indian J Med Res. 2015 Jan, doi:10.4103/0971-5916.154479	This research reports that about 50% of adenocarcinomas can be characterized based on the mutation profile, which has led to development of targeted therapy drugs in this indication.
14	Emerging therapeutic agents for advanced non-small cell lung cancer	Ruqin Chen, Rami Manochakian, Lauren James, Abdel-Ghani Azzouqa, Huashan Shi, Yan Zhang et al.	Published 23 rd April 2020, Doi: https://doi.org/10.1186/s13045-020-00881-7	This secondary research covers the unprecedented rise of immunotherapy and targeted therapy in the treatment of advanced NSCLC. 17 new medications have been approved for NSCLC from 2010-2020.

15	Targeted therapy for non-small cell lung cancer: current standards and the promise of the future	Bryan A. Chan and Brett G.M. Hughes	Translational lung cancer research vol. 4,1 (2015): 36-54. doi:10.3978/j.issn.2218-6751.2014.05.01	This secondary research highlights the importance of classifying NSCLC on the basis of histology and driver mutations and the fact that recent research has shown such mutations to be counter-acted by monoclonal antibodies (mAb) or small molecule tyrosine kinase inhibitors (TKI).
16	Immunotherapy for Advanced Non-Small Cell Lung Cancer: A Decade of Progress	Misty Dawn Shields, MD, PhD; Julian A. Marin-Acevedo, MD; and Bruna Pellini, MD	American Society of Clinical Oncology Educational Book 2021 :41, e105-e127	This review article makes it abundantly clear that patients with advanced non-small cell lung cancer now have a variety of treatment options, ranging from single-agent immunotherapy to quadruple therapy, which includes a dual immune checkpoint inhibitor plus chemotherapy or an immune checkpoint inhibitor plus chemotherapy plus anti-vascular endothelial growth factor drugs.
17	FDA Approves First Targeted Therapy for Lung Cancer Mutation Previously Considered	-	FDA Press Release, May 28, 2021	The USFDA approved Lumakras (Sotorasib) as the first in line targeted therapy for KRAS G12C mutated advanced stage NSCLC patients who have received at least one prior line of therapy. Earlier, this mutation was

	Resistant to Drug Therapy			considered to be resistant to drug usage.
18	Targeting BRAF mutations in non-small cell lung cancer	Connor Gerard O'Leary, Vladamir Andelkovic, Rahul Ladwa1 et al.	Published Dec 2019, Princess Alexandra Hospital, Brisbane, Australia; Translational Research Institute, Brisbane, Australia; Royal North Shore Hospital, Sydney, Australia; and various other institutes	BRAF mutation is a rare kind of mutation present in NSCLC patients, however Immunotherapy is beginning to show promise as an active therapy in BRAF mutated NSCLC in both V600E and non-V600E subtypes.
19	Two-Drug Combination Approved for Lung Cancers with BRAF Mutations	National Cancer Institute Staff	July 18 th , 2017	On June 22 nd 2017, FDA approved targeted combination therapy for NSCLC, i.e. dabrafenib and trametinib, which will be used to treat patients with metastatic NSCLC who have an

				alteration in their BRAF gene called V600E mutation.
20	U.S. Food and Drug Administration (FDA) Accepts Mirati Therapeutics' New Drug Application for Adagrasib as Treatment of Previously Treated KRASG12C-Mutated Non-Small Cell Lung Cancer	Mirati Therapeutics Press Release	15 th Feb, 2022	Mirati (Adagrasib) has had its NDA (New Drug Application) accepted by the US FDA for the treatment of KRAS G12C mutated patients, who received at least one prior line of therapy. It is currently being reviewed by the FDA for accelerated approval.

3 Methodology

This is secondary research, comprised of three elements:

- A PEST analysis of the Indian lung cancer market, including Political, Economic, Social, Technological, Legislative and Environmental factor analysis. It incorporates various sources from publicly available databases and gathers them in a comprehensive study.
- Identification of top lung cancer players in the Indian oncology market, and their products currently approved in India.
- A cost analysis of various NSCLC products in India.

This is followed by a summarization of the findings and some key takeaways.

Study Design: Secondary quantitative research and secondary qualitative research are used to find relevant data and information about oncology drugs pricing in India, from various sources available in the public domain.

Setting: India

Data Collection: Secondary data collection done via articles, reports, peer-reviewed papers, government-published documents, and databases.

Data Analysis: Software used are Excel from Microsoft 365 package.

4 Discussion

4.1 PEST Analysis

4.1.1 Political Factors

Indian Pharma industry, as a whole, is influenced by various political factors surrounding it. Any impacts observed on the Indian pharma industry will translate to the oncology market, and in turn, the NSCLC market in India. Some of these factors include:

- Bilateral Relations:
 - **Indo-China Relations:** China has a history of repeated border incursions into Indian territory, and recent times have been no exception, with recent violations of Indian territory by China near the Sino-Indian border. Chinese and Indian

troops have engaged in aggressive melee, face-offs and skirmishes at locations along the Sino-Indian border, including near the disputed Pangong Lake in Ladakh. All this has led to increased political tensions between India and China, with both sides resorting to tightening security around borders. India has also moved to ban Chinese applications, with 176 such applications banned. In such a political scenario, Indian pharma industry has also been affected.

There is a growing clamour in India for boycotting trade with China amidst recent political tensions between the two countries. India relies on China for API. An estimated 70 per cent of API requirements of India's pharmaceutical industry are sourced from China. Given this, restricting or banning the import of APIs would cause significant disruption to the Indian pharmaceutical industry which had \$40 billion in revenues in 2018-19, according to Pharmexcil.

The Pharma industry needs time to switch from China to other API markets. Chinese API is the cheapest and easiest to procure. Experts are of the opinion that while self-reliance from China is possible in a year's time, switching to another country means testing their API over a period of time. In short, we need material from China currently. But China has also increased its prices over the last few months. Therefore, independence from China can be a long opportunity which will help India escape China's monopoly over API and become self-reliant.

- **Indo-US Relations:** India and the United States have enjoyed a pleasant diplomatic relationship over the years. The United States seeks an expanded trade relationship with India that is reciprocal and fair. In 2019, overall U.S.-India bilateral trade in goods and services reached \$149 billion. U.S. energy exports are an important area of growth in the trade relationship.

India and the United States cooperate closely at multilateral organizations, including the United Nations, G-20, Association of Southeast Asian Nations (ASEAN) Regional Forum, International Monetary Fund, World Bank, and World Trade Organization. The United States welcomes India joining the UN

Security Council in 2021 for a two-year term, and supports a reformed UN Security Council that includes India as a permanent member. India is an ASEAN dialogue partner, an Organization for Economic Cooperation and Development partner, and an observer to the Organization of American States. India is also a member of the Indian Ocean Rim Association (IORA), at which the United States is a dialogue partner. In 2019, the United States joined India's Coalition for Disaster Resilient Infrastructure to expand cooperation on sustainable infrastructure in the Indo-Pacific region.

However, there are concerns regarding free trade with the U.S. and its impact on the Indian pharma industry. Concerns of the US on policies and practices of India in trade issues, highlighted in the 'National Trade Estimate Reports on Foreign Trade Barriers' and on the protection and enforcement of intellectual property rights (IPRs), highlighted in the 'Special 301 Reports' give an indication of the issues that the US would want to address in the FTA. The Special 301 Reports have been raising matters with regard to the Patents Act of India, such as narrow patentability standards – which puts a check on pharmaceutical innovations that do not show therapeutic efficacy – and lack of protection of test data submitted to regulatory authorities (data exclusivity). Resolution of these issues to the satisfaction of the US could lead to the amendment of the Patents Act, but that could impact the Indian pharma industry. The IPR chapter of the re-negotiated NAFTA agreement (NAFTA 2.0), on the lines of TPA 2015, reflects the standard of patent protection in the US, which the administration would seek its FTA partners to have in place. There are three key provisions in the IPR chapter of NAFTA 2.0, which if incorporated into the Patents Act, would severely hit the Indian pharma industry.

One, it provides for patents for all innovations, which includes new uses of a known product, new methods of using a known product or new processes of using a known product. But section 3(d) of India's Patents Act allows innovations of this nature, in pharmaceutical products, only if the innovations prove therapeutic efficacy. Section 3(d) not only checks the 'evergreening' of patents and frivolous

patents, thereby providing more space for generic manufacturers, but also contributes in ensuring the quality of innovations by filtering in only meritorious innovations. An FTA with the US could lead to the removal of this section from the Indian Patents Act; in fact, the US has been making this demand for a long time.

In short, amendments to the Patents Act at the insistence of the US will pave the way for 'evergreening' of pharmaceutical patents in India, thereby curtailing competition in the market. The pharmaceutical industry is one of the few in which India has a price advantage globally, which has earned it the 'pharmacy of the world' tag. An FTA with the US will severely shake the foundation stones on which the Indian pharma industry has been built upon.

- **Indo-Russian Relations:** There have been recent talks that India's hesitance to condemn Russia puts the country's pharma industry in compromising position. Many Indian pharmaceutical companies do extensive business with Russia and Ukraine. According to Business Standard, India exported more than \$591 million in pharmaceutical goods to Russia last fiscal year and \$181 million to Ukraine. Year on year, those figures represented growth rates of 7% and 44%, respectively. According to Reuters, no Indian companies, pharmaceutical or otherwise, have pulled out of Russia.

For example, Dr. Reddy's Laboratories told Reuters that it is bracing for sales disruptions but has not taken any action against the country. In India, Dr. Reddy's manufactures and distributes Russia's Sputnik V COVID-19 vaccine.

A *Mint* report from June 11, 2022 observes that as a result of Russia's invasion of Ukraine, the West has imposed a number of sanctions on the country. The crisis began on February 24, when Russian President Vladimir Putin declared a military offensive against the East European country. This however means that India can latch onto opportunities in the Russian market. Denis Alipov, Russia's envoy to

India, stated on June 10, 2022 that Indian pharmaceutical companies could replace demand for Western companies in Russia.

- Political Scenario in India: India is one of the few developing countries with a National Cancer Control Programme. The programme envisions tobacco-related cancer control, early detection and treatment of uterine cervical cancer, and distribution of therapy services, pain relief, and palliative care through health infrastructure enhancement. Changes in tobacco use, the 'Knowledge, Attitude, Practice' (KAP) pattern, compliance with screening programmes, changes in referral practises, and a shift in stage distribution are all suggested surrogate outcome measures. (via Ministry of Health and Family Welfare, Government of India)

The Indian government's policy interventions in the pharmaceutical sector are pushing for creating an environment for innovation so that India can become a leader in discovery of pharmaceuticals and medical technology, remarked Prime Minister Narendra Modi on Nov 19, 2021. This indicates that India is prepared to push its price advantage in the world pharma domain, and this overall growth will aid the pharma sector. Given the current circumstances, we can expect the Indian lung cancer market to grow in the coming years.

- Price Control in India: In India, NPPA regulates the prices of all Drugs as per the Drug Price Control Order (DPCO) 2013. NPPA stands for National Pharmaceutical Pricing Authority. According to a 6th November, 2020 press release by Ministry of Chemicals and Fertilizers, Government of India, on November 7, 2020, the NPPA stated that the decision received unanimous support from all stakeholders. Based on feedback from pharmaceutical companies following the implementation of the NPPA notification, it was discovered that during this exercise, 526 brands of 42 anti-cancer drugs saw price reductions of up to 90%.²³

For example, the price of Erlotinib 150 mg tab under Brand Birlotib was reduced from Rs 9999/- to Rs 891.79. Although this represents a pleasant scenario for patients and

affordable cancer care, it presents a major business blockade for NSCLC drug manufacturers in India.

4.1.2 Economic Factors

Plenty of economic factors abound, affecting the lung cancer market in India. The Asia-Pacific region's lung cancer market, which comprises of developing countries such as India and China, is forecasted to worth 170B USD by 2027, growing at a CAGR of 7.65% from 2022-2027.²⁴ The spread of cancer is driving the APAC market growth. Some other economic factors that influence the lung cancer market in India are:

- **Rapid Industrialization:** Both India and China are developing nations and are pushing for rapid industrialization to aid economic growth. This leads to increased business across sectors including pharma, and thus becomes a driving factor in lung cancer market growth.
- **DPCO:** Drug Price Control Order, 2013, exercise of the powers conferred by section 3 of the Essential Commodities Act, 1955, (10 of 1955), and supersession of the Drug (Prices Control) Order, 1995, except as respect to things done or omitted to be done before such supersession, is an order by the Central Government of India to control rising drug prices across therapies in India. This only allows for an annual increase in drug prices, for any company at the start of the year.²⁵
- **Inflation:** Inflation has a detrimental affect on manufacturing cost of drugs, however due to an in-place DPCO (Drug Price Control Order) of 2013 in India, mid-year increase in drug prices is prohibited. This affects business and lowers the profits of pharma companies selling lung cancer products in India.
- **Falling INR:** The Indian Rupee has shown a downward trend against the US Dollar in the last 10 years and Business Today reported on May 9, 2022 that the Rupee has dropped 51 paise to an all-time low of Rs 77.41 against the US dollar in early trade.²⁶ This drop in value is not good news for Foreign Drug companies' India units, because it delays the introduction of imported medicine. It also erodes the profitability of several imported drugs. This, coupled with the DPCO really affects business for foreign pharma companies in India.
- **Average Medical expenditure in India:**

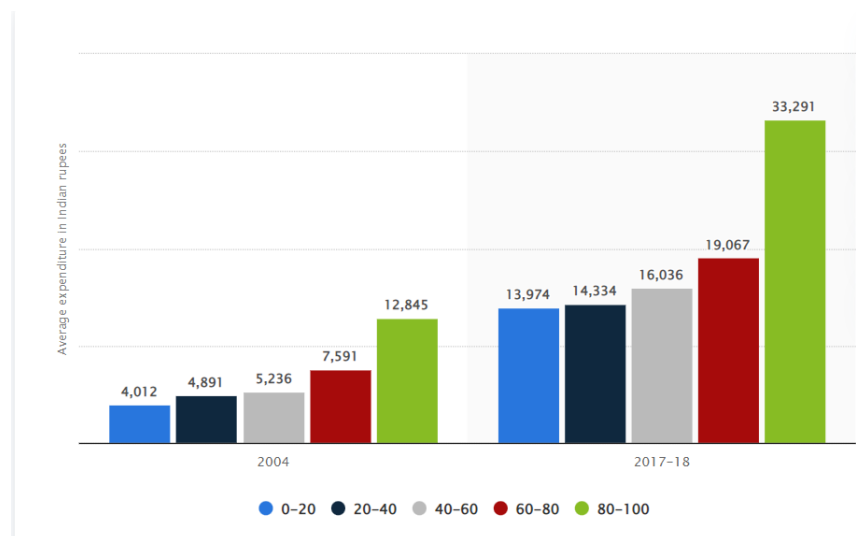


Figure 4.1: Average medical expenditure in current price per hospitalization case in India in 2004 to 2018, by consumption group (Source: <https://www.statista.com/statistics/1267167/india-average-medical-expense-in-current-price-per-hospitalization-case-by-consumption-group/>)

The average medical expenditure per hospitalization has increased in India several fold across all age groups from 2004 to 2017-18, as depicted by the bar chart. Oncology medicines are usually more expensive than any given indication's medicine, thus an increase in medical expenditure per hospitalization is good news and is understood to have a positive impact on lung cancer drug purchase in India.

4.1.3 Social Factors

The impact of socio-cultural factors in a country is felt across industries. This naturally means that the pharmaceutical industry is no exception. We observe that a number of such factors influence the NSCLC market in India. Some of them are discussed below:

- Level of lung cancer awareness:** There is a study titled "Level of Awareness of Various Aspects of Lung Cancer Among College Teachers in India: Impact of Cancer Awareness Programmes in Prevention and Early Detection" authored by Abhishek Shankar , Shubham Roy , Abhidha Malik and various other authors²⁷, which chronicles the results of a Pink Chain campaign, which was a campaign on cancer awareness. The results of this study concluded that after conducting cancer awareness events in various colleges between 2011-2013, the level of knowledge regarding lung cancer significantly improved after 6 months, with the results sustaining after one year. The awareness even caused a significant change in smoking and drinking habits among the college teachers. Another significant finding from this study was that major reasons for not going for check-up were

ignorance (83.1 %), fear (30.1 %) and lethargic attitude (29.3 %) initially, but over time, lack of time, lethargic attitude and hesitation became important factors after knowing various aspects of lung cancer.

What this tells us is that India has an issue when it comes to cancer awareness, as college professors and teachers are supposed to belong to uplifted, educated echelons of our society. One would assume that the level of cancer awareness would be high and treatment hesitancy would be low, however we still see those issues persisting. Cancer awareness programmes are a positive and effective activity and a requirement to initiate change, as demonstrated by the study. However, if the study's results are anything to go by, one would be worried that ignorance, being the reason for majority of the population to avoid lung cancer check-ups, is not an encouraging testament to the fact that there is still a long way to go when it comes to cancer awareness in India.

This does not bode well for the NSCLC market in India.

- **Lifestyle:** MOFHW, India published a report on 50 years of cancer care in India, titled 'CANCER PREVENTION AND CONTROL IN INDIA', which states that tobacco is the most widely recognized cause of cancer, accounting for 40 to 50 percent of malignancies in men and 20 percent of cancers in women. The report also states that dietary habits are thought to be responsible for 10 to 20% of malignancies in India.

According to the Global Adult Tobacco Survey India, 2016-17, about 267 million adults (15 years and older) in India (29 percent of all adults) use tobacco. As tobacco use includes cigarette smoking, a major risk factor for NSCLC, we can say that a large chunk of the population of India stands at a potential lung cancer risk, among other health adversities.

- **Age of the Population:** Lung cancer is diagnosed in about two out of every three people over the age of 65, and the majority of those diagnosed are over the age of 45. At the time of diagnosis, the average patient is 71 years old.²⁸ In India, approximately 139 million people over the age of 60 live there, accounting for more than 10% of the entire population. With 319 million individuals over the age of 60, the proportion of older persons is predicted to nearly quadruple to 19.5 percent in 2050. This indicates that one out of every five Indians is going to be over the age of 65. Given the very first statistic in

this section (majority of lung cancer diagnosed are over 45), and the fact that India has an ageing population, we can say that the potential patient pool for NSCLC should be on the rise.

- **Change in Food and Exercise Habits:** India's HDI (Human Development Index) has been steadily increasing. Based on consumption expenditure, education, and health, this index accurately reflects living conditions. According to the United Nations, India's HDI in 2014 was 0.586, up 5.77 percent from 2012. India's HDI was 0.647 in 2018.²⁹ Talking about physical exercise, a fitness survey demonstrated that compared to the 2019 data, where just 26% of Indians practised yoga, 11% cardio workouts, and 10% body-weight exercises, the 2020 data indicated a nearly 60% increase in all activities.³⁰

Thus, as healthy lifestyle adopters increase in India, one can assume that the risk of cancers including NSCLC will come down.

4.1.4 Technological Factors

Cancer research has really picked up the pace in terms of technology in recent years. Lung cancer too, hasn't been alienated from this progress and is constantly receiving new advancements when it comes to bettering the diagnosis and treatment of the disease. It includes research related to early stage detection, adjuvant, neoadjuvant, immuno therapies and also the recent rise of targeted therapy in NSCLC. Some key recent technological advances in the NSCLC field are as follows:

- **Sotorasib Approval:** The FDA granted accelerated approval to sotorasib (brand name Lumakras), a RAS GTPase family inhibitor, on May 28, 2021, for adult patients with KRAS G12C mutated locally advanced or metastatic non-small cell lung cancer who have received at least one prior systemic therapy, as determined by an FDA approved test.³¹
- **Mirati FDA application accepted:** Mirati Therapeutics, Inc. (Nasdaq: MRTX), a clinical-stage targeted oncology company, announced on February 15, that the US Food and Drug Administration (FDA) has approved adagrasib for the treatment of patients with non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy and have the KRASG12C mutation.³²

- **Advancements in Immunotherapy:** An immune checkpoint inhibitor is a medication that prevents immune system cells from attacking cancer by blocking proteins on their surface. Some recent examples of approved immune checkpoint inhibitors are:
 - Atezolizumab (Tecentriq)
 - Cemiplimab (Libtayo)
 - Durvalumab (Imfinzi)
 - Nivolumab (Opdivo)
 - Pembrolizumab (Keytruda)³³
- **Rise in other Targeted Therapies:** Apart from the already discussed Sotorasib and Adagrasib, there are plenty of other recently approved classes of drugs that come under targeted therapy for NSCLC. These include Anaplastic lymphoma kinase (ALK) Inhibitors, EGFR inhibitors, BRAF inhibitors, ROS1 inhibitors and more.³²
- **Radiotherapy Advances:** Some recent advances in the radiotherapy space for lung cancer include stereotactic ablative radiation therapy (SABR) and stereotactic body radiation therapy (SBRT).³⁴

4.2 COST ANALYSIS OF NSCLC MARKET

The cost analysis in this study doesn't cover all the drugs currently being marketed for NSCLC in India, rather it just focuses on notable products sold by top lung cancer market players in India. The products, along with the molecule name are listed followed by a tabular representation of prices gathered via various online sources.

4.2.1 Roche

Roche is a known pharma behemoth of the world. In 2020, it was ranked 2nd, just behind Johnson and Johnson, as the second largest pharmaceutical company in the world in terms of revenue.³⁵

Notable NSCLC products by Roche, currently being marketed/available in India are:

4.2.1.1 **Tecentriq (Atezolizumab):**

Roche released the monoclonal antibody atezolizumab, marketed as Tecentriq, for the treatment of lung and bladder cancer in India in 2018. In the approved indications, Tecentriq has shown to extend survival and improve quality of life, according to Roche. "For two forms of cancers: non-small cell lung cancer (NSCLC) and urothelial carcinoma, a type of bladder and urinary tract cancer," the medicine has been approved in India.³⁵

4.2.1.2 **Rozlytrek (Entrectinib)**

Rozlytrek (Entrectinib) is an ALK inhibitor that has been approved by the FDA for people with ROS1- NTRK Gene Fusion-Positive Solid Tumors and Positive, Metastatic Non-Small Cell Lung Cancer in 2019.³⁸

This drug is not directly marketed in India but is available for purchase via imports.

4.2.2 Pfizer

Pfizer is no anomaly when there is discussion of world's biggest pharmaceutical companies. In 2004, it was ranked number 1 among all Pharma MNCs & number 4 among all Pharma Companies by Business World.^{Error! Reference source not found.} Notable NSCLC products Pfizer India currently markets are:

4.2.2.1 Lorbriqua/Lorbrena (Lorlatinib)

Lorlatinib was first approved by the FDA in 2018 for the treatment of patients with ALK-positive metastatic NSCLC whose disease progressed after receiving crizotinib and at least one other ALK inhibitor for metastatic disease, or for those whose disease progressed after receiving alectinib or ceritinib as the first ALK inhibitor for metastatic disease.³⁹ The FDA granted accelerated clearance for this indication to Lorlatinib, an oral kinase inhibitor, based on tumour response rate and duration of response in a subgroup of patients with ALK-positive metastatic NSCLC in a phase 2 clinical trial. The FDA granted accelerated clearance for this indication to Lorlatinib, an oral kinase inhibitor, based on tumour response rate and duration of response in a subgroup of patients with ALK-positive metastatic NSCLC in a phase 2 clinical trial.

As of 2021, Pfizer's LORBRENA (lorlatinib) has been approved by the US Food and Drug Administration (FDA) as a first-line treatment for anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).⁴¹

Lorlatinib is available in India with the brand name Lorbriqua.

4.2.2.2 Xalkori/Crizalk (Crizotinib)

Crizotinib, also known as Xalkori, is an anti-cancer drug available as capsule that works by inhibiting the enzymes ALK and ROS1. It was first approved for advanced stage metastatic NSCLC in USA in the year 2011. In 2016, its approval was expanded to include the treatment of ROS-1 Positive Non-Small Cell Lung Cancer.⁴¹

In India, Xalkori may be available with the brand name 'Crizalk'.

4.2.3 AstraZeneca

AstraZeneca has had its presence in the Indian market since 1979. During this period, it has been associated with quality healthcare and is one of the biggest names in the world pharmaceutical industry. It also has a glowing oncology portfolio and has been one of the pioneers of cancer research through the years.

Some of the NSCLC products by AZ, available or currently being marketed in India are:

4.2.3.1 Tagrisso (Osimertinib)

Osimertinib is used to treat NSCLC with certain specific mutations. It is available in the form of tablets. Tagrisso (osimertinib) is a tyrosine kinase inhibitor that works by inhibiting epidermal growth factor receptor activation (EGFR). The EGFR gene enables cancer cells to proliferate and divide uncontrollably in the lungs.⁴²

Tagrisso was first approved by the FDA in late 2015. Very recently, in 2020, Tagrisso was approved in the US for the adjuvant treatment of patients with early-Stage EGFR-mutated Non-Small Cell Lung Cancer.⁴³

4.2.3.2 Imfinzi (Durvalumab)

Imfinzi is an immunotherapy drug used to treat NSCLC. It is taken in the form of injections. It was first approved by the FDA in the year 2016 for bladder cancer and later approved for the treatment of NSCLC in 2018 for Unresectable Stage III Non-Small Cell Lung Cancer.⁴⁴

4.2.4 Bristol Myers Squibb

Bristol Myers Squibb (BMS) is an American Pharmaceutical company. It is one of the world's largest pharmaceutical companies and consistently ranks among the Fortune 500 companies. In 2021, it ranked 82 on the Fortune 500 and reported its total revenue as \$46.4 Billion.⁴⁵

An NSCLC product currently marketed by BMS in India is:

4.2.4.1 Opdivo/Opdyta (Nivolumab)

Opdyta, molecule name Nivolumab is a monoclonal antibody drug that belongs to the immunotherapy class of NSCLC treatment. It is taken in the form of injections. Besides NSCLC, it is also approved for a number of other indications in oncology. It is approved for melanoma, urothelial cancer and colorectal cancer treatments. It was first approved by the US FDA in the year 2014 for lung cancer and later in 2015 for advanced lung cancer. Opdivo is also cleared for NSCLC treatment in metastatic NSCLC patients with PDL1 $\geq$ 1%, in combination with Yervoy (Ipilumab), also manufactured by BMS.⁴⁶

Opdivo is currently being marketed in India with the brand name Opdyta.

4.2.5 Merck

Merck and Co, sharing its name with its German counterpart, is an American Multinational Pharmaceutical company. Usually mentioned in the same breath as the Pfizers and Johnson and Johnsons of the world, Merck is one of the largest pharmaceutical companies on the planet, coming in at the 71st spot on the Fortune 500 list 2022.⁴⁷

Merck currently sells a very important NSCLC product in India, namely:

4.2.5.1 Keytruda (Pembrolizumab)

Keytruda, or Pembrolizumab is a monoclonal antibody used in the treatment of advanced stage NSCLC. It is an injectible drug, which was first approved for treatment by the US FDA in 2018, for Patients with Metastatic Nonsquamous NSCLC with No EGFR or ALK Genomic Tumor Aberrations. It went on to have a flurry of approvals, often spanning other indications such as colorectal cancer and renal cell carcinoma.⁴⁸

4.2.6 Notable Omissions

This list excludes some prominent drugs used for the treatment of NSCLC, for the simple reason that many of them have lost their exclusivity, and generics have taken over their market share. That is why that becomes a different discussion altogether where we can compare generics and biosimilars of anti-NSCLC drugs. A glaring omission is Avastin, a prominent chemotherapy used in NSCLC, whose omission is explained by the already mentioned criteria. Other prominent drugs, similarly, excluded from this discussion include,

- Cisplatin.
- Carboplatin.
- Paclitaxel (Taxol)
- Albumin-bound paclitaxel (nab-paclitaxel, Abraxane)
- Docetaxel (Taxotere)
- Gemcitabine (Gemzar)
- Vinorelbine (Navelbine), and many more.

Selecting drugs that haven't lost their market exclusivity makes for a healthier discussion for price competency, gross-to-net ratios, and therapy costs.

One might notice that the current selection exclusively consists of targeted therapies and immunotherapy drugs, which just goes to show the rise in prominence of the two categories in recent years over traditional chemotherapy.

4.3 Tabular Representation of Price

Table 4.1: MRP and Discounted Prices, NSCLC Drugs India

Sr no	Brand Name	Molecule	Manufacturer	Class	SKU	M.R.P* (source)	Discounted Price* (Source)
1	Tecentriq	Atezolizumab	Roche	Immunotherapy (Monoclonal antibody)	1200 mg/20 mL injection (1 vial)	Rs 3,96,725/- (Tata 1mg, Apollo Pharmacy)	Rs 1,25,000-3,30,000/- (IndiaMart), Rs 325314.50/- (Apollo Pharmacy), Rs 3,37,126/- (PharmEasy)
2	Tecentriq	Atezolizumab	Roche	Immunotherapy (Monoclonal antibody)	840 mg/14 mL injection (1 vial)	Rs 2,77,708/- (Apollo)	Rs 89,900/- (IndiaMart), Rs 2,27,720/- (Apollo)
3	Rozlytrek	Entrectinib	Roche	ALK and ROS1 inhibitors	200 mg tab (90 unit bottle)	N/A (Drug not marketed in India)	Rs 1,81,000/- (IndiaMart)
4	Lorbriqua	Lorlatinib	Pfizer	ALK and ROS1 inhibitors	100 mg tab (30 unit bottle)	Rs 3,12,000/- (Apollo Pharmacy)	Rs 1,08,000/- (IndiaMart), Rs 2,55,840/- (Apollo)
5	Lorbriqua	Lorlatinib	Pfizer	ALK and ROS1 inhibitors	25 mg tab (30 unit bottle)	Rs 1,02,000/- (Mr Med Pharmacy)	Rs 78,336/- (Mr Med)
6	Crizalk/Xalko ri	Crizotinib	Pfizer	ALK and ROS1 inhibitors	200 mg cap (60 unit bottle)	Rs 1,00,177/- (Netmeds)	Rs 80,142/- (Netmeds)
7	Crizalk/Xalko ri	Crizotinib	Pfizer	ALK and ROS1 inhibitors	250 mg cap (60 unit bottle)	Rs 1,06,207/- (Apollo)	Rs 85,016/- (Netmeds), Rs 90,276/- (Apollo)

8	Tagrisso	Osimertinib	AstraZeneca	EGFR inhibitor	80 mg tab (10 unit pack)	Rs 2,04,435/- (Apollo Pharmacy)	Rs 1,83,992/- (Apollo Pharmacy), Rs 1,73,770/- (PharmEasy)
9	Tagrisso	Osimertinib	AstraZeneca	EGFR inhibitor	40 mg tab (10 unit pack)	Rs 2,02,391/- (Netmeds)	Rs 1,61,913/- (Netmeds)
10	Imfinzi	Durvalumab	AstraZeneca	Immunotherapy (Monoclonal antibody)	120 mg/2.4 mL injection (1 vial)	Rs 45,500/- (Tata 1 Mg)	Rs 44,900/- (Tata 1 Mg)
11	Imfinzi	Durvalumab	AstraZeneca	Immunotherapy (Monoclonal antibody)	500 mg/10 mL injection (1 vial)	Rs 1,89,505/- (Apollo)	Rs 1,55,459/- (Apollo)
12	Opdivo/Opdyta	Nivolumab	BMS	Immunotherapy (Monoclonal antibody)	10 mg/mL (100 mg vial)	Rs 99,500/- (Tata 1 mg)	Rs 79,600/- (PharmEasy), Rs 50,000-55,000 (IndiaMart)
13	Opdivo/Opdyta	Nivolumab	BMS	Immunotherapy (Monoclonal antibody)	10 mg/mL (40 mg vial)	Rs 39,800/- (Tata 1 Mg)	Rs 22,000-28,000/- (IndiaMart)
14	Keytruda	Pembrolizumab	Merck	Immunotherapy (Monoclonal antibody)	100 mg/4 mL (4 mL vial)	Rs 2,36,000/- (Tata 1 mg)	Rs 2,01,025/- (PharmEasy), Rs 90,000-1,48,000/- (IndiaMart)

4.4 GTN Ratios For Each SKU

There are two types of therapies in the current cost analysis selection. They are targeted therapy and immunotherapy. If we tabulate the GTN (Gross to net) ratios for all the drugs and establish a median discount for the drugs that have a range of pricing, we can compare the GTN ratios for all the brands.

Table 4.2: Median GTN for NSCLC Drugs

Therapy	Brand	SKU	GTN (range)	GTN (median)
Immunotherapy	Tecentriq	1200 mg/20 mL (20 mL vial)	15%-68%	42.0%
	Tecentriq	840 mg/14 mL (14 mL vial)	18%-68%	43.0%
	Imfinzi	120 mg/2.4 mL injection (1 vial)	N/A	1.3%
	Imfinzi	500 mg/10 mL injection (1 vial)	N/A	18.0%
	Opdivo/Opdyta	10 mg/mL (100 mg vial)	20%-50%	35.0%
	Opdivo/Opdyta	10 mg/mL (40 mg vial)	30%-45%	38.0%
	Keytruda	100 mg/4 mL (4 mL vial)	15%-62%	38.0%
Targeted Therapy	Lorbriqua	100 mg tab (30 unit bottle)	18%-65%	42.0%
	Lorbriqua	25 mg tab (30 unit bottle)	N/A	23.0%
	Crizalk/Xalkori	200 mg cap (60 unit bottle)	N/A	20.0%
	Crizalk/Xalkori	250 mg cap (60 unit bottle)	N/A	20.0%
	Tagrisso	80 mg tab (10 unit pack)	10%-15%	12.5%
	Tagrisso	40 mg tab (10 unit pack)	N/A	20.0%

4.5 Comparison by Brands

Based on table 4.1, we can do a straightforward comparison of the median GTN across brands. Such a comparison has been done in Figure 4.2.

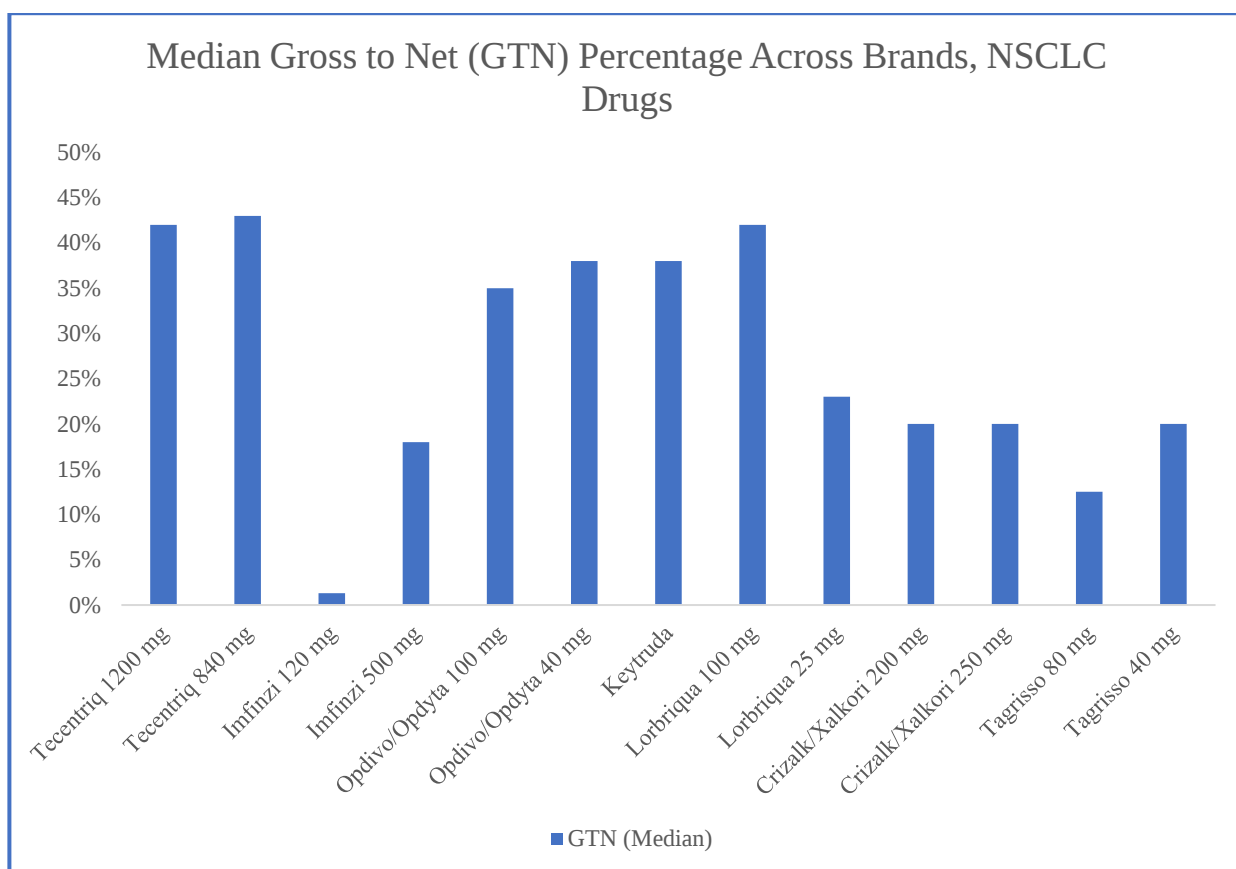


Figure 4.2: Median GTN % across brands, NSCLC Drugs

Some definite conclusions from this chart are:

- The highest GTN discount is offered by Roche for Tecentriq 840 mg (43%), closely followed by Tecentriq 1200 mg (42%) and Pfizer's Lorbriqua 100 mg (42%).
- The lowest GTN discount recorded in this study is courtesy of AstraZeneca's Imfinzi 120 mg. (1.3%)
- The average GTN offered by the covered NSCLC drugs is 27.13%. However, this average is slightly skewed by one oddity in the data, Imfinzi 120 mg's 1.3% GTN. If we were to exclude Imfinzi 120, the average GTN stands at 29.29%.
- The most expensive NSCLC drug in terms of M.R.P is Tecentriq 1200 mg, whose cost per 1 vial of 20 mL stands at INR 3,96,725/-, it is also the most expensive drug after discount, costing a whopping INR 3,37,126/- at its most expensive.
- On the other hand, the drug with the lowest M.R.P among those studied is Opdivo 10 mg's 40 mL vial, costing INR 39,800/- and INR 28,000/- at its most expensive after discount.

4.6 Comparison between Immunotherapy and Targeted Therapy

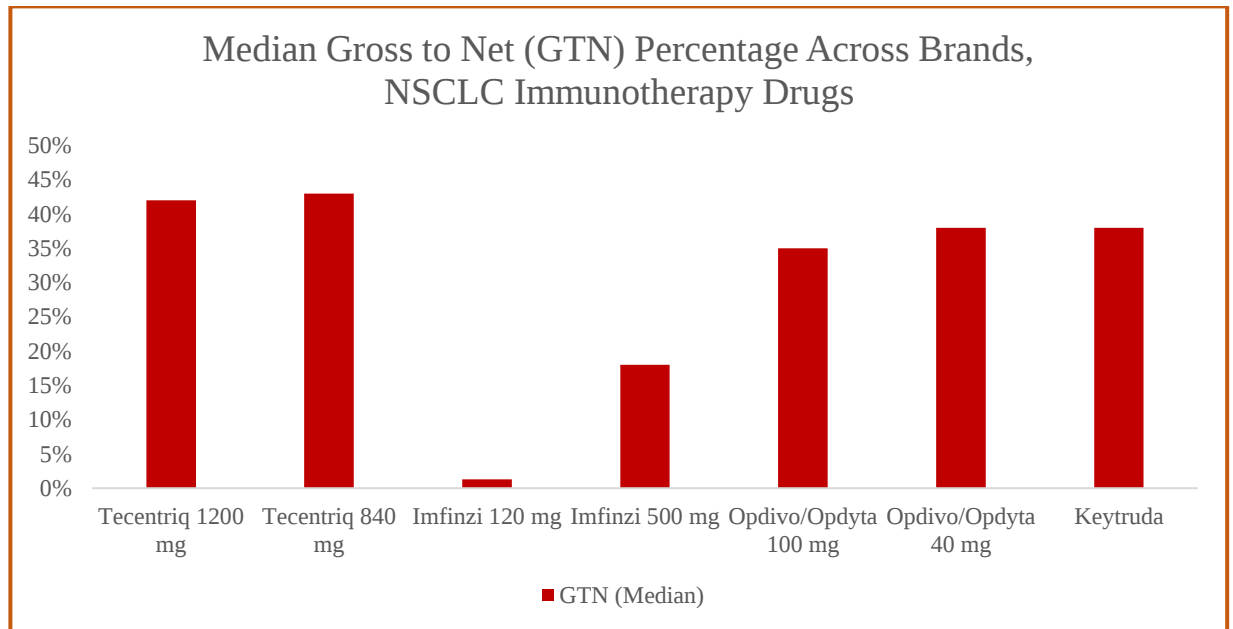


Figure 4.3: Median Gross to Net (GTN) Percentage Across Brands, NSCLC Immunotherapy Drugs

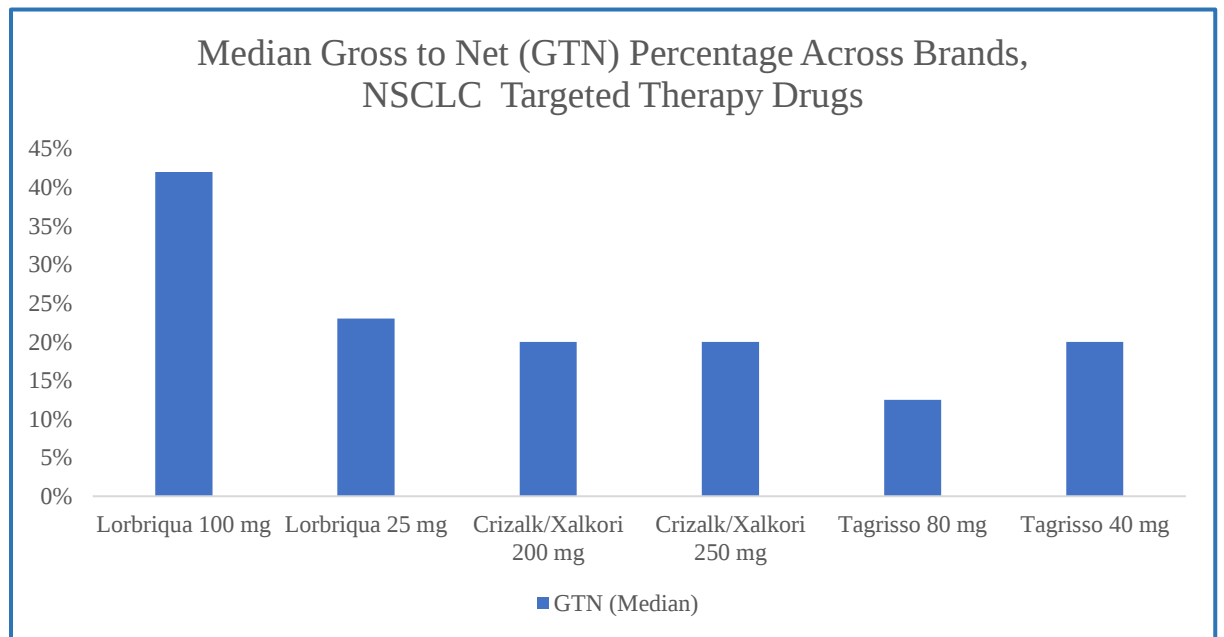


Figure 4.4: Median Gross to Net (GTN) Percentage Across Brands, NSCLC Targeted Therapy Drugs

Based on figures 4.3 and 4.4, we can draw the following conclusions:

- 5 immunotherapy drugs exceed the 30% GTN mark, against just one from targeted therapies, which indicates that in general, immunotherapy drugs offer better discounts in India currently as compared to targeted therapy drugs.
- Average GTN offered in immunotherapy drugs stands at 30.75% while the same in case of targeted therapy drugs stands at 22.91%. Thus, this just goes to solidify the previous point of immunotherapy NSCLC drugs offering a heftier discount as compared to targeted therapies in general.

4.7 GTN Comparison by Manufacturer

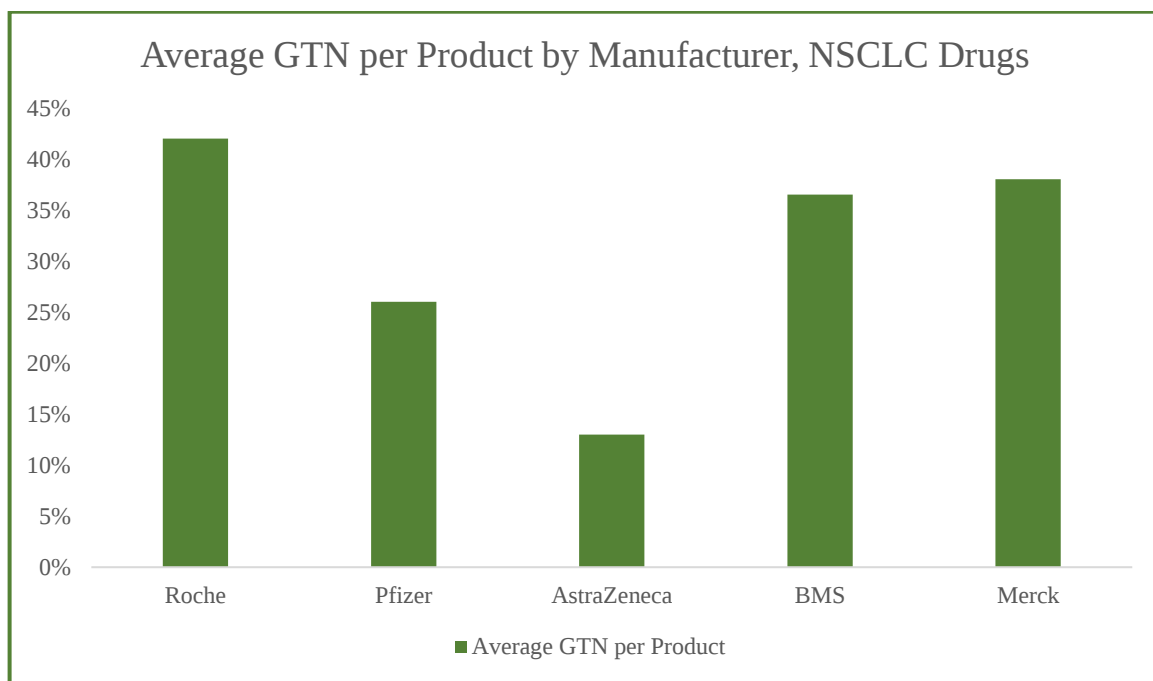


Figure 4.5: Average GTN/Product by Manufacturer, NSCLC Drugs

As obvious from Fig 4.5,

- Roche is the anticancer company in India that provides the highest average GTN discount on its NSCLC products (42%), followed by Merck (38%).
- AstraZeneca has the lowest GTN per product (13%) across all top NSCLC companies in India.

4.8 Final Words

A through PEST analysis of the NSCLC market in India was conducted, and all the relevant political, economic, social, and technological factors affecting it were analysed. We have successfully identified the top NSCLC market players in India and listed down their prominent NSCLC oncology products. We have listed down the gross and net price for each product and its every SKU. We then proceeded to find out the median GTN ratio for each product and compared the GTN by brand, type of therapy and company.

Cost of therapy for each drug would have made for an interesting discussion for each drug will depend on the compliance factor, persistence, adoption curves, erosion curves, combination therapy dynamics, cannibalization between lines of therapies, duration of therapy and dosage. That kind of information, apart from the dosage and duration of therapy is usually concealed by companies and not revealed in the public domain. So that presents a limitation for including cost of therapy in this study.

5 Conclusion and Recommendations

In conclusion, we can summarize the following:

- Roche, Pfizer, AstraZeneca, BMS and Merck are the top oncology market players in India.
- India aims to become independent in the API market long term, which may open doors driving down input costs in the country and aid the pharmaceutical industry.
- India-Russia relations may detrimentally affect the NSCLC market.
- DPCO (Drug Price Control Order), 2013, doesn't allow companies to increase prices in the middle of the year.
- Factors such as increasing average age and increasing lung cancer awareness may positively impact the NSCLC market. Similarly, factors like improving lifestyle may negatively affect the NSCLC market.
- Increasing medical expenditure is likely to aid NSCLC market in future.
- Compared to chemotherapy, immunotherapy and targeted therapy have shown rapid growth in recent years and earned multiple approvals for drugs across companies. There are plenty of immunotherapy and targeted therapy products currently in

development across companies and we might just be entering the golden era of advanced cancer care.

- When talking about the most expensive NSCLC drug in India according to MRP and net price, it is the Tecentriq injection, which costs INR 3,96,725/- per 1 vial of 20 mL, and is also the most expensive drug after discount, costing a whopping INR 3,37,126/- at its most expensive.
- When discussing the cheapest NSCLC drug in India, it is Opdivo 10 mg's 40 mL vial, costing INR 39,800/- and INR 28,000/- at its most expensive after discount.
- The highest GTN% was offered in Tecentriq 840 mg (43%) and the lowest in Imfinzi 120 mg (1.3%)
- On an average, immunotherapy drugs provided 30.75% GTN per product while targeted therapy drugs provided about 23%, which shows that immunotherapy drugs are providing more patient friendly discounts.
- By manufacturer, Roche was found to be providing the most discount (42%) and AstraZeneca the least (12.5%).

A few recommendations based on these findings are:

- India's cancer data is lacking, because we do not gather medical data extensively, for example claims data in U.S. captures a wide variety of patient data, which, although anonymously, gives insight into the burden of a disease and the target population. It also reveals important parameters like treatment rate, biomarker testing rates, gene mutation rates and more. This gaping lack of patient data will affect pricing of drugs in India. We need to step up the gathering of medical data in the country in an efficient and accessible way.
- Companies must capitalize on the fact that lung cancer awareness is severely lacking in the country. They must be prepared to sponsor awareness programmes in the country because that will improve the treatment rate and diagnosis of the disease.
- The therapy costs for most NSCLC drugs are still unbelievably high for a country like India, where the per capita income is still exceptionally low. This, added to the fact that most Indians pay for healthcare out of pocket, ensures that most do not get to avail expensive therapies such as cancer therapy. Thus, to increase the number of

new and continuing prescriptions, more GTN discounts must be made available by the companies, especially for targeted therapies.

- There is a need for government sponsored social healthcare programs for cancer patients that covers at least a part of cancer therapy in afflicted patients.

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Abbreviations

1. WHO: World Health Organisation
2. FDA: Food and Drug Administration (US)
3. SCLC: Small cell lung cancer
4. NSCLC: Non-small cell lung cancer
5. PEST: Political, Economic, Social and Technological (Analysis)
6. GTN: Gross-to-net
7. BMS: Bristol-Myers-Squibb
8. KRAS: Kirsten rat sarcoma viral oncogene homolog
9. ALK: Anaplastic Lymphoma Kinase
10. ROS: 'Orphan' receptor tyrosine kinase
11. BRAF: Serine/threonine-protein kinase B-Raf
12. EGFR: Epidermal growth factor receptor
13. NPCA: National Price Control Authority
14. DPCO: Drug Price Control Order
15. SABR: Stereotactic ablative radiation therapy
16. SBRT: Stereotactic body radiation therapy
17. NTRK: Neurotrophic tropomyosin receptor kinase