Market Assessment Study to Evaluate the Trends of Immuno-Oncology Drug Prescription for Melanoma in the US Market

By

Shraddha Singh

Dissertation submitted in partial fulfillment of the requirements of the degree

MBA Hospital and Health Management

Academic year, 2017-2019

The IIHMR University, Jaipur

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INSTITUTE OF HEALTH
MANAGEMENT RESEARCH
(WHO Collaborating Centre for District Health System Based on Primary Health Care)

IIHMR UNIVERSITY

TO WHOMSOEVER MAY CONCERN

This is to certify that **Dr. Shraddha Singh**, student of MBA Hospital and Health Management from The IIHMR University, Jaipur has undergone internship training at **PharmaAce Analytics Pvt. Ltd., Pune** from **February 4th, 2019** to **May 3rd, 2019**.

The Candidate has successfully carried out the study designated to her during internship training and her approach to the study has been sincere, scientific and analytical.
The Internship is in fulfillment of the course requirements.

I wish her all success in all her future endeavors.

Col. (Dr.) Ashok Kaushik
Dean, Academics and Student Affairs
The IIHMR University, Jaipur

17 May 2019

Col. (Dr.) Ashok Kaushik
Dean, Academic and Student Affairs (Guide)
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PharmaACE

The certificate is awarded to

Ms. Shraddha Singh

In recognition of having successfully completed her internship in the department of

Market Research

And has successfully completed her project on

"Market Assessment Study to evaluate the trends of Immuno-oncology drug prescription for Melanoma in the US market"

3rd May 2019

She comes across as a committed, sincere and diligent person who has a strong drive and zeal for learning.

We wish her all the best for her future endeavors!

For PharmaACE Innovations LLP

Rashi Chawla

HR Lead

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THE IIHMR UNIVERSITY, JAIPUR

CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled **Market Assessment Study to Evaluate the Trends of Immuno-Oncology drug prescription for melanoma in the US Market** submitted by **Dr. Shraddha Singh** Enrolment No- **IIHMR- 670** under the supervision of Col. Dr. Ashok Kaushik, Dean Academics and Student Affairs The IIHMR University, Jaipur for award of MBA in Hospital and Healthcare Management of the University carried out during the period from February 4, 2019 to May 3, 2019 embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other institute or other similar institution of higher learning.

Shraddha

Signature

Dr. Shraddha Singh

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Last but not the least I would like to express my gratitude for my parents and for their constant encouragement and faith in me during my summer internship.

Above all, I would like to thank God for giving me the strength to manage the difficulties which I faced during this period.

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1. List of Figures

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3. List of Symbols and Abbreviations

- MOA: Mechanism of Action
- ROA: Route of Administration
- IO: Immuno-oncology
- Adj. Mel: Adjuvant Melanoma
- Met Mel: Metastatic Melanoma
- RFS: Relapse Free Survival
- PFS: Progression Free Survival
- OS: Overall Survival

Market Assessment Study to evaluate the trends of Immuno-oncology drug prescription for Melanoma in the US market

A INTRODUCTION: [1,2,3,4]

Immuno-oncology Therapy:[5]

Definition:

Immuno-oncology refers to the use of the body's natural defenses to treat cancer. It works by stimulating the immune system instead of fighting the tumors, avoiding disturbance in functionality of healthy cells.

Introduction of novel immune-oncology therapies with lesser side effects is driving growth of the global immune-oncology drugs market. Improved therapeutic outcomes have led to increasing success rates against cancer, owing to in-depth understanding of the disease pathophysiology, functioning of the tumor cells, and effective ways to tackle with the same. Moreover, immuno-oncology therapies have lesser side effects compared to conventional cancer therapies such as chemotherapy, radiation therapy, and others.

Biomarkers in Immuno-Oncology Therapy:

Biomarkers are biologic molecules, cells, or processes found in tissues or body fluids (such as blood) that are a sign of a normal or abnormal process or disease.

Melanoma Disease Overview:

- **Definition:** Melanoma is an invasive neoplasm of melanocytes, the melanin-producing cells, and accounts for ~1% of all skin cancers
- **Demography:**
- The prevalence in 2016 was 1.17M
- ~76k new cases in melanoma out of which 5% are Stage lV
- Out of the total new cases in 2016, 61% were male and 39% female

- **Diagnosis:** Biopsy (Shave, Punch, Incisional and Excisional, Optical; FNA(Fine Needle Aspiration), Surgical Lymph Node, Sentinel Lymph Node); Imaging test; Blood test
- **Characteristics:** The edges are irregular, ragged, notched, or blurred.

  The colour is not the same all over (Ugly Duckling Sign), May include different shades of brown or black, or sometimes with patches of pink, red, white, or blue.

  The spot is larger than 6mm across, although melanomas can sometimes be smaller than this. The mole is changing in size, shape, or colour.
- **Treatment:** Primary treatment options: Surgery, Radiation therapy, Chemotherapy
- **Further therapy options:** Immunotherapy, Targeted Therapy, Oncolytic Virus Therapy
- **Prognosis**: Average 5-year survival rate is 15-20%[1] and average 10-year survival rate is 10% for Stage lV melanoma

B OBJECTIVES

1. To evaluate the current trends and scope of IO for Melanoma in US Market
2. To study the full IO clinical trials pipeline of Melanoma

C Literature Review:

Melanoma Disease Burden: According to a study by Franklin C et al. Eur J Surg Oncol. (2017)[3], Malignant melanoma contributes in majority cases of skin cancer related fatality and have an increased incidence in the past years. It has very poor prognosis and the treatment remains a tough challenge. In recent years, improved knowledge and better understanding of the role of immune system led to the development and approval of several immunotherapies. Incidence rate of melanoma has been increasing and it is now the 5th and 7th most common cancer. The Surveillance, Epidemiology and End Results (SEER) data shows that among Caucasians, there has been a 60% increase in incidence over the last 30 years. For many years, there has continued to be a high rate of death from metastatic melanoma with an estimated 10,130 deaths from melanoma in 2016[8.] Margaret L Axelrod et al., in her study stated that treatment and prognosis of metastatic melanoma has changed substantially since the discovery of Immune Checkpoint Inhibitors (ICI), agents that enhance the anti-tumor immune response.[11]

Immuno Therapy: Evidences that melanoma tumor cells are highly immunogenic and a better understanding of T-cell immune checkpoints have changed the therapeutic approach to advanced melanoma. Instead of targeting the tumor directly, immunotherapy targets and activates the immune response using checkpoint inhibitors, monoclonal antibodies, vaccines, and adoptive T cell therapy.[5] The Report, titled, "Trends in the global immuno-oncology landscape," published in Journal of Nature Reviews Drug Discovery in 2018 stated that a 67% increase is seen in the number of active immuno-oncology pipeline agents in a year, showing the unprecedented expansion in the I-O Drug Market[7]**.** The Cross-sectional study article published in JAMA Network Open Journal stated that the percentage of US patients who are eligible for checkpoint inhibitor drugs increased from 1.54% in 2011 to 43.63% in 2018 and the percentage of patients estimated to respond to checkpoint inhibitor drugs was 0.14% in 2011 and increased to 12.46% in 2018[4] which will shift the whole treatment paradigm towards the Immuno therapies. Study by Tala Achkar and Ahmad A Tarhini and published in Journal of Hematology and Oncology evaluated various Immunotherapies drug class to assess potential benefit of I-O Therapies.

Checkpoint inhibitors are currently being tested in the adjuvant setting with initial data for ipilimumab suggesting efficacy in this context. Ipilimumab (PD-L1 Inhibitor), a monoclonal antibody against the cytotoxic T-lymphocyte antigen 4 (CTLA-4) as well as nivolumab and pembrolizumab targets the programmed cell death protein 1 (PD-1) prolongs Overall Survival in patients with advanced melanoma. The latter substances seem to have an increased response rate and more tolerable safety profile compared to ipilimumab. The combination of a CTLA-4 + a PD-1 inhibitor seems to be superior to the monotherapies, especially in patients with PD-L1 negative tumours[3]. Talimogene laherparepvec (TVEC) is the first oncolytic virus approved in the therapy of metastatic melanoma offering a treatment option especially for patients with limited disease.

Advancement in the treatment of melanoma have focused on overcoming tumor-induced immune suppression and were initially established in the adjuvant setting with the use of IFN-α and HDB IL-2 in the treatment of metastatic disease[5]**.** A Randomized Control Study on treatment-naïve Melanoma patients, published in Journal of Hematology and Oncology evaluated the survival benefit of patients in form of OS, PFS and RFS as primary endpoint of the study established that Pd-L1/ PD-L1 Antibody in increase the Overall Survival Rate of the patient[47]**.**

According to a Randomized Control Studies done by Pyo JS, Kang G (2017), Estimated ORRs of immunotherapy and chemotherapy were 0.224 and 0.108, respectively. The Odds ratios for ORR of nivolumab/ ipilimumab, pembrolizumab and nivolumab 3 mg/kg were 8.54, 5.39 and 4.35, respectively, compared with chemotherapy alone.[3] Due to the efficacy shown by both CTLA-4 and PD-1 blocking antibodies, scientists have investigated the possibility of more effective treatment therapy by combining the 2 modes of treatments. One study looked at the combination therapy of Nivolumab and Ipilimumab, which established that combination therapy provided faster and deep tumor regression suggesting that Nivolumab and Ipilimumab can act synergistically.[4] Several studies have been performed to validate interferon-alpha (IFN-α) as an adjuvant in immunotherapy treatments against resected melanomas. Mocelli et al.[18] conducted a meta-analysis including the results of 14 trials on the use of IFN-α as an adjuvant and found a 12% reduction in the risk of death; however, only one study using high doses of IFN-α established a significant impact of the treatment on overall survival.

Conclusion: Immuno-oncology Therapy is leading to a transformational shift in treatment paradigms for patients with cancer from Conventional therapies to Targeted Therapies. Development of new drug class such as PD-1/ PD-L1 Antibody, CT-L4 Inhibitors, Targeted Therapies lead to more efficient treatment tailored according to the individual's genetic condition, while minimizing toxicities. Clinical trials are currently underway in patients with BRAF mutation-associated melanoma by combining a BRAF-1 and IFN-α inhibitor to determine whether the combination might have greater potency than monotherapy. The potential of immunotherapy is vast with durable responses in a proportion of patients with poor prognosis. The future of immunotherapy relies upon the intelligent application of research and clinical trials to clinical practice, so that immunotherapy can be effective for a wider population and maintain its growth.[6]

D Methodology

RESEARCH QUESTION

What are the current market trends and scope in Immuno-oncology drug for Melanoma in US Market?

HYPOTHESIS: NA

MATERIAL AND METHODS:

Study Design: Analytical and Observational

Setting: US Market

Study Population: NA

Sampling Technique: Quota Sampling

Data Collection Procedure:

1) Primary Data provided by the client
2) Secondary Data from the Oncology studies and Government sites

Duration of Study: 3 months

ETHICAL CONSIDERATION

1. The identity of patients and oncologists were be kept anonymous while collecting data
2. The Actual name of products has been blinded due to confidentiality issues of clients

E Project Findings:

I. Disease Burden:

Table 9 Table showing yearly Incidence of Melanoma according to Race

Category[8]	Incidence (Per 100,000)
Non-Hispanic Whites	27
Hispanics	5
African- American	1
Asian/ Pacific Islanders	1

Table 10 Table shows Condition of occurrence of Melanoma according to Age and Gender

Age Group[9]	Condition
<50 years	Female > Male
By 65 years	Male: Female= 2:1
By 80 years	Male: Female=3:1

Table 11 Table showing Lifetime Risk of getting Melanoma according to Race

Race[10]	Lifetime Risk of getting Melanoma (Per 100,000)
Caucasians	2500
Hispanics	500
African American	100

Table 12 Table showing 5 years survival rate according to stage

SEER Stage[11]	Clinical Staging	5 years relative Survival Rate
Localized	Stage I & II	98%
Regional	Stage III	64%
Distant	Stage IV	23%
All SEER Stage Combined	All Stages Combined	92%

Table 13 Table showing Estimated cases of Melanoma in 2019

<table>
<tr><th colspan="3">Incidence[12]</th><th colspan="2">Deaths</th></tr>
<tr><td colspan="3">192,310</td><td colspan="2">7,230</td></tr>
<tr><th colspan="2">Invasive (Epidermis + Dermis)</th><th>Non- Invasive (Epidermis)</th><th>Men</th><th>Women</th></tr>
<tr><td colspan="2">96,480</td><td rowspan="2"></td><td rowspan="2">4,740</td><td rowspan="2">2,490</td></tr>
<tr><th>Men</th><th>Women</th></tr>
<tr><td>57,220</td><td>39,260</td><td></td><td></td><td></td></tr>
</table>

II. Drugs Approved for Treatment of Melanoma:[13]

Immunotherapies

- Intron A (high-dose interferon alfa-2b)
- Sylatron (peginterferon alfa-2b)
- Proleukin / IL-2 (interleukin-2)
- Keytruda (pembrolizumab): Anti PD-1 Antibody
- Opdivo (nivolumab): Anti PD-1 Antibody
- Opdivo (nivolumab) and YERVOY (ipilimumab) Combination
- Yervoy (ipilimumab): Anti CTLA-4 Antibody

Targeted Therapies

- Braftovi (encorafenib) and Mektovi (binimetinib) Combination
- Cotellic (cobimetinib) and Zelboraf (vemurafenib) Combination
- Mekinist (trametinib): MEK Inhibitor
- Mekinist (trametinib) and Tafinlar (dabrafenib) Combination
- Tafinlar (dabrafenib): B-RAF Inhibitor
- Zelboraf (vemurafenib): B-RAF Inhibitor

Chemotherapy

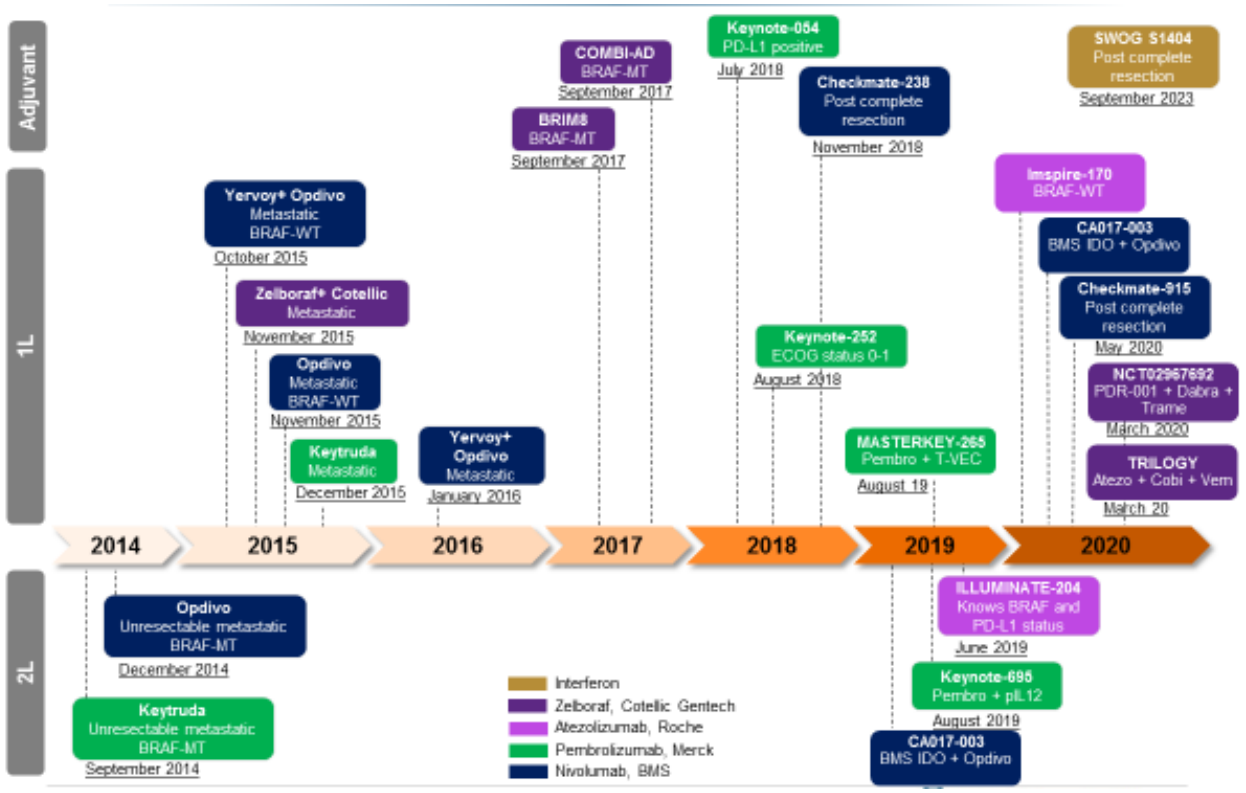
- DTIC (dacarbazine)

Oncolytic virus therapy

- Imlygic (talimogene laherparepvec "T-Vec")

III. Melanoma Approval Timeline:

Figure 8 Figure showing complete timeline for the approval of Melanoma Medication



- This figure shows the complete timeline of the approved drug for Melanoma according to the Line of Therapy, along with the name of studies through which the FDA Approval was granted

IV. InlineProducts:

Brand Name (Molecular Name); Manufacturer	Mechanism of Action	Indication	Dosage	FDA Approval
Opdivo (nivolumab) BMS[14]	PD 1 Inhibitor	Adj. Mel; Met Mel	Infusion 240mg every 2 weeks up to a year	2014
Keytruda (pembrolizumab) Merck[15]	PD 1 Inhibitor	Adj. Mel; Met Mel	Infusion 200 mg every 3 weeks for up to a year (until disease progression or unacceptable toxicity)	2014
Yervoy (ipilimumab) BMS[16]	PD-L1 Inhibitor	Adj. Mel; Met Mel	Infusion First: 10mg/kg every 3 weeks up to 4 doses Subsequently: 10mg/kg every 12 weeks up to 3 years	2011

Table 14 Table showing Approved Drugs for Melanoma with their dosing

Brand Name (Molecular Name); Manufacturer	Mechanism of Action	Indication	Dosage	FDA Approval
Tafinlar Novartis (Acquired from GSK)[17]	BRAF Inhibitor	Adj. Mel; Met Mel	150 mg orally taken twice daily, approximately 12 hours apart as a single agent or with trametinib	2013
Mekinist Novartis (Acquired from GSK)[18]	MEK Inhibitor	Adj. Mel; Met Mel	Trametinib: 2mg (via 0.5 or 2mg tablets	2013
Braftovi[19]	BRAF Inhibitor	Met Mel	450 mg orally once daily	2018
Mektovi[20]	MEK Inhibitor	Met Mel	45 mg twice daily in combination with encorafenib	2018

Brand Name (Molecular Name); Manufacturer	Mechanism of Action	Indication	Dosage	FDA Approval
Zelboraf[21]	BRAF Inhibitor	Met Mel	960 mg (four 240 mg tablets) twice daily	2017
Cotellic[22]	MEK Inhibitor	Met Mel	60 mg (three 20 mg tablets) once daily	2017
Opdivo + Yervoy[23]	PD-1+ PD-L1 Inhibitor	Adj. Mel; Met Mel	Opdivo: 3mg/kg weekly Yervoy: 1mg/ kg weekly	2016
Braftovi + Mektovi[24]	BRAF+ MEK Inhibitor	Met Mel	Braftovi: 450 mg orally once daily Mektovi: 45 mg twice daily	2018

Brand Name (Molecular Name); Manufacturer	Mechanism of Action	Indication	Dosage	FDA Approval
Tafinar + Mekinist[25]	BRAF+ MEK Inhibitor	Adj. Mel; Met Mel	Oral (Capsule + Tablet) Dabrafenib: 150mg (75mg bid) + Trametinib: 2mg(via 0.5 or 2mg tablets)	2013
Zelboraf + Cotellic[26]	BRAF+ MEK Inhibitor	Met Mel	Zelboraf: 960 mg (four 240 mg tablets) twice daily; Cotellic: 60 mg (three 20 mg tablets) once daily	2017

- Currently 9 drugs for Monotherapy and 4 combinations are approved for Melanoma in the US Market.

V. Attribute Analysis:

For Inline Products:

Table 15 Table showing attributes of approved drugs

Drug (Molecular Name)	Approval Date	Attributes
Opdivo (nivolumab)[14]	2014	Indicated for the treatment of patients with BRAF V600 wild as well as mutation type unresectable or metastatic melanoma Indicated for the adjuvant treatment of patients with melanoma with involvement of lymph nodes or metastatic disease who have undergone complete resection Indicated in combination with ipilimumab for the treatment of patients with unresectable or metastatic melanoma under accelerated approval based on progression-free survival
Yervoy (ipilimumab)[16]	2011	Indicated for the treatment of unresectable or metastatic melanoma in adults and pediatric patients (12 years and older) Indicated for the adjuvant treatment of patients with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy Indicated in combination with nivolumab for the treatment of patients with unresectable or metastatic melanoma under accelerated approval based on progression-free survival
Keytruda	2014	Indicated for the treatment of patients with

(pembrolizumab)[15]		unresectable or metastatic melanoma
Braftovi (encorafenib)1[9]	2018	Indicated, in combination with binimetinib, for the treatment of patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation Not indicated for treatment of patients with wild-type BRAF melanoma
Mektovi (binimetinib)[20]	2018	Indicated in combination with encorafenib for patients with unresectable or metastatic melanoma with the BRAF V600E or V600K mutations
Tafinlar (dabrafenib)[17]	2013	Indicated as a single agent for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation Indicated, in combination with trametinib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations
Mekinist (trametinib)[18]	2013	Indicated, as a single agent or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations Indicated, in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, and involvement of lymph node(s), following complete resection
Cotellic (cobimetiniob)[22]	2015	Indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutation, in combination with vemurafenib Not indicated for treatment of patients with wild-type BRAF melanoma
Zelboraf (vemurafenib)[21]	2011	Indicated for the treatment of patients with unresectable or metastatic melanoma with

		BRAFV600E mutation Not recommended for use in patients with wild-type BRAF melanoma
Imlygic (talimogene laherparepvec "T-Vec")		Indicated for the local treatment of unresectable cutaneous, subcutaneous, and nodal lesions in patients with melanoma recurrent after initial surgery Have not shown to improve OS

For Pipeline Products:

Drug	Mechanism of Action		Study Results
PDR001+ Dabrafenib+ Trametinib[22]	BRAF/ MEK Inhibitor	N=423 Previously untreated patients with Advanced Melanoma	The median PFS was 9.3 months in the dabrafenib-trametinib group and 8.8 months in the dabrafenib-only group Hazard ratio for progression or death in the dabrafenib-trametinib group, 0.75 The overall response rate was 67% in the dabrafenib-trametinib group and 51% in the dabrafenib-only group At 6 months, the interim overall survival rate was 93% with dabrafenib-trametinib and 85% with dabrafenib alone The rate of cutaneous squamous-cell carcinoma was lower in the dabrafenib-trametinib group than in the dabrafenib-only group (2% vs. 9%) whereas pyrexia occurred in more patients (51% vs. 28%) and was more often severe (grade 3, 6% vs. 2%) in the dabrafenib-trametinib group
Cobimetinib+ Atezolizumab[23]		N=152 (27	Atezolizumab + cobimetinib had manageable safety and clinical activity

		December 2013 and 9 May 2016)	irrespective of KRAS/BRAF status **CONS:** The most common all-grade treatment-related adverse events (AEs) were diarrhea (67%), rash (48%) and fatigue (40%)
NKTR-214 + nivolumab + ipilimumab[24]		N=38 Advanced Treatment-Naïve 1L Melanoma Patients (Stage IV)	Responses were observed in 7/11 (63%) efficacy-evaluable patients (2 CR and 5 PR) [◊]. Median time to response was 1.7 months. DCR, also known as disease control rate (CR + PR + 3 SD)
Avelumab+ Bevacizumab[25]		N=52	Avelumab showed durable responses, promising survival outcomes, and an acceptable safety profile in patients with previously treated metastatic melanoma The confirmed ORR was 21.6%, complete response, 7.8%; partial response, 13.7%). Median PFS and OS were 3.1 months and 17.2 months respectively Thirty-nine patients (76.5%) had a treatment-related adverse event (TRAE), most commonly infusion-related reaction (29.4%), fatigue (17.6%), and chills (11.8%); 4 patients (7.8%) had a grade 3 TRAE. Five patients (9.8%) had an immune-related TRAE (all were grade 1/2). No grade 4 TRAEs or treatment-related deaths were reported.

PDR001[26]		N=61	Preliminary trial results suggested that the drug is well-tolerated and safe ORRs were higher in PD-L1+ pts, corroborating previous findings that PD-L1 expression enriches for response to anti-PD1 agents in certain tumor types
IMCgp100+ Durvalumab and/or Tremelimumab[27]			The therapy was safe and triggered long-lasting responses in patients with both skin and eye melanoma Patients experienced a prolonged response to treatment and longer survival times. Seventy-three percent survived for a year after treatment, compared with 25 to 45 percent with other treatments
CMP-001+ Pembrolizumab[28]		N=68	Combining CMP-001 with Keytruda resulted in objective, durable tumor responses without triggering major toxicity issues in PD-1-resistant advanced melanoma patients, the study reports. **CONS:** Acute adverse effects related to treatment mainly included fever, nausea and/or vomiting, headache, hypotension, and rigors

VI. Trends:

Figure 9 Pie chart showing percentage of patients with different treatment methods

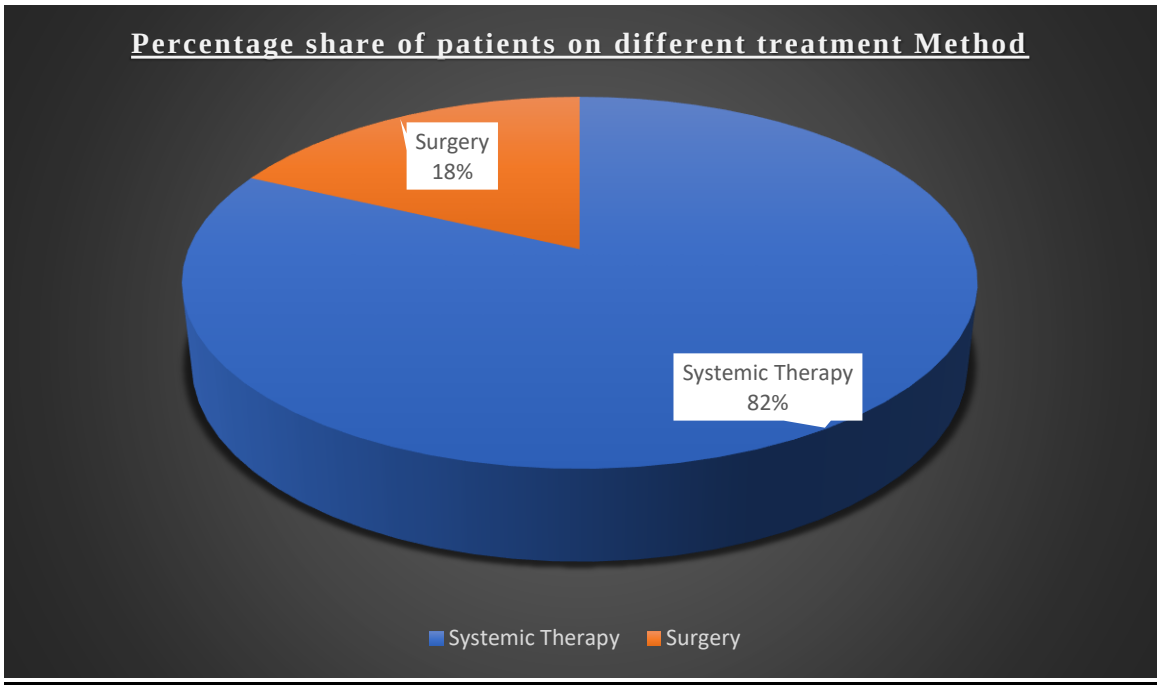


Figure 10 Pie chart showing Percentage share of patients on different Line of Therapy

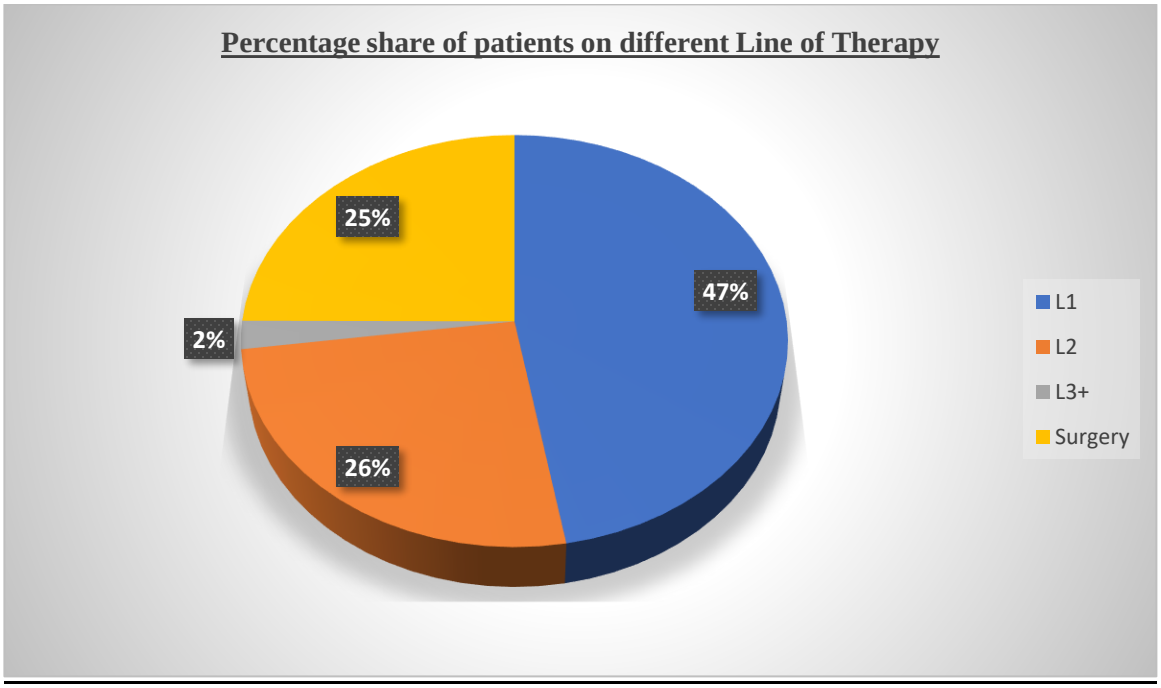


Figure 11 Pie chart showing Percentage share of patients on treated by different Drug class

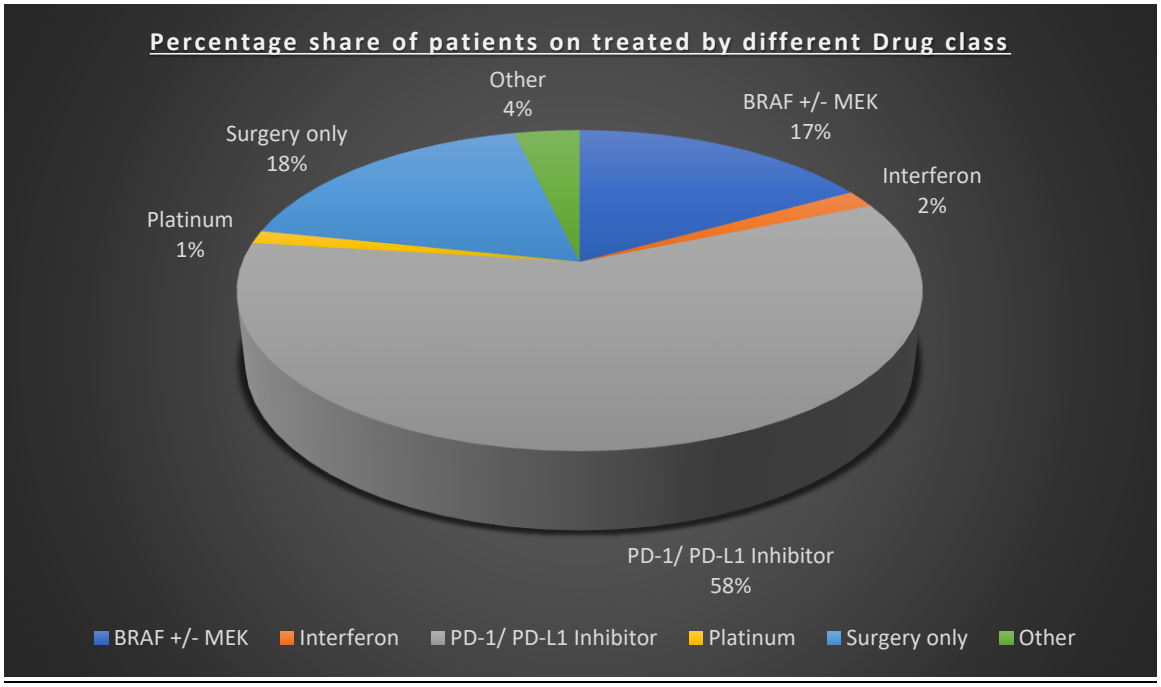
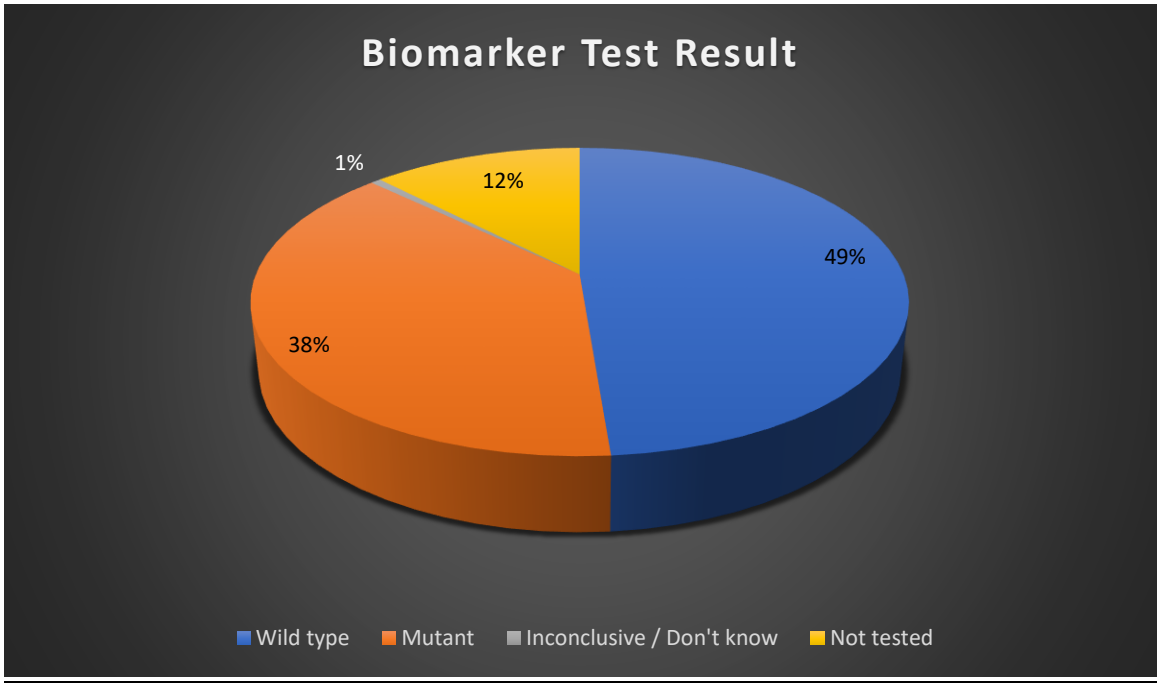


Figure 12 Pie chart showing Biomarker Test Result



VII. Pipeline Analysis

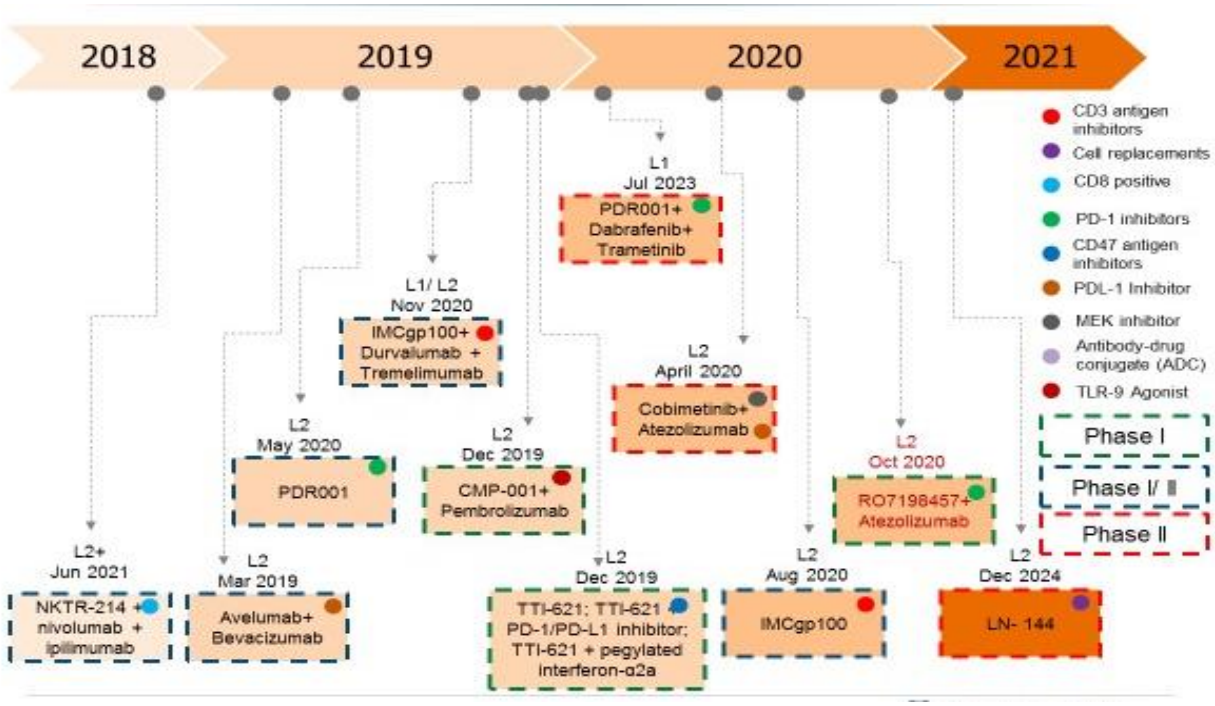
Table 16 Table showing various Pipeline drugs under development in Melanoma

Drugs	NCT ID Company	# Pts, Pt Population	Phase	Primary Completion Date (CT.gov)	Study Completion Date (CT.gov)
PDR001+ Dabrafenib+ Trametinib[29]	NCT02967692 Novartis Pharmaceuticals	538 Unresectable or metastatic BRAF V600 mutant melanoma	III	Jul 2019	July 2023
Cobimetinib+ Atezolizumab[30]	NCT03108131 Genentech, Inc.	60 Metastatic Melanoma	II	April 2020	April 2020
LN- 144[31]	NCT02360579 Iovance Biotherapeutics, Inc.	164 Metastatic Melanoma	II	Mar 2020	Dec 2024
NKTR-214 + nivolumab + ipilimumab[32]	NCT02983045 Bristol-Myers Squibb	480 Metastatic melanoma	I|II	Jun 2020	Jun 2021
Avelumab+ Bevacizumab[33]	NCT03167177 NantKwest, Inc.	67 Metastatic Melanoma progressed on or after chemotherapy and anti-PD-1/PD-L1 therapy	I|II	Jan 2019	Mar 2019

Drugs	NCT ID Company	# Pts, Pt Population	Phase	Primary Completion Date (CT.gov)	Study Completion Date (CT.gov)
PDR001[34]	NCT02404441 Novartis Pharmaceuticals	319 Metasatic Melanoma	I|II	May 2020	May 2020
IMCgp100+ Durvalumab and/or Tremelimumab[35]	NCT02535078 Immunocore. Ltd	85 Advanced Melanoma	I|II	Nov 2019	Nov 2020
CMP-001+ Pembrolizumab[36]	NCT03084640 Checkmate Pharmaceuticals	76 Previously received an anti-PD-1/PD-L1 therapy for advanced cutaneous melanoma	I	Oct 2019	Dec 2019
TTI-621; TTI-621 + PD-1/PD-L1 inhibitor; TTI-621 + pegylated interferon-α2a[37]	NCT02890368 Trillium Therapeutics Inc.	240 Metastatic Melanoma	I	Dec 2019	Dec 2019
RO7198457+ Atezolizumab[38]	NCT03289962 Genentech, Inc.	567 Locally advanced or Metastatic Melanoma	I	Sept 2020	Oct 2020

VIII. PIPELINE OVERVIEW:

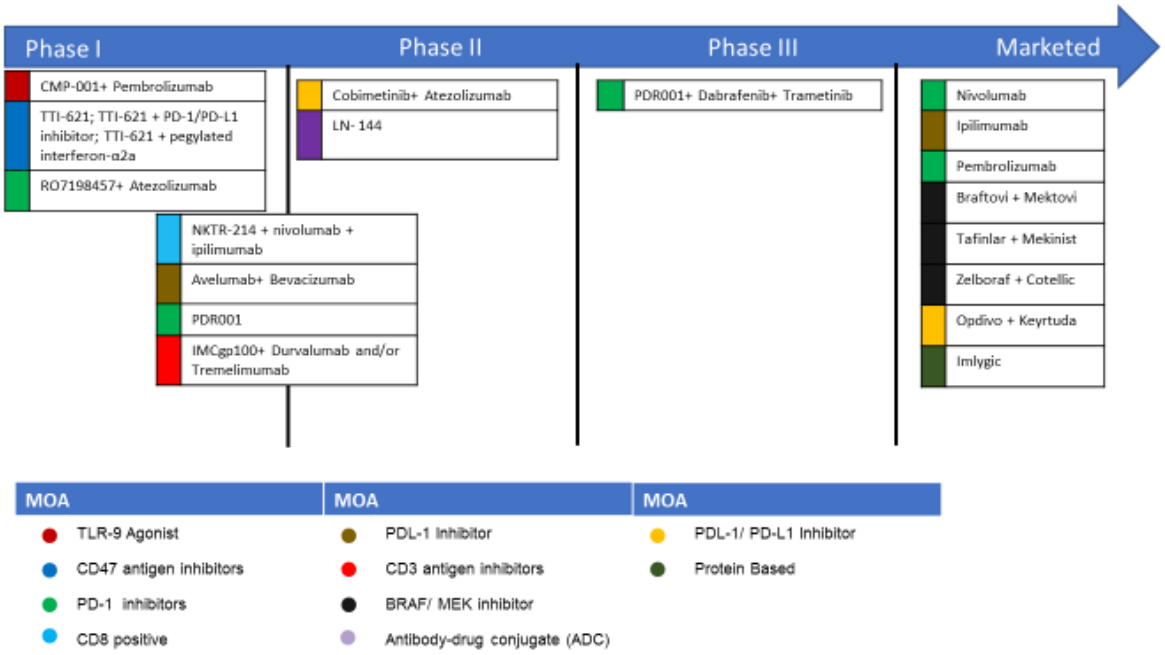
Figure 13 Figure showing Pictorial representation of Pipeline drugs



F Results

CI Landscape:

Figure 14 Figure showing Complete CI Landscape of Melanoma



- Table 16 shows that there are currently 10 major drugs in the pipeline for Melanoma.
- It includes 1 drug in Phase III, 2 drugs in Phase II and & drugs in the initial stages in the pipeline
- The total CI Landscape of Melanoma along with their mechanism of action is shown in **Figure 7**
- **Figure 2** shows that approx. 85% of the patients rely on Systemic Therapy for the treatment of Melanoma
- **Figure 5**further shows the status of Biomarker Testing (Pd-1), which plays an important role in diagnosis as well as deciding the treatment
- **Figure 4**explores the percentage of patients on different drug classes for Melanoma, where the major percentage consists of PD-1/ PD_L1 inhibitor

G Discussion

This study shows:

- Market for I-O Therapy is booming at a very fast rate
- Many new I-O drugs are coming in near future which will greatly affect the whole treatment modality of Melanoma
- With the advancement of technology, there is evolution of various new Biomarker Test, which is useful in Diagnosis as well as Treatment for Melanoma
- Majority of patients are prescribed I-O Drugs for the treatment Melanoma
- New I-O drugs are coming up which are in the Mid and Late Phase of Clinical Trials

H Conclusion

In this section, the findings are summarized, and their implications discussed. This section may also include suggestions for future work.

1) I-O has the maximum percentage of share of new patients among other treatment methods.
2) Many new drugs are in the pipeline for Melanoma
3) More and more physicians are opting Biomarker Test to choose the treatment to be prescribed to the patients
4) Advancement in technologies and research has paved new way for new and innovative treatment methods to evolve

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