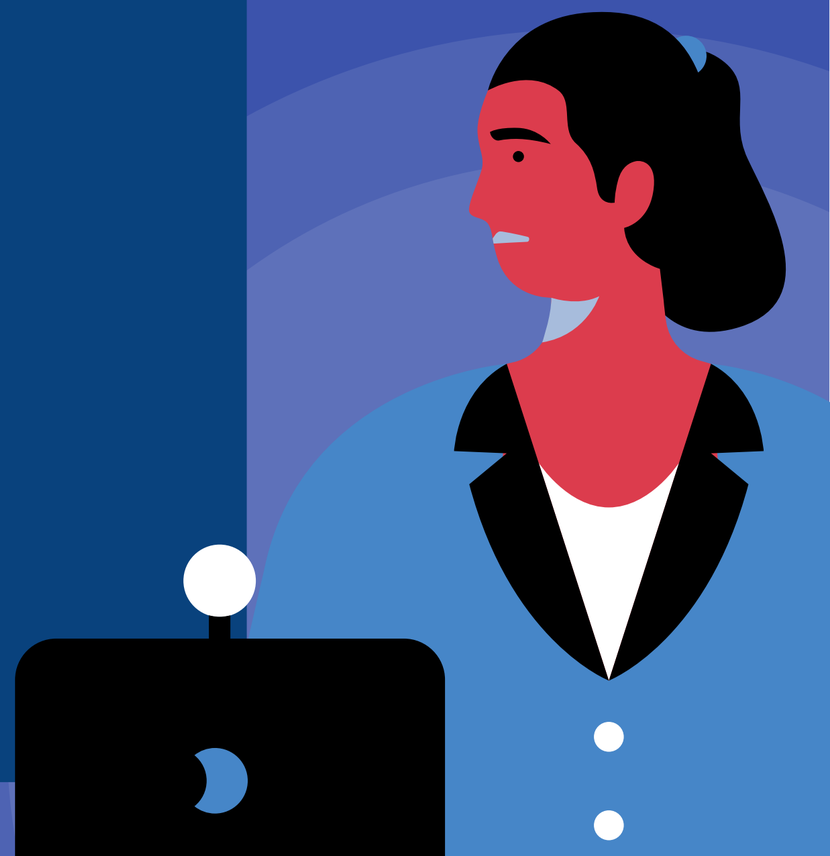
FDA Approvals of Cancer Medicines for Localized vs. Advanced Disease, 2006-Current Day

By: David Wilborn and Dr. Steven Joffe

Content Outline

Topics for discussion



What are the Major Components?

1. Differences between early and late stage disease and their associated treatments
2. Disparities in the amount of treatments that the FDA approves to treat early versus late stage disease.
3. What is the FDA and through what pathways can they approve drugs?

- **Hypothesis**: We hypothesize that there is a greater amount of approvals for drugs that treat advanced cancers versus drugs that treat early stage cancer.

Early Versus Late Stage Disease

- What dictates what is early or late stage cancer?
- How do this influence and inform the objective of the therapeutics they receive?

Stage 1

At this stage, the cancer isn't deeply grown into any tissue, has not reached the lymph nodes, and hasn't spread.

Stage 2

At the this stage, the cancer has grown deeper into the tissue and although it may have spread to the lymph nodes, hasn't metastasized.

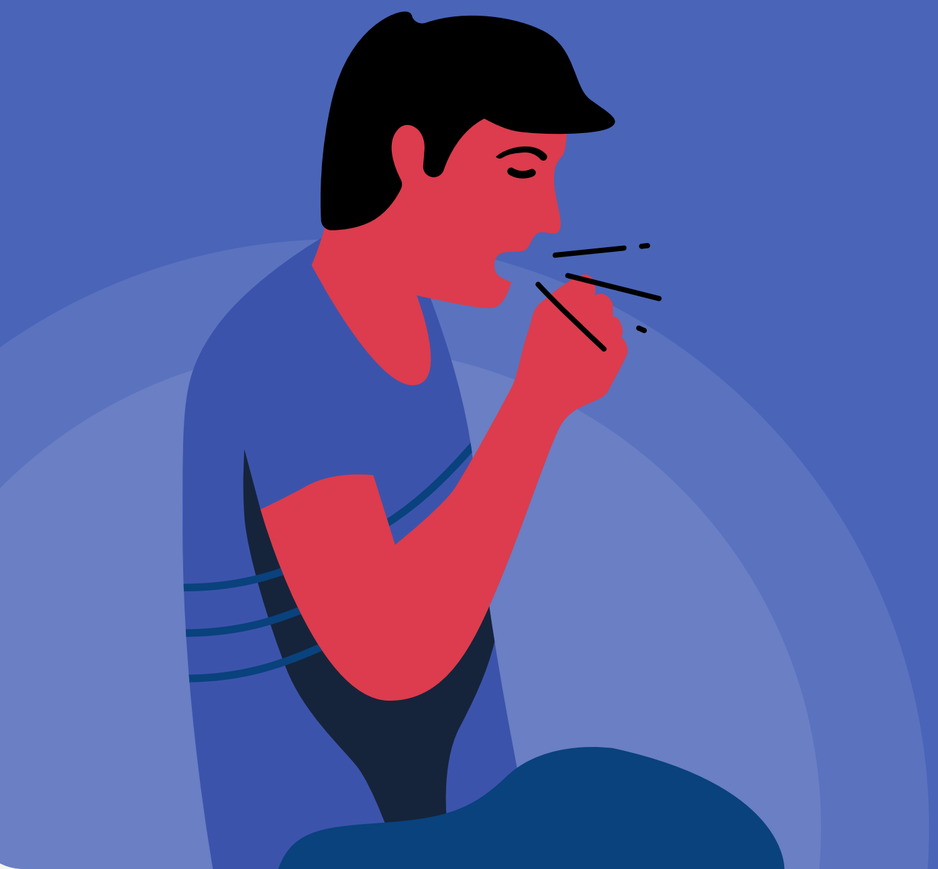
Stage 3

At this stage, the cancer is often called "locally advanced" as it has grown in size, and may have spread to nearby lymph nodes tissues, and organs.

Stage 4

At this stage, the cancer is known as "metastatic cancer" because it has spread to distant parts of the body.

So What Does the FDA Do and what's its significance?



Rising Number of Accelerated Approvals

"The U.S. Food and Drug Administration approved a record 43 new drugs last year through fast-track programs that skip or shorten major steps other drugs must pass, or 73% of total new drugs. That compares with 10 expedited drugs, or 38% of the total, approved 10 years ago." (Wall Street Journal 2019)

Who's Pushing This?

- Drug Makers
- Doctors
- Patients
- Policy Makers

How does This Effect what Types of Drugs Are Approved

- Different endpoints
- Single-Arm Trials
- Less Long-term Efficacy
- Reinforces the lack of early stage therapies

What did This Project Aim to do?

Aim 1

To ascertain the disparity, if one exists, between numbers of drug approvals in early versus late stage cancer treatments

Aim 2

Identify characteristics of drug approvals for late stage versus early stage disease

Aim 3

Use findings to propose policy, institutional, and academic solutions in effort to improve health outcomes

METHODS

Data abstracted through various sources and placed into Google Sheet

Data converted from Google Sheet format to an Excel Sheet

Descriptive analysis done using STATA

Generic drug name	Manufacturer	Disease	Specific Indication (Exact Text)	Approval explicitly includes	Advanced or Adjuvant?	Line:	New Approval or Additional Indication?	Date of Approval	Type of Drug	Type of Approval
Ixabepilone	Bristol-Myers Squibb	Breast Cancer	Metastatic or locally	No	Advanced	Second or Greate	New Approval	10/16/2007	Small Molecule	Regular Approval
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Degarelix	Ferring Pharmaceuticals Inc	Prostate Cancer	Advanced prostate c	No	Advanced	First	New Approval	12/24/2008	Small Molecule	Regular Approval
Everolimus	Novartis Pharmaceuticals Cc	Renal Cell Carcinoma	Advanced renal cell	No	Advanced	Second or Greate	New Approval	3/30/2009	Small Molecule	Regular Approval
Pazopanib	GlaxoSmithKline	Renal Cell Carcinoma	Advanced Renal Cel	No	Advanced	First	New Approval	10/19/2009	Biologic	Regular Approval
Cabazitaxel	Sanofi-Aventis	Prostate Cancer	Metastatic hormone-	No	Advanced	Second or Greate	New Approval	6/17/2010	Small Molecule	Regular Approval
Eribulin	Eisai Inc	Breast Cancer	Metastatic breast ca	No	Advanced	Second or Greate	New Approval	11/15/2010	Small Molecule	Regular Approval
Ipilimumab	Bristol-Myers Squibb	Melanoma	Unresectable or met	No	Advanced	First	New Approval	3/25/2011	Biologic	Regular Approval
Vandetanib	AstraZeneca Pharmaceutica	Thyroid Cancer	Medullary thyroid ca	No	Advanced	First	New Approval	4/6/2011	Biologic	Regular Approval
Abiraterone Acetate	Centocor Ortho Biotech, Inc.	Prostate cancer	Metastatic castration	No	Advanced	Second or Greate	New Approval	4/28/2011	Small Molecule	Regular Approval
Everolimus	Novartis Pharmaceuticals Cc	Neuroendocrine Tumors of Panc	Progressive neuroen	No	Advanced	First	Additional Indica	5/5/2011	Small Molecule	Regular Approval

User: Steven Joffe

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1 . ta Year_of_Approval

Year_of_App |
      roval |      Freq.     Percent        Cum.
------------+-----------------------------------
       2006 |          8        2.65        2.65
       2007 |          8        2.65        5.30
       2008 |          4        1.32        6.62
       2009 |          4        1.32        7.95
       2010 |          5        1.66        9.60
       2011 |          8        2.65       12.25
       2012 |         13        4.30       16.56
       2013 |         13        4.30       20.86
       2014 |         12        3.97       24.83
       2015 |         23        7.62       32.45
       2016 |         14        4.64       37.09
       2017 |         27        8.94       46.03
       2018 |         37       12.25       58.28
       2019 |         27        8.94       67.22
       2020 |         47       15.56       82.78
       2021 |         39       12.91       95.70
       2022 |         13        4.30      100.00
------------+-----------------------------------
      Total |        302      100.00

2 . ta Line_

      Line_ |      Freq.     Percent        Cum.
------------+-----------------------------------
      First |        132       44.00       44.00
First, Seco |         16        5.33       49.33
Second or G |        152       50.67      100.00
------------+-----------------------------------
      Total |        300      100.00

3 . ta Advanced_or_Adjuvant_

Advanced_or |
  _Adjuvant_ |      Freq.     Percent        Cum.
-------------+-----------------------------------
    Adjuvant |         23        7.62        7.62
    Advanced |        272       90.07       97.68
        Both |          5        1.66       99.34
```

Findings

Advanced or Adjuvant

```
3 . ta Advanced_or_Adjuvant_
```

Advanced_or_Adjuvant_	Freq.	Percent	Cum.
Adjuvant	23	7.62	7.62
Advanced	272	90.07	97.68
Both	5	1.66	99.34
Other	2	0.66	100.00
Total	302	100.00	

Accelerated or Regular

```
7 . ta Type_of_Approval
```

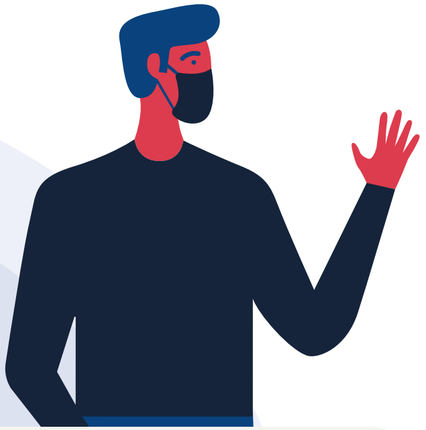
Type_of_Approval	Freq.	Percent	Cum.
Accelerated Approval	64	21.26	21.26
Accelerated to Regular Approval	9	2.99	24.25
Regular Approval	228	75.75	100.00
Total	301	100.00	

Line of Treatment

```
2 . ta Line_
```

Line_	Freq.	Percent	Cum.
First	132	44.00	44.00
First, Second or Greater	16	5.33	49.33
Second or Greater	152	50.67	100.00
Total	300	100.00	

How Did I Contribute?



Literature Review

Located and read relevant literature to get a grasp on fundamentals of cancer treatments

Abstraction

I did the abstraction from the sites and input the data into the spreadsheet.

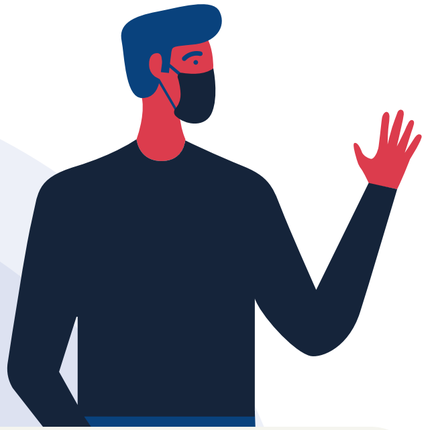
Searching

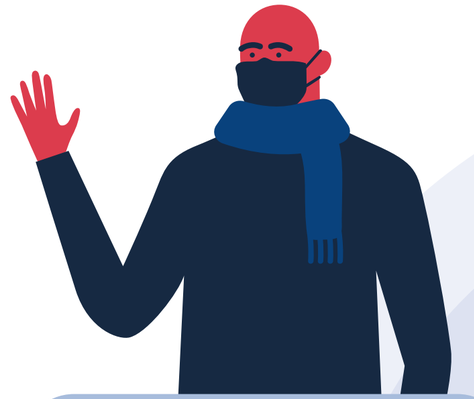
If the FDA database didn't include the information that I needed, I went and searched for it in other resources like PubMed.

Collaborating

Met with mentor regularly to clarify questions

What Did I Learn?





Characterization

Being able to characterize data in a very efficient manner is just as important as inputting the correct data

Observation

When we observe certain phenomena, it's important to keep in mind that there may not be single overarching cause, but multiple smaller causes that funnel things in a particular direction

Treatment in Practice

In the treatment of a disease such as as cancer where its very treatment causes lots of toxicity, there's a delicate balance to be struck

What's Next?

Next steps are to investigate if findings are attributable to private industry decisions, FDA regulatory policies, academic conventions, funding agency stipulations, or a mixture?