

## Supplementary Online Content

Marquart J, Chen EY, Prasad V. Estimation of the percentage of US patients with cancer who benefit from genome-driven oncology. *JAMA Oncology*. Published online April 17, 2018. doi:10.1001/jamaoncol.2018.1660

**eAppendix 1.** Yearly Cancer Statistics

**eAppendix 2.** Data Sources by Malignancy

**eAppendix 3.** Pie Charts Estimating Patients Eligible for Genomically Targeted Therapy

**eAppendix 4.** Pie Charts Estimating Patients Who Could Benefit from Genomically Targeted Therapy

**eAppendix 5.** Pie Charts Estimating Patients Eligible for Genomically Informed Therapy

**eAppendix 6.** Pie Charts Estimating Patients Who Could Benefit from Genomically Informed Therapy

**eAppendix 7.** Pie Charts Estimating Patients Eligible for and who could Benefit from Adjuvant Therapy

**eFigure 1.** Percent of US metastatic Cancer Patients Who May be Eligible for and Benefit from Genomically Informed Treatment

**eFigure 2.** Growth of Genome Targeted and Informed Therapy Over Time With Fitted Linear Regression

This supplementary material has been provided by the authors to give readers additional information about their work.

## eAppendix 1. Cancer Statistics by Year:

2006: <https://www.ncbi.nlm.nih.gov/pubmed/16514137>  
2007: <https://www-ncbi-nlm-nih-gov/pubmed/17237035>  
2008: <https://www-ncbi-nlm-nih-gov/pubmed/18287387>  
2009: <https://www-ncbi-nlm-nih-gov/pubmed/19474385>  
2010: <https://www-ncbi-nlm-nih-gov/pubmed/20610543>  
2011: <https://www.ncbi.nlm.nih.gov/pubmed/21685461>  
2012: <https://www.ncbi.nlm.nih.gov/pubmed/22237781>  
2013: <https://www.ncbi.nlm.nih.gov/pubmed/23335087>  
2014: <https://www.ncbi.nlm.nih.gov/pubmed/24890451>  
2015: <https://www.ncbi.nlm.nih.gov/pubmed/25559415>  
2016: <https://www.ncbi.nlm.nih.gov/pubmed/26742998>  
2017: <https://www.ncbi.nlm.nih.gov/pubmed/28055103>  
2018: <https://www.ncbi.nlm.nih.gov/pubmed/29313949>

## eAppendix 2. Data Sources by Malignancy:

Below are the detailed breakdowns and evidence used for each malignancy, the mutations involved in genomically targeted and informed therapy, as well as the drugs approved for the specific targets.

### Non-Small Cell Lung Cancer(NSCLC):

-Yearly Statistics from Cancer Statistics section, 2018 Lung Cancer deaths = 154,050  
-NSCLC frequency = 85% Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/>

### Mutations:

#### EGFR:

Frequency: 15%(10-20%), Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346098/>

Best Overall Response Rate:

2006-2012: 10.6% Gefitinib, FDA drug label

2013-2018: 65%, Osimertinib and Erlotinib, from FDA drug label

Drugs	Approval Dates
Erlotinib	4/16/10, 5/14/13, 10/18/16(Originally approved in 2004)
Afatinib	7/12/13, 1/12/18
Gefitinib	7/13/15(Originally approved in 2003)
Osimertinib	11/13/15, 3/31/17

#### ALK:

Frequency: 4.5%(2-7%), Source: <https://www.ncbi.nlm.nih.gov/pubmed/20979469>

Best Overall Response Rate:

2011-2012: 56%(50-61%) Crizotinib, FDA drug label

2013-2016: 65% Crizotinib, FDA drug label

2017-2018: 79%, Alectinib, from FDA drug label

Drugs	Approval Dates
Crizotinib	8/26/11, 11/20/13
Ceritinib	4/29/14, 5/26/17
Alectinib	12/11/15, 11/6/17
Brigatinib	4/28/17

**ROS1:**

Frequency: 2%(1.7%), Source: <https://www.ncbi.nlm.nih.gov/pubmed/22215748>

Best Overall Response Rate 2016-2018: 66%, Crizotinib, from FDA drug label

Drugs	Approval Dates
Crizotinib	3/11/16

**BRAF:**

Frequency: 2%(1-3%), Source: <https://www.ncbi.nlm.nih.gov/pubmed/29057232>

Best Overall Response Rate 2017-2018: 63%, Dabrafenib and Trametinib, from FDA drug label

Drugs	Approval Dates
Dabrafenib and Trametinib	6/22/17

**Breast Cancer:**

-Yearly Statistics from Cancer Statistics section, 2018 Breast Cancer deaths = 41,400

**Mutations:**

**HER2:**

Frequency: 17%(15-20%), Source: <https://www.ncbi.nlm.nih.gov/pubmed/25332249>

Best Overall Response Rate:

2006-2012: 16% Trastuzumab, FDA drug label

2013-2018: 43.6%, Ado-Trastuzumab emtansine, from FDA drug label

Drugs	Approval Dates
Trastuzumab	11/16/06(originally in 1998)
Lapatinib	3/13/07, 1/29/10
Pertuzumab	6/8/12, 9/30/13
Ado-Trastuzumab Emtansine	2/22/13

**BRCA:**

Frequency: 2%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2408797/pdf/83-6691407a.pdf>

Best Overall Response Rate 2018: 59.9%, Olaparib, from FDA drug label

Drugs	Approval Dates
Olaparib	1/12/18

## Melanoma:

-Yearly Statistics from Cancer Statistics section, 2018 Melanoma deaths = 9320

### Mutations:

#### **BRAF V600E and V600K:**

Frequency: 50%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3600117/>

Best Overall Response Rate:

2011-2012: 48.4%, Vemurafenib, FDA drug label

2013-2014: 57% Dabrafenib+Trametinib, FDA drug label

2015-2018: 70%, Cobimetinib, FDA drug label

Drugs	Approval Dates
Vemurafenib	8/17/11
Dabrafenib	5/29/13
Trametinib	5/29/13
Trametinib w/ Dabrafenib	1/10/14, 11/20/15
Cobimetinib	11/10/15

## Colorectal Cancer:

-Yearly Statistics from Cancer Statistics section, 2018 Colorectal Cancer deaths = 50,630

### Mutations:

#### **KRAS Wild Type:**

Frequency: 57%, Source: <https://www.ncbi.nlm.nih.gov/pubmed?term=18316791>

Best Overall Response Rate:

2006-2011: 10.8% Cetuximab, FDA drug Label

2012-2018: 18%, Cetuximab, FDA drug label

Drugs	Approval Dates
Panitumumab	9/27/06
Cetuximab	10/2/07, 7/6/12(originally approved in 2004)

## Ovarian Cancer:

-Yearly Statistics from Cancer Statistics section, 2018 Ovarian Cancer deaths = 14,070

### Mutations:

#### **BRCA:**

Frequency: 15%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5524247/>

Best Overall Response Rate:

2014-2015: 34%, Olaparib, FDA drug label  
 2016-2018: 54%, Rucaparib, FDA drug label

Drugs	Approval Dates
Olaparib	12/19/14
Rucaparib	12/19/16

## Gastroesophageal Cancer(including GIST):

-Yearly Statistics from Cancer Statistics section, 2018 Gastric+Esophageal Cancer deaths = 26,650

### Mutations:

#### HER2:

Frequency: 17.9%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4870069/>  
 Best Overall Response Rate 2010-2018: 12%, Trastuzumab, from FDA drug label

Drugs	Approval Dates
Trastuzumab	10/20/10

### Frequency of GIST:

GIST involves multiple organ systems but with over 60% gastric (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4880518/pdf/nihms771882.pdf>) and being overall less than 1% of all gastrointestinal malignancies(<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4487456/>) it is a small percentage. With the low overall prevalence, the vast majority of GIST being non-metastatic (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4039646/>), and 85% mutation rate for KIT (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4487456/>) we felt that using 1% of gastric for an overall number was a reasonable and generous estimate of the small percentage KIT mutation positive metastatic GIST that contributes to total genomic cancer therapy.

**Frequency:** 1%(per above)

Best Overall Response Rate 2006-2018: 67.3%, Imatinib, FDA drug label from 2006

Drugs	Approval Dates
Imatinib	12/19/08, 1/31/12(originally approved in 2001)

## Chronic Myeloid Leukemia(CML):

-Yearly Statistics from Cancer Statistics section, 2018 CML deaths = 1090

### Mutations:

#### Ph+:

Frequency: 100%,

Best Overall Response Rate 2006-2018: 95.3%, Imatinib, from FDA drug label

Drugs	Approval Dates
Imatinib	9/27/06, 1/25/13(originally approved in 2001)
Dasatinib	6/28/06, 10/28/10, 11/9/17
Nilotinib	10/29/07, 6/17/10

Ponatinib	12/14/12
Bosutinib	12/19/17

## Chronic Lymphocytic Leukemia(CLL):

-Yearly Statistics from Cancer Statistics section, 2018 CML deaths = 4510

### Mutations:

#### **17p Deletion:**

Frequency: 7%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4116834/>

Best Overall Response Rate:

2014-2015: 47.6%, Ibrutinib, FDA drug label

2016-2018: 80.2%, Venetoclax, FDA drug label

Drugs	Approval Dates
Ibrutinib	7/28/14
Venetoclax	4/11/16

## Acute Myeloid Leukemia(AML):

-Yearly Statistics from Cancer Statistics section, 2018 AML deaths = 10670

### Mutations:

#### **IDH2:**

Frequency: 11%, Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3145345/>

Best Overall Response Rate 2017-2018: 40.3%, Enasidenib

Source: <http://www.bloodjournal.org/content/early/2017/06/05/blood201704779405?ssochecked=true>

Drugs	Approval Dates
Enasidenib	8/1/17

### Mutations:

#### **FLT3:**

Frequency: 10.8%, Source: <http://www.bloodjournal.org/content/118/20/5366>

Best Overall Response Rate 2017-2018: 5.4%, Midostaurin,

Source: <http://www.nejm.org/doi/full/10.1056/NEJMoa1614359>

Drugs	Approval Dates
Midostaurin	4/28/17

## Acute Lymphocytic Leukemia(ALL):

-Yearly Statistics from Cancer Statistics section, 2018 ALL deaths = 1470

### Mutations:

#### **Ph+:**

Frequency: 25%(20-30%), Source: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4091825/>  
 Best Overall Response Rate 2006-2018: 19%, Imatinib, from FDA Drug Label

Drugs	Approval Dates
Imatinib	10/19/06

## Microsatellite Instability High(MSI):

-Yearly Statistics from Cancer Statistics section, 2018 MSI Deaths

Breast: 41,400

Colorectal: 50630

Endometrial: 11,350

Small Cell Lung: 23,107

Thyroid Cancer: 2,060

Adrenal Cortical: 1,020

Esophageal: 15,850

Cervical: 4,170

Glioblastoma: 8,751

Renal Cell Carcinoma(RCC): 14,970

Pancreatic: 44,330

Small Intestine: 1,450

Prostate Adenocarcinoma: 29,430

Cholangiocarcinoma: 3,790

Sarcoma: 4,990

## Mutation Frequency:

Malignancy	Frequency	Source
Breast	1.70%	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467167/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5467167/</a>
Colorectal	4.00%	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594190/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4594190/</a>
Endometrial	28.3%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Small Cell Lung	2.00%	<a href="https://www.ncbi.nlm.nih.gov/pubmed/28596308">https://www.ncbi.nlm.nih.gov/pubmed/28596308</a>
Thyroid	29.7%	<a href="http://clincancerres.aacrjournals.org/content/7/11/3444">http://clincancerres.aacrjournals.org/content/7/11/3444</a>
Adrenal Cortical	0.054%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Esophageal	0.033%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Cervical	0.023%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Glioblastoma	0.013%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
RCC	0.011%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Pancreatic	0.011%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Small Intestine	18.00%	<a href="https://www.ncbi.nlm.nih.gov/pubmed/12627520">https://www.ncbi.nlm.nih.gov/pubmed/12627520</a>
Prostate	0.011%	<a href="https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/">https://www-ncbi-nlm-nih-gov/pmc/articles/PMC5467167/</a>
Cholangiocarcinoma	0.05%	<a href="http://cco.amegroups.com/article/view/12260/12685">http://cco.amegroups.com/article/view/12260/12685</a>
Sarcoma	0.03%	<a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5576142/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5576142/</a>

Best Overall Response Rate 2017-2018: 39.6%, Pembrolizumab, from FDA drug label

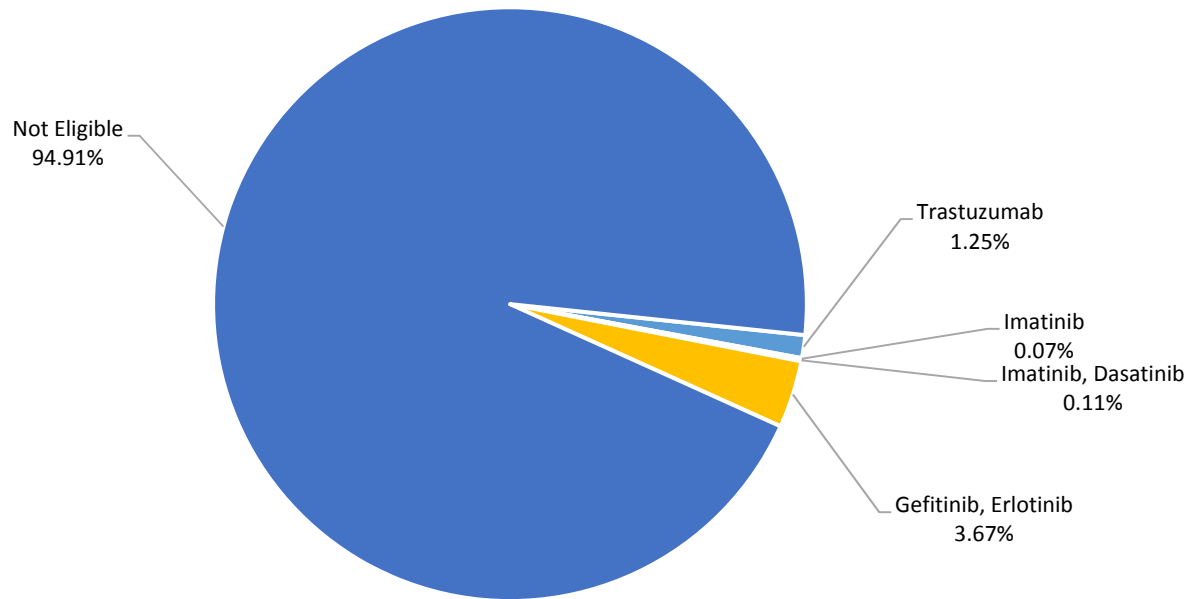
Drugs	Approval Dates
-------	----------------

Pembrolizumab	5/23/17
Nivolumab	8/1/17

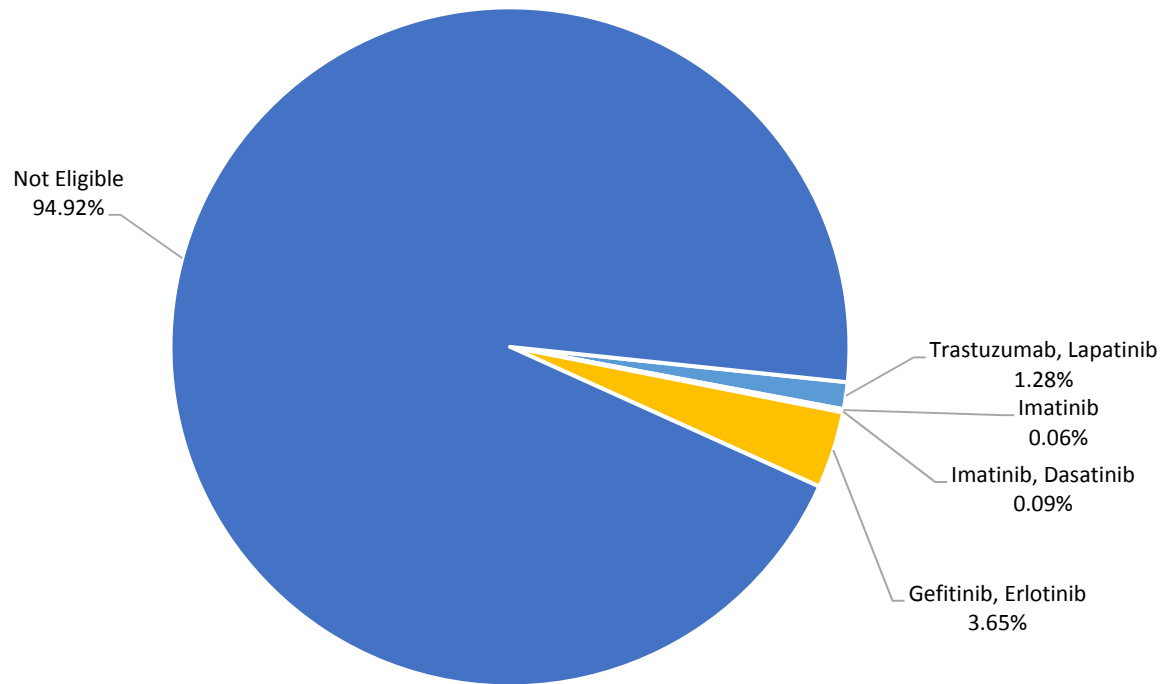
### **eAppendix 3. Pie Charts Estimating Patients Eligible for Genomically Targeted Therapy**



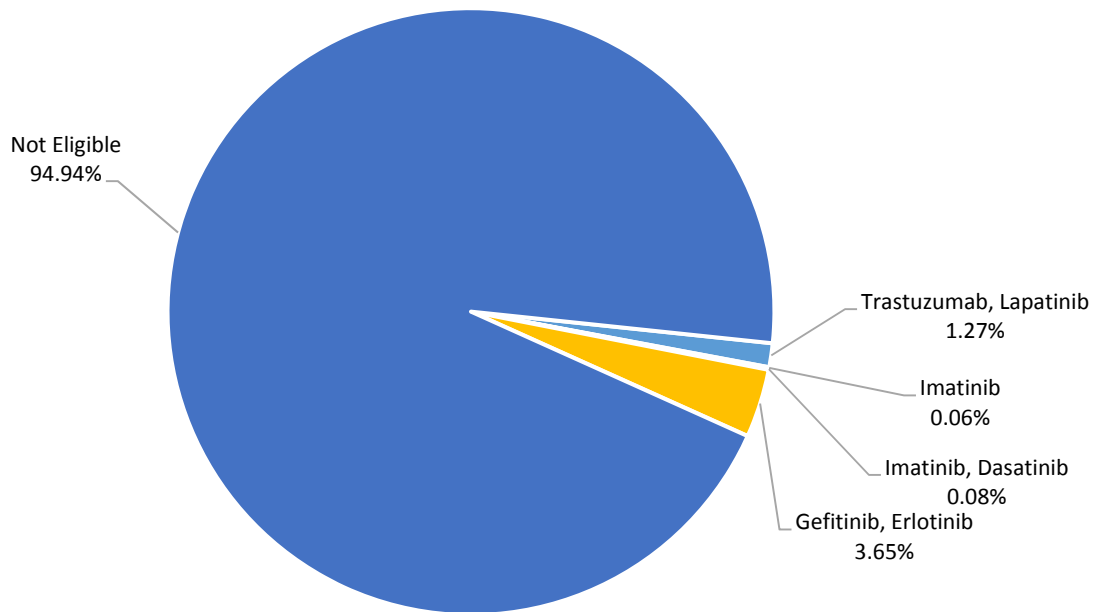
2006



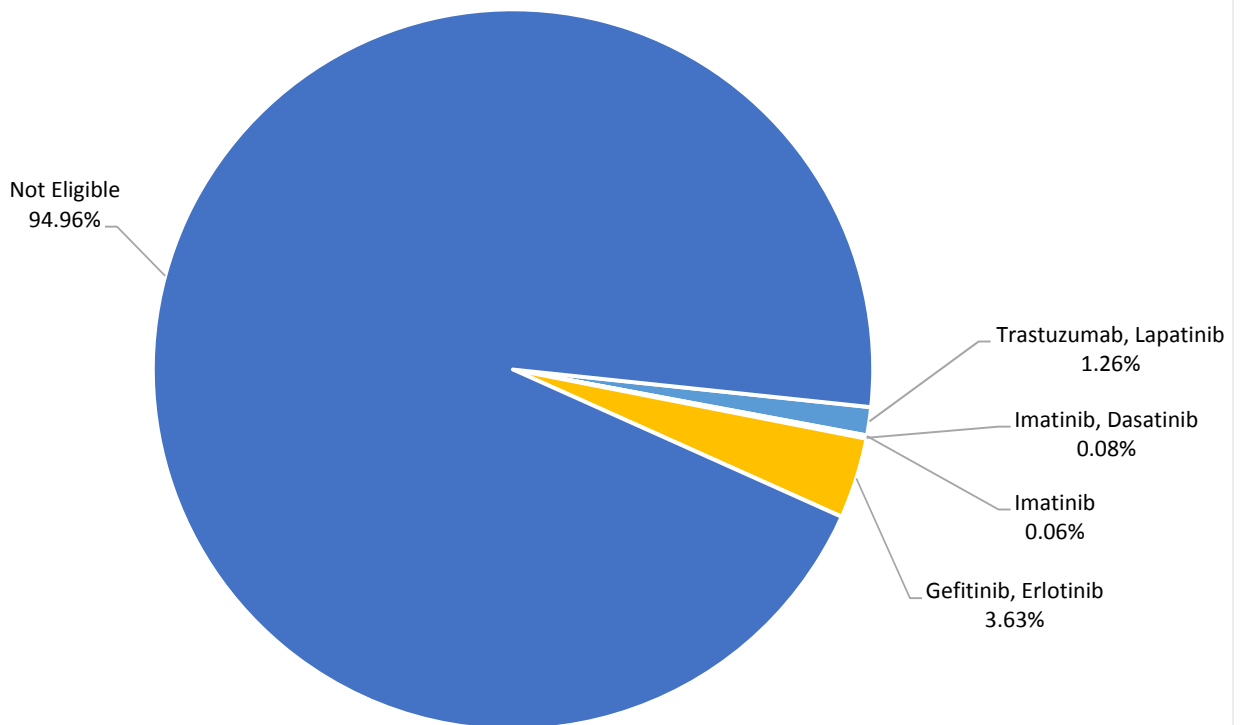
2007



2008

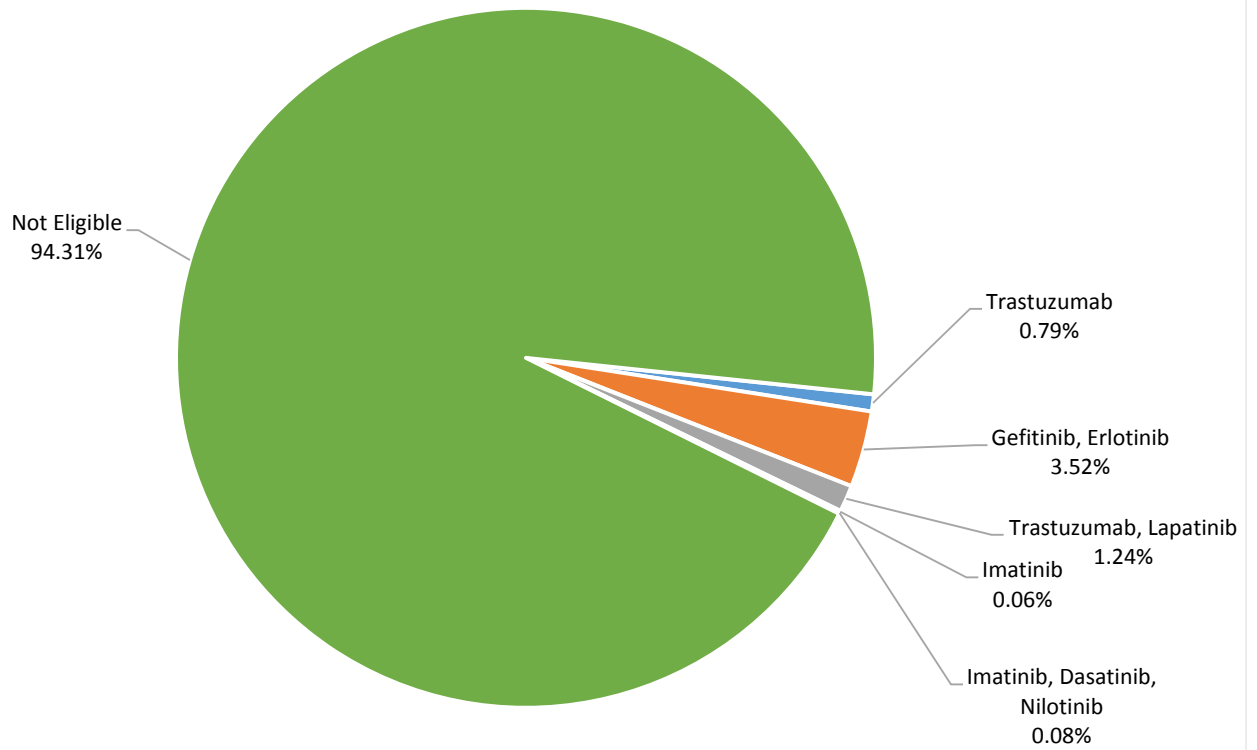


2009

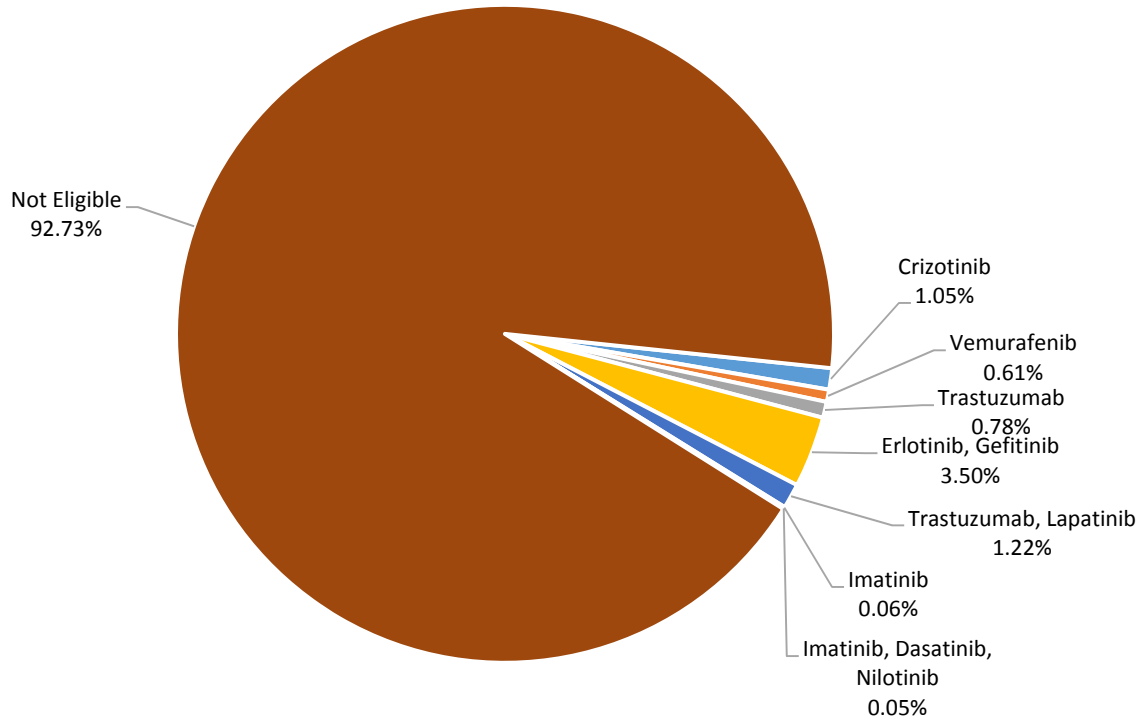




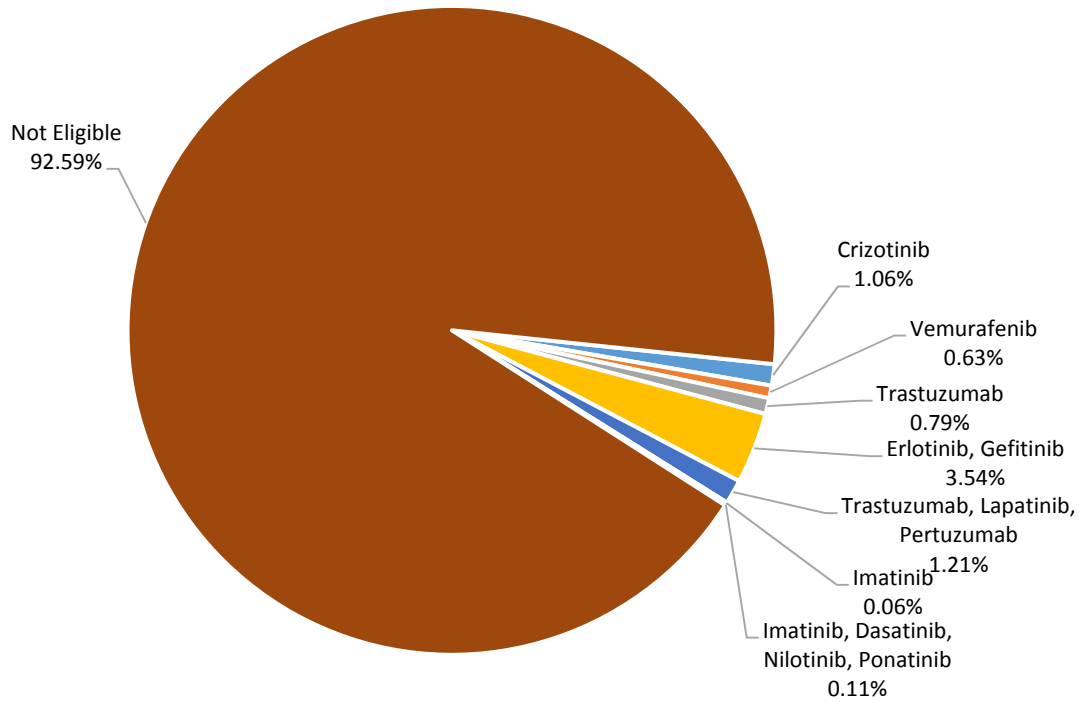
2010



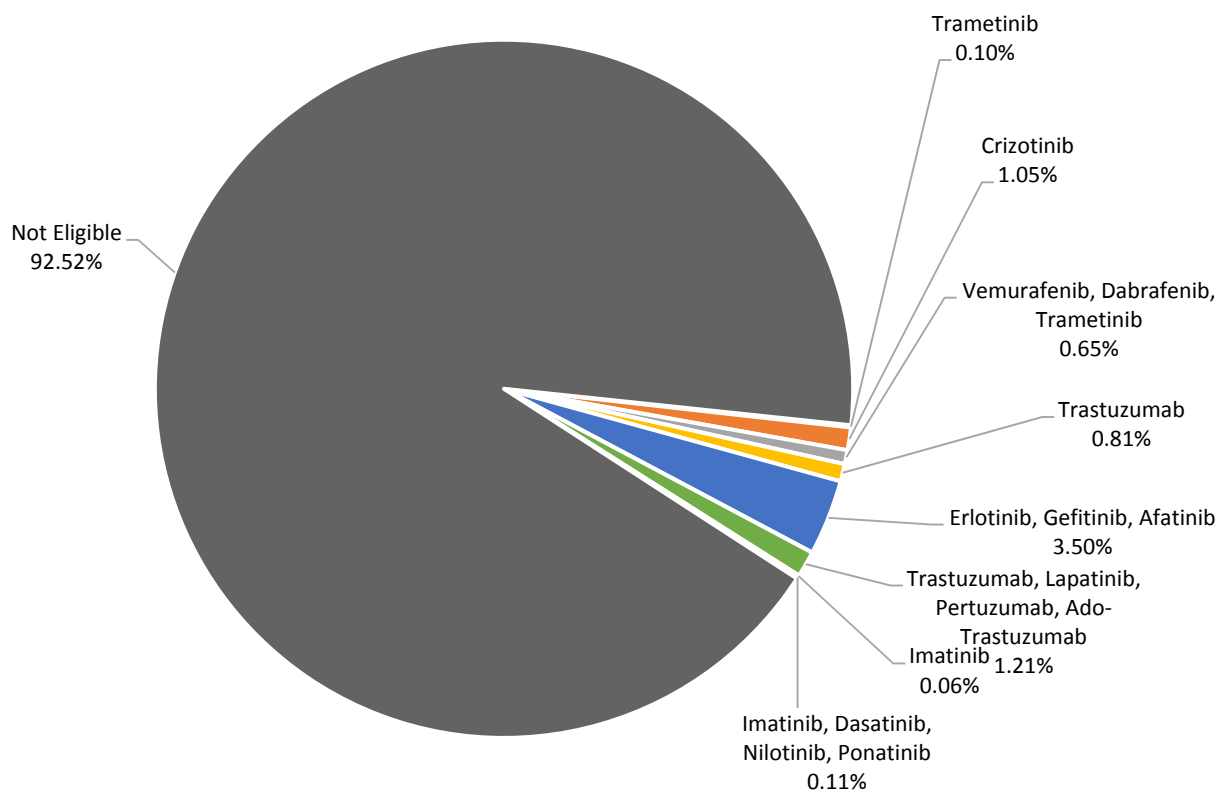
2011



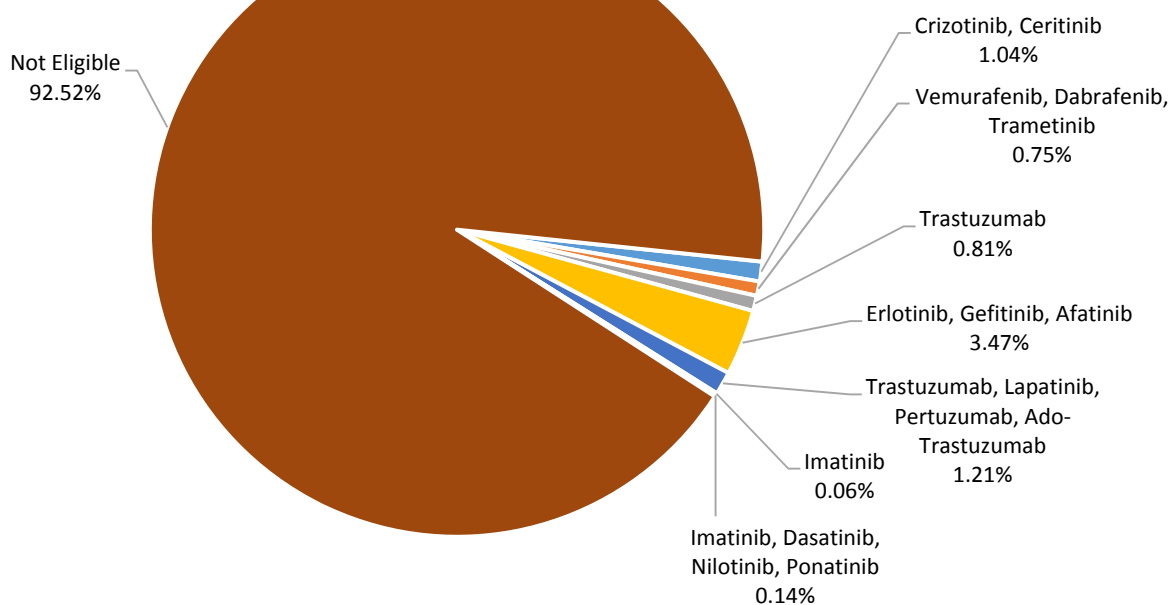
2012



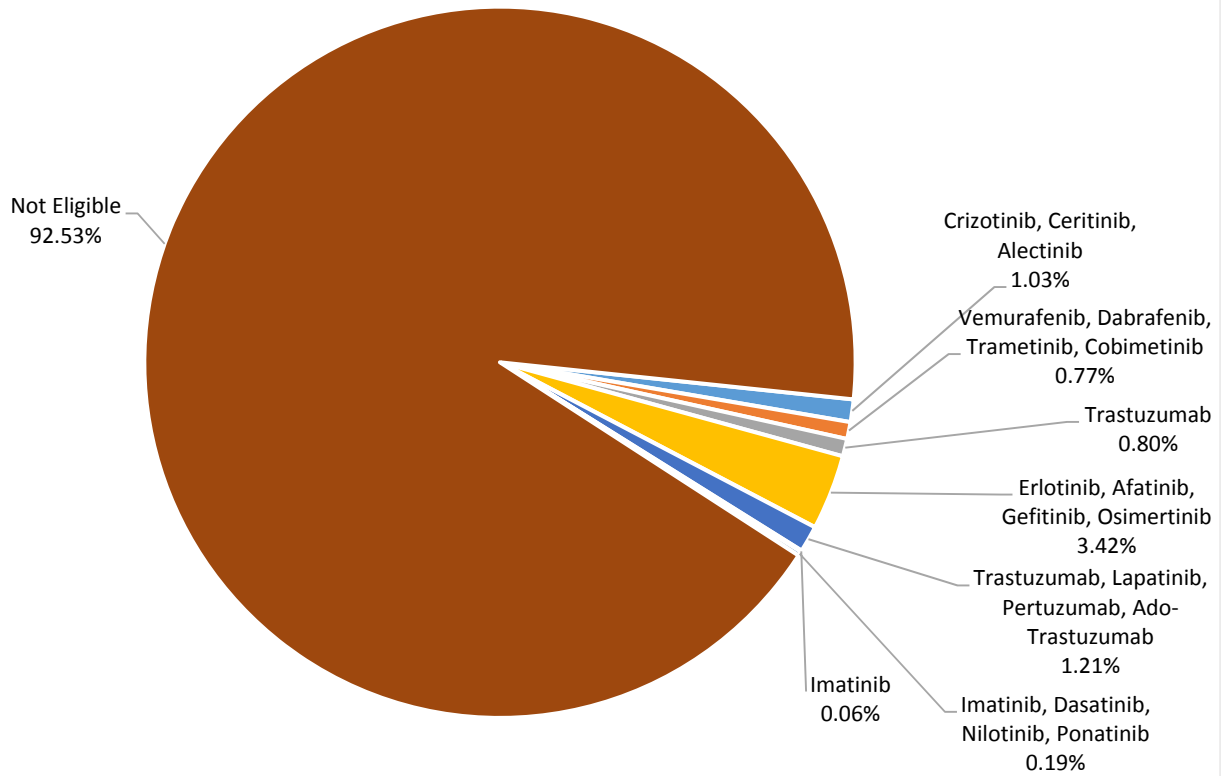
2013



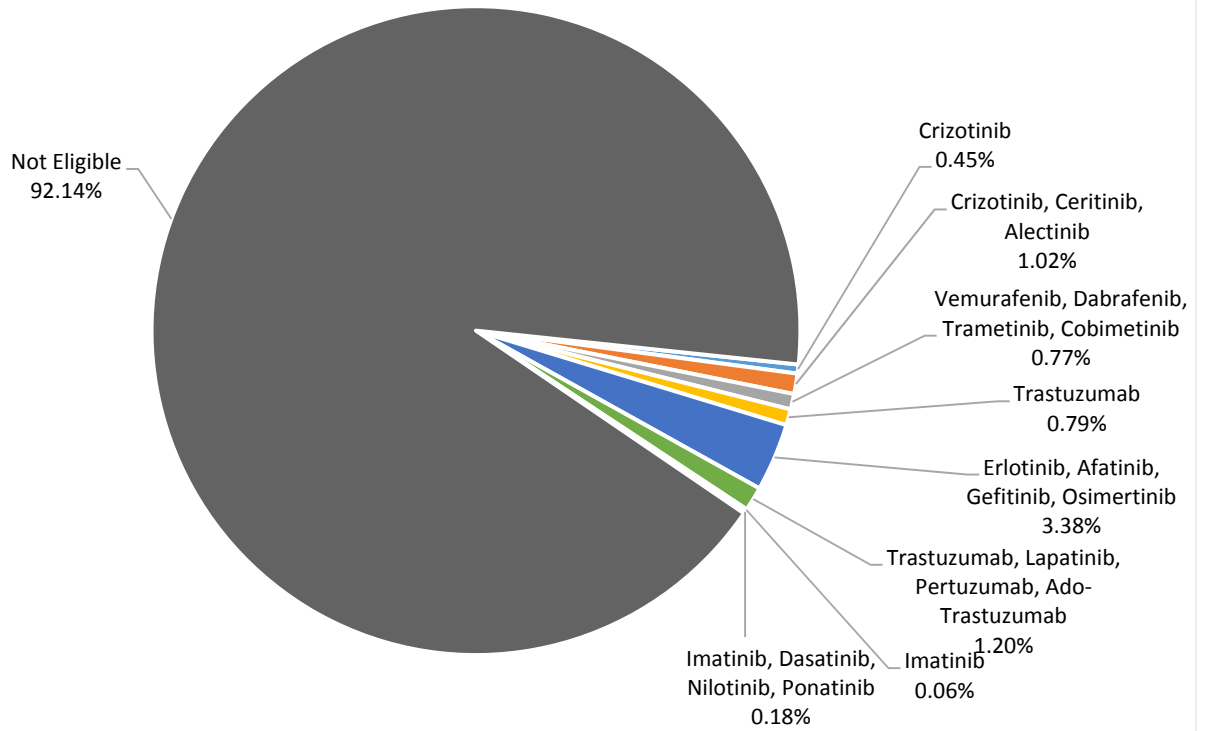
2014



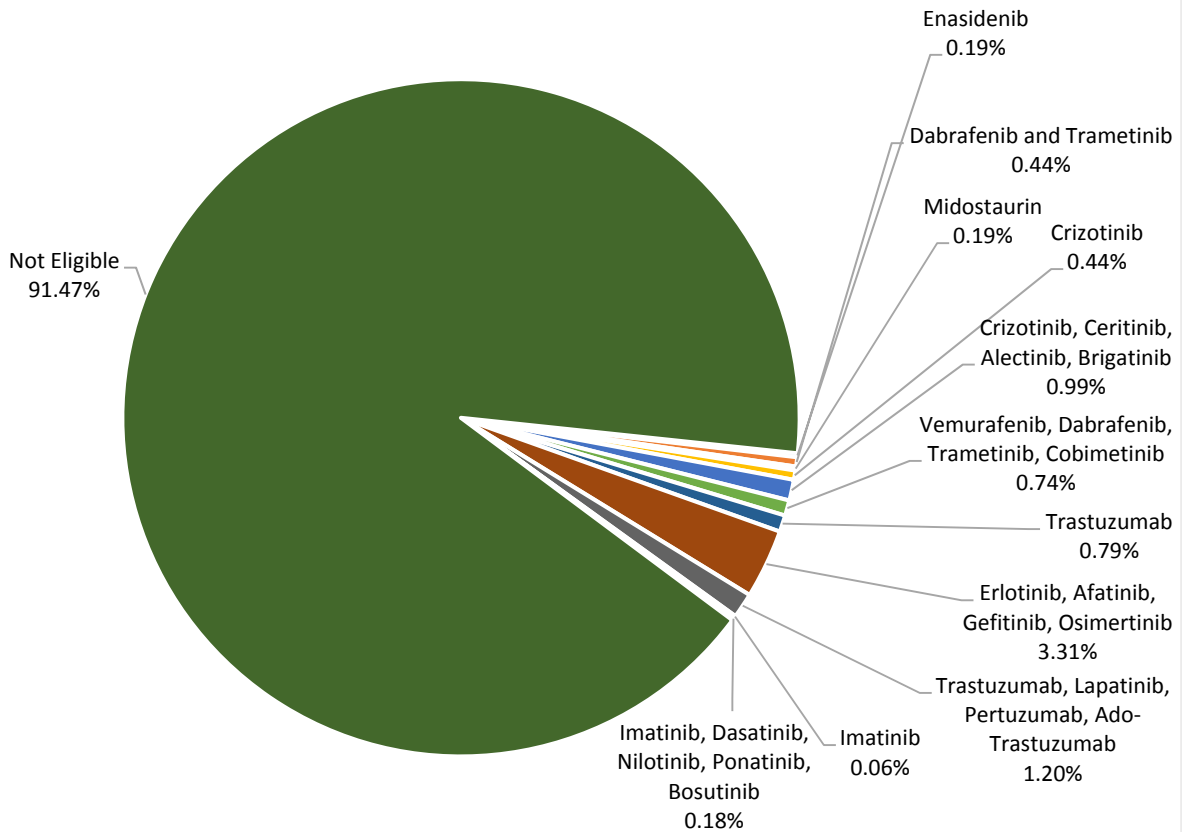
2015



2016

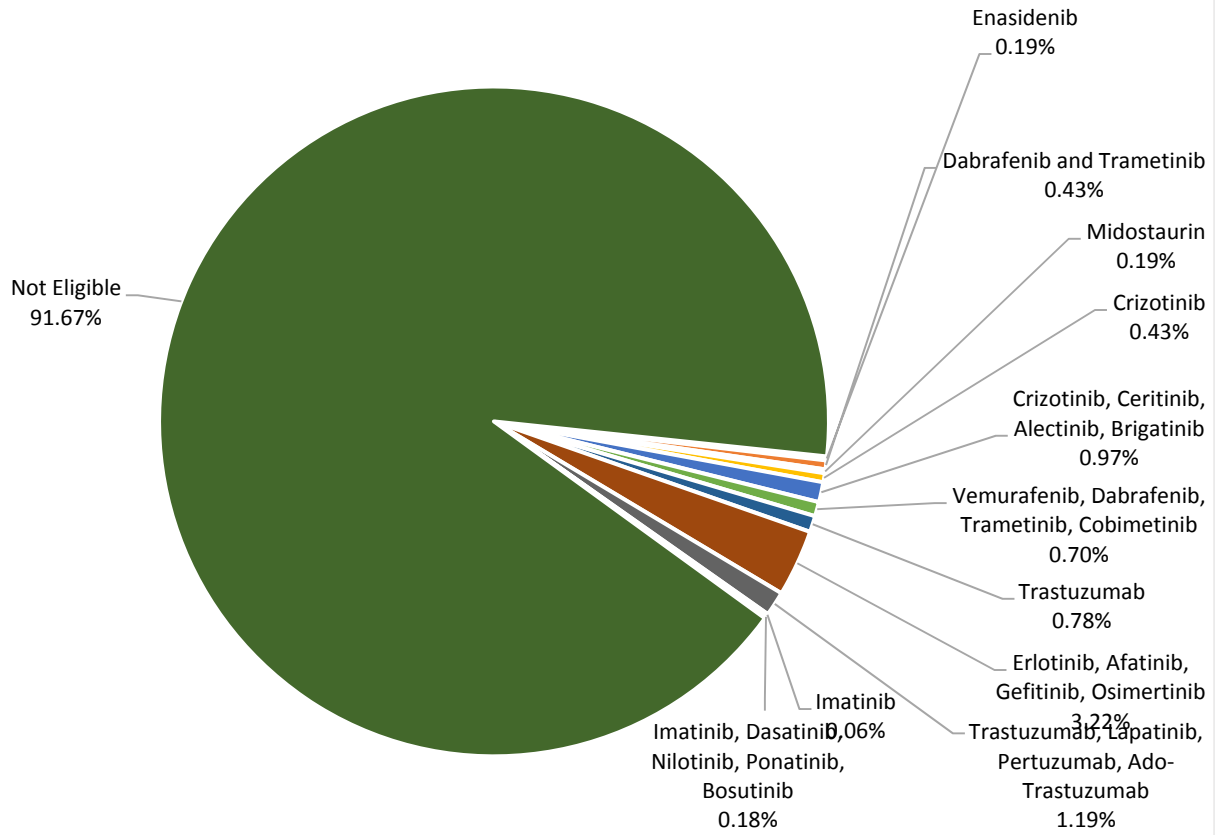


2017



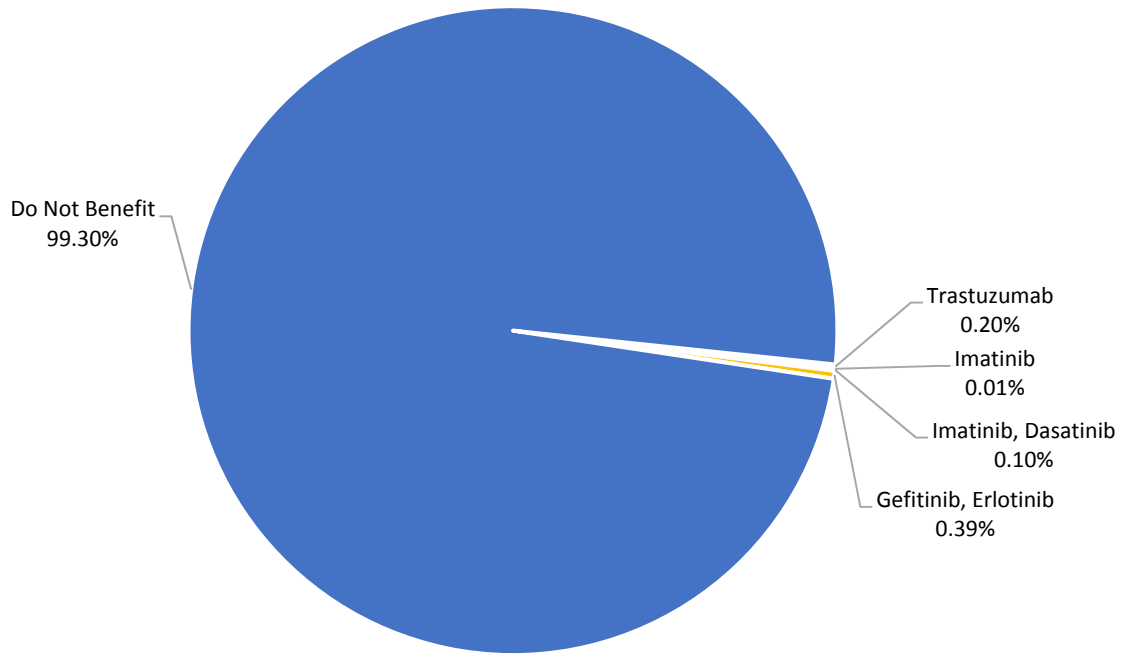


2018

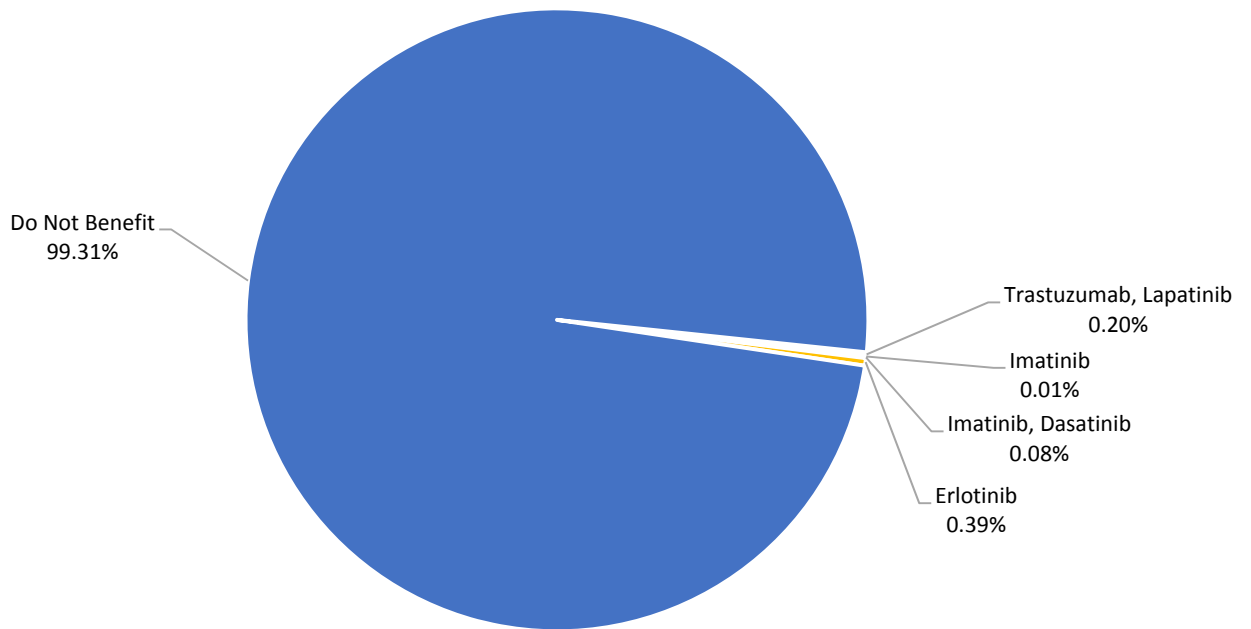


# **eAppendix 4. Pie Charts Estimating Patients Who Could Benefit from Genomically Targeted Therapy**

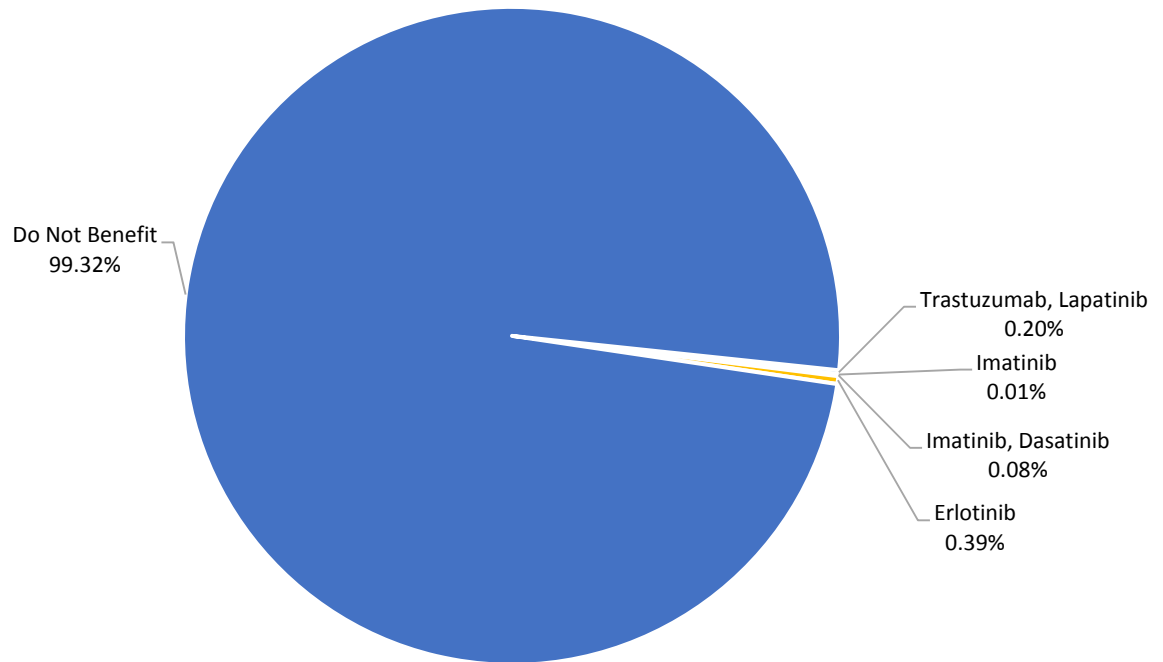
2006



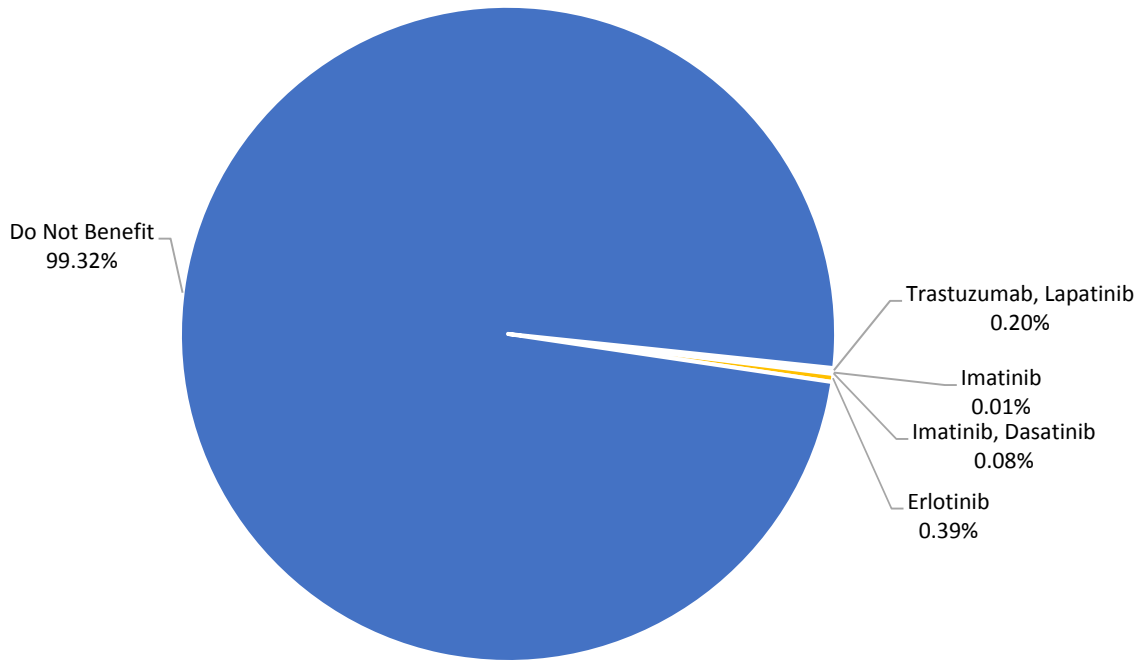
2007



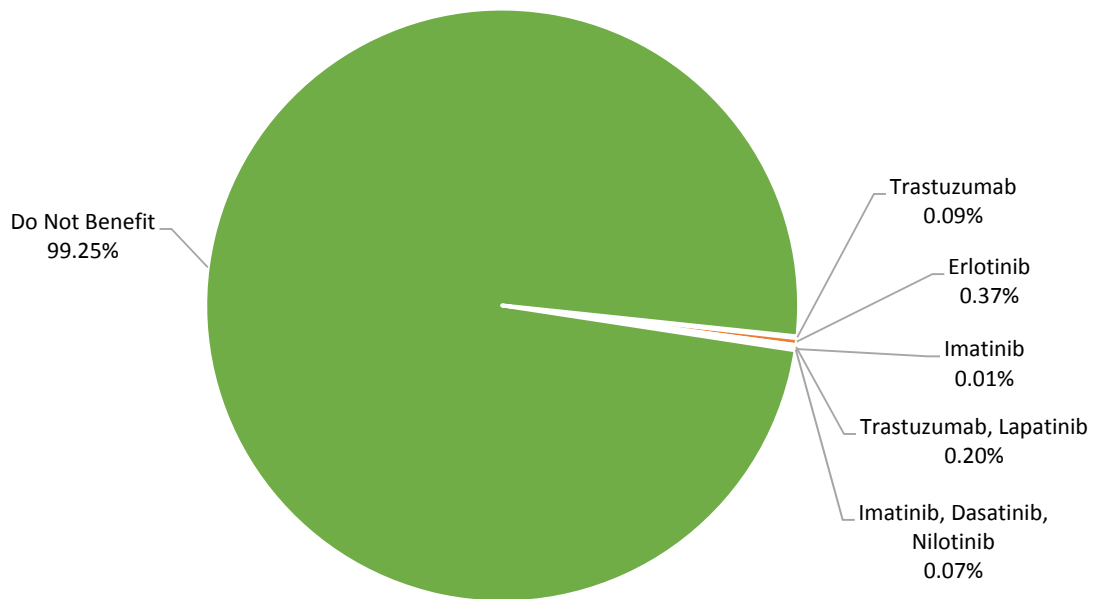
2008



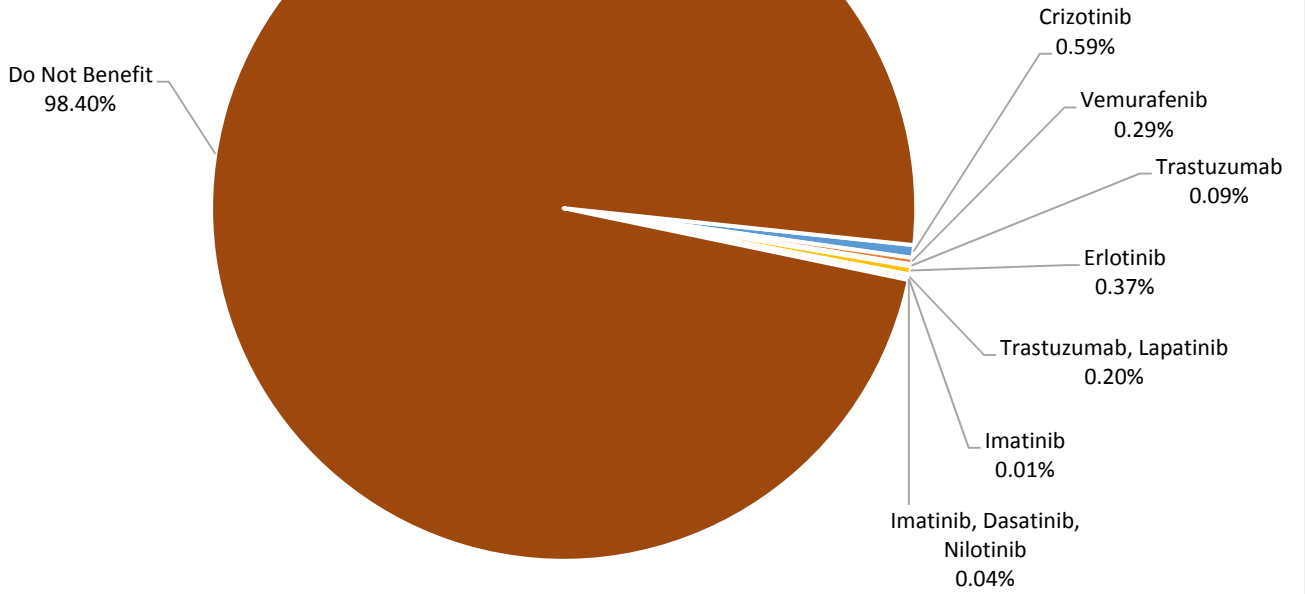
2009



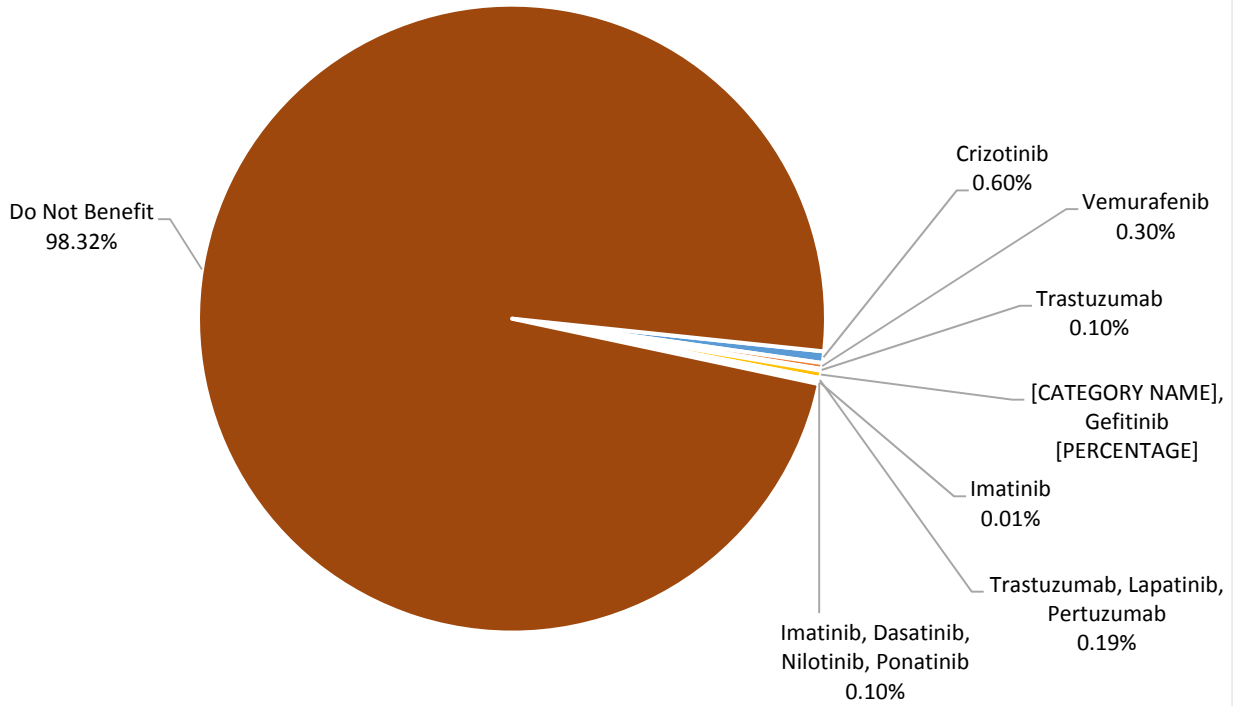
2010



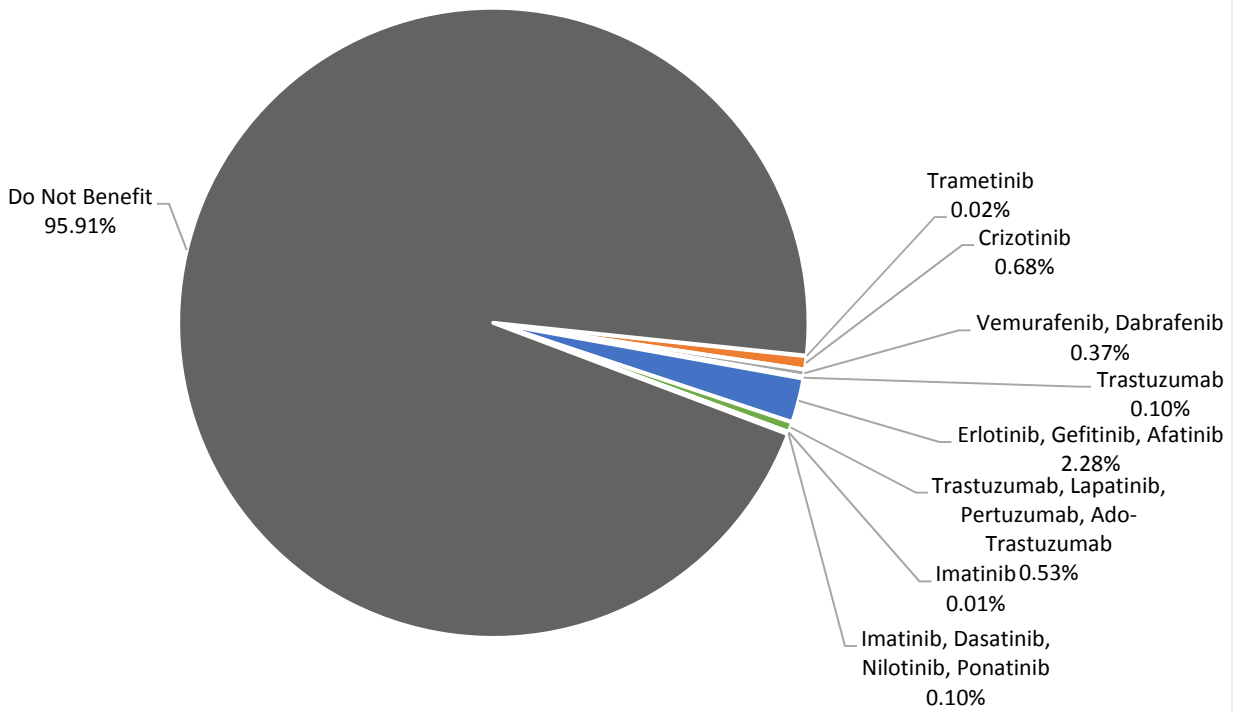
2011



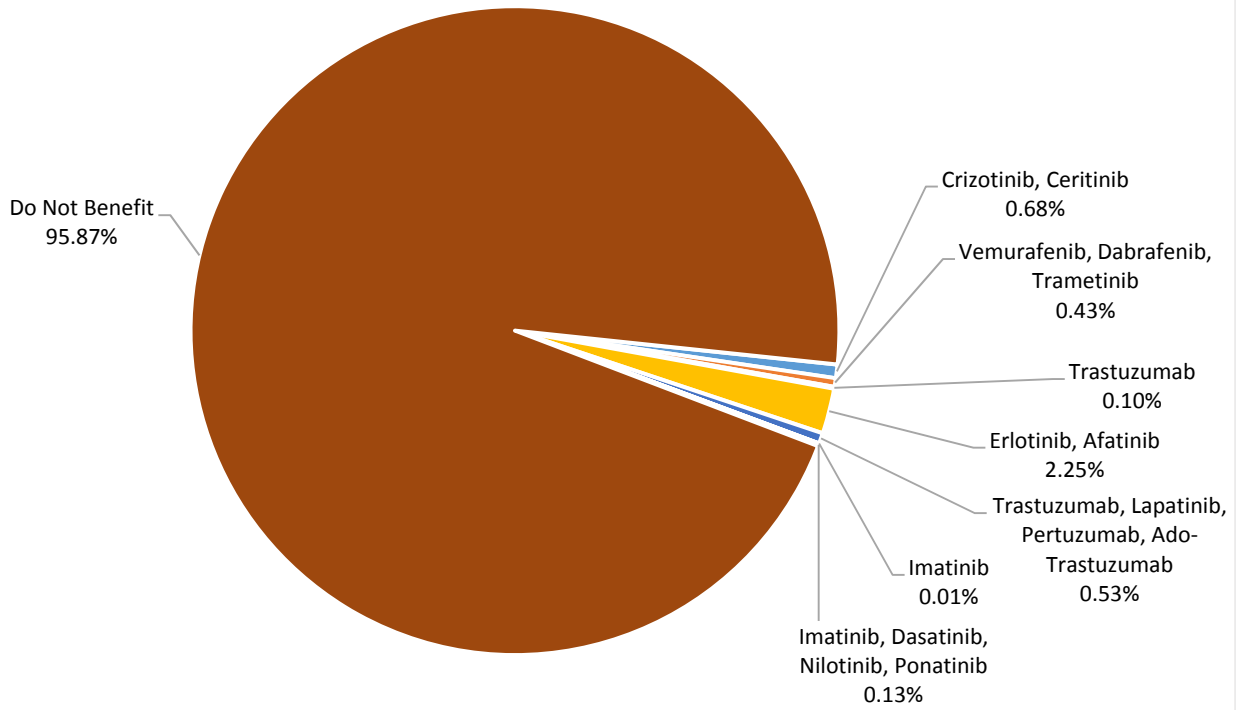
2012



2013

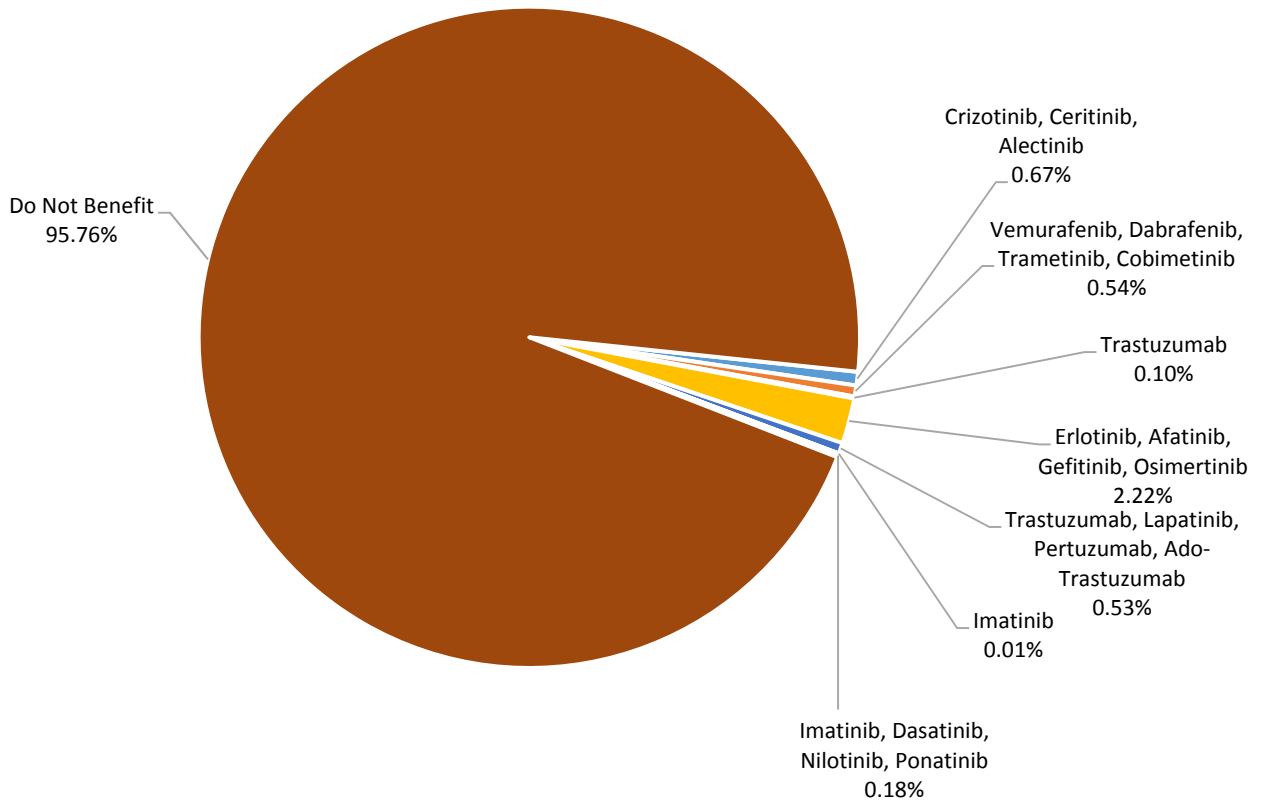


2014

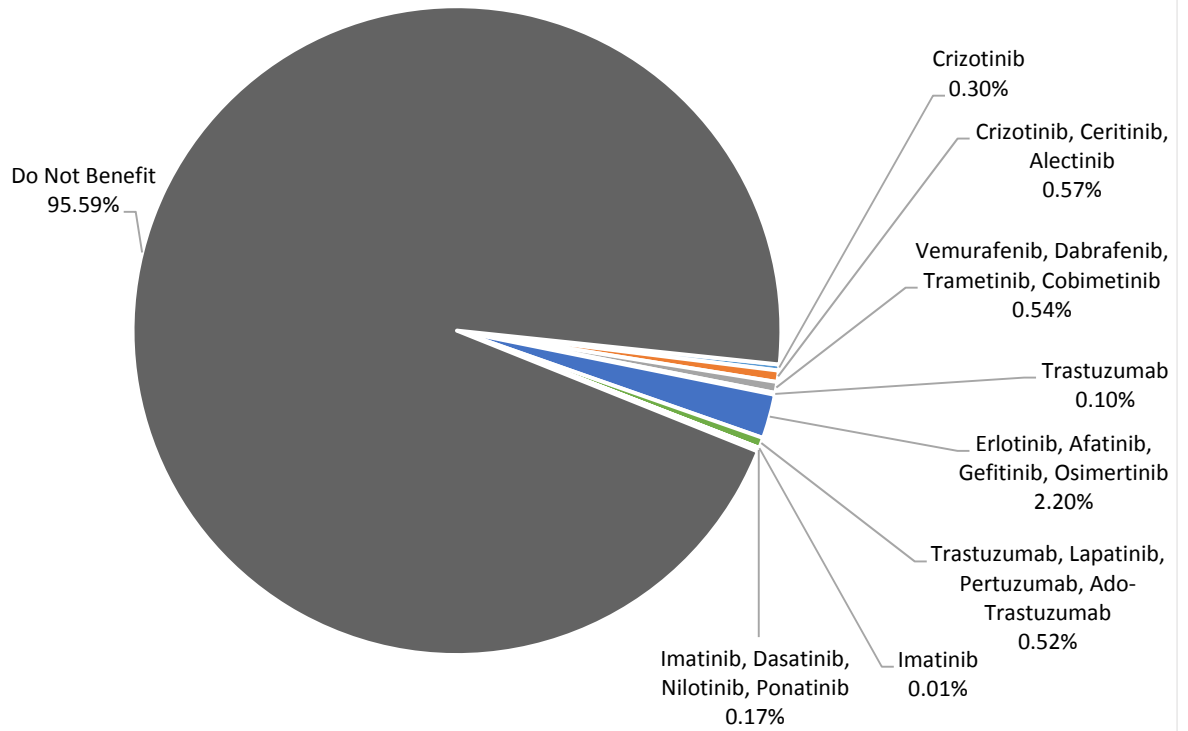




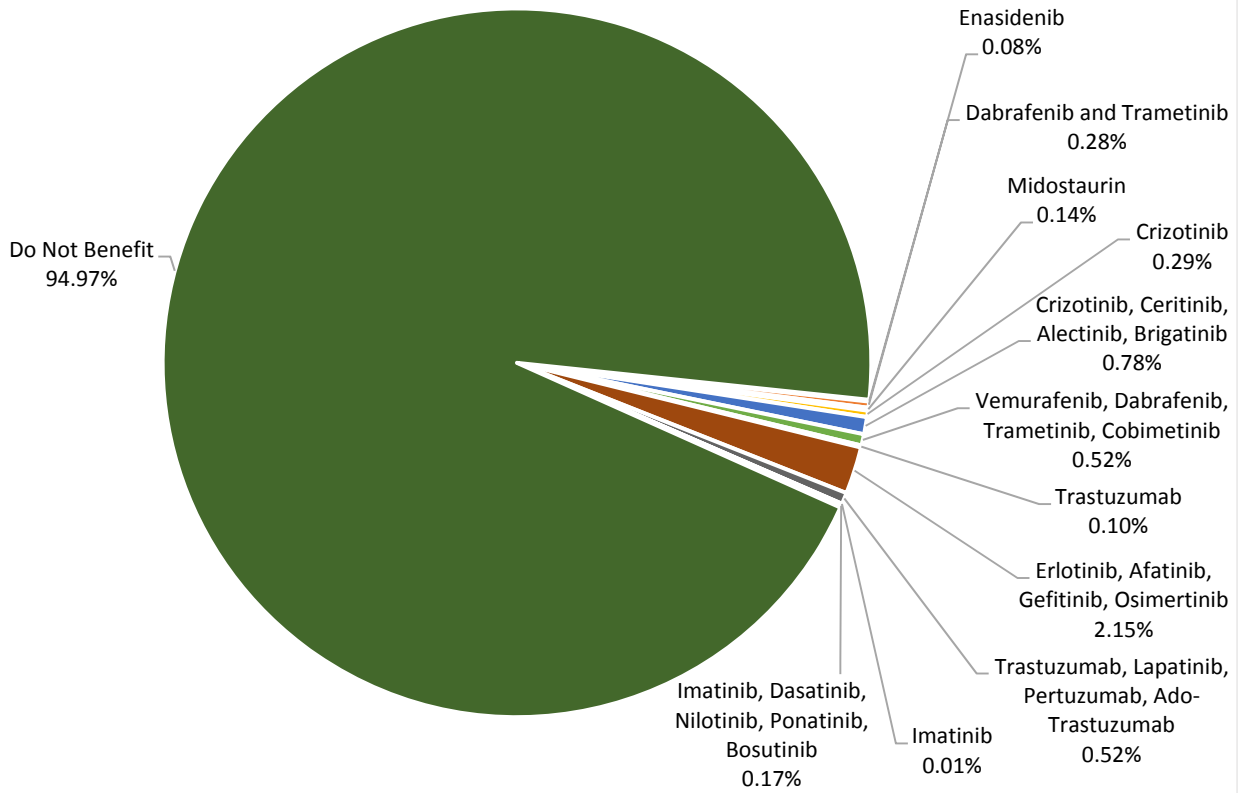
2015



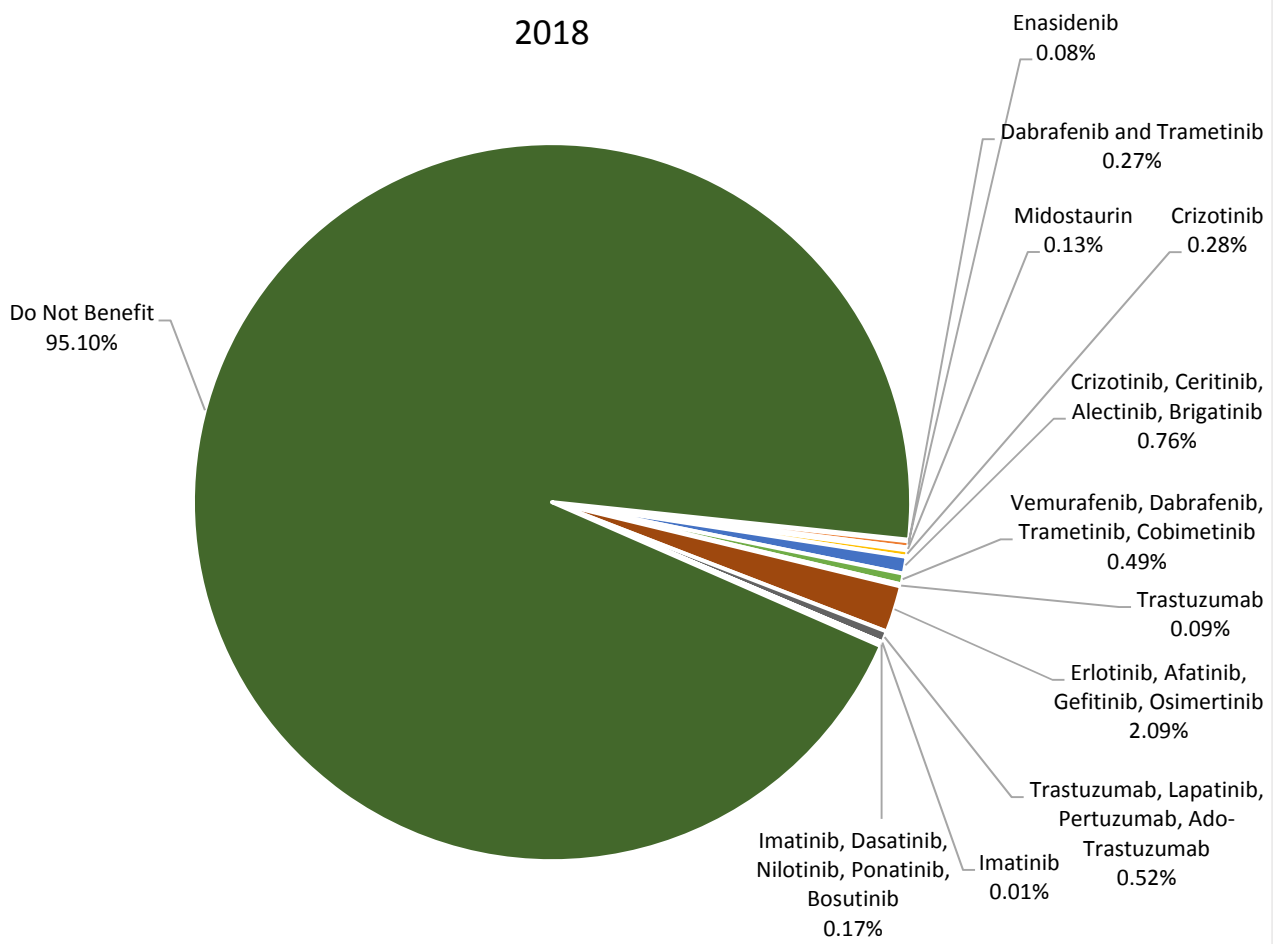
2016



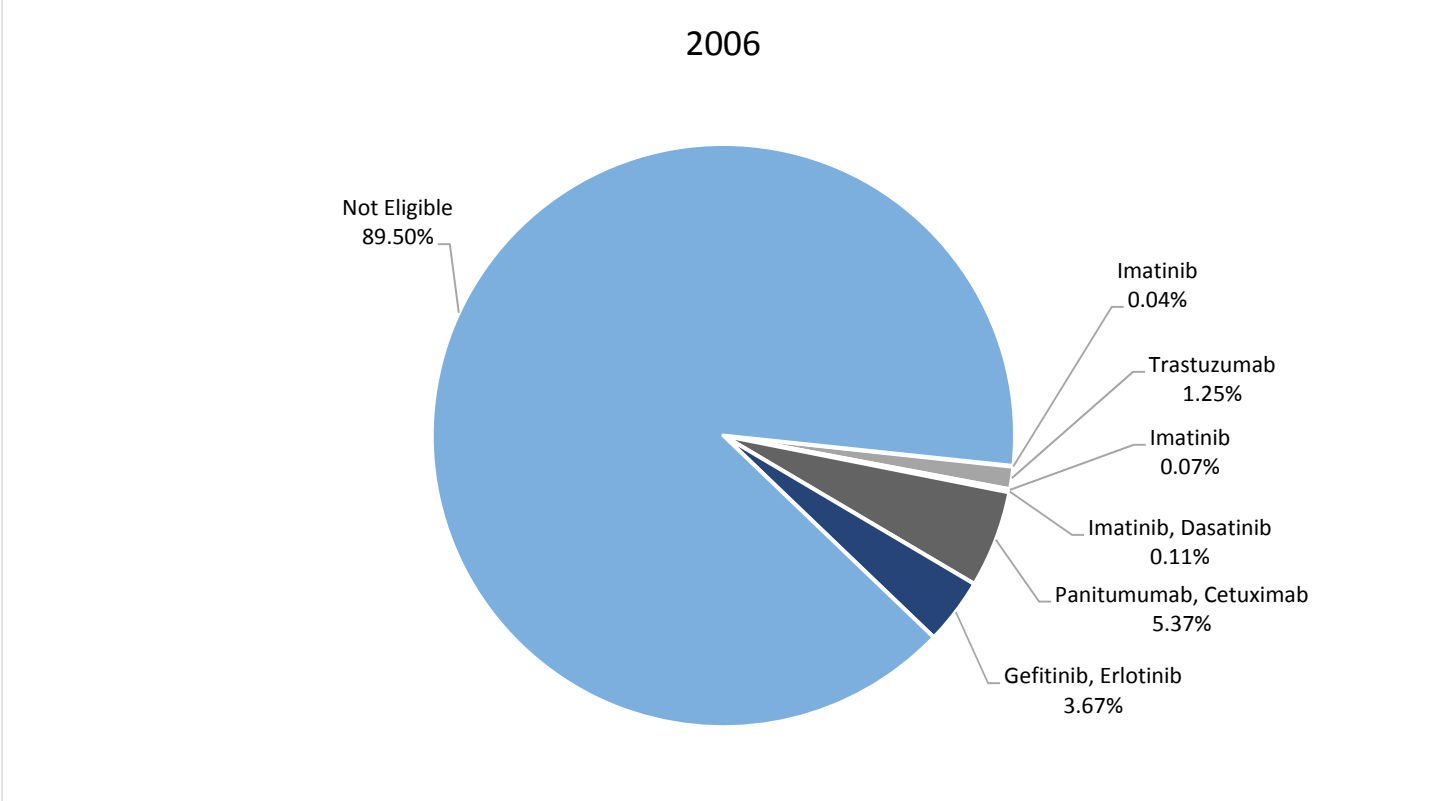
2017



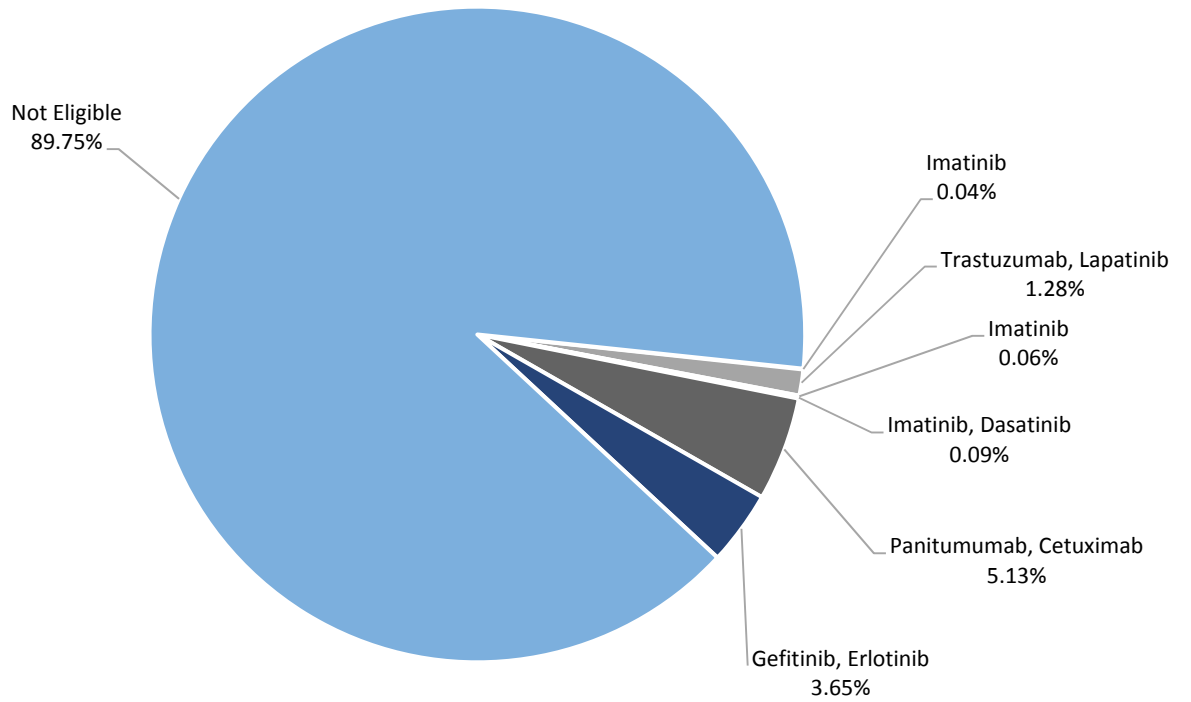
2018



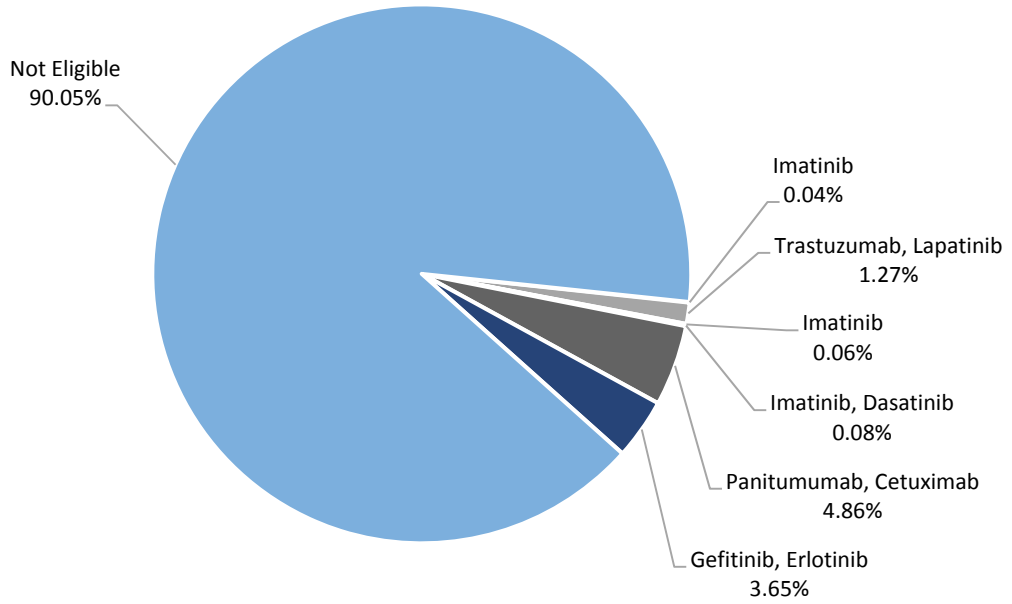
# eAppendix 5. Pie Charts Estimating Patients Eligible for Genomically Informed Therapy



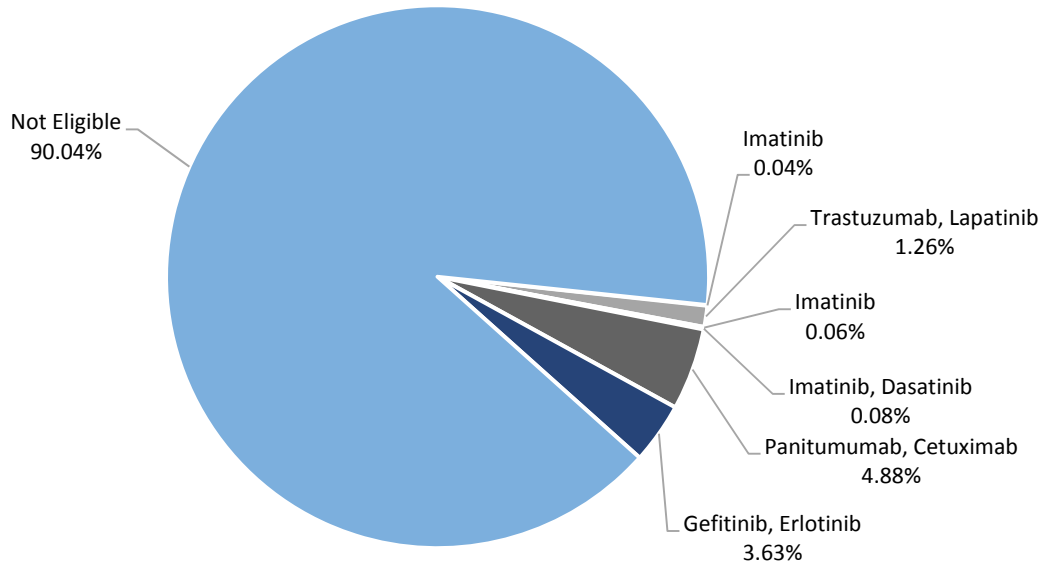
2007



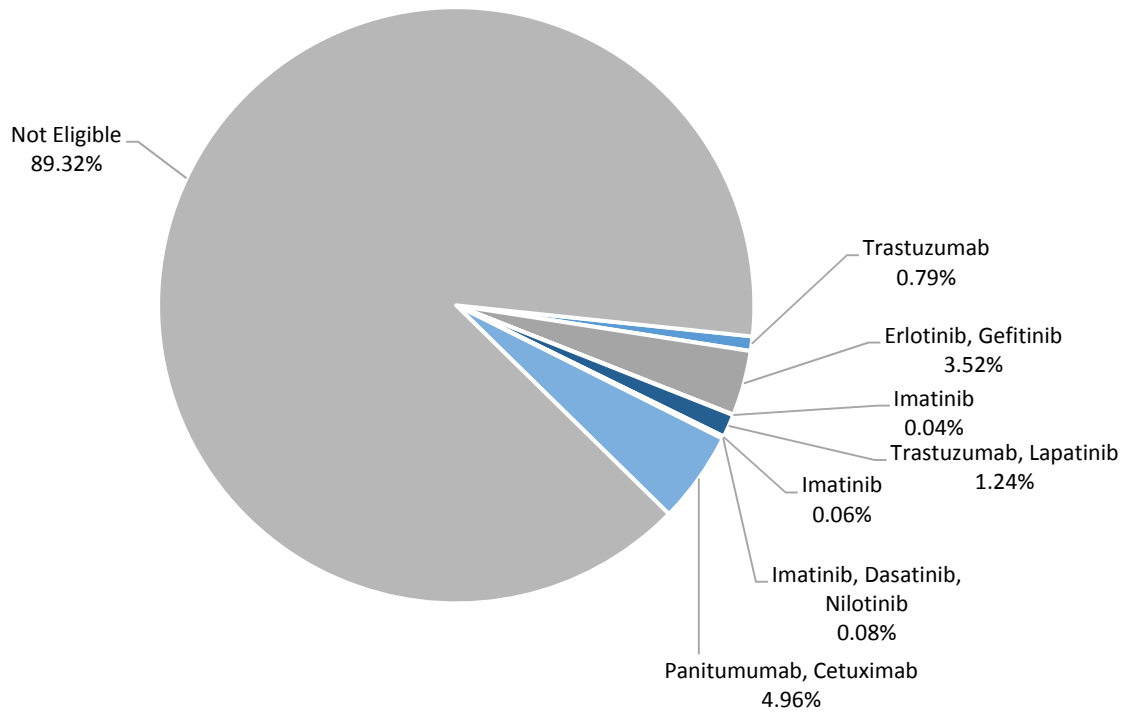
2008



2009

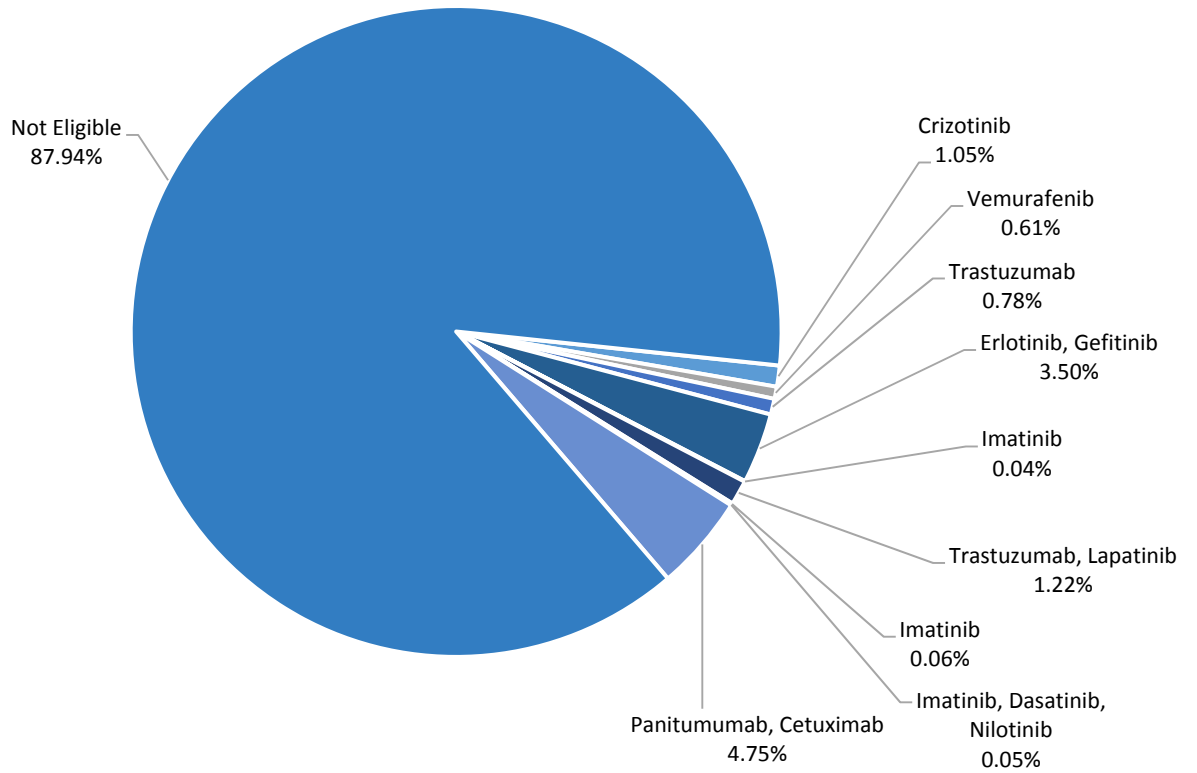


2010

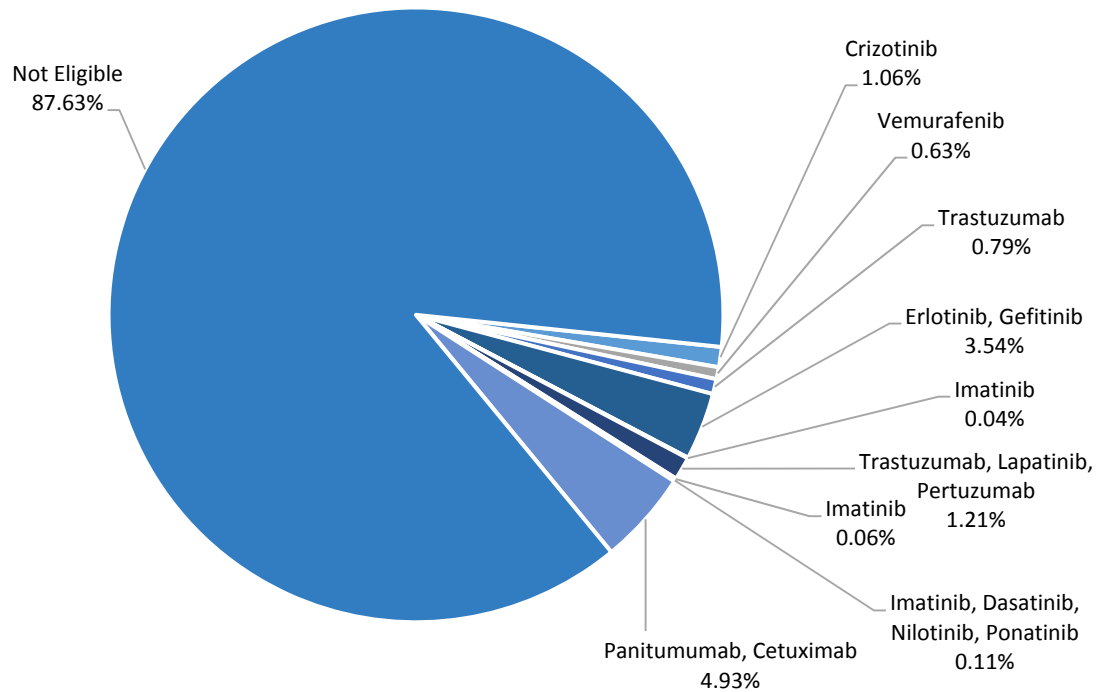




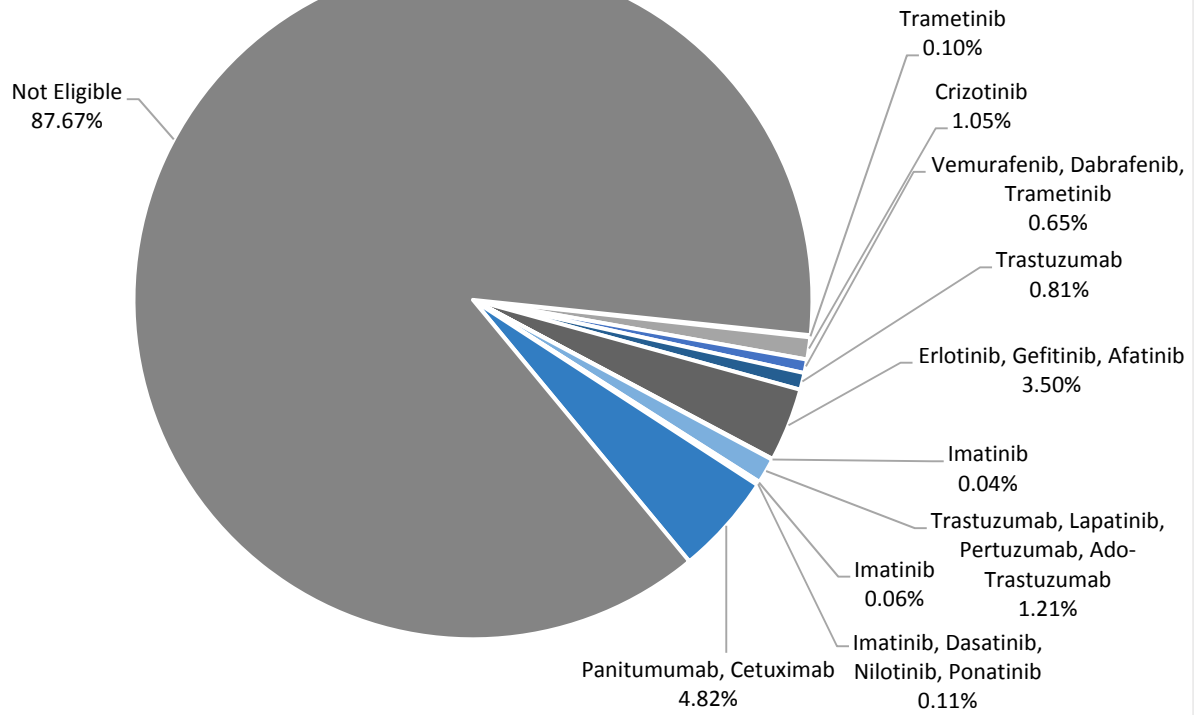
2011



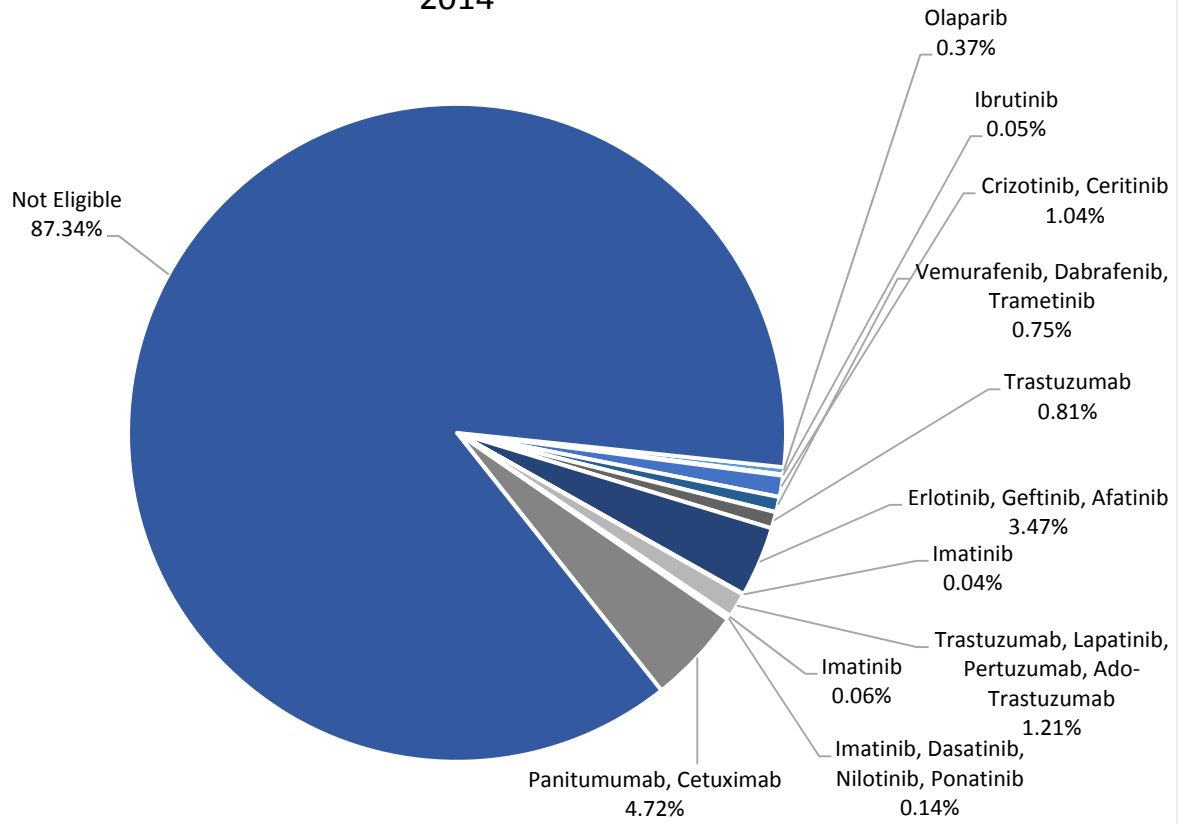
2012



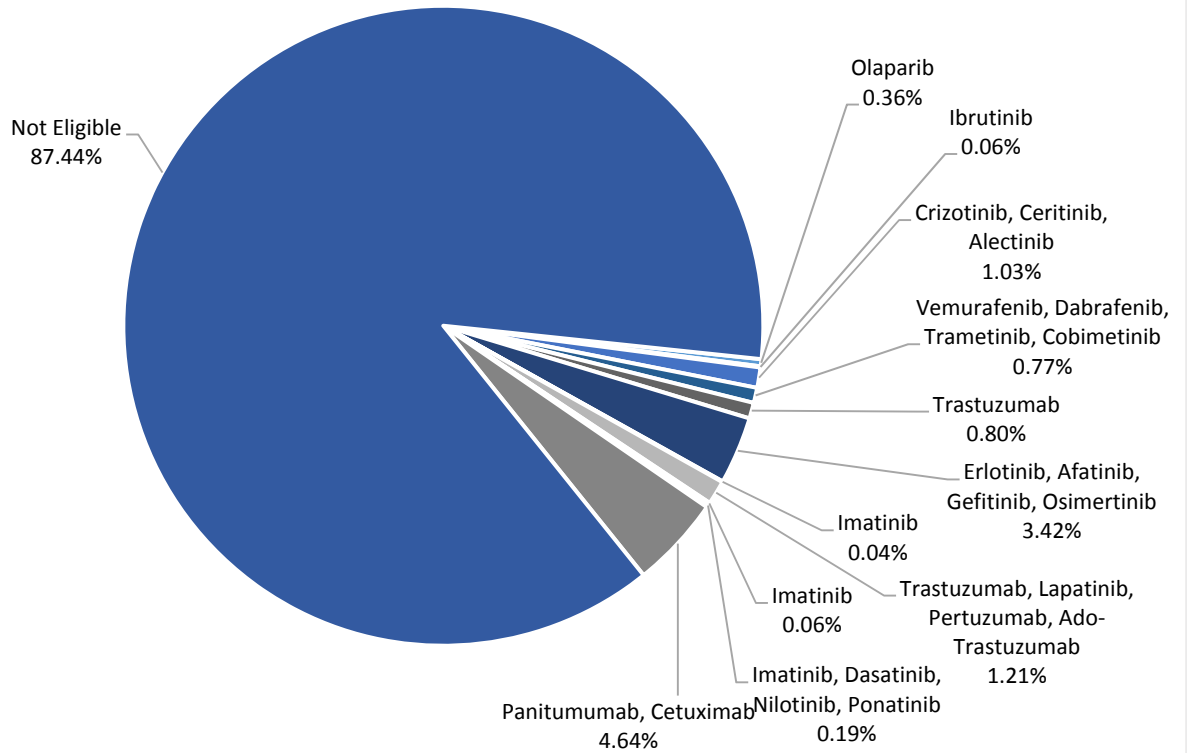
2013



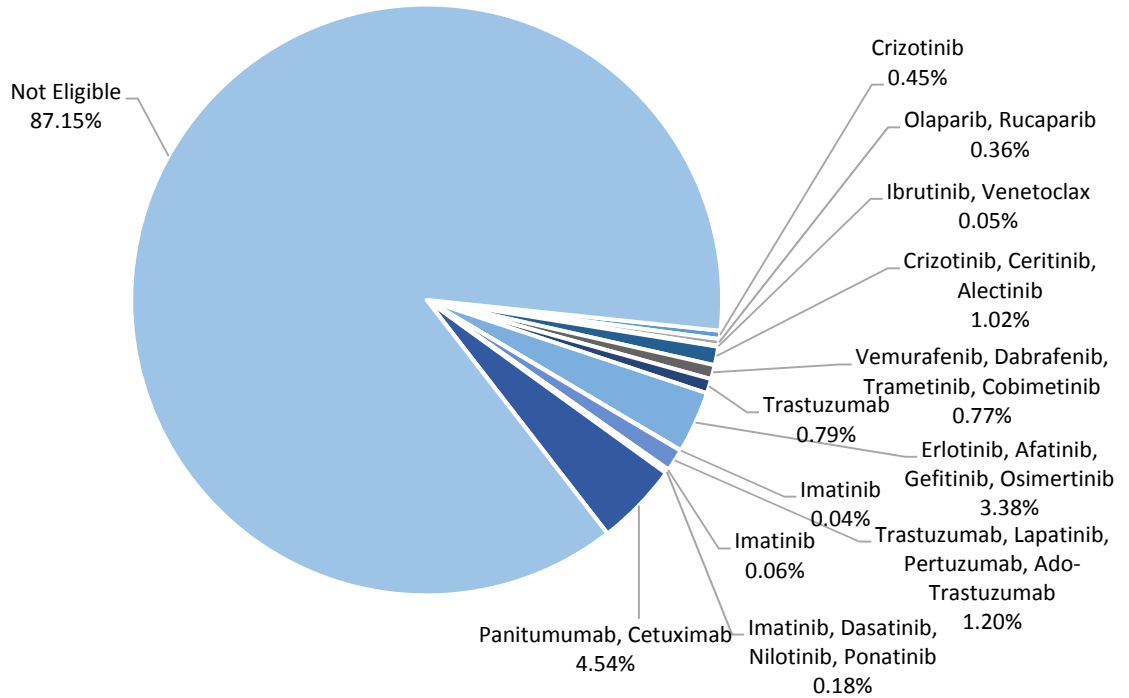
2014



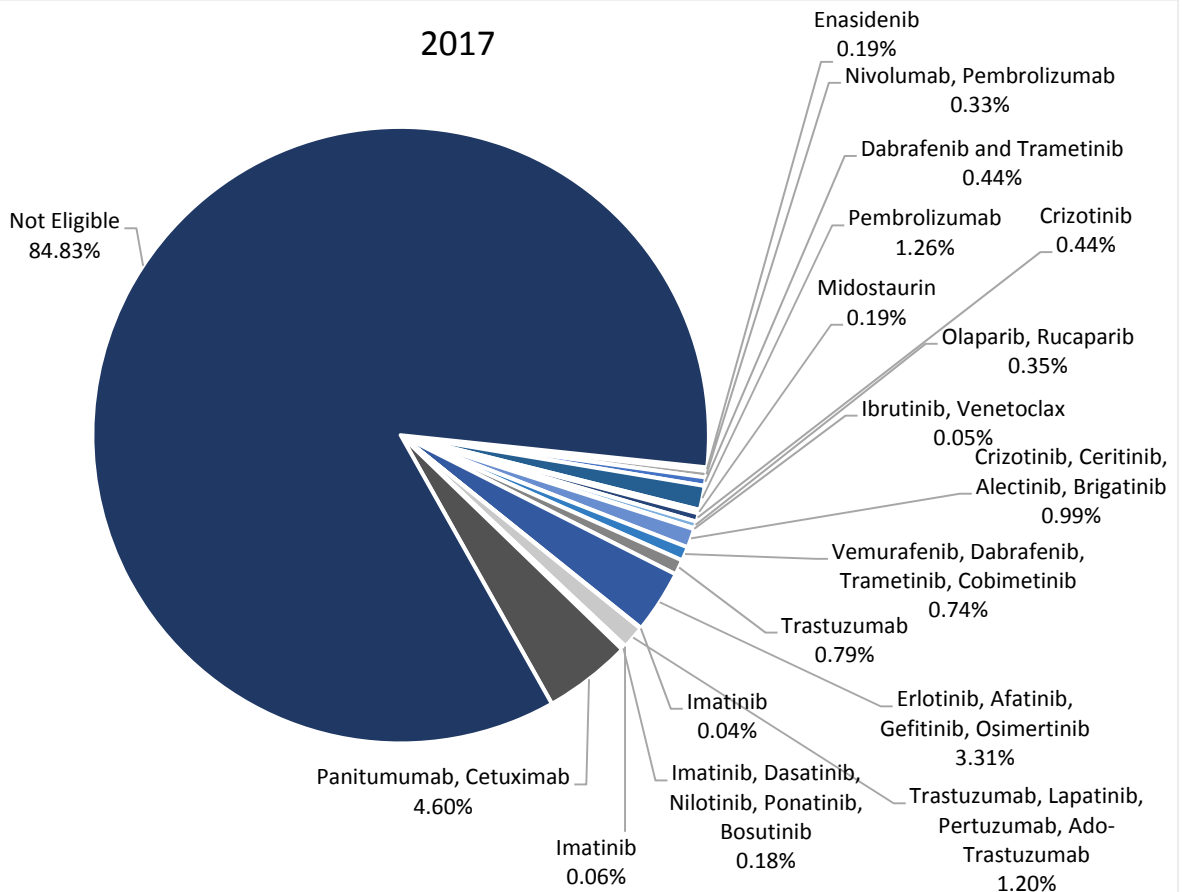
2015



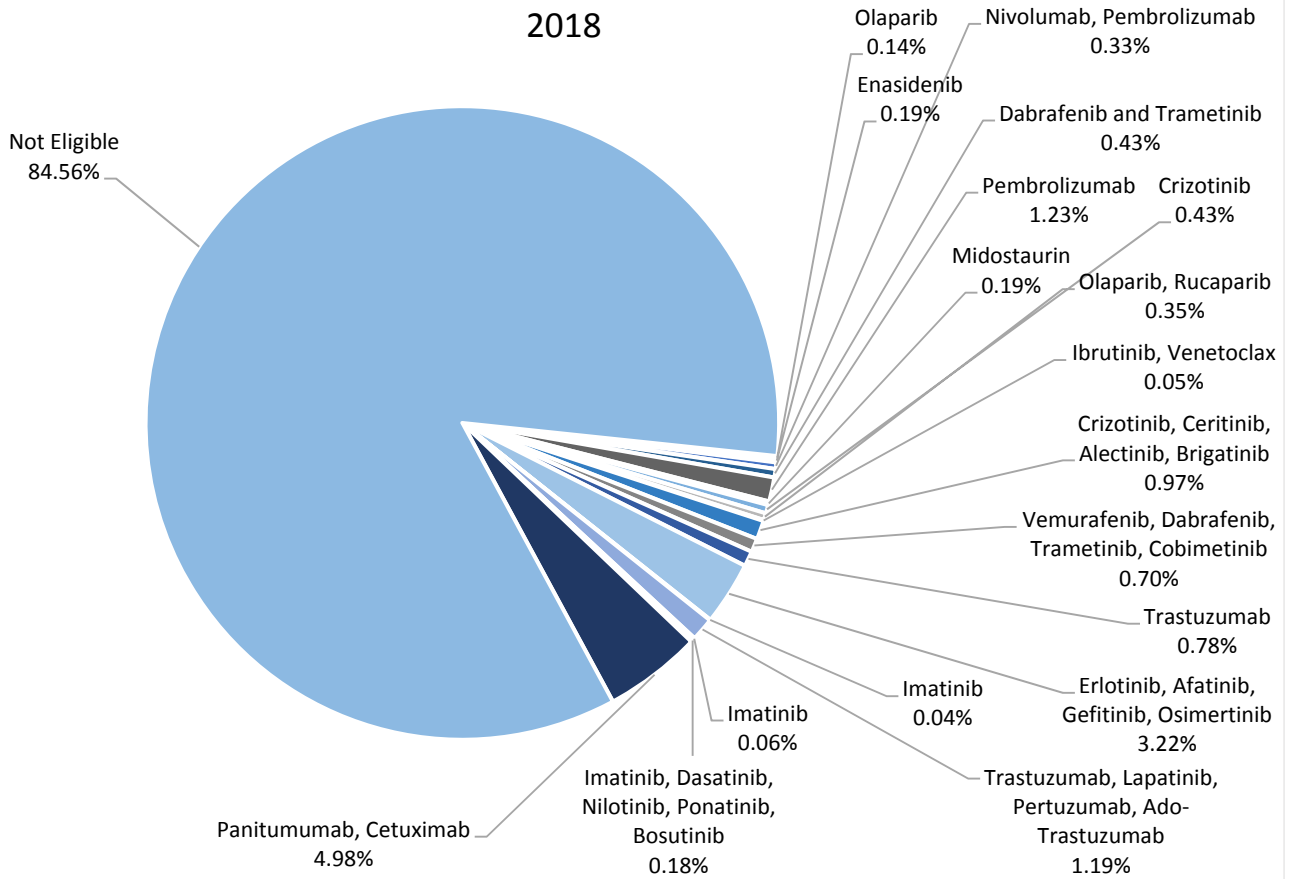
## 2016



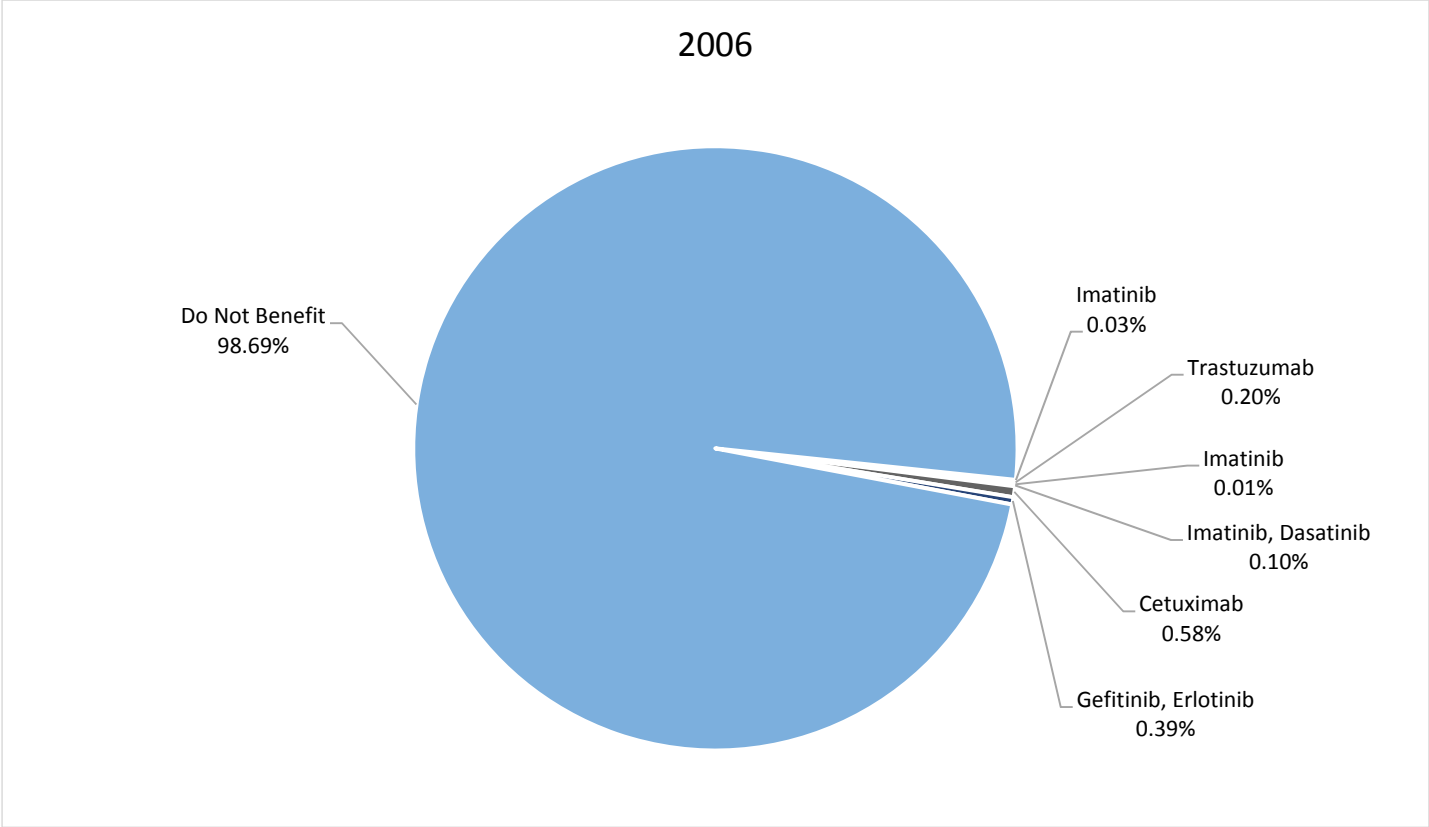
## 2017



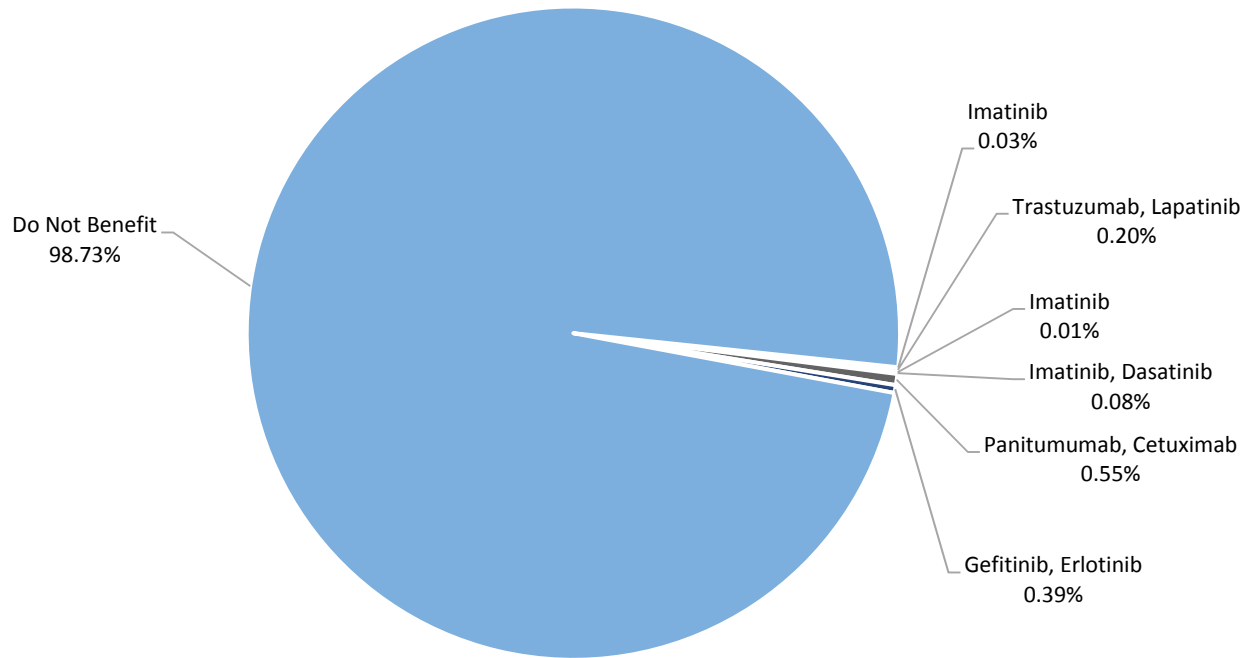
2018



# eAppendix 6. Pie Charts Estimating Patients Who Could Benefit from Genomically Informed Therapy

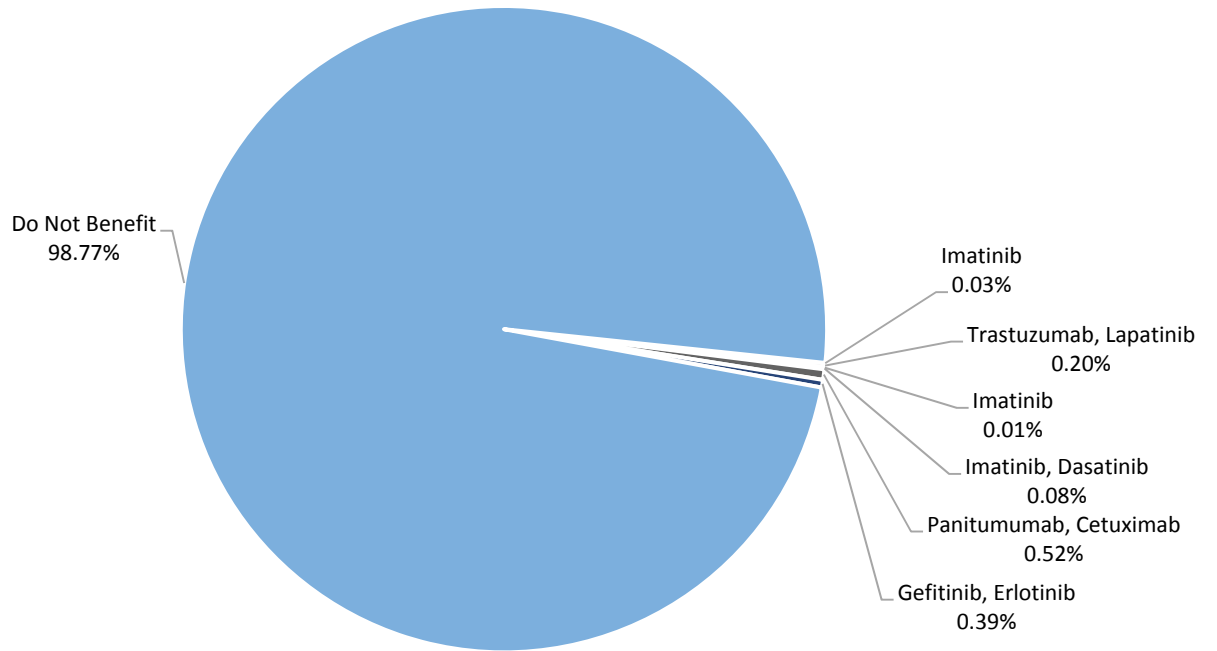


2007

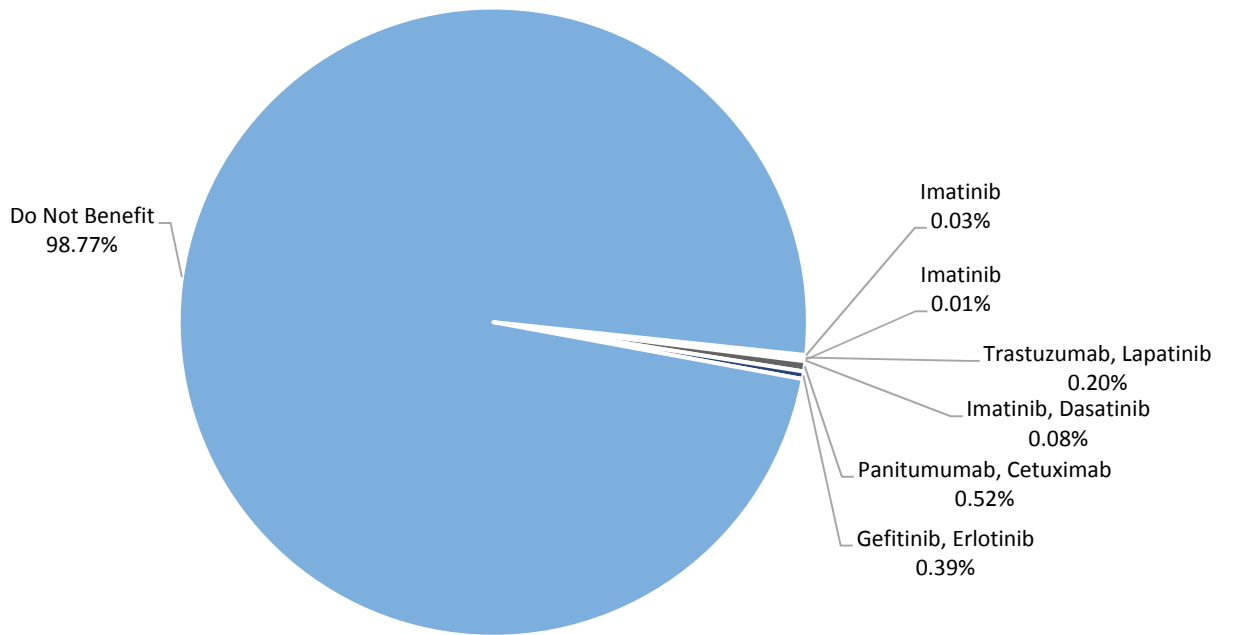




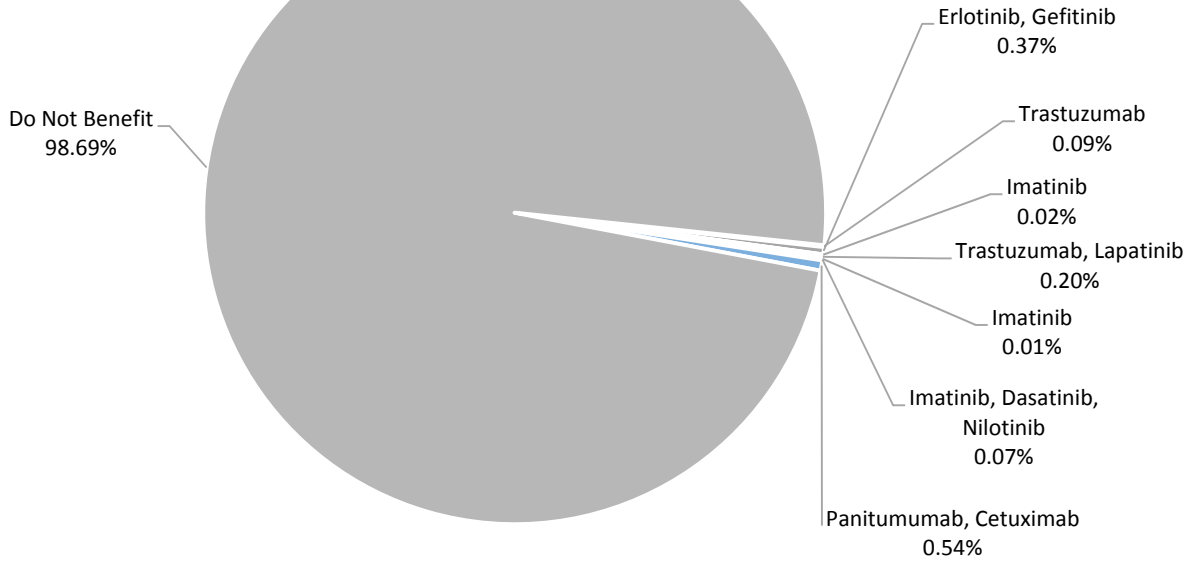
2008



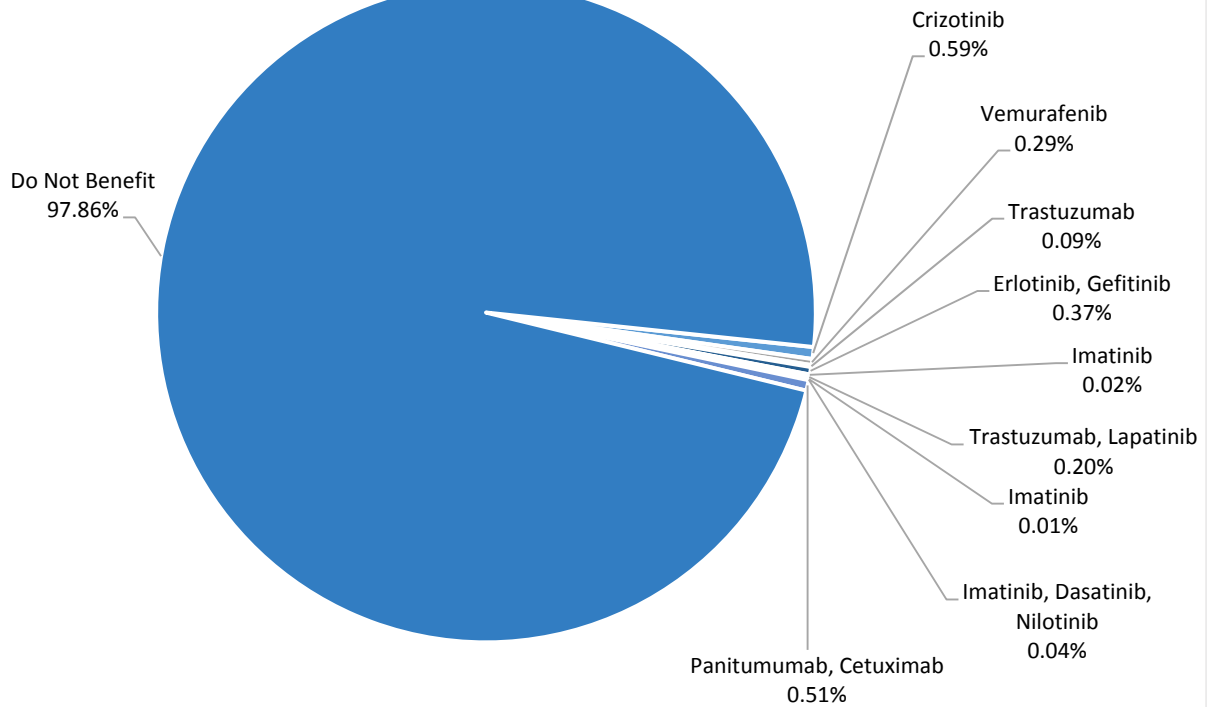
2009



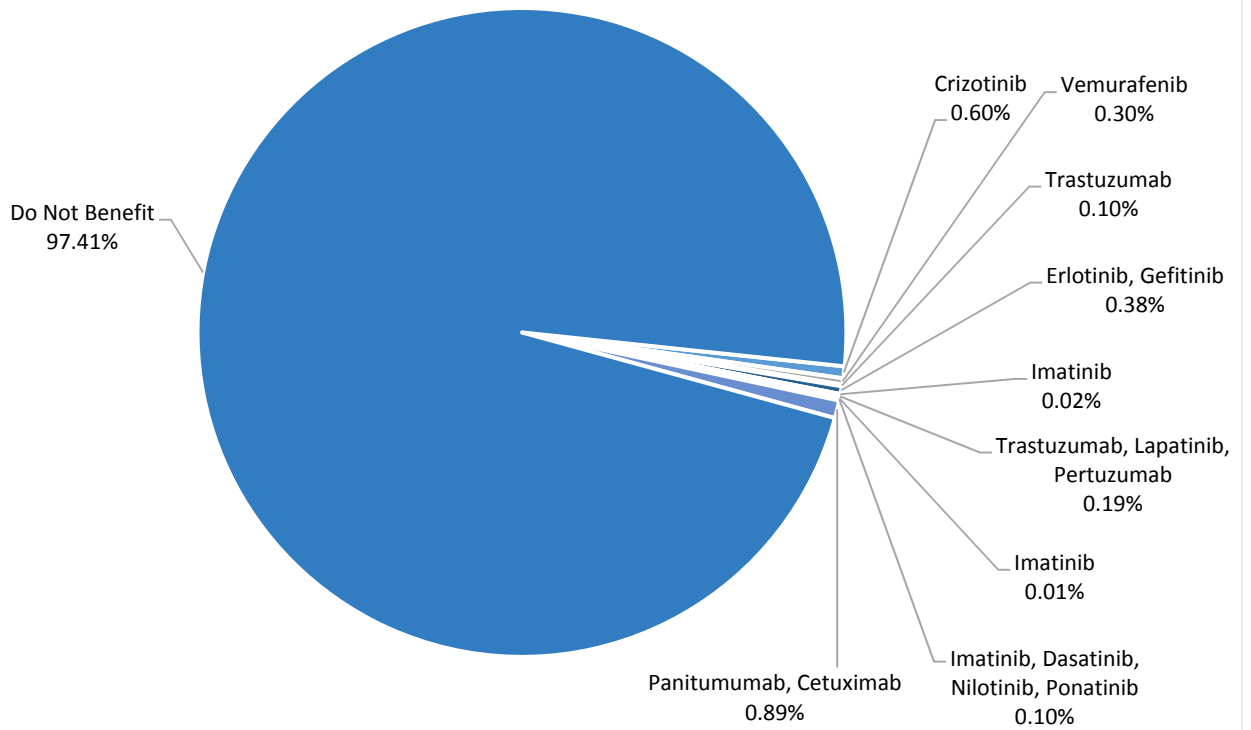
2010



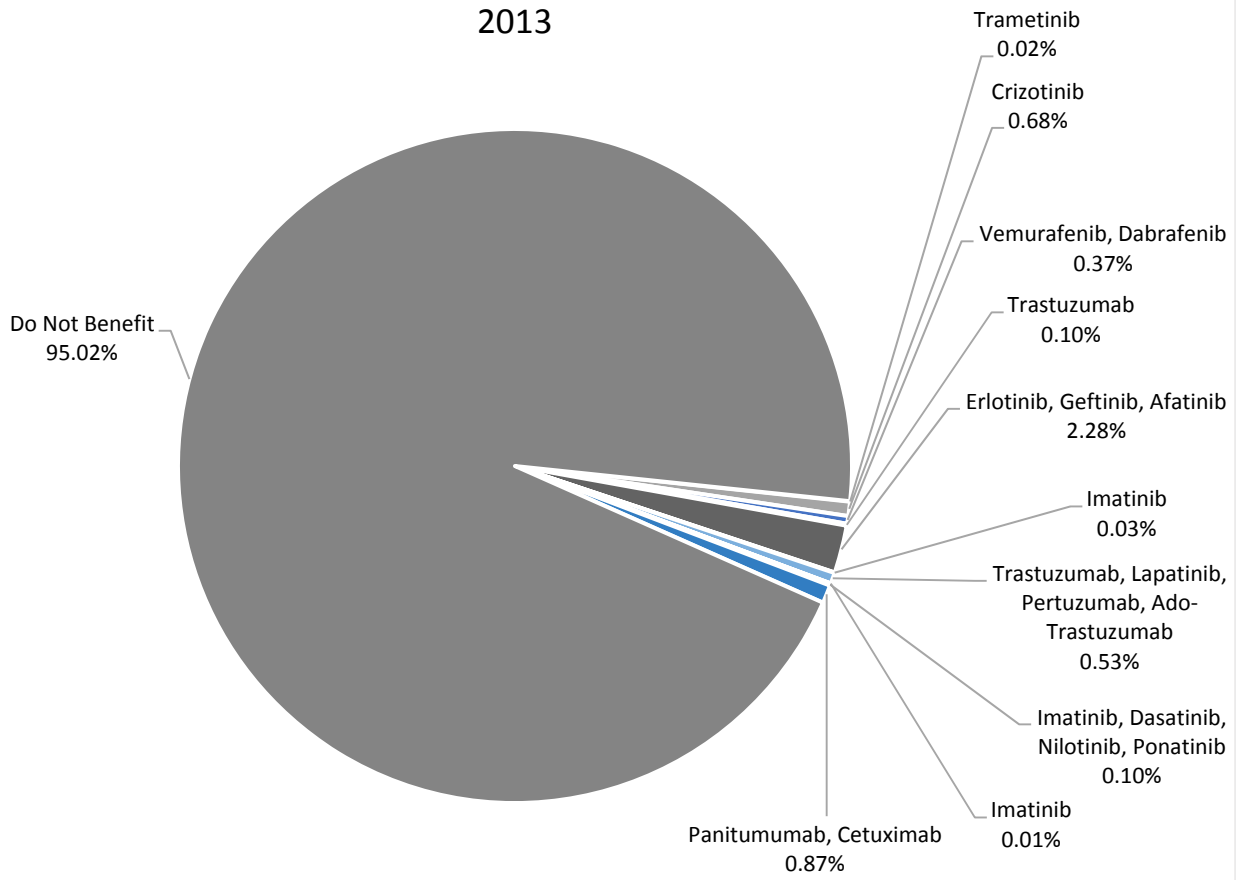
2011



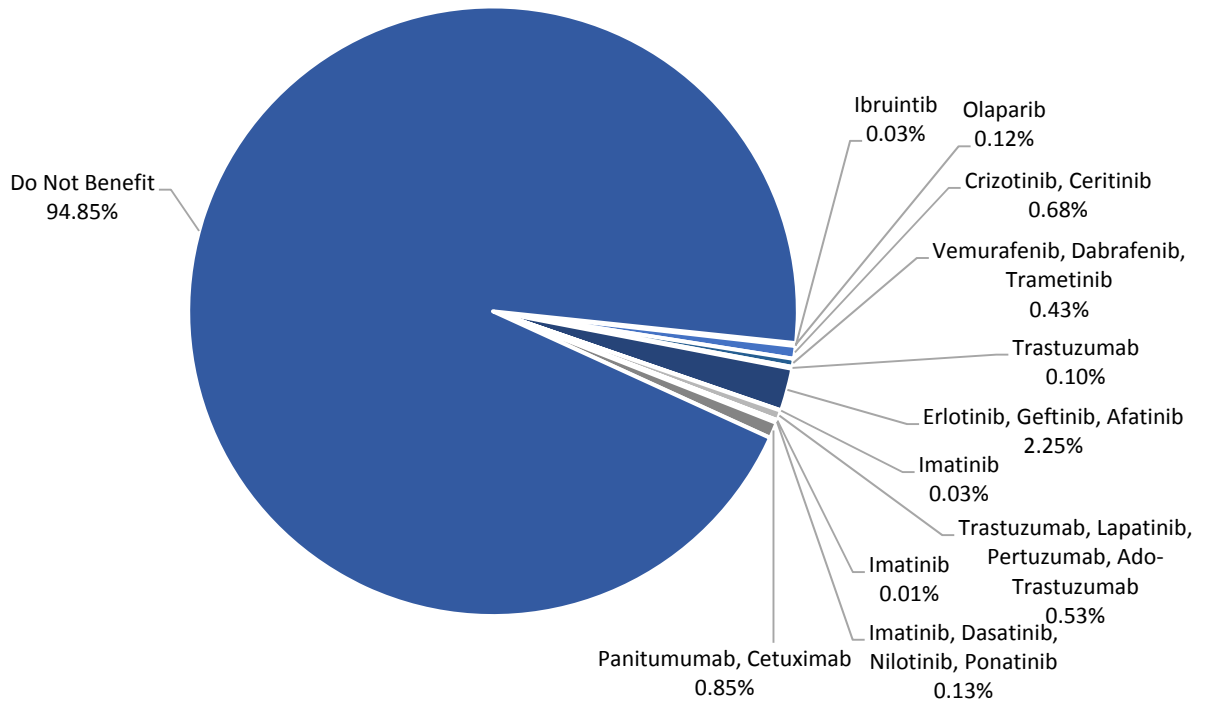
2012



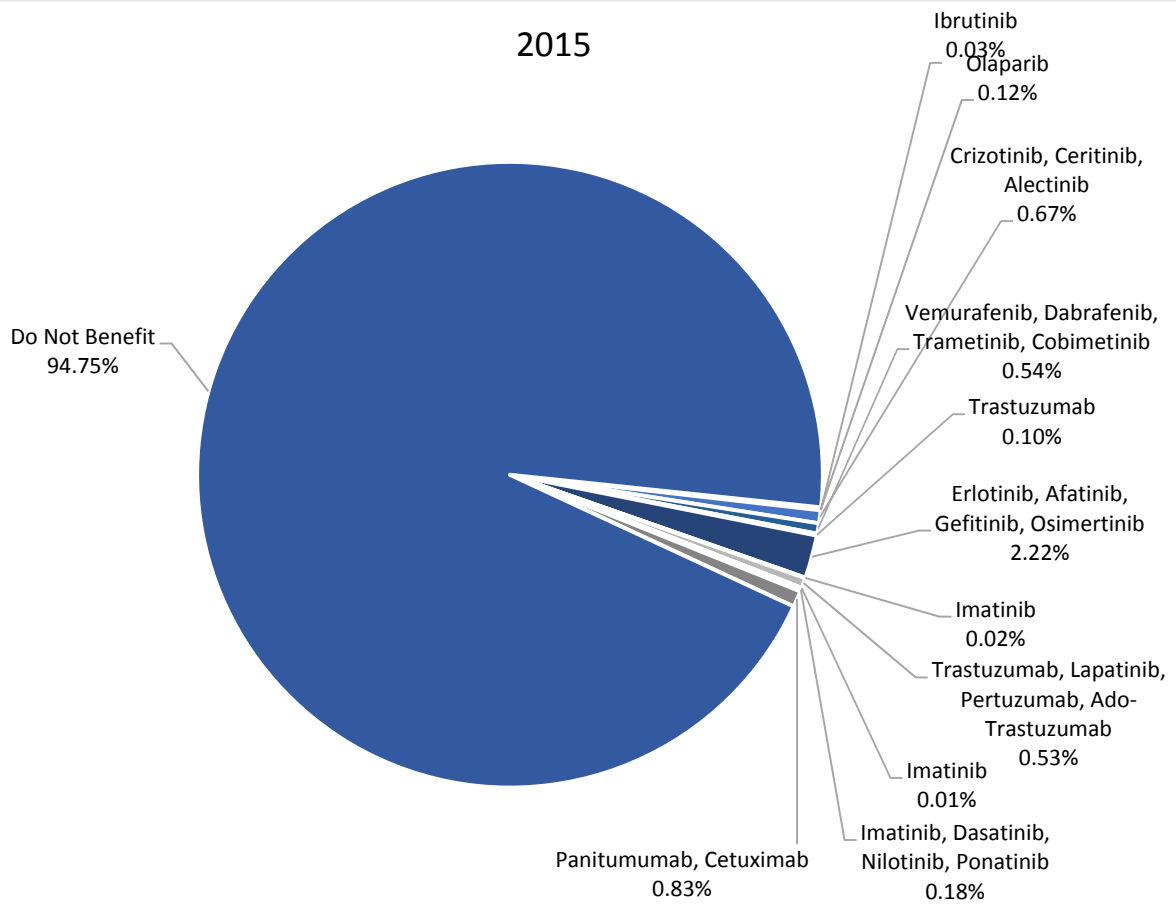
2013

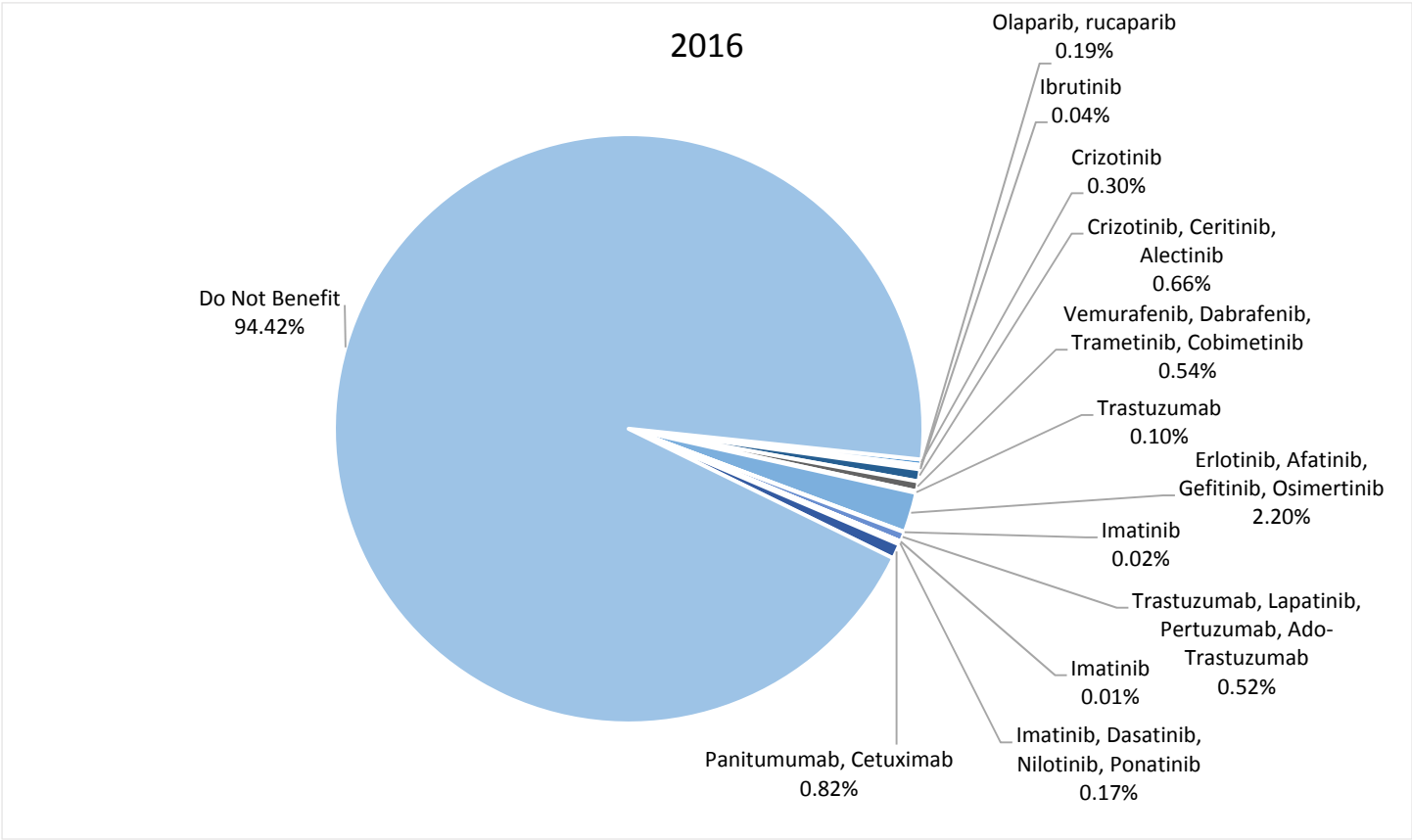


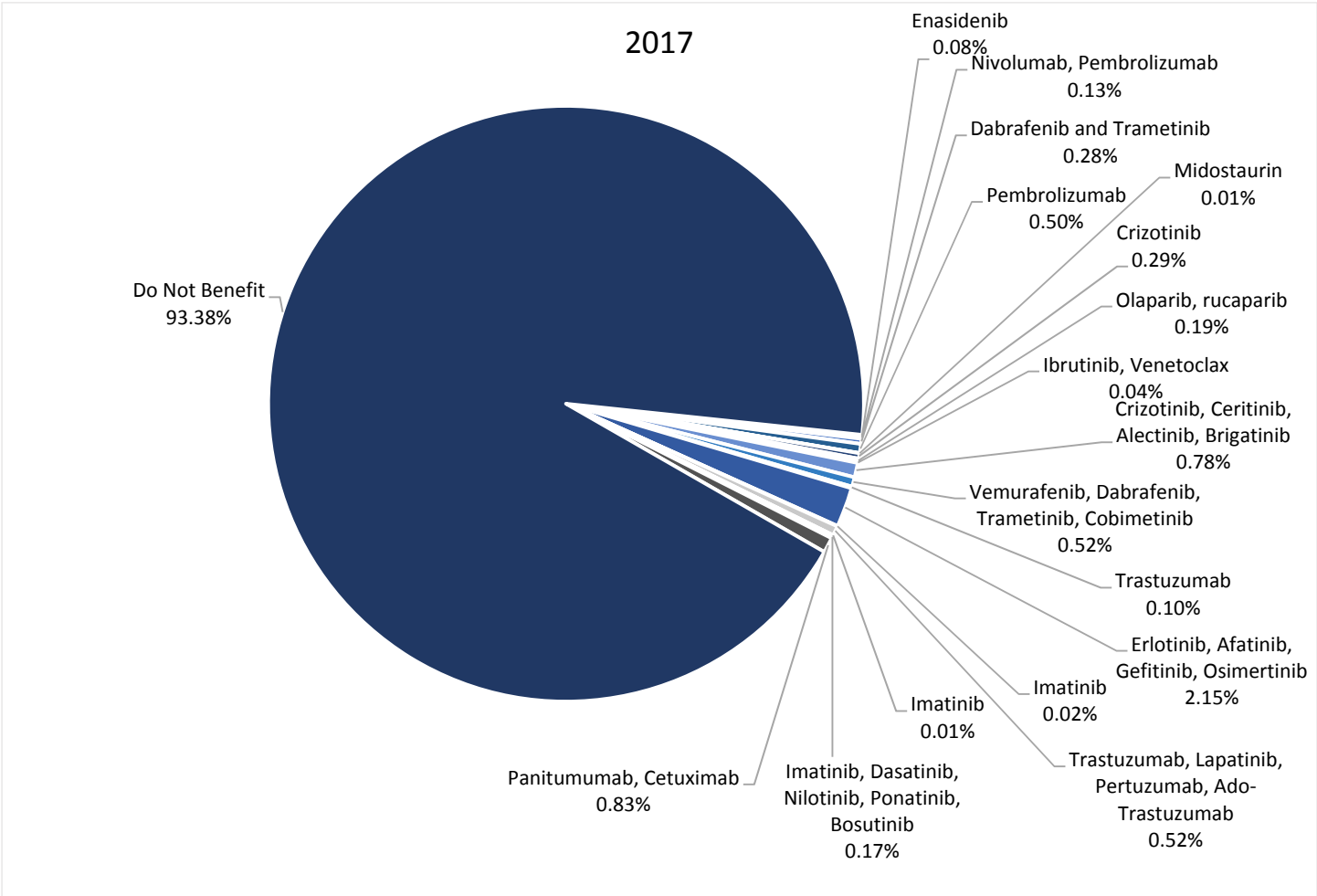
2014



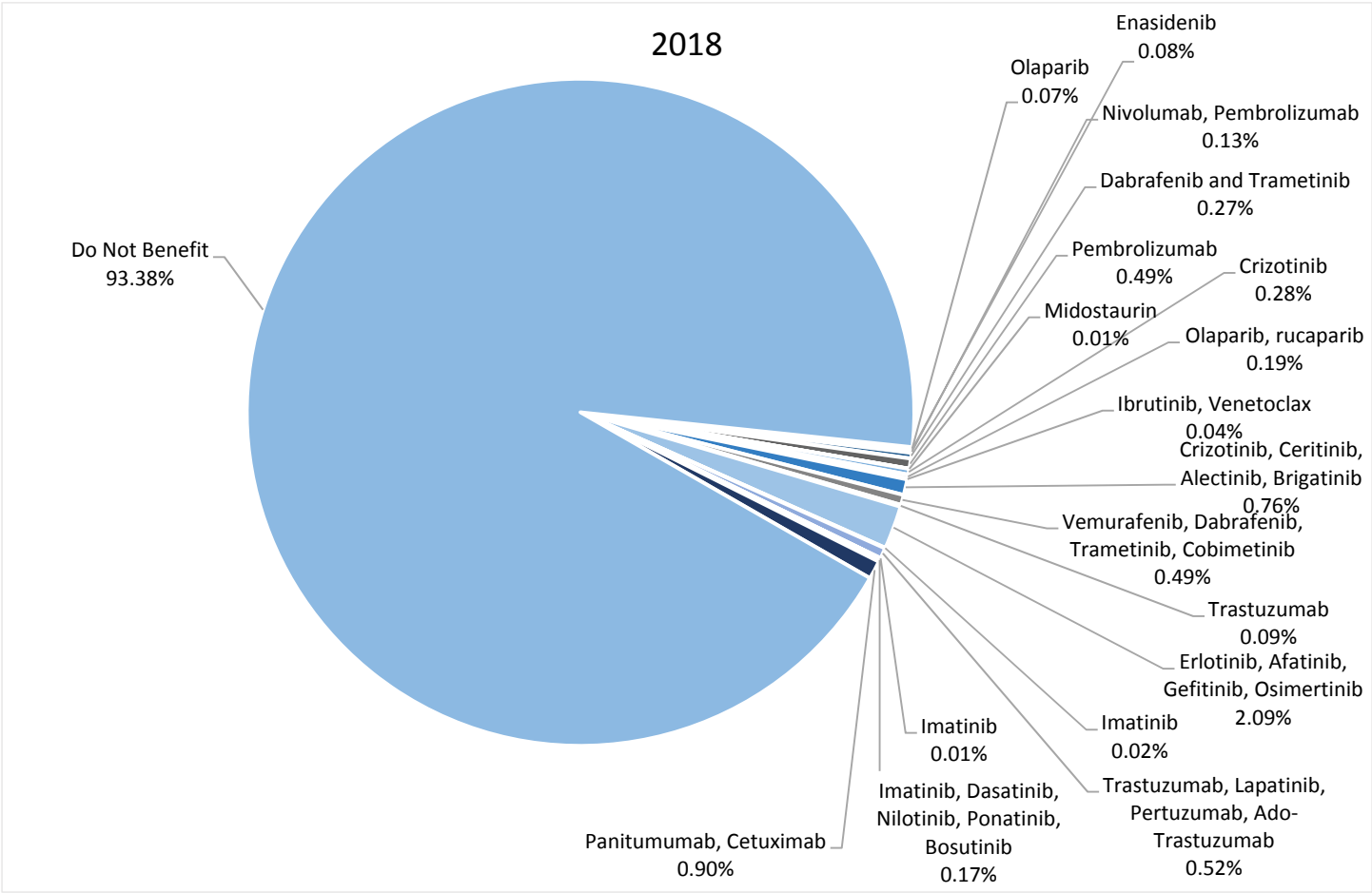
2015



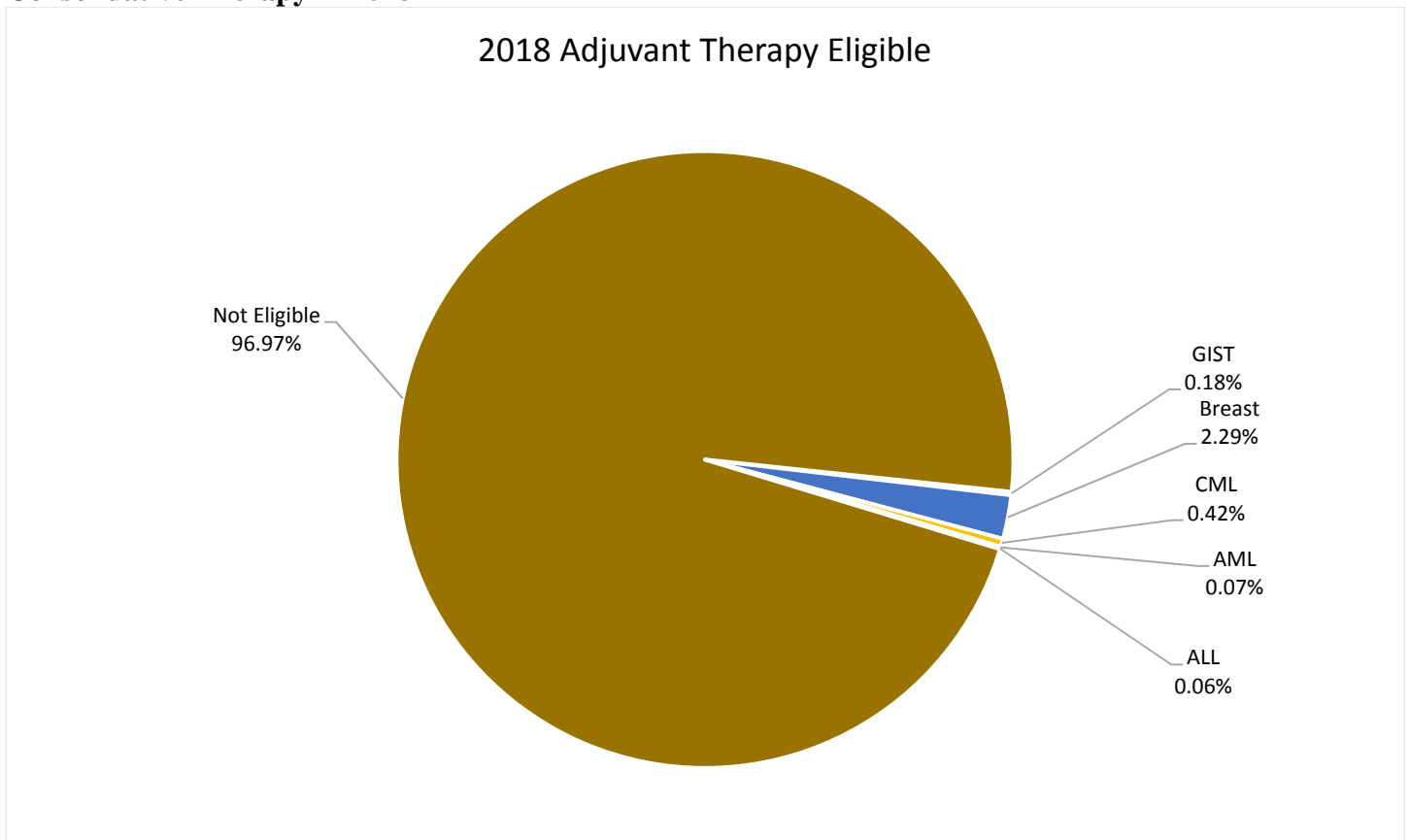




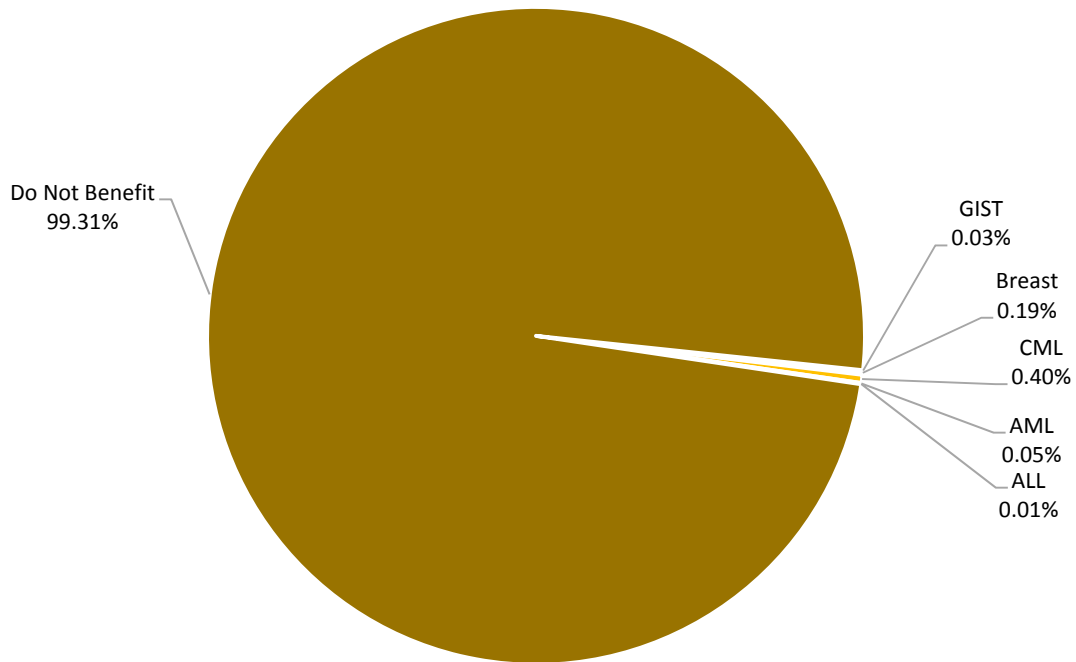




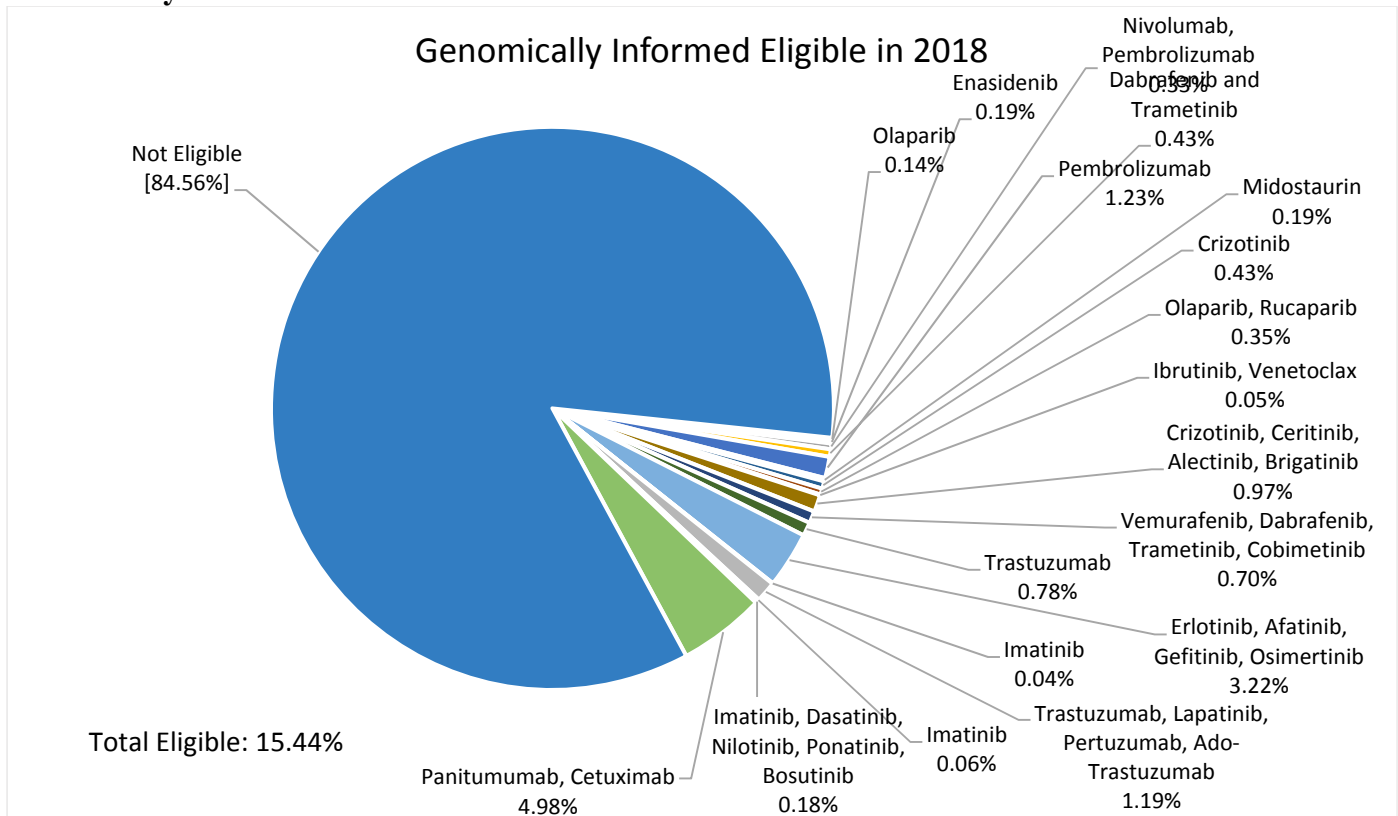
**eAppendix 7. Pie Charts Estimating Patients Eligible for and who could Benefit from Adjuvant and Consolidative Therapy in 2018**

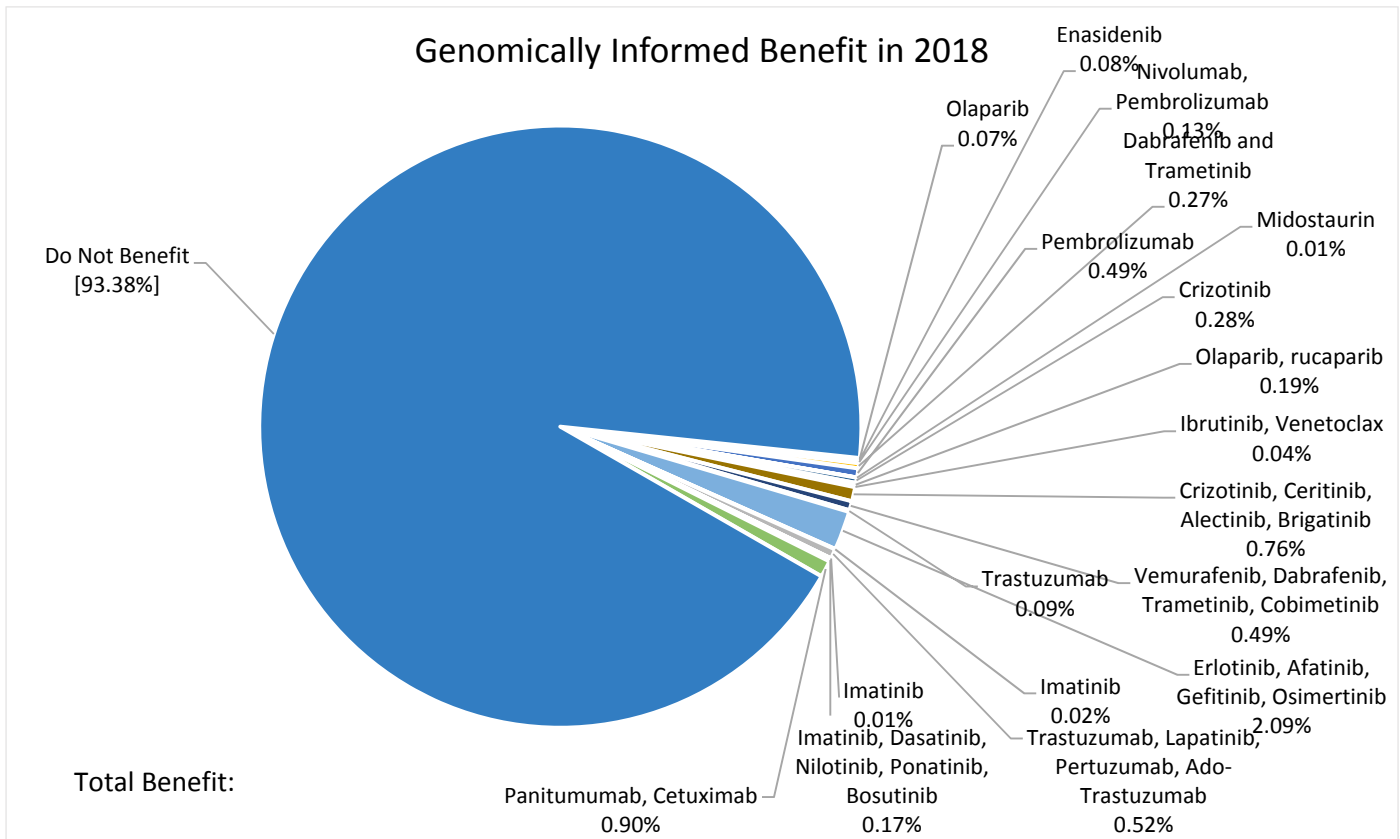


## 2018 Adjuvant Therapy Benefit



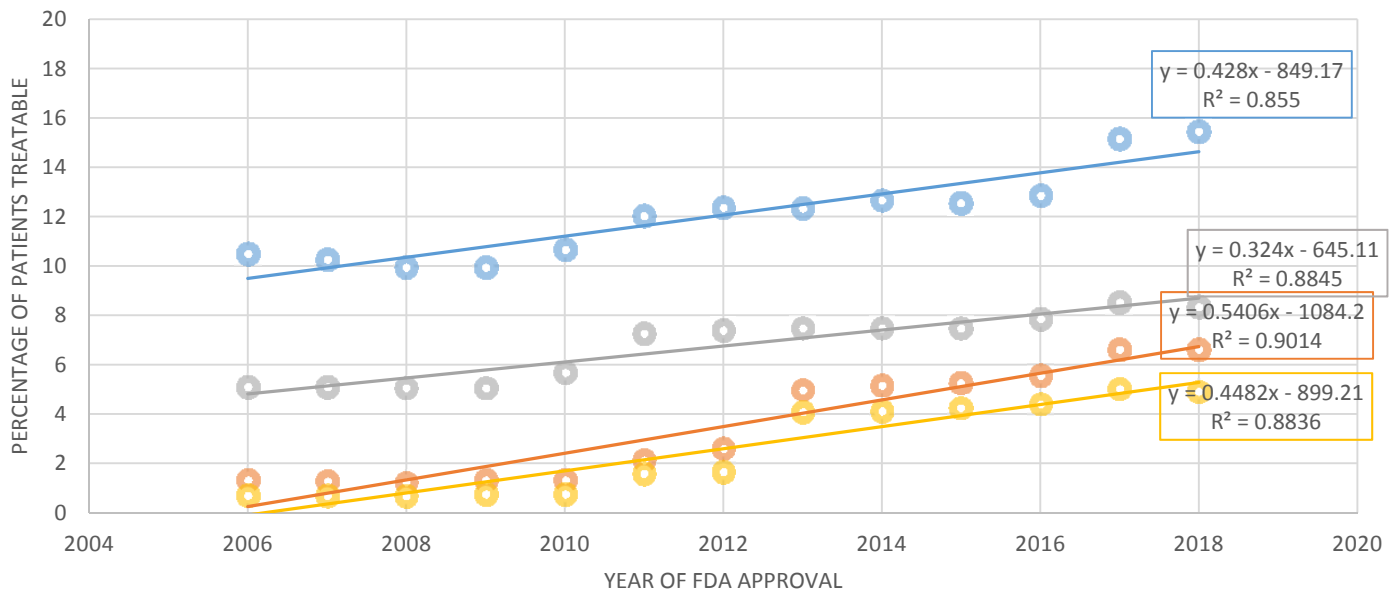
**eFigure 1. Percent of US Metastatic Cancer Patients Who May Be Eligible for and Benefit from Genomically Informed Treatment**





**eFigure 2. Growth of genome targeted and informed therapy over time with fitted linear regression.**

## Genome Therapy Over time



- Genome Informed Eligible Patients
- Genome Targeted Eligible Patients
- Genome Informed Benefit Patients
- Genome Targeted Benefit Patients
- Linear (Genome Informed Eligible Patients)
- Linear (Genome Informed Benefit Patients)
- Linear (Genome Targeted Eligible Patients)
- Linear (Genome Targeted Benefit Patients)