# Supplemental Online Content

DeMartino PC, Miljković MD, Prasad V. Potential cost implications for all US Food and Drug Administration oncology drug approvals in 2018. *JAMA Intern Med*. Published online November 9, 2020. doi:10.1001/jamainternmed.2020.5921

**eTable.** 2018 FDA oncology approvals
**eAppendix.** Assumptions and references used for estimating eligible population and prices

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

**eTable 1.** 2018 FDA oncology approvals

| Drug | New drug or new indication | Displaced therapy | Price of displaced therapy per patient | Number eligible in US | Gross price per patient | Net price per patient | NET projected total cost |
|---|---|---|---|---|---|---|---|
| Olaparib | New indication | Capecitabine | $461 | 740 | $177,721 | $177,261 | $131,172,811 |
| Afatinib | New indication | Cisplatin and pemetrexed | $49,494 | 6,550 | $125,555 | $76,061 | $497,969,436 |
| Lutetium Lu 177 | New drug | Octreotide | $84,706 | 8,785 | $201,200 | $116,494 | $1,023,279,782 |
| Abiraterone acetate | New indication | None | $0 | 25,000 | $5,100 | $5,100 | $127,500,000 |
| Apalutamide | New drug | None | $0 | 6,815 | $146,946 | $146,946 | $1,001,435,354 |
| Durvalumab | New drug | None | $0 | 11,680 | $148,204 | $148,204 | $1,731,024,308 |
| Abemaciclib | New indication | None | $0 | 20,710 | $119,351 | $119,351 | $2,471,755,068 |
| Brentuximab | New indication | Bleomycin | $427 | 2720 | $226,828.80 | $226,401 | $615,811,605 |
| Nilotinib | New indication | Imatinib | $5,869 | 400 | $108,793 | $102,925 | $41,169,823 |
| Blinatumomab | New indication | None | $0 | 840 | $179,458 | $179,458 | $150,744,760 |
| Rucaparib | New indication | None | $0 | 6,150 | $138,627 | $138,627 | $852,553,590 |
| Nivolumab & ipilimumab | New indication | Sunitinib | $104,540 | 11,860 | $141,936 | $37,395 | $443,505,678 |
| Osimertinib | New indication | Gefitinib | $89,572 | 17,680 | $365,003 | $275,431 | $4,869,622,909 |
| Dabrafenib & trametinib | New indication | None | $0 | 3,670 | $216,075 | $216,075 | $792,996,388 |
| Tisagenlecleucel | New indication | Per SCHOLAR-1 | $54,000 | 5,900 | $373,000 | $319,000 | $1,882,100,000 |
| Dabrafenib & trametinib | New indication | Bleomycin | $0 | 80 | $176,789 | $176,789 | $14,143,111 |
| Venetoclax | New indication | Bendamustine | $41,456 | 3,930 | $135,228 | $93,772 | $368,525,006 |
| Pembrolizumab | New indication | None | $0 | 2,550 | $48,620 | $48,620 | $123,982,020 |

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|---|---|---|---|---|---|---|---|
| Pembrolizumab | New indication | None | $0 | 150 | $126,413 | $126,413 | $18,961,956 |
| Bevacizumab | New indication | None | $0 | 18,020 | $75,323 | $75,323 | $1,357,311,450 |
| Encorafenib & binimetinib | New drug | Vemurafenib | $68,360 | 2,900 | $281,726 | $213,365 | $618,759,834 |
| Ipilimumab & nivolumab | New indication | None | $0 | 2,040 | $213,662 | $213,662 | $435,871,367 |
| Enzalutamide | New indication | None | $0 | 6,165 | $143,018 | $143,018 | $881,705,477 |
| Ribociclib | New indication | None | $0 | 20,710 | $158,921 | $158,921 | $3,291,244,798 |
| Ivosidenib | New drug | None | $0 | 1,090 | $112,425 | $112,425 | $122,543,332 |
| Mogamulizumab-kpkc | New drug | Vorinostat | $42,027 | 510 | $226,855 | $184,828 | $94,262,099 |
| Nivolumab | New indication | None | $0 | 10,780 | $23,032 | $23,032 | $248,280,379 |
| Lenvatinib | New indication | Sorafenib | $73,930 | 22,250 | $43,368 | ($30,563) | -$680,016,960 |
| Moxetumomab pasudotox | New drug | None | $0 | 190 | $74,010 | $74,010 | $14,061,957 |
| Duvelisib | New drug | Ofatumumab | $58,527 | 3,930 | $154,875 | $96,348 | $378,648,072 |
| Duvelisib | New drug | Add | $0 | 1,340 | $88,943 | $88,943 | $119,182,950 |
| Dacomitinib | New drug | Gefitinib | $93,467 | 5,893 | $156,240 | $62,773 | $369,923,882 |
| Cemiplimab-rwlc | New drug | None | $0 | 9,000 | $100,100 | $100,100 | $900,900,000 |
| Talazoparib | New drug | Capecitabine | $420 | 740 | $93,385 | $92,965 | $68,793,927 |
| Pembrolizumab | New indication | None | $0 | 38,510 | $77,793 | $77,793 | $2,995,794,566 |
| Lorlatinib | New drug | None | $0 | 1,570 | $139,926 | $139,926 | $219,684,417 |
| Pembrolizumab | New indication | None | $0 | 22,250 | $48,620 | $48,620 | $1,081,803,900 |
| Brentuximab | New indication | Vincristine | $69 | 2,300 | $154,037 | $153,968 | $354,127,265 |
| Emapalumab | New drug | Alemtuzumab | $0 | 250 | $182,359 | $182,359 | $45,589,635 |
| Glasdegib | New drug | None | $0 | 4,365 | $47,982 | $47,982 | $209,443,067 |
| Venetoclax | New indication | None | | 4,635 | $71,917 | $71,917 | $333,334,456 |
| Gilteritinib | New drug | Mitoxantrone, etoposide, cytarabine | $246 | 3,280 | $141,750 | $141,504 | $464,132,208 |
| Atezolizumab | New indication | Docetaxel | $1,470 | 79,300 | $101,134 | $99,665 | $7,903,417,295 |
| Pembrolizumab | New indication | Etoposide and cisplatin | $385 | 830 | $84,745 | $84,361 | $70,019,399 |

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|---|---|---|---|---|---|---|---|
| Olaparib | New indication | None | $0 | 3,240 | $124,978 | $124,978 | $404,928,674 |
| Tagraxofusp-erzs | New drug | CHOP | $899 | 150 | $635,681 | $634,782 | $95,217,326 |

**eAppendix. Assumptions and references used for estimating eligible population and prices**

Notes:

1. Quoted indications from FDA. https://www.fda.gov/drugs/resources-information-approved-drugs/hematologyoncology-cancer-approvals-safety-notifications)
2. Adult weight 83kg and BSA 1.9$m^2$ (average adult measures in U.S. per CDC 2019)
3. All estimates use 2018-2019 U.S. population unless noted otherwise (329 million)
4. Approvals below are listed chronologically by approval date
5. American Cancer Society incidence/mortality data was extracted from: https://cancerstatisticscenter.cancer.org
6. SEER data extracted from: SEER Preliminary Cancer Incidence Rate Estimates for 2017, and diagnosis years 2000 to 2017, SEER 18, National Cancer Institute. Bethesda, MD, https://seer.cancer.gov/statistics/preliminary-estimates/
7. When incidence rather than mortality data were used to estimate the population eligible for an advanced/metastatic indication, it is noted just below the "Number eligible in U.S." line with justification (13 approvals)

**Olaparib:** For patients with "deleterious or suspected deleterious germline BRCA-mutated, HER2-negative metastatic breast cancer who have been treated with chemotherapy either in the neoadjuvant, adjuvant, or metastatic setting"

American Cancer Society (ACS) estimates 42,260 deaths from breast cancer (BC) in 2019.
HER2 negative BC accounts for 70% of all breast cancer. Source: https://www.ncbi.nlm.nih.gov/pubmed/3798106
5% of all patients with new BC diagnosis have BRCA mutation. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3870050/
Number eligible in U.S. (annual): 1,480 incident patients with metastatic HER2 negative BRCA mutated cancer
Given concurrent approval of talazoparib for overlapping indication, 50% market share: 740

Cost: Median duration of therapy 8.2 months on study. Dose 300mg twice daily. $1.204 per mg

*Subtraction of displaced therapy*: Capecitabine, comparator arm of study. Median duration 3.4 months on study. Dose capecitabine 2500mg/m2 daily x14 days and repeated in 21 day cycles. $0.002 per mg.

**Afatinib:** "first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have non-resistant epidermal growth factor receptor (EGFR) mutations as detected by an FDA-approved test"

ACS estimates 154,050 deaths from lung cancer in 2019.
NSCLC frequency = 85% of lung cancers. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
EGFR mutation frequency in NSCLC = 15% (10-20%). Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346098/
Number eligible in U.S.: 19,640 patients with metastatic NSCLC and EGFR mutation
Given approval of dacomitinib and osimertinib with overlapping indication, 33% market share used: 6,547

Cost: Median duration of therapy 11 months on study. Dose 40mg daily. $9.512 per mg.

*Subtraction of displaced therapy:* Cisplatin and pemetrexed, comparator arm on study. Median duration of exposure not reported. Median PFS for this arm of 5.4 months (7 cycles). Cisplatin, 75 mg/m2, and pemetrexed, 500 mg/m2, once every 21 days. $7.398 per mg pemetrexed and $0.3 mg cisplatin.

**Lutetium Lu 177:** "treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults"

Annual incidence of GEP-NET 3.56 per 100,000 people = 11,712 cases GEP-NET in US per year. No data available regarding proportion of GEP-NETs with increased somatostatin receptor expression though expert opinion stating a

"majority" have high level expression; we estimate 75% of GEP-NETs have high somatostatin receptor expression.
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5824320/
Number eligible in U.S.: 8,784 patients with GEP-NET

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as national data for GEP-NET mortality were limited whereas the above reference was deemed to provide a rigorous estimate.

Cost: 4 doses given on study. Dose 7.4 GBq once every 8 weeks. $5,030 per mci.

*Subtraction of displaced therapy:* Octreotide (high dose depot) comparator arm on study. Median duration of 8 doses. Octreotide 60mg every 4 weeks. $176 per mg IM formulation.

**Abiraterone acetate:** "in combination with prednisone for metastatic high-risk castration-sensitive prostate cancer (CSPC)"

ACS estimates 33,330 deaths from prostate cancer in 2019.
A "majority" of newly diagnosed metastatic prostate cancer is responsive to androgen deprivation therapy (ATD); for our analysis we assumed 75% are responsive to ADT. Source: https://www.ncbi.nlm.nih.gov/pubmed/27431496
Number eligible in U.S.: 24,998 patients with metastatic CSPC

Cost: Median duration of therapy 24 months on study (12-months for our analysis). Dose 1000mg daily. $0.0141 per mg.

**Apalutamide:** "non-metastatic castration-resistant prostate cancer (CRPC)"

ACS estimates 174,650 new cases of prostate cancer in 2019.
94% of prostate cancer is localized at diagnosis (SEER).
8.3 per 100 person years develop CRPC. Source: https://www.ncbi.nlm.nih.gov/pubmed/22910034
Number eligible in U.S.: 13,630 incident cases of non-metastatic CRPC
Given concurrent approval of enzalutamide with overlapping indication, 50% market share: 6,815

Cost: 61% of patients remained on apalutamide through median follow-up of 20.3 months on study (12-months for our analysis). Dose 240mg daily. $1.700 per mg.

**Durvalumab:** "for patients with unresectable stage III non-small cell lung cancer (NSCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy"

ACS estimates 228,150 new cases of lung cancer in 2019.
NSCLC frequency = 85%. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
28.4% of NSCLC presenting as stage III disease and 21.2% of those with stage III receive chemoradiotherapy.
Source: https://www.ncbi.nlm.nih.gov/pubmed/30543349
Number eligible in U.S.: 11,680 incident cases of stage III NSCLC receiving chemoradiotherapy

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as the indication requests specifically stage III disease. Existing national mortality data does not allow for identification of this subset.

Cost: Median duration 40 weeks on study. Dose of 10mg/kg once every two weeks. $8.928 per mg.

**Abemaciclib:** "in combination with an aromatase inhibitor as initial endocrine-based therapy for postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer"

ACS estimates 42,260 deaths from breast cancer (BC) in 2019
70% of patients with metastatic BC have HR-positive disease
HER2 negative BC accounts for 70% of all BC. Source: https://www.ncbi.nlm.nih.gov/pubmed/3798106

Number eligible in U.S.: 20,710 new incident cases of advanced/metastatic BC with HR positive and HER2 negative.

Cost: Median of 16 cycles received on study (limited to 12 cycle for analysis). Dose of 150mg twice daily. $1.105 per mg.

**Brentuximab:** "adult patients with previously untreated stage III or IV classical Hodgkin lymphoma (cHL) in combination with chemotherapy"

ACS estimates 8110 new incident cases of HL in 2019.
SEER data estimates 12.2% of HL occurs in those < 20 years of age (excluded). 6% will have non-classical HL (excluded). 41% will have "distant" disease at diagnosis (extrapolated to be stage 3/4).
Number eligible in U.S.: 2,720 cases of cHL stage 3 or 4 in adults

Cost: Mean number of doses was 10.8 (max 12) on study; to 11 doses for analysis. Dose of 1.2mg/kg. $206.208 per mg.

*Subtraction of displaced therapy:* Bleomycin on comparator arm. Mean of 11 doses bleomycin received on study with dose of 10 unit/m2. $2.045 per mg.

**Nilotinib:** "For pediatric patients 1 year of age or older with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia in chronic phase (Ph+ CML-CP) or Ph+ CML-CP resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy"

SEER incidence rate (2012-2016) of 0.6 cases of CML per 100,000 for ages 1-19. 2019 U.S. Yields an estimated 1,974 new incident cases of pediatric CML per year.
5% of CP CML is resistant to initial imatinib therapy and 3% are intolerant of imatinib. Source: https://www.ncbi.nlm.nih.gov/pubmed?term=12637609
Estimate 100 incident CML with imatinib resistance and 60 intolerant of imatinib. Estimate 15% market share for first line nilotinib.
Number eligible in U.S.: 400 incident cases of pediatric Ph+ CML-CP.

Cost: Limited to 12-months of therapy. Dose of 230mg/$m^2$ twice daily. Estimated average pediatric BSA 1$m^2$. $0.657 per mg

*Subtraction of displaced therapy:* No comparator on study. Used imatinib to estimate comparator cost with 12-month duration. Dose of 340mg/m2. $0.048 per mg

**Blinatumomab:** "For the treatment of adult and pediatric patients with B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%"

SEER incidence (2012-2016) 1.7 cases of ALL per 100,000 for all ages yields an estimated 5,590 new incident cases of ALL. 75% of ALL is B-cell. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5520400/
30% of adult ALL and 10% of pediatric ALL with complete morphologic remission following induction/consolidation have positive MRD. > 50% ALL occurs in persons < 20 years of age. We used a conservative estimate that 20% of adults/children with B-cell ALL with CR1 have positive MRD. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6027091/
Number eligible in U.S.: 840 incident cases of B-cell ALL in CR1 with positive MRD

Cost: Median number of cycles received on study was 2 (max 4). Dose of 28mcg/day x28 days. $114.450 per mcg

**Rucaparib:** "for the maintenance treatment of recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response (CR or PR respectively) to platinum-based chemotherapy"

ACS estimates 13,980 deaths from ovarian cancer in 2019

44% of patients having a CR or PR to platinum-based therapy for recurrent disease. Source: https://www.ncbi.nlm.nih.gov/pubmed/1999708
Number eligible in U.S.: 6,150 cases of recurrent disease having a CR or PR to second line (or greater) platinum therapy.

Cost: Mean duration of therapy not reported for the entire study population. On study, the safety population had median treatment duration of 8.3 months and this duration was used for the analysis. Dose of 600mg twice daily. $0.464 per mg.

**Nivolumab + ipilimumab:** To be used "in combination for the treatment of intermediate or poor risk, previously untreated advanced renal cell carcinoma (RCC)"

ACS estimates 14,830 deaths from kidney cancer in 2020.
RCC account for 80% of all primary renal neoplasms.
Source: https://www.ncbi.nlm.nih.gov/pubmed/29562145
Number eligible in U.S.: 11,860 incident cases of advanced RCC with intermediate/poor risk disease

Cost: Median duration of treatment on study was 7.9 months. Dose of nivolumab (240mg) plus ipilimumab (1mg/kg) every 3 weeks for 4 doses followed by maintenance nivolumab monotherapy (240mg) every 2 weeks. Nivolumab $27.419mg. Ipilimumab $150.028 per mg.

*Subtraction of displaced therapy:* Sunitinib as comparator on study. Median duration of exposure of 7.8 months. Dose of 50mg daily x4 weeks followed by two weeks off. $13.403 per mg

**Osimertinib:** "For the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R mutations"

ACS estimates 154,050 deaths from lung cancer in 2019.
NSCLC frequency = 85%. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
EGFR mutation frequency in NSCLC = 15% (10-20%). Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346098/
90% of EGFR mutations involve L858R or exon 19 del. Source: https://www.ncbi.nlm.nih.gov/pubmed/17318210
Number eligible in U.S.: 17,680 incident cases of metastatic NSCLC with EGFR mutation (L858R mutation of exon 19 deletion)
Given approval of dacomitinib and afatinib with overlapping indication, 33% market share used: 5,893

Cost: Median duration of treatment of 16.2 months on study (limited to 12 months). Dose 80 mg once daily. $12.674 per mg

*Subtraction of displaced therapy:* Gefitinib as comparator on study (as was erlotinib, equivalent pricing).
Median duration of exposure of 11.5 months. Dose of 250mg daily. $1.039 per mg.

**Dabrafenib plus trametinib:** "for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations... and involvement of lymph node(s), following complete resection"

ACS estimates 96,480 incident cases of melanoma in 2019.
SEER (2009-2015) 9% of incident melanoma is regional.
45% of melanoma has BRAF mutation. V600E mutations account for 74% and V600K mutations account for 20% of all BRAF mutations. Source: https://www.ncbi.nlm.nih.gov/pubmed/21343559
Number eligible in U.S.: 3,670 incident cases of regional melanoma with BRAF V600E or V600K mutations

Cost: Median duration of treatment of 11 months on study. Dose of dabrafenib 150mg twice daily plus trametinib 2mg daily. $1.041 per mg dabrafenib and $171.213 per mg trametinib.

**Tisagenlecleucel:** "for adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma"

Institute for Clinical and Economic Review (ICER 2018) performed budget impact analysis for axicabtagene ciloleucel for same indication/population. Source: https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf
Number eligible in U.S.: 5,900 cases of relapsed/refractory DLBCL having previously received at least 2 lines of therapy.

*Note:* ICER estimate was based upon incidence rather than mortality data in estimating the eligible population. Deemed appropriate given perceived rigor of estimate.

Cost: $373,000 per dose.

*Subtraction of displaced therapy:* No comparator arm on study.
ICER group previously estimated, from salvage regimens on SCHOLAR-1 study, average salvage regimen costing $54,000 and this was used for our analysis.
https://icer-review.org/wp-content/uploads/2017/07/ICER_CAR_T_Final_Evidence_Report_032318.pdf

**Dabrafenib plus trametinib:** "for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory local/regional treatment options"

ACS estimates 52,070 incident cases of thyroid cancer.
SEER (2012-2016) estimates 0.8% of all thyroid cancer is anaplastic carcinoma
20% of anaplastic thyroid cancer have BRAF V600E mutation. Source:
https://www.ncbi.nlm.nih.gov/pubmed/17453004
Number eligible in U.S.: 80 incident cases of advanced anaplastic thyroid cancer with BRAF V600E mutation.

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population. Perceived equivalence for this rare tumor type.

Cost: Median duration of treatment was 9 months on study. Dose of dabrafenib 150mg twice daily plus trametinib 2mg daily. $1.041 per mg dabrafenib and $171.213 per mg trimetinib.

**Venetoclax:** "for patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy"

ACS estimates 3,930 deaths from CLL in 2019. Using mortality as a surrogate for disease receiving second (or later) line of therapy should provide a conservative/underestimation of population size.
Number eligible in U.S.: 3,930 cases of CLL having received at least one prior therapy.

Cost: Median duration of therapy 22.1 months on study. To account for lower doses at initiation, we limited the duration to 11 months for our calculation. Dose of 400mg daily. $1.025 per mg.

*Subtraction of displaced therapy:* Bendamustine, comparator on study. Duration of 6 cycles. Dose 70mg/m2 on days 1 and 2 of cycle. $25.975 per mg.

**Pembrolizumab:** "for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥1)"

ACS estimates 4,250 deaths from cervical cancer in 2019.
Estimated 60% of cervical cancer expresses PD-L1. Source:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6367228/
Number eligible in U.S.: 2,550 cases metastatic cervical cancer with PD-L1 expression.

Cost: Median duration of treatment 2.9 months on study (median of 5 doses). Dose of 200mg every 3 weeks. $48.620 per mg.

**Bevacizumab:** "for patients with epithelial ovarian, fallopian tube, or primary peritoneal cancer in combination with carboplatin and paclitaxel, followed by single-agent bevacizumab, for stage III or IV disease after initial surgical resection"

ACS estimates 22,520 incidence cases ovarian cancer in 2019.
SEER (2009-2015) estimates 59% distant and 21% regional disease at diagnosis.
Number eligible in U.S.: 18,020 incident cases of stage III or IV disease

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population. Deemed appropriate given front-line indication and perception that mortality data underestimated eligible population.

Cost: For the "bevacizumab throughout" group (demonstrated the PFS improvement), patients planned to receive 21 cycles of bevacizumab 15mg/kg once every 3 weeks. Only 24% of patients on study completed the 21 cycles; for our analysis we limited duration to 11 cycles. $5.5 per mg.

**Pembrolizumab:** "for the treatment of adult and pediatric patients with refractory primary mediastinal large B-cell lymphoma (PMBCL), or who have relapsed after two or more prior lines of therapy"

ACS estimates 74,200 incident cases of non-Hodgkin lymphoma (NHL) in 2019.
2% of NHL is PMBCL. Source: https://www.ncbi.nlm.nih.gov/pubmed?term=9704731
Estimate that 10% of incident PMBCL will be relapsed/refractory. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6477766/
Number eligible in U.S.: 150 cases of relapsed/refractory PMBCL

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as no national mortality data was available for this tumor.

Cost: Median duration of response estimated to be 9.7 months (no duration of therapy reported on study). Dose 200mg every 3 weeks (13 doses for our analysis). $48.620 per mg.

**Encorafenib plus binimetinib:** "for patients with unresectable or metastatic melanoma with a BRAF V600E or V600K mutation"

ACS estimates 6,850 deaths from melanoma in 2020.
45% of melanoma has BRAF mutation. V600E mutations account for 74% and V600K mutations account for 20% of all BRAF mutations. Source: https://www.ncbi.nlm.nih.gov/pubmed/21343559
Number eligible in U.S.: 2,900 incident cases metastatic melanoma with BRAF V600E or V600K mutation

Cost: Median duration of treatment of 50 weeks on study with dose of binimetinib 45mg twice daily ($4.429 per mg and encorafenib 450mg daily ($0.903 per mg).

*Subtraction of displaced therapy:* Vemurafenib, comparator on study. Median duration of exposure 27 weeks with dose 960mg twice daily. $0.188 per mg.

**Ipilimumab plus nivolumab:** "for the treatment of patients 12 years of age and older with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer (mCRC) that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan"

ACS estimates 51,020 deaths from colorectal cancer in 2019.
4% of patients with mCRC have MSI-H or dMMR disease. Source: https://www.ncbi.nlm.nih.gov/pubmed/19165197 and https://www.ncbi.nlm.nih.gov/pubmed/25139339
Number eligible in U.S.: 2,040 incident cases of mCRC with MSI-H or dMMR disease

Cost: Median of 4 doses ipilimumab and 24 doses of nivolumab received on study (limited to 17 doses nivolumab for our analysis). Dose of nivolumab 3mg/kg and ipilimumab 1mg/kg every 3 weeks x4 doses followed by nivolumab 3mg/kg every 2 weeks. Nivolumab $27.419 per mg and ipilimumab $150.028 per mg.

**Enzalutamide:** "for patients with castration-resistant prostate cancer (CRPC)". Previously approved for metastatic disease; our analysis is limited to patients with non-metastatic disease only to reflect newly eligible population.

ACS estimates 174,650 new cases of prostate cancer in 2019.
8.3 per 100 person years develop CRPC and 15% will have metastatic disease. Source:
https://www.ncbi.nlm.nih.gov/pubmed/22910034
Number eligible in U.S.: 12,330 incident cases of CRPC (non-metastatic)
Concurrent approval on apalutamide for overlapping indication, each drug given 50% market share: 6,165

Cost: Median duration of treatment 18.4 months on study (limited to 12 for analysis). Dose of enzalutamide 160mg daily. $2.483 per mg.

**Ribociclib:** "in combination with an aromatase inhibitor for pre/perimenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer, as initial endocrine-based therapy"

ACS estimates 42,260 deaths from breast cancer (BC) in 2019
70% of patients with metastatic BC have HR-positive disease
HER2 negative BC accounts for 70% of all BC. Source: https://www.ncbi.nlm.nih.gov/pubmed/3798106
Number eligible in U.S.: 20,710 new incident cases of advanced/metastatic HR positive and HER2 negative BC.

Cost: Median duration of treatment 15.2 months on study (limited to 12 for analysis). Dose 600mg daily (3 weeks on, 1 week off). $1.051 per mg.

**Ivosidenib:** "for adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test"

ACS estimates 10,920 deaths from AML in 2019
IDH1 mutation occurs in 6-16% of AML, 10% used for analysis. Source:
https://www.ncbi.nlm.nih.gov/pubmed/24699305
Number eligible in U.S.: 1,090 cases of relapsed or refractory AML with IDH1 mutation

Cost: Median treatment duration of 4.1 months on study with dose of 500mg daily. $1.828 per mg.

**Mogamulizumab:** "for adult patients with relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy"

Incidence of 7.5 per million new incident cases of cutaneous T-cell lymphoma (CTCL) per year
Source: https://www.ncbi.nlm.nih.gov/pubmed/24005876
MF accounts for 55% and SS for 5% of all cases of CTCL. Source:
https://www.ncbi.nlm.nih.gov/pubmed/17540844
29% of MF presents advanced (stage IIB or greater)
Source: https://www.ncbi.nlm.nih.gov/pubmed/22850569
Assumed all SS is advanced
Number eligible in U.S.: 510 incident cases advanced relapsed/refractory MF or SS

Cost: Median treatment duration of 6 cycles on study with dose of 1mg/kg weekly for first 28-day cycle followed by 1mg/kg on day 1 and 15 of subsequent 28-day cycles. $195.228 per mg.

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as no national mortality data was readily available for this tumor type.

*Subtraction of displaced therapy:* Vorinostat, comparator on study. Median duration of exposure 84 days on study. Dose of 400mg daily. $1.251 per mg.

**Lenvatinib:** "for first-line treatment of patients with unresectable hepatocellular carcinoma (HCC)"

ACS estimates 31,780 deaths from liver cancer in 2019
SEER (2012-2016) estimates 70% of all liver/bile duct cancers are HCC
Number eligible in U.S.: 22,250 cases of unresectable HCC

Cost: Median treatment duration of 5.7 months on study with dose of 8-12 mg daily depending upon weight (8mg dose used for our analysis). $31.702 per mg.

*Subtraction of displaced therapy:* Sorafenib, comparator on study. Median duration of exposure 3.7 months on study. Dose 400mg twice daily. $0.833 per mg.

**Nivolumab:** "for patients with metastatic small cell lung cancer (SCLC) with progression after platinum-based chemotherapy and at least one other line of therapy"

ACS estimates 154,050 deaths from lung cancer in 2019
SCLC accounts for 14% of all lung cancers. Source: https://www-ncbi-nlm-nih-gov.liboff.ohsu.edu/pubmed/27269741
Estimate that 50% of those with metastatic SCLC with progression following two lines of therapy are fit enough for third line therapy
Number eligible in U.S.: 10,780 cases of metastatic SCLC with progression after two lines of therapy

Cost: Median treatment duration of 3.5 doses on study with dose of 3mg/kg every two weeks (rounded to 240mg per FDA label). $27.419 per mg.

**Moxetumomab pasudotox:** "for adult patients with relapsed or refractory hairy cell leukemia (HCL) who received at least two prior systemic therapies, including treatment with a purine nucleoside analog (PNA)"

Estimate 1240 new cases of HCL per year in U.S. Source: https://www.ncbi.nlm.nih.gov/pubmed/31068044
Little data available to estimate number of patients with R/R disease following two lines of therapy. We estimated 15% incidence of R/R disease having received at least two prior systemic therapies.

Number eligible in U.S.: 190 cases of relapsed/refractory HCL eligible for third line therapy

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as no national mortality data was readily available for this tumor type.

Cost: Study did not report median duration of treatment. 63% of patients completed the planned 6 cycles; we estimated mean duration of treatment on study to be 3.5 cycles. Dose of 0.04mg/kg on days 1, 3, 5 of each 28-day cycle. $2,114.58 per mg.

**Duvelisib:** "for adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) after at least two prior therapies"

ACS estimates 3,930 deaths from CLL per year in U.S. This estimate was used as proxy for number of patients eligible for duvelisib per year.
Number eligible in U.S.: 3,930 cases of R/R CLL after at least two prior therapies.

Cost: Median duration of 50 weeks on study (limited to 12 months). Dose of 25mg twice daily. $8.85 per mg .

*Subtraction of displaced therapy:* Ofatumumab, comparator on study. Median duration of exposure 23 weeks. Initial dose of 300 mg, followed one week later by 2000 mg once weekly for 7 doses, and then 2000 mg once every 4 weeks for 4 additional doses. $6.034 per mg.

**Duvelisib:** "for adult patients with relapsed or refractory follicular lymphoma (FL) after at least two prior systemic therapies"

SEER estimates 3.5 new cases per 100,000 of follicular lymphoma (2007-2016) with 88.4% 5-year survival. 11.6% of newly diagnosed patients with death in the first 5 years was used as proxy for number eligible; likely underestimating the true population.
Number eligible in U.S.: 1,340 cases of R/R FL after at least two prior therapies.

Cost: Median duration of treatment of 6.7 months on study. Dose of 25mg twice daily. $8.85 per mg

**Dacomitinib:** "for the first-line treatment of patients with metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletion or exon 21 L858R substitution mutations"

ACS estimates 154,050 deaths from lung cancer in 2019.
NSCLC frequency = 85%. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
EGFR mutation frequency in NSCLC = 15% (10-20%) and 90% of EGFR mutations in NSCLC are del19 or L858R.. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346098/
Number eligible in U.S.: 17,680 patients with metastatic NSCLC and EGFR mutation (del19 or L858R)
Given approval of afatanib and osimertinib with overlapping indication, 33% market share used: 5,893

Cost: Median duration of treatment 15.3 months. Dose of 45 mg daily. $9.644 per mg.

*Subtraction of displaced therapy:* Gefitinib, comparator on study. Median duration of exposure 12 months on study. Dose 250mg daily. $1.039

**Cemiplimab:** "for patients with metastatic cutaneous squamous cell carcinoma (CSCC) or locally advanced CSCC who are not candidates for curative surgery or curative radiation"

CSCC is not included in national cancer registries
Estimated 300,000 new cases of CSCC per year in U.S. and 3% of CSCC develop metastasis
Source: https://www.ncbi.nlm.nih.gov/pubmed/23375456
Number eligible in U.S.: 9,000 new cases CSCC with metastasis

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population. Tumor not listed in national registries.

Cost: Median duration of treatment 33 weeks on phase 2 study. Dose of 350mg every 3 weeks. $26 per mg.

**Talazoparib:** "for patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2 negative locally advanced or metastatic breast cancer"

ACS estimates 42,260 deaths from breast cancer (BC) in 2019.
HER2 negative BC accounts for 70% of all breast cancer. Source: https://www.ncbi.nlm.nih.gov/pubmed/3798106
5% of all patients with new BC diagnosis have BRCA mutation. Source:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3870050/
Number eligible in U.S.: 1,480 incident cases of BC with metastatic HER2 negative BRCA mutation
Given concurrent approval of olaparib for overlapping indication, 50% market share: 740

Cost: Median duration of treatment 6.1 months on study. Dose of 1mg daily. $510.30 per mg.

*Subtraction of displaced therapy:* Physician's choice comparator on study, capecitabine used most frequently (44%). Median duration of exposure on study not reported. Estimated to be 3.1 month exposure (median duration of response for the physician's choice arm).
Dose 1,250mg/$m^2$ twice daily x2 weeks with 21 day cycles. $0.002 per mg.

**Pembrolizunab:** "in combination with carboplatin and either paclitaxel or nab-paclitaxel as first-line treatment of metastatic squamous non-small cell lung cancer (NSCLC)"

ACS estimates 154,050 deaths from lung cancer in 2019
25% of all lung cancers are squamous NSCLC
Source: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html
Number eligible in U.S.: 38,510 incident cases of squamous NSCLC with metastasis

Cost: Mean duration of treatment 6.3 months on study (8 doses). Dose of 200mg every 3 weeks. $48.62 per mg.

**Lorlatinib:** "for patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) whose disease has progressed on crizotinib and at least one other ALK inhibitor for metastatic disease or whose disease has progressed on alectinib or ceritinib as the first ALK inhibitor therapy for metastatic disease"

ACS estimates 154,050 deaths from lung cancer in 2019
NSCLC frequency = 85% of lung cancers. Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
ALK rearrangements are found in 4% of NSCLC. Source: https://www.ncbi.nlm.nih.gov/pubmed/22327623
Estimated 30% of patients with metastatic NSCLC with ALK rearrangement will progress following prior therapy and live long enough to receive lorlatinib in later line.
Number eligible in U.S.: 1,570 cases of metastatic NSCLC with ALK rearrangement with disease progression on crizotinib (and one prior ALK inhib) or progressed on alectinib or ceritinib.

Cost: Median duration of treatment 8.3 months on study. Dose of 100mg daily. $5.619 per mg.

**Pembrolizunab:** "for patients with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib"

ACS estimates 31,780 deaths from liver cancer in 2019
SEER (2012-2016) estimates 70% of all liver/bile duct cancers are HCC
Number eligible in U.S.: 22,250 cases of HCC with progressive disease following sorafenib

Cost: Median duration of treatment 4.2 months on study (5 doses). Dose of 200mg every 3 weeks. $48.62 per mg.

**Brentuximab:** "for previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified"

SEER (2007-2016) estimates incidence rate of 1 case peripheral T-cell lymphoma per 100,00 persons (excluding sALCL)
Estimate 50% of PTCL (excluding sALCL) will express CD30. Source:
https://www.ncbi.nlm.nih.gov/pubmed/30522922
SEER (2007-2016) estimates incidence rate of 0.2 cases sALCL per 100,000 persons
Number eligible in U.S.: 2,300 incident cases of sALCL or other PTCL with CD30 expression

Cost: 6-8 cycles planned on study; 89% of patients received at least 6 cycles (6 cycles used for analysis). Dose of brentuximab 1.8mk/kg every 3 weeks. $171.84 per mg.

*Subtraction of displaced therapy:* Vincristine on comparator arm (CHOP). Median duration of exposure of 6 cycles. Dose 2mg x1 on day 1 of each cycle. $5.75 per mg.

**Emapalumab:** "for adult and pediatric patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy"

Incidence of 1 case of HLH per 100,000 persons under 18 years of age. Source:
https://www.ncbi.nlm.nih.gov/pubmed/19953651

Our analysis limited the estimated population to under 18 given less robust data in adults and majority of cases occurring in children.
33% of children will have relapse/refractory disease. Source: https://www.ncbi.nlm.nih.gov/pubmed/19953651
Number eligible in U.S.: 250 incident cases of R/R pediatric HLH

Cost: Median duration/dose on study not reported. We estimated median dose of 3mg/kg with duration of 6 weeks. $337.701 per mg and estimated average recipient to be 15kg.

*Subtraction of displaced therapy:* No comparator on study. Alemtuzumab presumed to be alternative.
Dose 1mg/kg divided over 4 days x1. $0 per mg.

**Glasdegib:** "for newly-diagnosed acute myeloid leukemia (AML) in patients who are 75 years old or older or who have comorbidities that preclude intensive induction chemotherapy"

SEER (2000-2016) estimates AML incidence rate of 23.2 per 100,000 aged 75-79, 28.6 per 100,000 aged 80-84 and 26.3 per 100,000 aged 85+
Limited the analysis to only those 75+ years of age given lack of consensus regarding percentage of patients with "comorbidities precluding intensive induction".
Number eligible in U.S.: 4,635 incident cases of AML in patients 75 years or older

Cost: Median duration of treatment 2.7 months on study. Dose of 100mg daily. $5.924 per mg.

**Venetoclax:** "in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy"

SEER (2000-2016) estimates AML incidence rate of 23.2 per 100,000 aged 75-79, 28.6 per 100,000 aged 80-84 and 26.3 per 100,000 aged 85+
Limited the analysis to only those 75+ years of age given lack of consensus regarding percentage of patients with "comorbidities precluding intensive induction".
Number eligible in U.S.: 4,635 incident cases of AML in patients 75 years or older.

Cost: Median duration of treatment 127 days on study. Dose of 600mg daily following ramp-up (assumed dose of 200mg daily across ramp-up period). $1.024 per mg.

**Gilteritinib:** "for treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation"

ACS estimates 10,920 deaths from AML in 2019
FLT3 mutation occurs in 30% of adult AML. Source: https://www.ncbi.nlm.nih.gov/pubmed/30651634
Number eligible in U.S.: 3,280 cases of R/R AML with FLT3 mutation

Cost: Median duration of treatment unavailable (results unpublished). FDA label recommends dose of 120mg daily and states, "treatment for a minimum of 6 months is recommended" and this was used for analysis. $6.563 per mg.

*Subtraction of displaced therapy:* Mitoxantrone, etoposide and cytarabine (MEC) was used for analysis (one of four comparators on study). Median duration of one cycle on study. Dose of mitoxantrone 8mg/m$^2$, etoposide 100mg/m$^2$ and cytarabine 1000mg/m$^2$ daily x5 days. $8.5 per mg mitoxantrone, $0.094 per mg etoposide, $0.010 per mg cytarabine.

**Atezolizumab:** "for the first-line treatment of patients with metastatic non-squamous, non-small cell lung cancer (NSq NSCLC) with no EGFR or ALK genomic tumor aberrations… in combination with bevacizumab, paclitaxel, and carboplatin"

ACS estimates 154,050 deaths from lung cancer in 2019
NSCLC frequency = 85% of lung cancers. Source:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864624/
25% of all lung cancers are squamous NSCLC
Source: https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html
EGFR mutation frequency in NSCLC = 15% (10-20%). Source:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4346098/
ALK rearrangements found in 5% of NSCLC. Source: https://www.ncbi.nlm.nih.gov/pubmed/26777916
Number eligible in U.S.: 79,300 incident cases of metastatic NSq NSCLC with no EGFR or ALK aberration.

Cost: Median duration of treatment of 8.2 months on study. Dose of 1200mg once every 3 weeks. $7.662 per mg.

*Subtraction of displaced therapy:* Docetaxel, comparator on study. Mean duration of 2.1 months on study. Dose of docetaxel 75mg/$m^2$ once every three weeks. $3.438 per mg.

**Pembrolizumab:** "for adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma (MCC)"

SEER (2000-2013) estimated 2,400 incident cases of MCC in 2013
26% present with regional lymph node involvement and 8.4% with metastatic disease. Source:
https://www.ncbi.nlm.nih.gov/pubmed?term=27198511
Number eligible in U.S.: 830 incident cases of MCC with regional or metastatic disease

Cost: Median duration of treatment 6.6 months (median of 10.5 doses) on study. Dose 2mg/kg once every 3 weeks. $48.62 per mg.

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population as no national mortality data was available for this tumor type.

*Subtraction of displaced threapy:* No comparator on study. Etoposide and cisplatin determined to be alternative. Reported median time to progression of 90 days for those with advanced disease treated with chemotherapy (reference below). This was used for duration of exposure. Dose 100mg/$m^2$ etoposide x3 days and 75mg/$m^2$ cisplatin x1 day with 21 day cycles. $0.094 per mg etoposide and $0.3 per mg cisplatin.
https://www.ncbi.nlm.nih.gov/pubmed/27431483

**Olaparib:** "for the maintenance treatment of adult patients with deleterious or suspected deleterious germline or somatic BRCA-mutated (gBRCAm or sBRCAm) advanced epithelial ovarian, fallopian tube or primary peritoneal cancer who are in complete or partial response to first-line platinum-based chemotherapy"

ACS estimates 22,520 incident cases ovarian cancer in 2019
SEER (2009-2015) estimates 59% distant and 21% regional disease at diagnosis
Germline BRCA mutation occurs in 15% of epithelial ovarian cancer and somatic mutation occurs in 3%. Source:
https://www.ncbi.nlm.nih.gov/pubmed?term=21720365
Number eligible in U.S.: 3,240 incident cases of advanced epithelial ovarian cancer with BRCA mutation.

*Note:* Incidence rather than mortality data were used for the estimation of this eligible population. Incidence data were deemed more precise given molecular subtype not reported with mortality data and front-line indication.

Cost: Median duration of treatment 24.6 months on study (12 months for analysis). Dose 300mg twice daily. $0.579 per mg.

**Tagraxofusp:** "for blastic plasmacytoid dendritic cell neoplasm (BPDCN) in adults and in pediatric patients 2 years and older"

Estimated incidence of BPDCN 0.45 cases per 1 million in U.S. Source:
http://www.bloodjournal.org/content/128/22/4789.abstract
Number eligible in U.S.: 150 incident cases of BPDCN

Cost: Median duration of treatment of 5 cycles. Dose 12mcg/kg daily on days 1-5 per 21-day cycle. $25.529 per mcg.

*Subtraction of displaced therapy:* No comparator on study. Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) determined to be alternative therapy. Duration of one cycle. Doses of 750mg/$m^2$ cyclophosphamide x1, doxorubicin 50mg/$m^2$ x1, vincristine 2mg x1 and prednisone 100mg daily x5 days. $0.569 per mg of cyclophosphamide, $0.8 per mg doxorubicin, $5.75 per mg of vincristine, $0.0082 per mg of prednisone.