CS Healthcare Database

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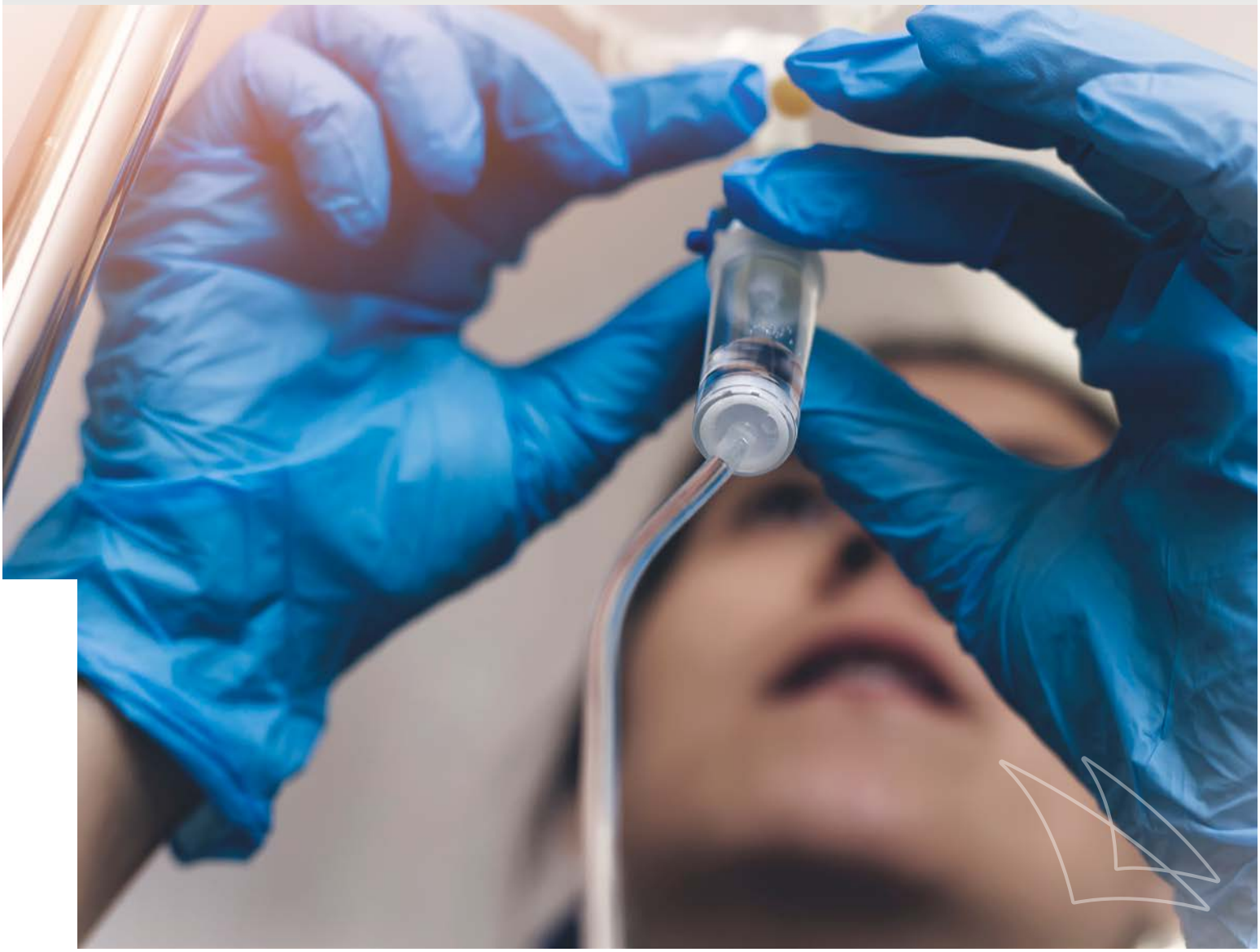
Therapeutic Journeys in cancer

Data-driven insights into immuno-oncology cancer care



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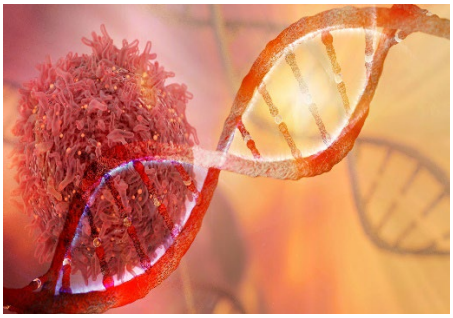
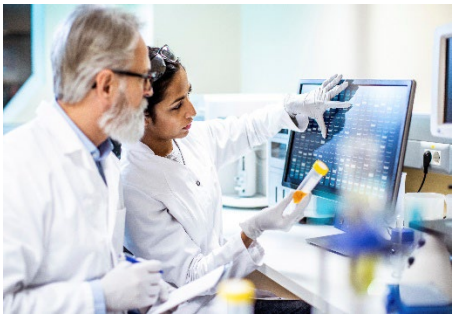
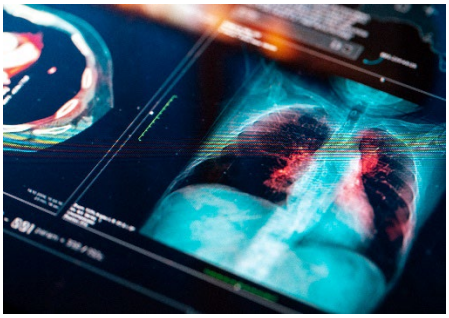
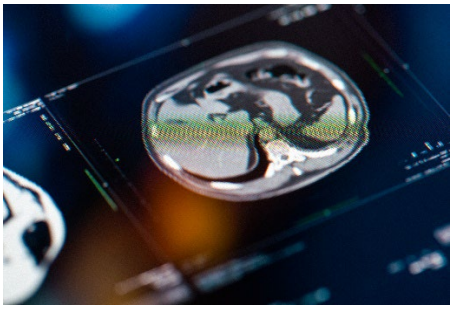
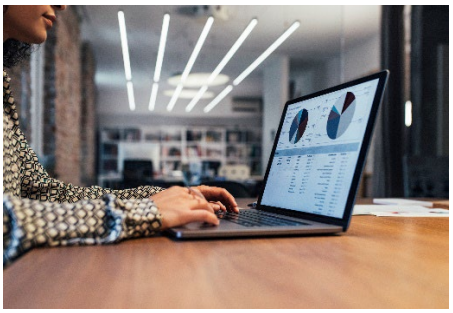










A letter from the Global Head of Securities Research

To our valued institutional clients and to the medical community,

In this report we draw from our new CS Healthcare Database to create representative patient journeys in cancer. As a core component of our alternative data initiative, we were provided access to a database that includes anonymized prescription claims records for roughly 120 million Americans, with additional medical claims data for up to half of this population. In total we analyzed billions of records using a seasoned team of data scientists and a world-class team of pharmaceutical sector experts. Our data assets are sourced through strategic partnerships with global companies. The report that follows contains specific insights into real-world immuno-oncology cancer care. With this data we assessed treatment choices, sequencing of treatments, brand market shares, duration of therapy versus clinical trial data, and financial burden. We hope the broader medical community, in addition to our traditional financial community clients, finds our work helpful and engages with us on future projects. We are thrilled to enhance our Research product with the unique signals available from our alternative data effort and we look forward to continuing to introduce new capabilities across a wide variety of health care topics and sectors.

Thanks and enjoy!

David Bleustein, Global Head of Securities Research

Executive summary

Proprietary database assessing prescription and medical claims records of around 120m US citizens. Claims data by indication and length of use, allows us to follow typical therapeutic journeys through a disease and enables a granular analysis of competitive market shares. For this specific area of immuno-oncology, we estimate the medical claims database covers around 5% of the US treated population.

Based on our proprietary Credit Suisse Healthcare Database, we present a deep dive into immuno-oncology (I-O), looking at PD-(L)1 treatment utilisation across tumour types. In 2021, worldwide I-O sales generated revenues of $36bn and we forecast c10% sales CAGR to 2027 before first patent loss at the end of 2028E. Our US database contains anonymised claims data from a subscriber database of c122m people representative of US demographics and incomes. We estimate the medical claims data covers around 5% of overall US claims for the PD-(L)1 class. We have claims data by indication and length of use, enabling a granular analysis of competitive market shares.

Immuno-oncology insights include:

- **Keytruda growing share in most settings.** The database allows us to break down drug claims by indication over time. We set out market shares by indication and a therapeutic breakdown for each key I-O agent.
- **Limited sequential use of these drugs across indications.** This highlights the very significant scope for novel/combination options in second-line settings post-PD-(L)1, particularly for non-small cell lung cancer (NSCLC). We note multiple catalysts in 2H22/23E for potential 2L NSCLC agents, including the Ipsen/Exelixis Cabometyx combo, the MRK/Eisai Lenvima combo, Sanofi's tusamitamab, Bristol Myers/Mirati's sitravatinib and AstraZeneca/Daiichi's DS-1062.
- **Real-world usage matches clinical trials.** We compare duration of real-world usage with clinical trial results across a number of commercially important cancer settings. Whilst it is too early to see uptake of adjuvant treatment, we note that we have seen no lengthening of average claims per treatment cycle.
- **We see 20-30% of apparent off-label use reimbursed for most drugs.** We see no difference in uptake or treatment duration whether commercial or government funded.

The Credit Suisse Healthcare Database

- **The proprietary CS Healthcare Database offers a unique insight into the treatment of various diseases in the US.** The full database contains healthcare claims covering both outpatient prescriptions for around c122m US citizens and a more limited sample size of medical claims funded by both commercial and government channels. We concentrate our analysis on trends from 2018 onwards in this report, which is when the PD-(L)1 class of drugs became well established. Over this period, the overall database has increased coverage from c115m active subscribers to 122m. This covers around one-third of the US population for Rx claims.
- **We estimate the medical claims database covers around 5% of the US treated population for oncology.** We base this on a calculation of total claims for each drug multiplied by our estimated net price. We compare these totals with the reported US sales data by each company and see a broad agreement of 5% of each drug over 2019-20. We understand that around half of organisations that contract with the database for Rx services submit medical claims to the database. This enables organisations to gain a more holistic understanding of overall healthcare spending. Clearly, in the area of cancer the number of medical claims submitted to the database appears to be significantly lower than the 10-15% that might be expected from the provider commentary. We assume that the highly specialised nature of cancer treatment means that many patients are funnelled into dedicated treatment networks and that organisations may see limited read-across for their broader healthcare spending from submitting these specific claims to the overall database. We do see the expected age and funding split of drugs suggesting to us that the sample size, whilst relatively small, is representative of age and funding status of the US population.
- **This overall database allows us to follow typical therapeutic journeys through a disease.** It allows us to view persistence and compliance on a therapy, common treatment cocktails, and transitions onto and off specific drugs. The database contains both medical and prescription claims, so we can see claims for drugs delivered in both office/hospital settings and those given in outpatient settings in an equivalent fashion. We have visibility into quantities of drug per Rx, and access to co-pay details for drugs, although not for medical claims. A number of specialist drugs supplied under a specialty pharmacy program are censored in our database as they are in other commercially available audit services.
- **Medical claims made under a permanent J code can be analysed,** together with any associated diagnosis codes. This may add some insights into the small number of specialty pharmacy drugs where the at-home delivery of these drugs is censored in other available audit data. However, claims for new drugs logged under a temporary J code are not captured, limiting utility to trends in established drugs given in an office setting. There is a significant lag in the submission of medical claims data to the database, which suggests its utility is focused on observing longer-term usage trends.
- **Our second report using our database looks at the immuno-oncology segment of the cancer market.** This is an important growth area and one where there is little visibility in current audit data sources on the detailed use of drugs today by indication and no guide on longevity of treatment or follow-on treatment options.

Figure 1: Credit Suisse Healthcare Database: Insights from US healthcare claims

Year	Overall Subscribers m	Avg Subscribers m	Subscribers with claims m	Overall Claimants			Cancer Mx claimants	
				Rx m	Mx m	of which Rx & Mx m	Overall cancer Mx m	PD(L)1
2017	114.5	105.8	50.7	31.6	20.7	15.3	0.74	9,151
2018	112.3	104.1	53.0	32.3	20.3	15.0	0.71	12,527
2019	118.1	103.9	57.9	33.4	21.6	15.3	0.73	16,603
2020	111.2	103.0	61.2	36.0	20.4	15.0	0.69	18,217
2021	121.9	113.1	61.9	43.6	20.3	15.6	0.70	18,660

Source: Credit Suisse Healthcare Database (Rx claims = prescription claims, Mx claims = medical claims)

“Keytruda is gaining share of new patient starts with lung, GI and breast cancers contributing the most to patient growth. We see a good correlation between the use of the drug in the real-world setting vs the clinical studies that led to the drug approvals in certain indications. Surprisingly, no evidence yet of expanding use into earlier settings, although limited evidence of re-use highlights scope for post PD-(L)1 combinations or novel therapies, especially for non-small cell lung cancer (NSCLC).

Immuno-oncology key conclusions and charts

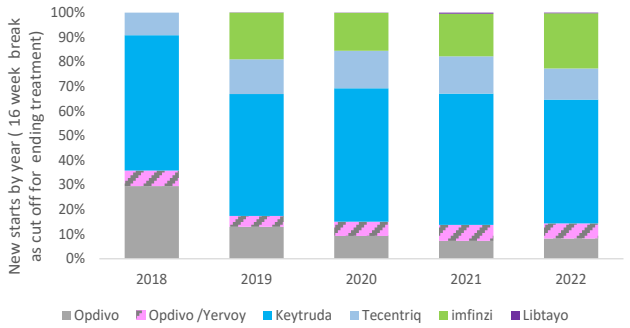
- **Keytruda gaining share in most settings.** We can look at new patient starts by year and by disease. Lung is the largest cancer setting, and has contributed the most to overall PD-(L)1 patient growth, followed by GI (gastrointestinal) and breast. We have seen PD-(L)1 patient growth of 14% 2018-21. Use in skin cancers has shown 7% growth (and now accounts for 9% share of the 2021 market). GI has shown c36% CAGR to be roughly the same size as the skin cancer market today.
- **Real-world use in line with studies.** Where we could match the setting with an underlying study (using diagnosis codes and concomitant drug claims), we saw a good correlation between the use of the drug in the real-world setting and in the underlying study. For example, for Imfinzi, we saw an average of 12.2 claims for treatment in the stage III PACIFIC setting and 28 weeks of treatment. Assuming that treatment correlates with time before progression, this compares with a median progression-free survival (PFS) of 20.8 weeks in the PACIFIC study.
- **11% of patients receive Imfinzi for >12 months of treatment** for Stage III non-small cell lung cancer (NSCLC). This compares with 20% in PACIFIC-R.
- **Surprisingly, no evidence yet of lengthening use with move to earlier settings.** The database shows a gradual decline in apparent treatment length and claims per treatment across most drugs and settings. This is not what we would expect, as we would expect the use of PD-(L)1 drugs to be expanding into earlier metastatic settings (and adjuvant setting) where patients should be able to take more cycles. We do not believe that this can be explained by expansion into new tumour types where initial use is normally in later lines with short treatment times, as it is also evident in use across narrowly defined indications. We believe it may partly reflect incomplete data in later cohorts with patients still on therapy, although this should not impact the 2018 to 2020 cohorts significantly. It is too early to see any treatment times in the adjuvant setting in this dataset.
- **Little use of less frequent dosing options.** We note that recent approvals of monthly (Imfinzi November 2020) or six-weekly dosing (Keytruda April 2020) are not reflected in growing apparent treatment intervals in the real-world data, suggesting only a limited adoption of what should be a simpler, more acceptable dosing regimen. For Keytruda, we see a stable average dosing interval of around 3.3 weeks from 2018 through to 1H21. We would expect this to change as more earlier-stage patients are treated with PD-(L)1 therapy, enabling less frequent visits to their oncologists and thus benefitting from more convenient dosing intervals.
- **We see no difference in the use of drugs by patient funding type.** We see no difference in access to drugs for commercial or government funding channels, and length of treatment is comparable, suggesting no differential financial pressures reducing compliance.
- **Very limited sequential use of these drugs across indications.** We look at treatment in the six months following completion of a treatment course of PD-(L)1 drugs (assuming a 16-week break means completion). In some settings such as 1L NSCLC, we see only some apparent re-use of PD-(L)1 drugs, with Keytruda being the most used either as re-treatment or after other drugs. This evidence of current limited later stage re-use highlights the very significant scope for novel/combination options in second-line settings post-PD-(L)1, particularly for non-small cell lung cancer (NSCLC). We note multiple catalysts in 2H22/23E for potential 2L NSCLC agents, including the Ipsen/Exelixis Cabometyx combo, the MRK/Eisai Lenvima combo, Sanofi's tusamitamab, BMY/Mirati's sitravatinib and AZN/Daiichi's DS-1062. See Figure 2 for key studies.
- **Off-label use appears to be common** and seems to be up to 20-30% of use in some cases. However, we caveat that some apparent off-label use will be treating secondary tumours of "on-label" primary tumours and the ICD-10 diagnostic code typically does not reflect this granularity of use. We would assume that bone and brain tumours are in many cases likely to be metastases of underlying tumours. Bone and brain tumours together account for c7% of 2020 Imfinzi use and 12-15% use of Opdivo, Keytruda and Tecentriq. We include use here as being "on-label" in this report. Diagnostic codes are not specific enough for us to allocate individual claims to specific indications in only 4% of the overall claims in our database.

Figure 2: Pipeline for drugs in 2L: lung cancer, post Keytruda chemo combo

COMPANY	DRUG	TRIAL	STAGE	COMMENT
Novartis	canakinumab	CANOPY-2	P3 2L all-comers	March 2021: did not meet primary endpoint of overall survival
Roche/Ipsen/Exelixis	Tecentriq + Cabometyx	CONTACT-01	P3 2L all-comers	Nov 2021: recruitment completed. Early reponse seen in P1 COSMIC-021 trial. P3 data due 2H22E.
Sanofi	tusamitamab ravtansine	CARMEN-LC03	P3 CEACAM5 high	CEACAM-5 overexpressed in c.20% of lung adenocarcinaomas. Data due 2023E. P2 in combo with ramucirumab due 2H22E. ASCO'22 data raise concerns on eye safety.
Merck/Eisai	Keytruda + Lenvima	LEAP-008	P3 2L all-comers	Data due in 2023E.
Bristol Myers Squibb/Mirati	Opdivo + sitravatinib	SAPPHIRE	P3 2L all-comers	Data due in 2H22E (estimated primary completion Sept 2022).
AZN	Dato-Dx (DS-1062)	TROPION-Lung01	P3 2L all-comers	Data due in late 22/early 2023

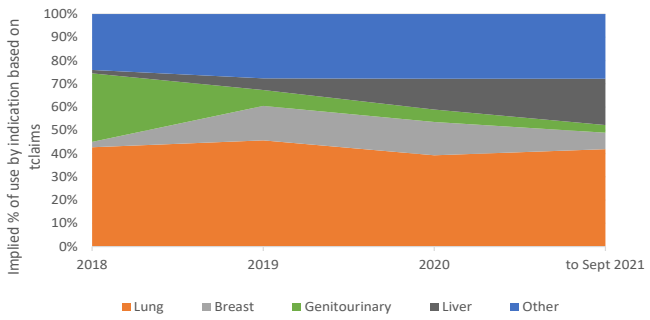
Source: Company data, Credit Suisse

Figure 3: Share of new overall lung patient starts over time



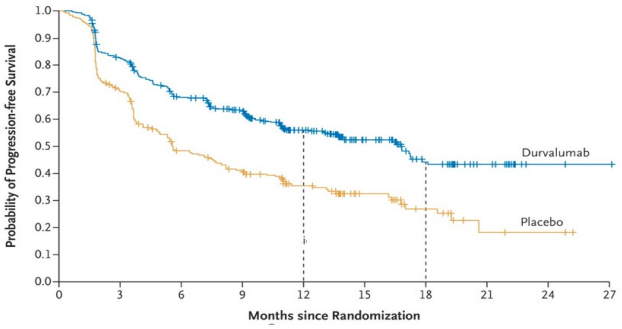
Source: Credit Suisse Healthcare Database

Figure 4: Use of Tecentriq by indication over time



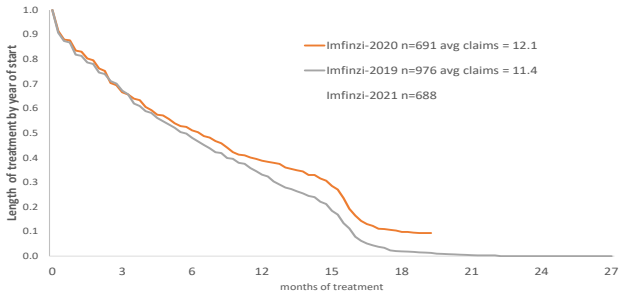
Source: Credit Suisse Healthcare Database

Figure 5: Progression-free survival in the Intention-to-Treat Population in PACIFIC study of Imfinzi in Stage III NSCLC



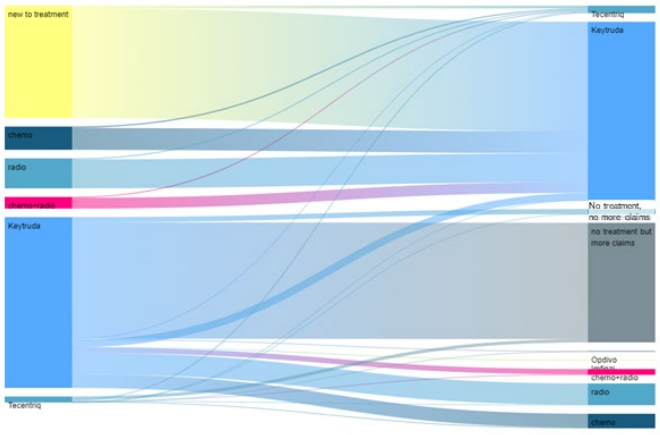
Source: Company data

Figure 6: Imfinzi real-world time on therapy from CS database. Compares favourably with PACIFIC trial



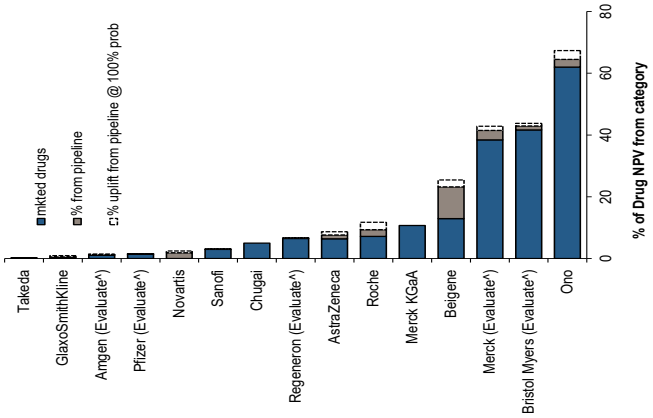
Source: Credit Suisse Healthcare Database

Figure 7: 1L NSCLC (all comers). Before and after Keytruda

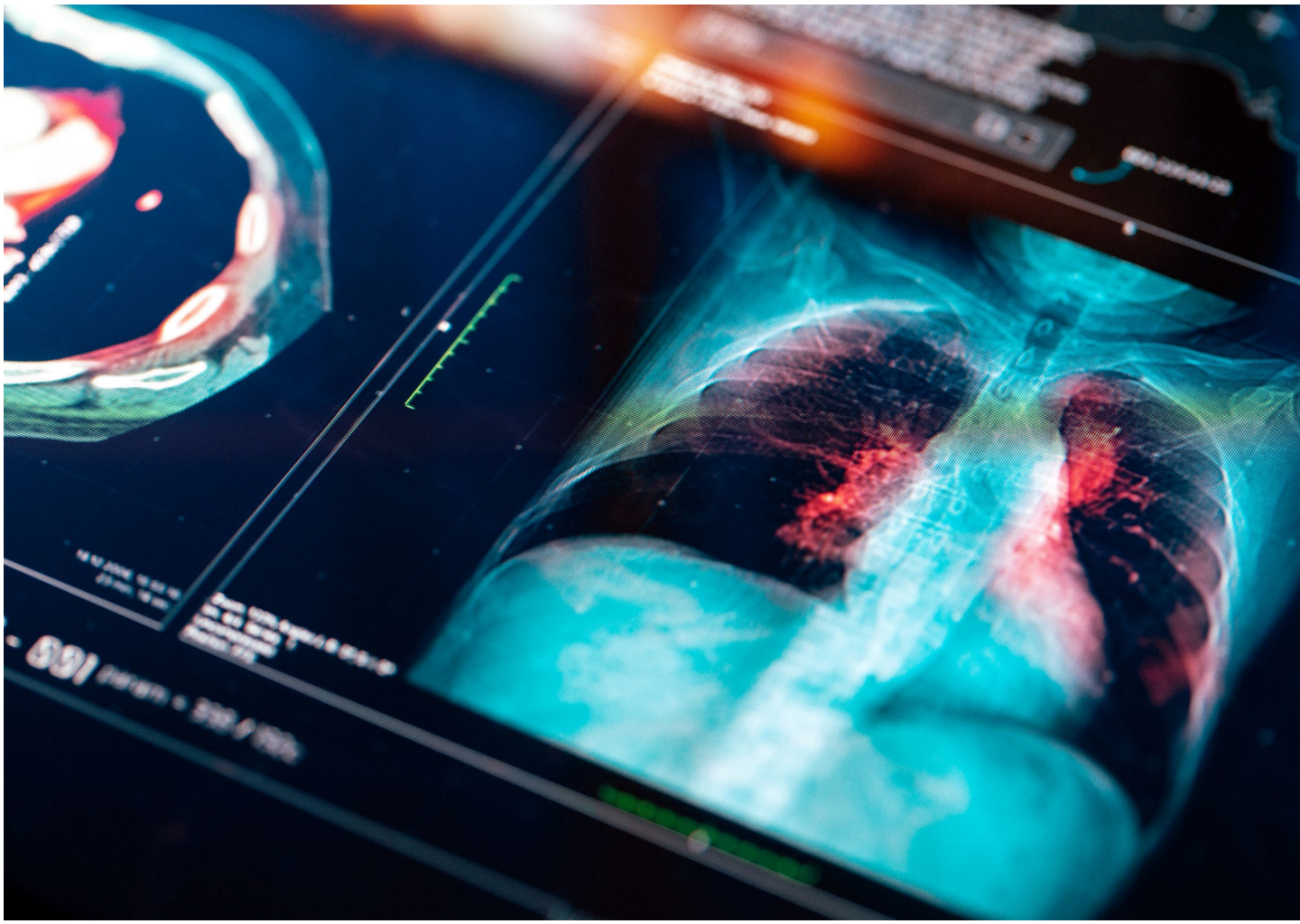


Source: Credit Suisse Healthcare Database

Figure 8: Importance of PD-(L)1 drugs to company NPVs



Source: Credit Suisse, Credit Suisse PharmaValues Database; US major forecasts used from Evaluate Pharma



“Real world use of Keytruda and Imfinzi look comparable to the duration of therapy given in clinical studies. Where we could match the setting with an underlying study (using diagnosis codes and concomitant drug claims), we saw a good correlation between the use of the drug in the real-world setting for Imfinzi and Keytruda in specific lung cancer indications.

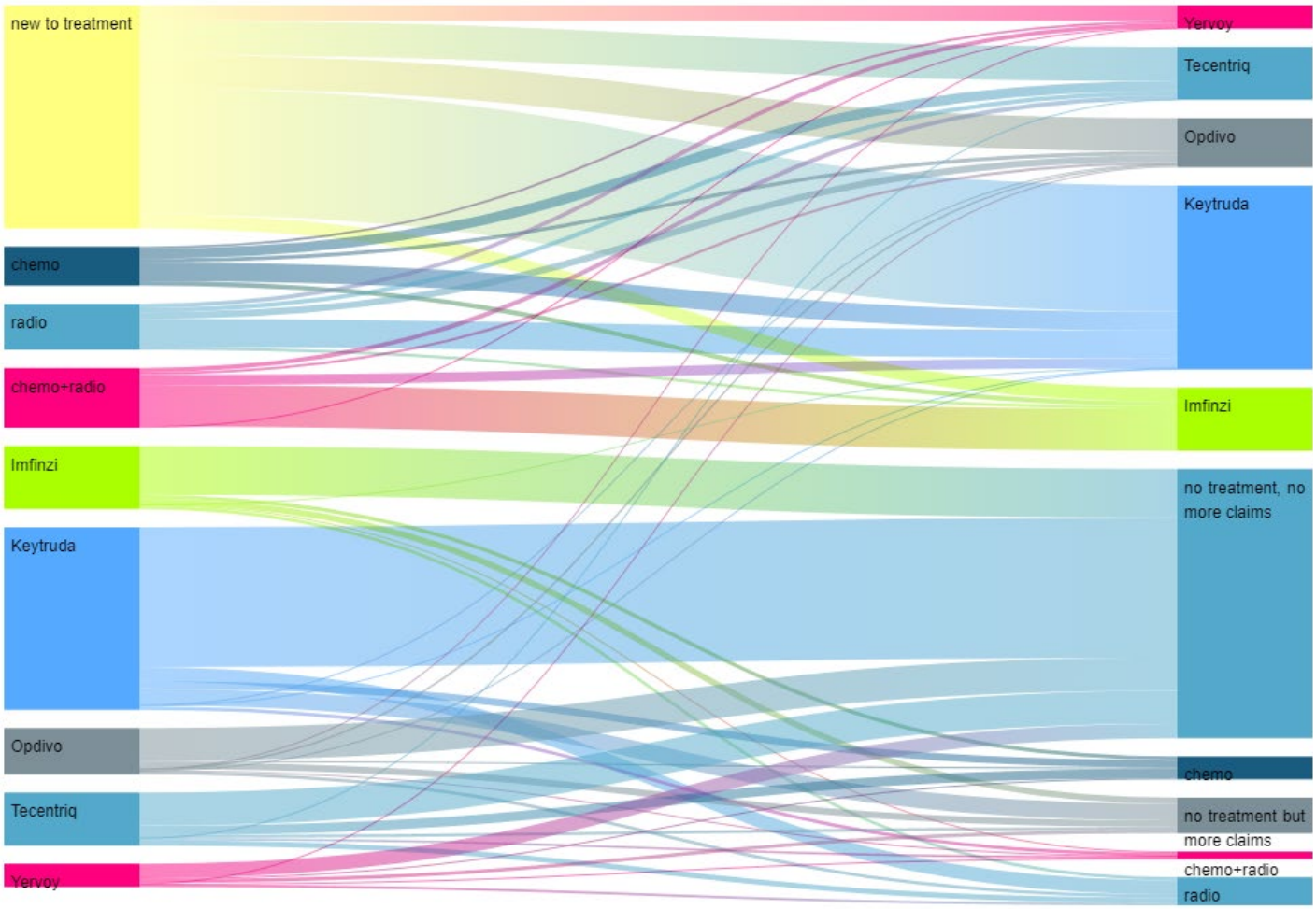
Patient journeys in lung cancer

- In this section, we look at transitions both onto, and away from, the main PD-(L)1 immuno-oncology drugs in patients in our database with a registered diagnosis of lung cancer. We look at the overall percentage of new patient starts, and show in the charts the next treatment options in the six months post initial treatment cycles. In the text, we comment on subsequent treatment options.
- We look at patient starts from 2018 to 2022 (acknowledging more limited 2022 start data) and patient transitions for cohorts covering 2019-2021 to allow for treatment completion.

All-comers in lung cancer

- In Figure 9, we look at transitions between treatments in overall lung cancer showing the lead-in from no treatment or prior chemo/radiotherapy to the first PD-(L)1 drug. This is the top of the figure with flow from left to right. At the bottom of the figure, again with a flow from left to right, we show the transition away from the PD-(L)1 drugs after the completion of treatment (with a new cycle noted if a patient stops treatment for more than 16 weeks). Here we do show Yervoy, which will double count patients who take Yervoy in combination with Opdivo.

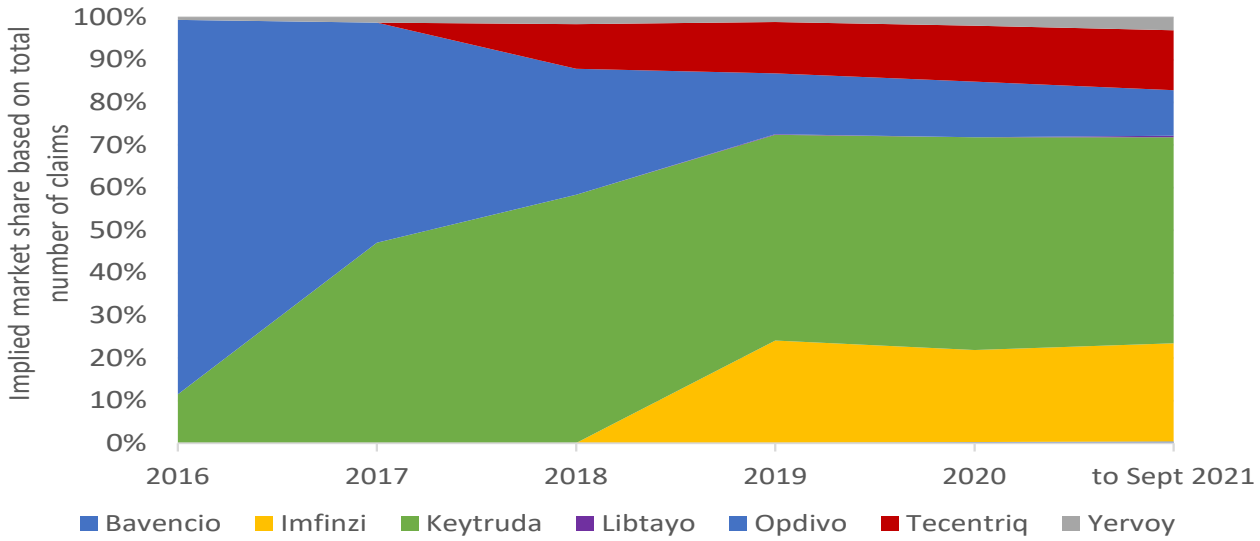
Figure 9: Lung cancer transitions 2019-2021 (excluding small numbers of Bavencio/Libtayo) but double counting Yervoy/Opdivo patients



Source: Credit Suisse Healthcare Database

Market share in lung cancer (all-comers)

Figure 10: PD-(L)1 market share in lung cancer implied by number of claims



Source: Credit Suisse Healthcare Database

1L metastatic NSCLC

- **Non-small cell lung cancer (NSCLC) makes up around 85% of lung cancers**. The proportion of patients with genetic drivers of disease that are treated by targeted therapies varies by geography, from 20% in US to 40% in RoW. PD-(L)1 therapies are utilised in patients without genetic drivers, and were first investigated in advanced settings post platinum-chemotherapy. Over time, studies have moved to earlier populations, and now PD-(L)1 therapy is considered the standard of care in 1L setting for many of these patients that lack targeted mutations. PD-(L)1 diagnostics further determine which drugs or combination of drugs are used.
- **US Merck's Keytruda is generally considered the 'gold standard' of care in 1L non-squamous NSCLC** when combined with platinum-chemotherapy, regardless of PD-1 status. Keynote-189 study was first published in May 2018. The study assessed Keytruda + chemo vs chemo in n=616 patients. Patients were treated with Keytruda until disease progression or up to a total of 35 cycles. Median PFS was 8.8mo in the Keytruda + chemo arm vs 4.9mo in the placebo arm. In August 2020, Keynote-189 was approved via the FDA real-time oncology review (RTOR) program, granting full approval to the Keytruda + chemo combination. The regimen was initially approved via the accelerated approval pathway in May 2017 based on the results of the Keynote-021 study.
- **In Keynote-189, the median duration of treatment was 7.4mo** (+/- 4.7mo) for the Keytruda arm and 5.4mo (+/- 4.3mo) for placebo. The median number of Keytruda doses observed was 10 (range 1-30). In Figure 12, we present real-world time on therapy based on our Credit Suisse Healthcare Database. In our analysis, we longitudinally follow individual NSCLC patients that start Keytruda + platinum therapy either in 2019 (n=1027), 2020 (n=1008) or 2021 (n=903). The average number of infusions observed was 9.6 in the 2019 cohort and 9 in the 2020 cohort. *The follow-up time for the 2021 cohort is insufficient for this analysis.*
- In Figure 13, we look at prior cancer-related claims before 3,050 patients took Keytruda in this setting and what treatments if any patients moved onto after stopping PD-(L)1 treatment for at least 16 weeks. We included patients who started treatment in 2019, 2020 or 2021 and who completed treatment before end-September 2021.
- For the follow-on treatments, we looked at claims in the following six months after they completed treatment. Post Keytruda treatment, in the following six months we see 3% of patients made no further claims and likely died or left the database. 66% made more claims that were not cancer treatment-related, suggesting remission/stable disease or palliative care. 31% went on to make more cancer-related claims. 8% involved further I-O treatment (roughly equally split between further Keytruda and Tecentriq). The remaining 23% of treatment claims cover chemo and radiation.

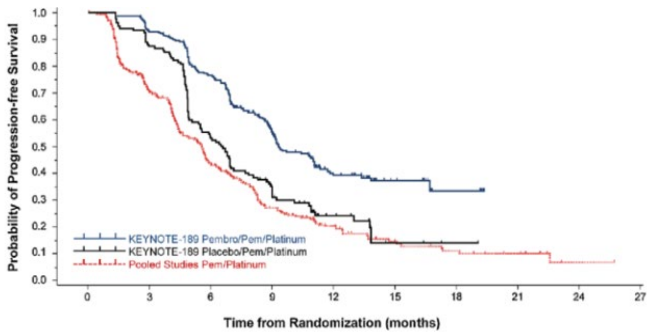
- **Unmet need for post-PD(L)1 therapies in lung cancer.** As highlighted, Immunotherapy is the current standard of care in previously untreated metastatic non-small cell lung cancer (1L NSCLC) without driver mutations. For patients who are PD-L1+ high (>50% expression), monotherapy I-O is preferred and chemo is added to the I-O regimen for PD-L1 low/negative patients. However, response rates are low (range c20-50%), and many patients relapse and so require subsequent care. For 2L patients, NCCN guidelines recommend chemotherapy if I-O was given in 1L. For those patients who receive only chemo in the 1L setting, then I-O is recommended in the 2L setting. The chemo of choice is typically docetaxel or pemetrexed.

- **Multiple 2L+ post-IO NSCLC studies reading out starting 2022.** Given the high unmet need in this area, many companies are exploring novel molecules and combinations in 2L NSCLC post-IO as we highlighted earlier in the note (see Figure 2 on page 11). Roche/Exelixis, Mirati/BMY and Eisai/MRK are exploring TKI + PD-1 combos in the 2L setting, with data from their P3 studies expected from 2H22E. Novel antibody drug conjugates are also being explored. Sanofi's CEACAM5 targeting ADC is being studied in a CEACAM5 biomarker selected subset of patients, with interim data readout possible in 2H22E. AZN/Daiichi are also investigating its TROP-2 targeting ADC, with data also expected in 2H22E.

Time on treatment

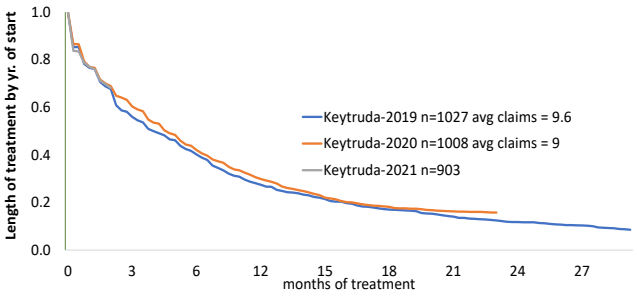
Keytruda + chemo in 1L NSCLC vs KEYNOTE-189

Figure 11: Progression-free survival in the Intention-to-Treat Population in Keynote-189 study of Keytruda + chemo in 1L NSCLC



Source: Company data

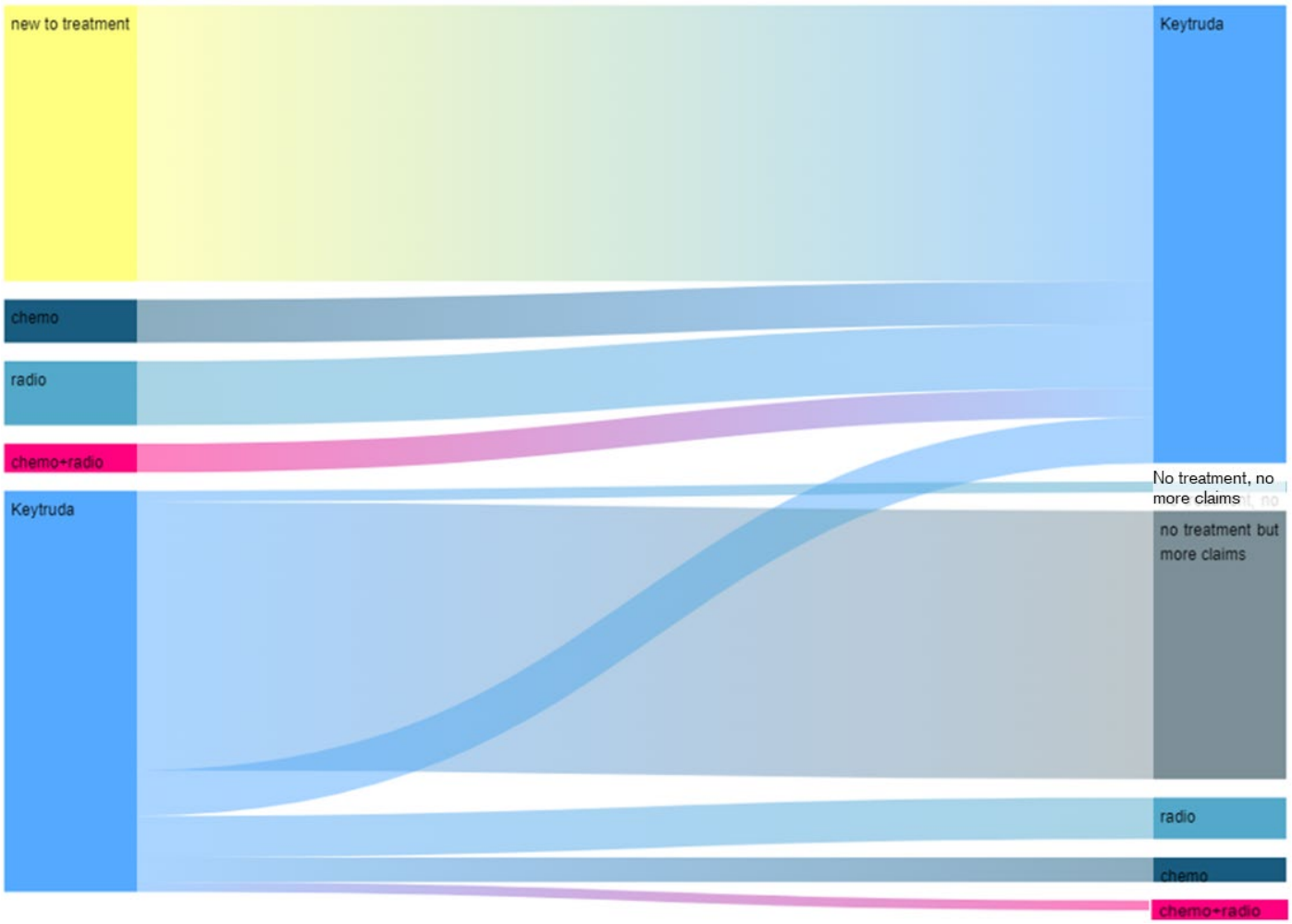
Figure 12: Keytruda + chemo in 1L NSCLC real-world time on therapy based on the Credit Suisse Healthcare Database



Source: Credit Suisse Healthcare Database

Patient journeys to/from Keytruda in lung cancer

Figure 13: 1L NSCLC. Treatments before and after Keytruda, for patients who started treatment in 2019, 2020 and 2021 who have progressed



Source: Credit Suisse Healthcare Database

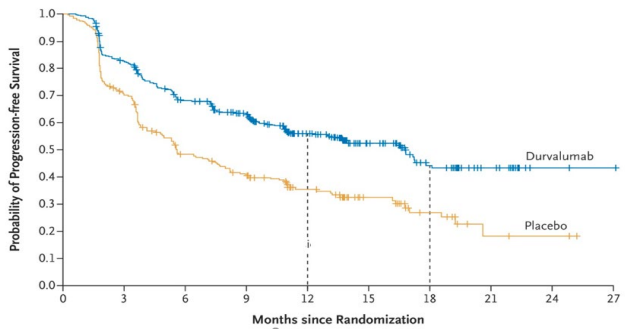
Stage III unresectable NSCLC

- **At diagnosis, cancers are classified by stage of disease**, indicating how advanced the cancer is. Stage 0, 1 and 2 (or Stage I and II) indicates the earlier stages of disease, where the disease is more localised and can often be removed by surgery (resection). When disease gets to Stage 3 (Stage III), not all tumours can be easily surgically removed, as the tumour has spread to lymph nodes, and thus some can be classified as unresectable. Once cancer reaches Stage 4 (Stage IV), the cancer has spread (metastasized) more widely around the body and may be present in other organs, tissue or even bones.
- **Initially, immunotherapy drugs were first assessed in metastatic cancer**, where the unmet need was highest. AZN's PACIFIC trial was one of the first studies to evaluate immuno-oncology agent Imfinzi in an earlier setting, Stage 3 unresectable stage of non-small cell lung cancer (unresectable stage 3 NSCLC) and for several years was the only immunotherapy agent approved in this setting.
- **The PACIFIC study assessed Imfinzi (durvalumab) vs placebo in Stage III unresectable cancer** following chemo-radiotherapy (CRT). Imfinzi was dosed every two weeks up to a maximum of 12 months. Initial results were published in November 2017. 713 patients were enrolled in the study and in the latest analysis, Imfinzi showed a median progression-free survival of 16.9mo vs 5.6mo on placebo. In February 2018, Imfinzi gained FDA approval for use in this setting and rapidly became the new standard of care. The approval allowed treatment to progression of disease or up to 12 months, per the study design. The median duration of treatment was 40.1 weeks (range, 1-54) for Imfinzi vs 28.0 weeks (range, 1-53) for placebo. The median number of infusions received was 20 (range, 1-27) in the durvalumab group and 14 (range, 1-26) in the placebo group.
- **In Figure 15, we present real-world time on therapy** based on our Credit Suisse Healthcare Database. In our analysis, we longitudinally follow individual patients that start Imfinzi therapy either in 2020 (n=691) or in 2021 (n=976). Our analysis shows that for patients starting treatment in 2019 and 2020, only 11% of patients continued to take Imfinzi beyond the 12-month period. The average number of infusions observed was 11.4 for the 2019 cohort and 12.1 for the 2020 cohort. *The follow-up time for the 2021 cohort is insufficient for this analysis.*
- **In September 2021, AZN published results from the PACIFIC-R real-world study** of Imfinzi in Stage 3 unresectable patients. Outcomes showed median treatment duration of 11 months, with 232 patients (of n=1155, so 20%) continuing to receive treatment for >12 months. The median number of infusions was 22.
- **In Figure 16, we look at prior cancer-related claims** and what treatments patients moved on to after taking Imfinzi for Stage III NSCLC. This data suggests that 18% of patients entered treatment in the PACIFIC setting without any evidence of prior cancer-related claims (new treatment, or new to the database). 71% made the expected chemo and radiation claims ahead of Imfinzi treatment (as per the PACIFIC labelling), with the remaining 11% we see having claimed only chemo (6%) or radiation (5%).
- **Following Imfinzi therapy, we see that 3% made no further claims at all** in the next six months after relevant treatment stopped. These individuals likely died, were in remission or left the database, perhaps moving to a different insurance coverage. 76% made no further cancer treatment-related claims for I-O/chemo or radiotherapy treatment, but did make other claims suggesting remission or stable disease or palliative care. 9% went on to receive further rounds of PD-(L)1 drugs, of which the majority went to Keytruda (5%) and 3% took more Imfinzi (after at least a 16-week interval). The remaining 13% took further radiotherapy / chemo or both.

Time on treatment

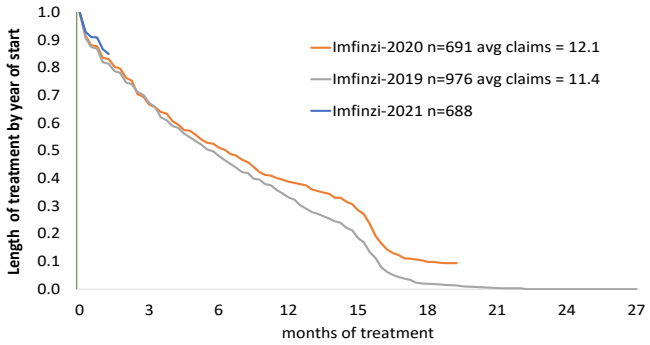
Imfinzi in Stage 3 unresectable lung cancer vs PACIFIC

Figure 14: Progression-free survival in the Intention-to-Treat Population in PACIFIC study of Imfinzi in Stage III NSCLC



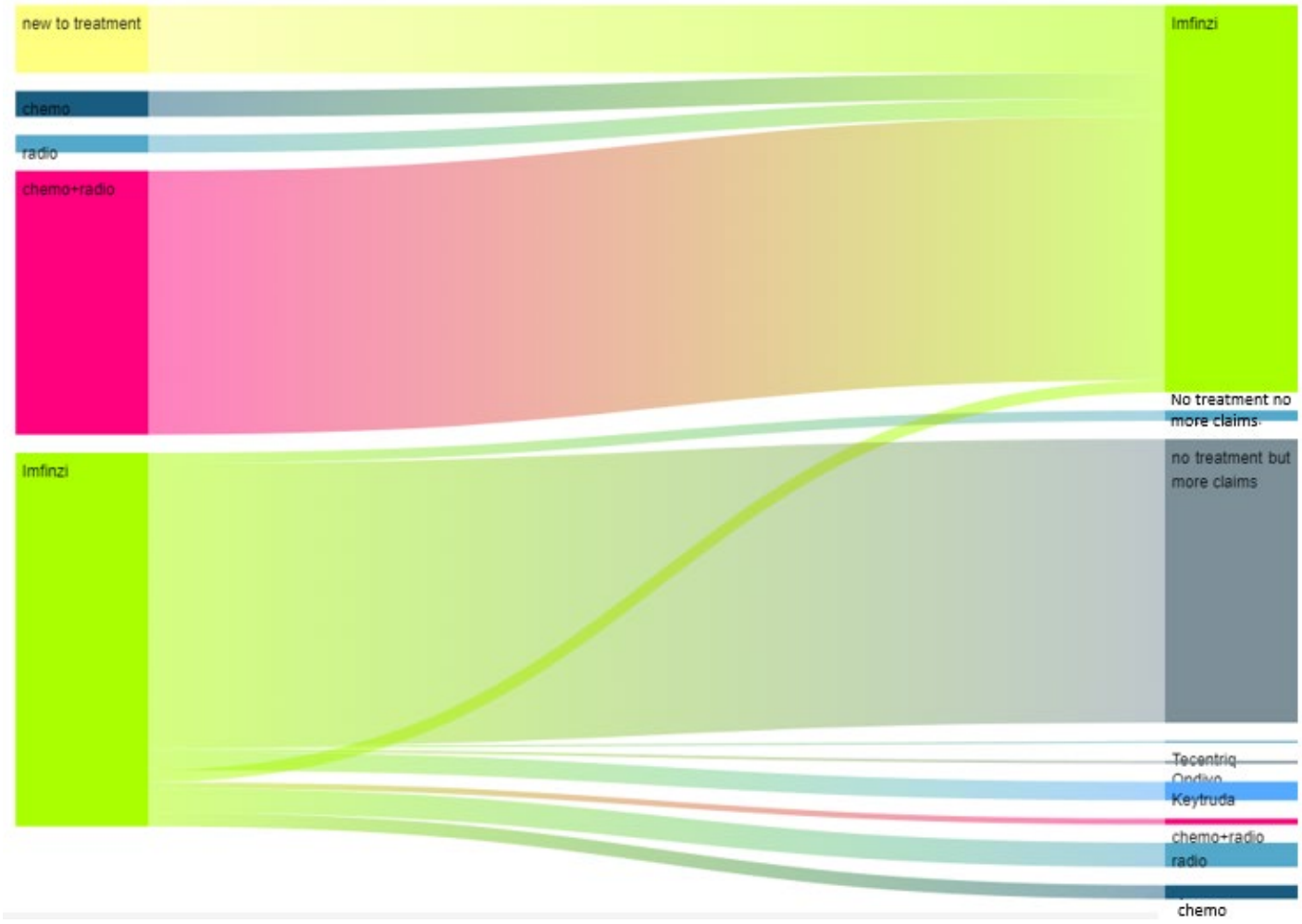
Source: Company data

Figure 15: Imfinzi real-world time on therapy based on the Credit Suisse Healthcare Database



Source: Credit Suisse Healthcare Database

Figure 16: Treatments before and after Imfinzi in Stage III NSCLC Treatments, for patients who started on Imfinzi in 2019, 2020 and 2021 who have progressed



Source: Credit Suisse Healthcare Database

SCLC

- **Small cell lung cancer (SCLC) makes up around 15% of lung cancers**. Historically, this tumour type has been hard to treat, given the aggressive nature and rapid doubling time. Chemotherapy was the standard of care for many years in this setting. Only Imfinzi and Tecentriq have shown benefit in previously untreated metastatic small cell lung cancer (1L SCLC), with both Opdivo and Keytruda P3 pivotal studies in 1L SCLC failing to show benefit.
- Immunotherapy is given uniquely in combination with etoposide (a type of chemo) only in the SCLC setting. Given this, we are able to identify SCLC patients in our database by looking for patients who are claiming for Imfinzi or Tecentriq + etoposide.

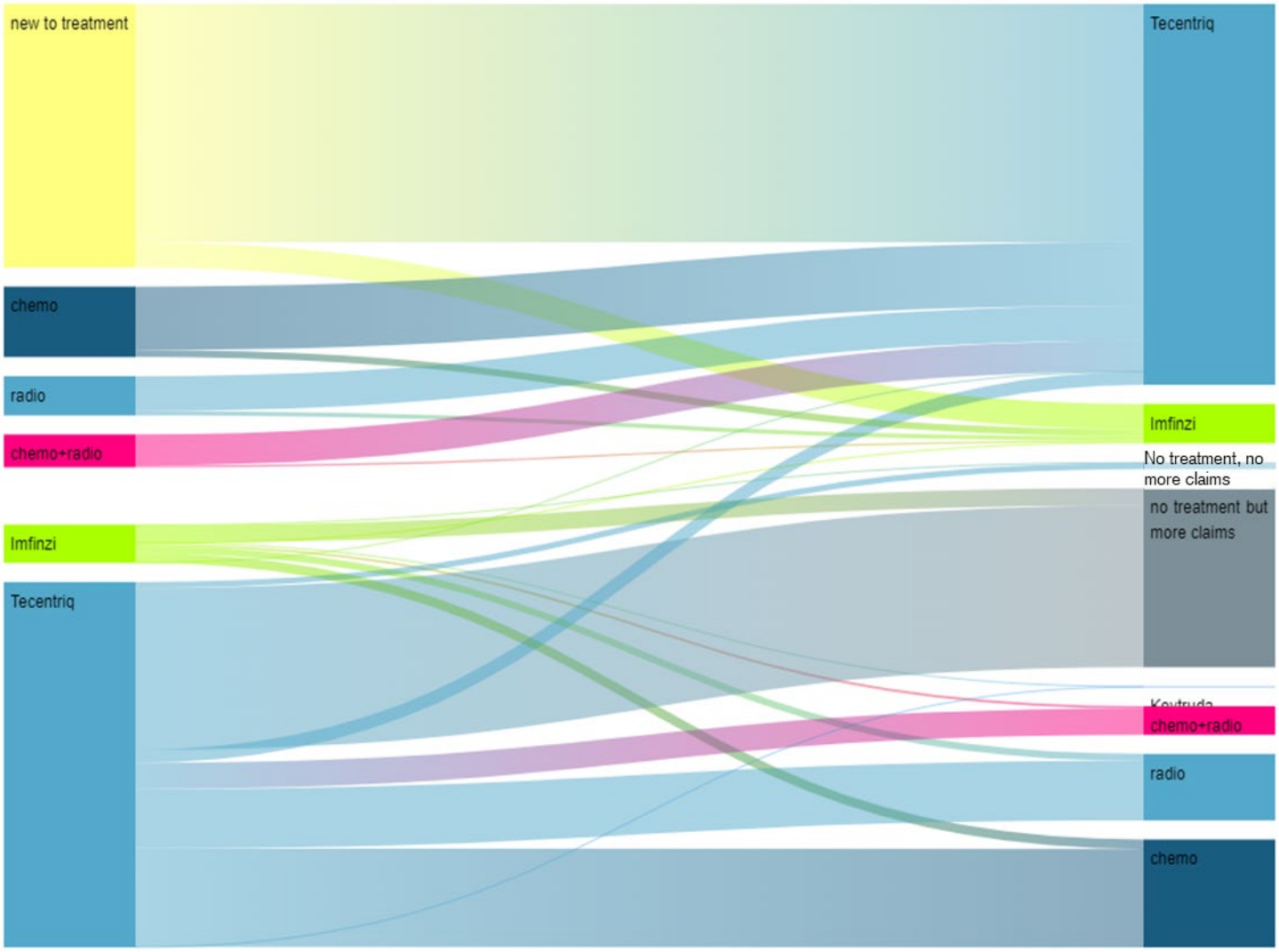
Tecentriq

- **Tecentriq was the first immunotherapy to show benefit in1L SCLC** as part of the IMPower133 trial. Results from this study were published in 2018. The study randomised n=403 patients 1:1 to receive either Tecentriq + chemo (etoposide + carboplatin) followed by Tecentriq monotherapy for maintenance or placebo. Patients were treated until progression of disease. Tecentriq showed mPFS of 5.2mo vs 4.3mo for the placebo group. In March 2019, Tecentriq received FDA approval, with the label stipulating treatment until progression. The median duration of treatment with Tecentriq was 4.7 months (range, 0-21), and the median number of atezolizumab doses received was seven (range, 1-30).
- Following the completion of Tecentriq, our data shows that over the next six months only 2% made no further claims and 44% made non-cancer treatment-related claims. 50% made further chemo/radiotherapy claims and 4% made more I-O-related claims. 52 out of 1,472 patients took more Tecentriq (after a 16-week break). One took Keytruda.
- Looking to the period after the initial six months post treatment to the end of the database, we saw no further I-O use.

Imfinzi

- **Imfinzi was the second immunotherapy to show benefit** in previously untreated metastatic small cell lung cancer (1L SCLC) as part of the CASPIAN study. The study results were first published in October 2019. The study randomised n=537 patients 1:1 to receive either Imfinzi + chemo (etoposide + platinum) followed by Imfinzi monotherapy for maintenance or placebo. Patients were treated until progression of disease. Imfinzi showed a mPFS of 5.1mo vs 5.4mo for the placebo group. In March 2020, Imfinzi received FDA approval, with the label stipulating treatment until progression.
- In CASPIAN, the median duration of therapy was 28 weeks (range 0-198) vs placebo being 23 weeks (range, 0-190), and the median number of infusions observed was seven (range 1-52). In Figure 21 we present real-world time on therapy based on our Credit Suisse Healthcare Database. In our analysis, we longitudinally follow individual SCLC patients that started Imfinzi therapy either in 2020 (n=98) or in 2021 (n=53). The average number of infusions observed was 7.6. *The follow-up time for the 2021 cohort is insufficient for this analysis.*
- Following the completion of Imfinzi over the next six months, only 2% made no further claims and 45% made non-cancer treatment-related claims. 49% made further chemo/radiotherapy claims, and 4% made more I-O-related claims. Four out of 159 patients took more Imfinzi (after a 16-week break), and one took Keytruda.

Figure 17: SCLC. Treatments before and after Tecentriq. For patients who started treatment in 2019, 2020 and 2021 and who have progressed

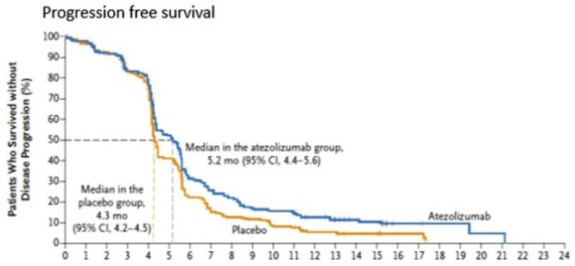


Source: Credit Suisse Healthcare Database

Time on treatment

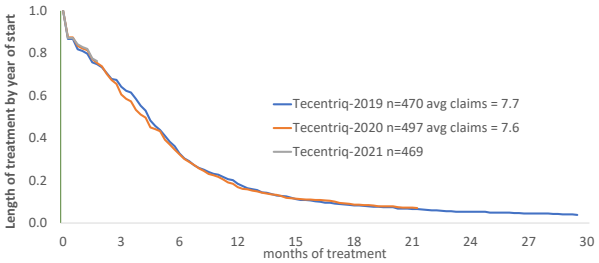
Tecentriq in 1L SCLC vs IMPower133

Figure 18: Progression-free survival in the Intention-to-Treat Population in IMPower133 study of Tecentriq in SCLC



Source: Company data

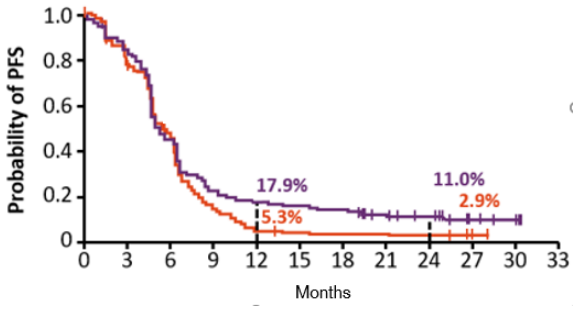
Figure 19: Tecentriq in SCLC real-world time on therapy based on the Credit Suisse Healthcare Database



Source: Credit Suisse Healthcare Database

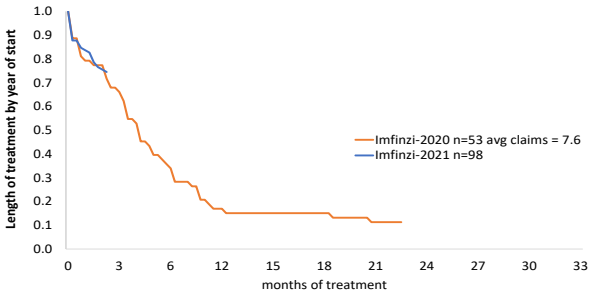
Imfinzi in 1L SCLC vs CASPIAN

Figure 20: Progression-free Survival in the Intention-to-Treat Population in CASPIAN study of Imfinzi in SCLC



Source: Company data

Figure 21: Imfinzi in SCLC real-world time on therapy based on the Credit Suisse Healthcare Database



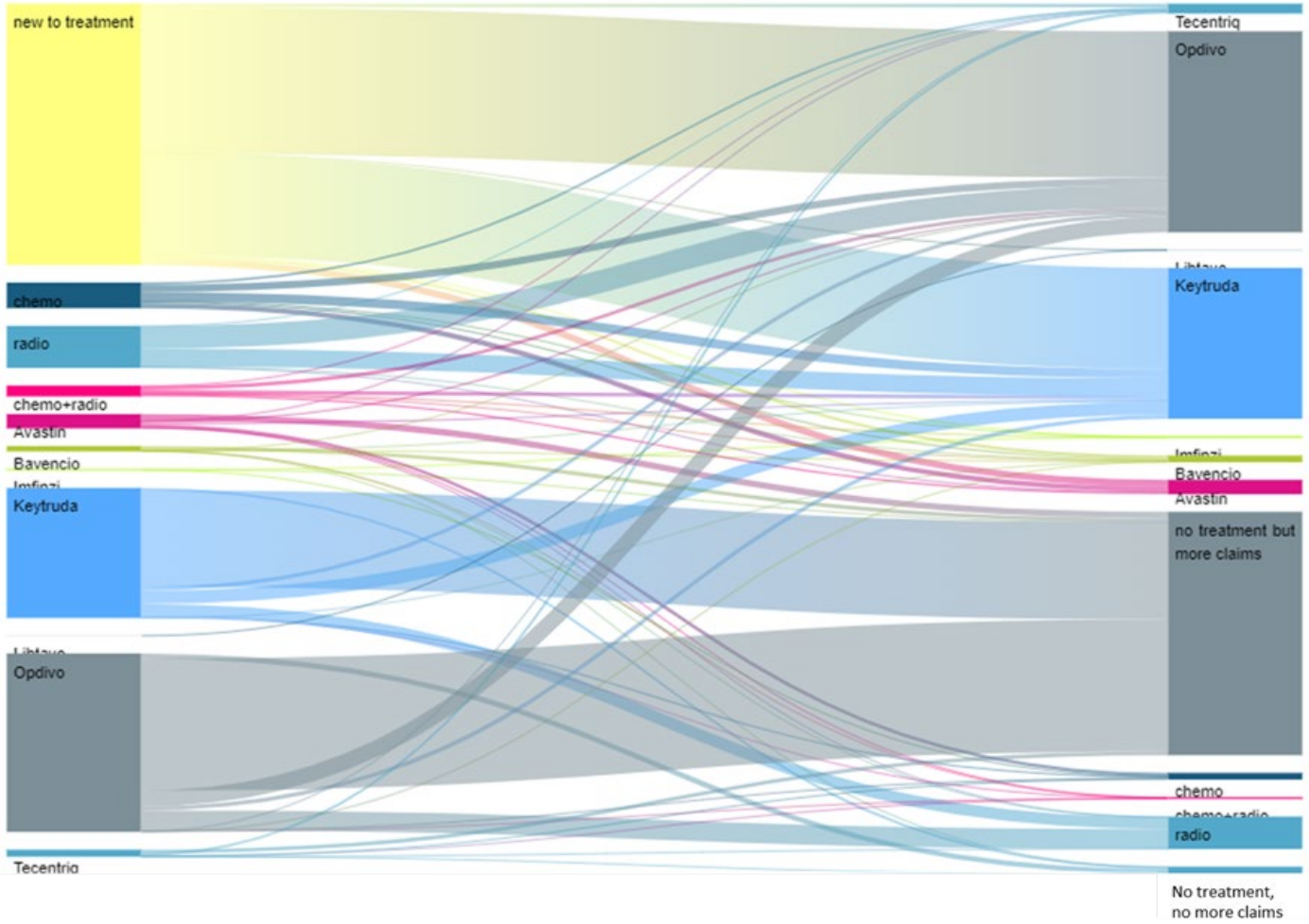
Source: Credit Suisse Healthcare Database

“In renal (kidney) cancer, around half of patients receiving Opdivo also claimed for Yervoy in their first few cycles.

Patient journeys in renal cancer

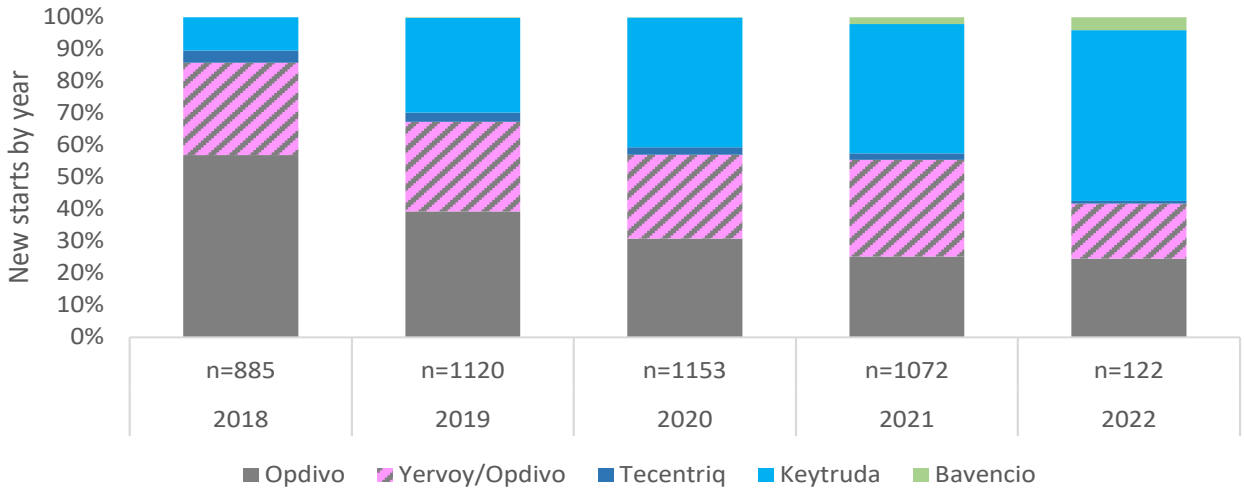
- In Figure 22, we detail patient journeys in renal cancer, and in Figure 23, we look at new patient starts on various PD-(L)1 drugs. Here the cohort size varies from 885 in 2018 to c1,100 from 2019-21 with n=122 for 2022 data.
- **Renal Cell Carcinoma (RCC) is the most common kidney cancer,** representing 80-90% of cases. RCC tends to be diagnosed early and of patients diagnosed with RCC, only 20-30% present with metastatic disease. The current standard of care for metastatic disease is either immunotherapy doublet (Opdivo + Yervoy) or immunotherapy + tyrosine kinase inhibitor (TKI).
- Amongst the PD-(L)1s, **Bristol Myers Squibb has dominated the RCC space**, with Opdivo considered a key backbone therapy. Opdivo was first approved for use in 2L RCC as monotherapy and subsequently moved to the 1L in combination with either its own Yervoy (CTLA-4 immunotherapy) or Exelexis' Cabometyx (TKI).
- **Opdivo + Yervoy was the first immunotherapy doublet to show benefit in 1L RCC**. Checkmate-214 P3 results were first published in April 2018. The study assessed Opdivo + Yervoy vs sunitinib, with n=1,096 patients randomised on a 1:1 basis. The progression-free survival was 11.6mo for Opdivo + Yervoy vs 8.4mo for the control arm. Opdivo was dosed every two weeks in the maintenance part of the trial.
- The median duration of treatment for the Opdivo + Yervoy arm was 7.9mo vs 7.8mo for the control. Assuming no missed doses, this implies a median of c15 Opdivo infusions over the period, with 3QW dosing for the first four cycles followed by 2QW dosing.
- In Figure 22, we look at transitions within the renal space. For clarity, we have removed small numbers of patients on Bavencio, Libtayo and Imfinzi patients. As patients taking Yervoy also took Opdivo, we have excluded these patients to avoid double counting.
- In this setting, there are a number of patients who appear to move from one PD (L) 1 drug and then, after treatment cessation for at least 16 weeks, back to the same drug (this is illustrated in Figure 22, for example, by patients moving from bottom left – post Opdivo – back to top right – on to Opdivo). This gives rise to some double counting of these patients who appear twice in this treatment view. Of note, there are very few transitions from one I-O to another I-O. Around 10% of patients for each drug appear to reinitiate therapy with the same drug after at least a 16-week break.
- **Yervoy use:** Of note, around 798 out of 1,620 patients who started Opdivo treatment in a renal setting also claimed for Yervoy in their first few cycles. Over the three years, we see a roughly 55/45% split in favour of Opdivo/Yervoy combination. For 2021 and 2022 new starters, the split was 50/50%.
- **Time on treatment:** In Figure 25, we present real-world time on therapy data based on our Credit Suisse Healthcare Database. In our analysis, we longitudinally follow individual RCC patients that start Opdivo + Yervoy therapy either in 2018 (n=370) or in 2019 (n=358), 2020 (n=314) or 2021 (n=321). The average number of Opdivo infusions observed was 11.5 in 2018, 8.9 in 2019 and 8.7 in 2020. *The follow-up time for the 2021 cohort is insufficient for this analysis.*
- Looking out beyond six months up to the end of the database cut-off, we see small numbers (c90 patients each) move to take further Keytruda and Opdivo treatment. This is not illustrated in Figure 22, which covers patients only in the six months post treatment.

Figure 22: Renal cancer transitions 2019-21 and ignoring Yervoy to avoid double counting Opdivo patients (small numbers of Bavencio patients <5 excluded)



Source: Credit Suisse Healthcare Database

Figure 23: Market share of new patient starts by drug in renal cell carcinoma (not claims)

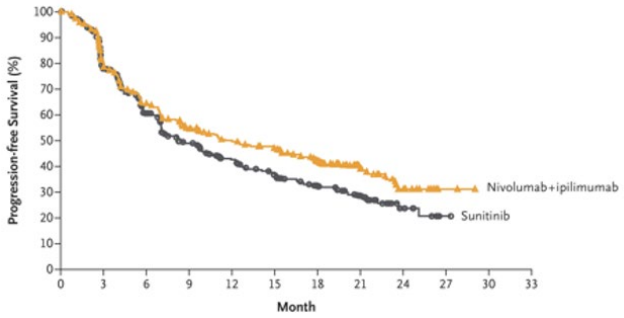


Source: Credit Suisse Healthcare Database

Time on treatment

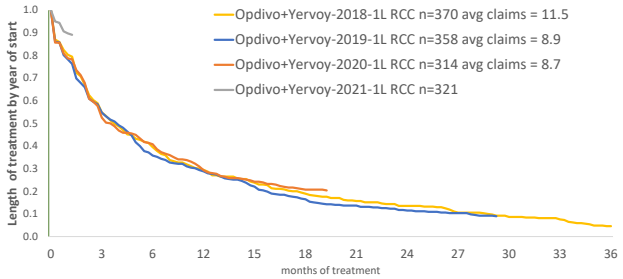
Opdivo + Yervoy in renal cancer vs Checkmate-214

Figure 24: Progression-free survival in Checkmate-214 study of Opdivo + Yervoy in 1L RCC



Source: Company data

Figure 25: Opdivo + Yervoy in 1L RCC real-world time on therapy based on the Credit Suisse Healthcare Database



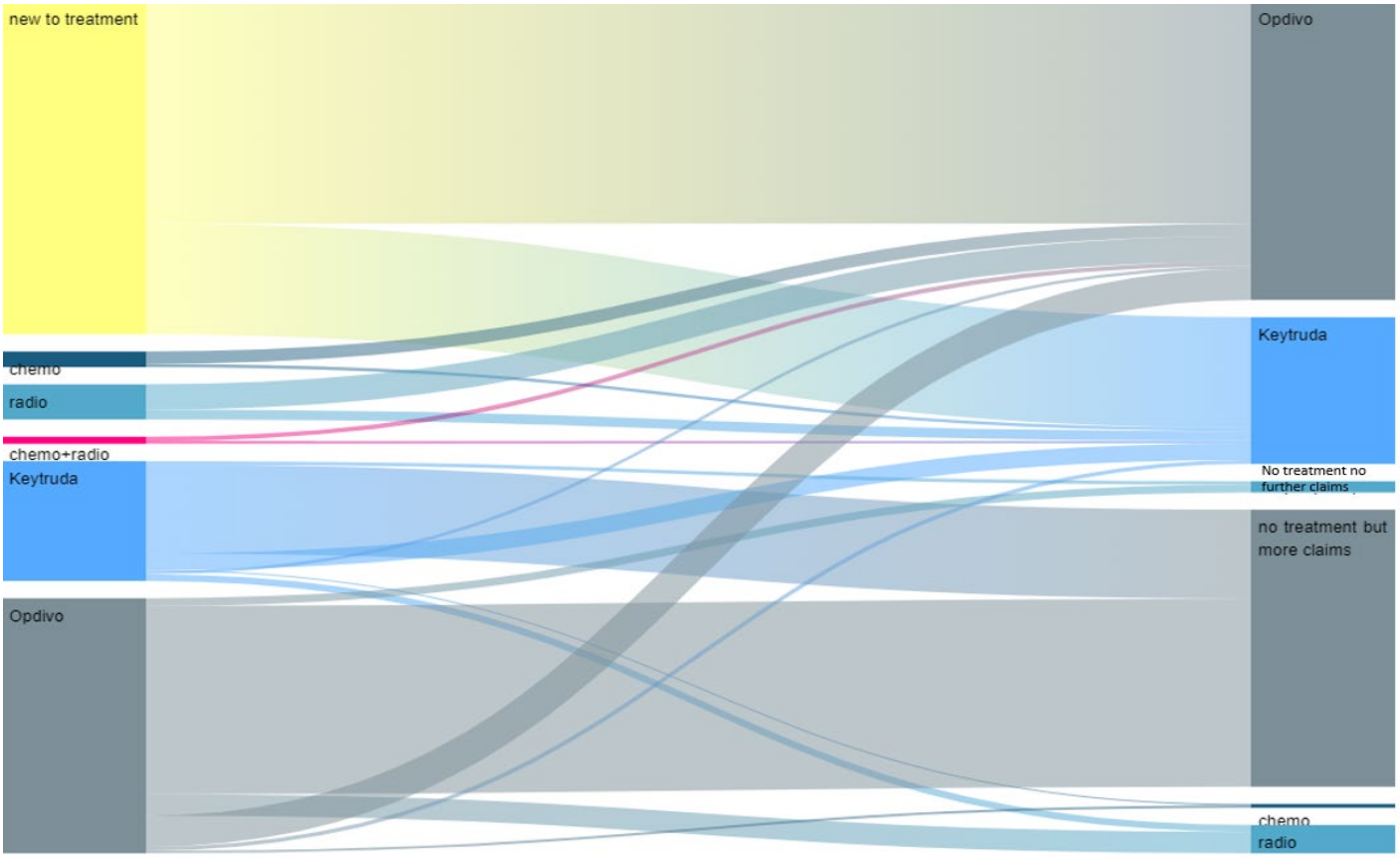
Source: Credit Suisse Healthcare Database

“Our data shows Keytruda appears to be gaining market share in the new melanoma patient starts over time.

Patient journeys in melanoma

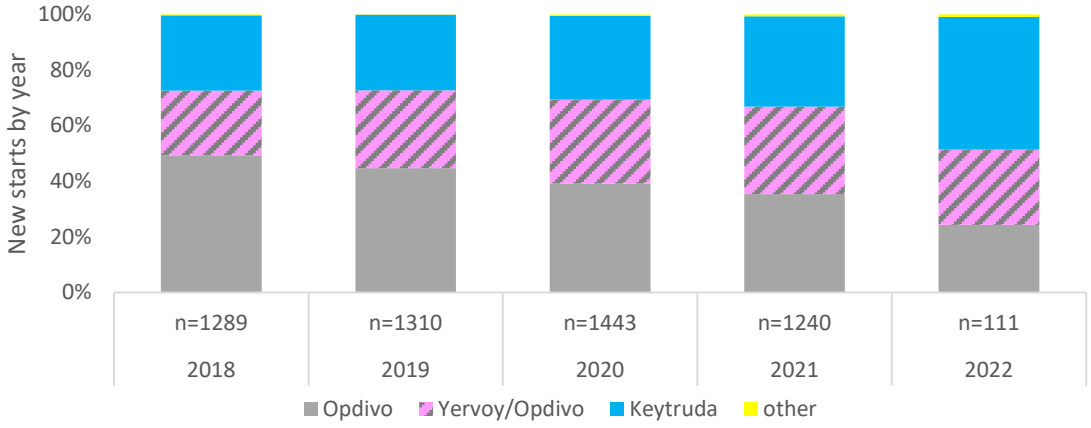
In Figure 26, we highlight transitions into PD-(L)1 drugs for melanoma and away from them after initial treatment cycles. We have excluded Yervoy to avoid double counting. However, in Figure 27, where we look at new patient starts, we have shown Opdivo and Opdivo Yervoy patients separately. Please note the small cohort of 2022 patients n=111 against n=1,300-1,400 in each of the previous years. Keytruda appears to be gaining share in this setting.

Figure 26: Melanoma transitions in 2019-21 (excluding small numbers of Bavencio/Libtayo/Tecentriq) and ignoring Yervoy to avoid double counting Opdivo patients



Source: Credit Suisse Healthcare Database

Figure 27: Share of new patient starts in melanoma



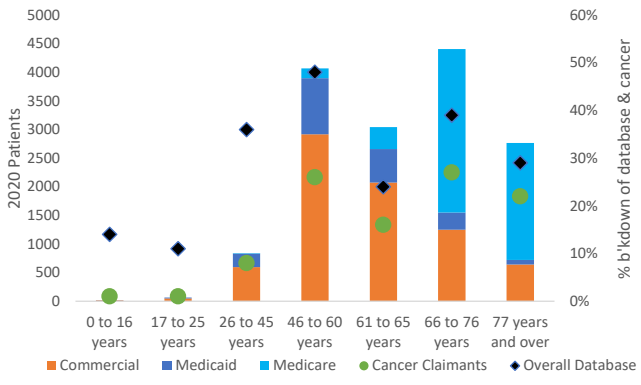
Source: Credit Suisse Healthcare Database

“We see no difference in access to drugs for commercial or government funding channels, and length of treatment is comparable, suggesting no differential financial pressures reducing compliance.

Funding of immuno-oncology drugs

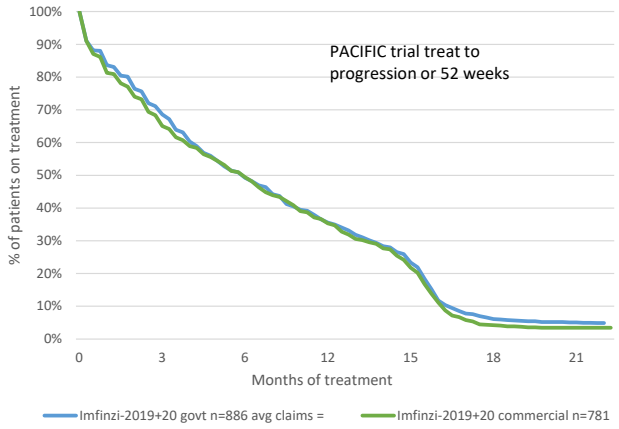
- Our overall database in 2021 covered some 123m subscribers for whom we have information on age cohort and funding status. In this database, 19% of subscribers are over 65 and 6% of the overall database is funded by Medicare, with a further 4% funded by Medicaid.
- We see 710,000 subscribers with cancer-related claims in the database. Of these, 38% are for Medicare, 8% for Medicaid and 54% are commercial funding. Of these patients, 64% are over the age of 60.
- Looking specifically at PD-(L)1 drugs, we see 15,000 claimants in 2020 and because of the lag of data, only 9,740 for 2021. In 2020, 47% of claimants were over the age of 65, and 36% of these claimants were funded by Medicare with a further 14% funded by Medicaid and 50% commercially.
- We therefore see no meaningful difference in sources of funding, suggesting that patients are accessing these drugs when required, irrespective of funding status.
- Looking at data for Imfinzi in the PACIFIC setting as an example, we also see no difference between the length of time on treatment for 886 patients who started treatment in 2019 and 2020 and were funded by government channels (Medicare or Medicaid), and 781 who were commercially funded.

Figure 28: Overall PD(L)1 funding by age cohort against a background of the overall CS Healthcare Database subscribers and cancer patients



Source: Credit Suisse Healthcare Database

Figure 29: A comparison of length of treatment in the PACIFIC setting with Imfinzi by government or commercial funding



Source: Credit Suisse Healthcare Database

“Across most indications, we see Keytruda as the dominant brand of choice as reflected in the highest proportion of claims.

Immuno-oncology drug share by indication

- In addition to looking at claims by drug, we can also look at the number of claims by indication, which gives us crude implied market shares in different disease areas. Across most indications, we see Keytruda as the dominant brand of choice, as reflected in the highest proportion of claims.
- In Figure 30, we highlight the patient starts by drug and indication for 2021. We have shaded in green where each drug has a current indication. In this analysis, we have lumped all lung cancers together and so a blanket shading of all the lung patient numbers is not fully accurate, as most drugs have limited indications by type and by stage of disease. We do not have similarly granular information on a patient's disease just using the ICD-10 diagnosis codes on claims.
- We highlight all tumours for Keytruda as potentially "on-label" as uniquely Keytruda has a pan-tumour indication for Microsatellite Instability-High (MSI-H) disease. Based on our individual drug profiles, we believe that 30-40% of claims could be classified as off-label, but that around half of these are likely to be used on metastatic settings (e.g., brain and bone), which will be based on underlying approved tumour settings. The breast indication for Tecentriq was withdrawn in August 2021 and is highlighted accordingly in orange.
- In the individual drug profiles, we provide more detail, highlighting the number of patients starting treatment by indication, the average number of claims, average duration of treatment and dosing interval.

Figure 30: 2021 patient starts. One treatment cycle based on treatment until 30-week break in treatment

	Bavencio	Imfinzi	Keytruda	Libtayo	Opdivo	Tecentriq	Yervoy	Total
Lung	**20**	**789**	**2358**	**18**	**599**	**690**	**300**	**4774**
Blood		**3**	**110**	**9**	**85**	**7**	**11**	**225**
Leukemia		1	19	4	16	2	4	46
Lymphoma		1	76	4	61	4	5	151
Myeloma		1	10	1	7	1	2	22
Breast	**3**	**10**	**592**		**17**	**90**	**7**	**719**
Gastrointestinal	**4**	**6**	**659**	**2**	**581**	**35**	**49**	**1336**
Other			2		2		2	6
Biliary	1		6		2	1	1	11
Colorectal	2	3	281	1	127	23	37	474
Esophageal		1	190		241	1	1	434
Gastric		1	139		181	1		322
Pancreatic	1	1	30		16	9	4	61
Genitourinary	**116**	**9**	**752**	**3**	**490**	**61**	**226**	**1657**
Bladder	101	5	357	1	64	46	7	581
Renal	15	4	384	1	422	14	217	1057
Gynaecological	**1**	**1**	**447**	**1**	**26**	**6**	**10**	**492**
Cervical			105	1	3	1	3	113
Endometrial	1		261		9	1	3	275
Ovarian		1	62		5	4	1	73
Head and Neck	**3**	**114**	**680**	**33**	**173**	**62**	**44**	**1109**
Liver	**5**	**27**	**382**	**1**	**272**	**342**	**98**	**1127**
Skin	**5**	**5**	**442**	**138**	**648**	**11**	**341**	**1590**
Cutaneous Squamous/Basal Cell		3	77	136	26	4	5	251
Melanoma		2	336	1	616	6	335	1296
Merkel Cell	5		29	1	6	1	1	43
Other	**42**	**134**	**2299**	**55**	**1190**	**534**	**621**	**4875**
Adrenal		2	97	1	45	17	18	180
Bone	11	37	799	5	292	202	153	1499
Brain	3	48	430	3	198	117	124	923
Mesothelioma			17		73		64	154
Nervous system		1	17	3	16	2	8	47
Neuroendocrine	3	11	30		29	55	19	147
Soft tissue		1	53	2	29	2	18	105
Abdomen		1	6		1			8
Unknown	**8**	**42**	**563**	**20**	**222**	**73**	**53**	**756**
Total	**207**	**1137**	**9174**	**271**	**4218**	**1904**	**1749**	**18660**

Note: Green shading indicates where a drug has the indication on its current label. Pale green for Keytruda represents the pan MSI-high tumour approval. The orange shading for Tecentriq in breast indicates the recent withdrawal from the market in this setting.
Source: Credit Suisse Healthcare Database

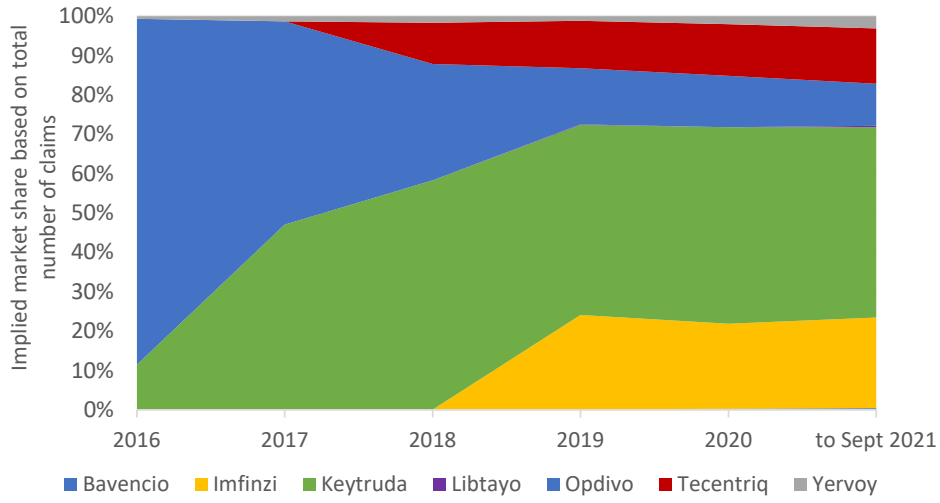
Lung

In lung cancer, we see Keytruda (in green in Figure 31) taking the lion's share of the market (c50% of claims), as expected, given the strength of the clinical data across settings in NSCLC (despite a lack of label in small-cell lung cancer). Imfinzi claims (in yellow in Figure 31) represent almost a quarter of lung cancer claims in our 2021 dataset (up to September 2021). Opdivo use in 2L lung cancer has declined relatively as I-O has become the standard of care in 1L setting. Tecentriq shows small YoY increases in market share of claims to c14% in 2021, likely driven by 1L approval in combo with Avastin and could benefit further in the future by uptake in an adjuvant PD-L1+ setting (approved in October 2021).

Breast

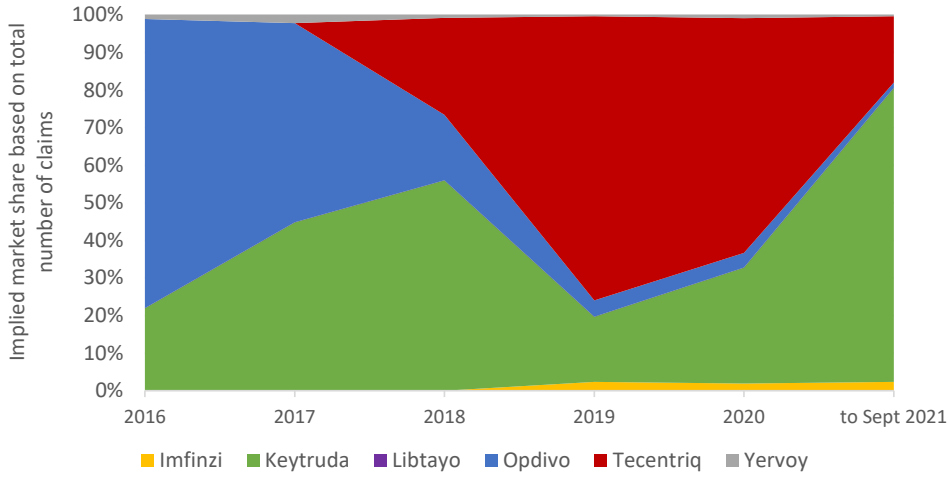
In **breast cancer**, we see Keytruda as becoming the dominant PD-1 therapy by 2021, driven by its broader label in PD-L1+ metastatic breast cancer with a choice of chemo (and Tecentriq withdrawal), as well as a recent approval in high-risk neoadjuvant TNBC (approved in July 2021).

Figure 31: Implied PD(L)1 market share in lung cancer based on total claims



Source: Credit Suisse Healthcare Database

Figure 32: Implied PD(L)1 market share in breast cancer based on total claims



Source: Credit Suisse Healthcare Database

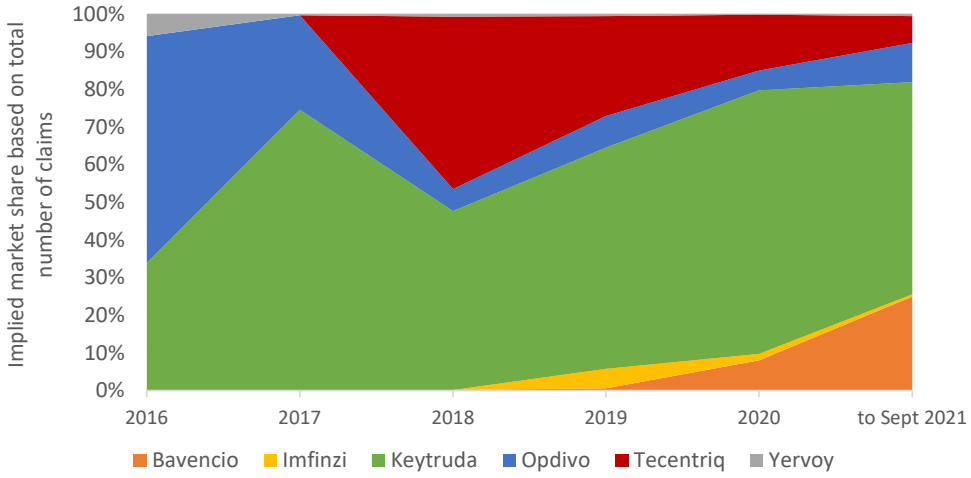
Bladder

In **bladder cancer,** we note the increasing penetration of Bavencio claims, reaching 11% of the total bladder cancer PD-(L)1 claims in our database in 2021, driven by growth of use in its unique 1L maintenance bladder cancer setting where competing PD-(L)1 molecules are not indicated. Keytruda is the dominant player by market share, while Tecentriq's share is in decline following the withdrawal of its FDA label on negative overall survival data.

Liver

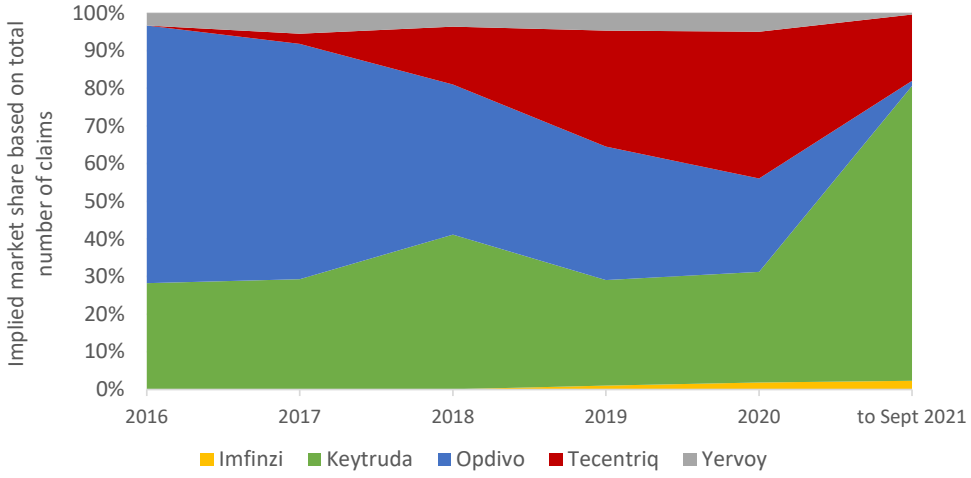
Keytruda is again the dominant PD-(L)1, with a step-up to close to 80% of claims in 2021 in HCC.

Figure 33: Implied PD(L)1 market share in bladder cancer based on total claims



Source: Credit Suisse Healthcare Database

Figure 34: Implied PD(L)1 market share in liver cancer based on total claims



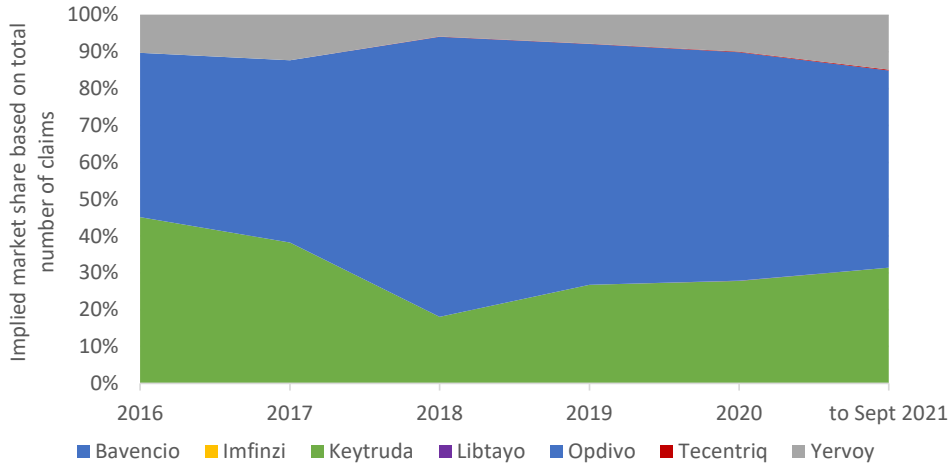
Source: Credit Suisse Healthcare Database

Melanoma

Renal

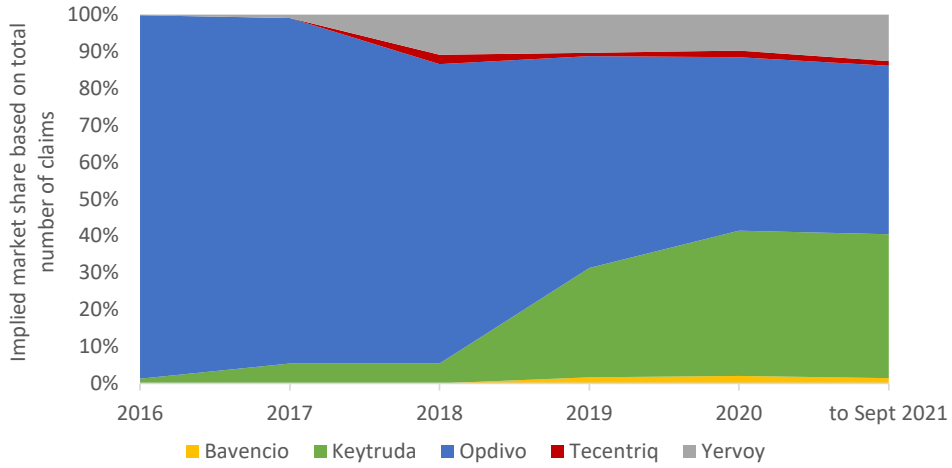
The one indication where Keytruda does not appear to have leading market share is **renal cell cancer**, where Opdivo is the clear favoured treatment with close to 50% share of the claims in our database by 2021, likely reflecting the strong data in 1L with both Yervoy and TKI Cabometyx.

Figure 35: Implied PD(L)1 market share in melanoma cancer based on total claims



Source: Credit Suisse Healthcare Database

Figure 36: Implied PD(L)1 market share in kidney cancer based on total claims

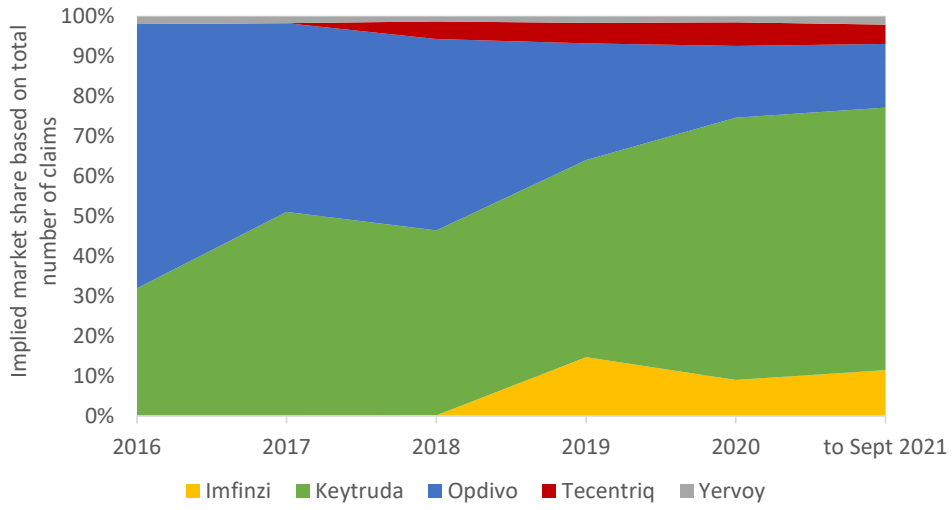


Source: Credit Suisse Healthcare Database

Head and neck

Keytruda is again the dominant PD-(L)1, with c65% share in head and neck by September 2021.

Figure 37: Implied PD(L)1 market share in head and neck cancer based on total claims



Source: Credit Suisse Healthcare Database

“Our database shows 20-30% of PD-(L)1 drug use occurs in tumour types where the drugs are not currently approved by FDA (known as “off label use”).

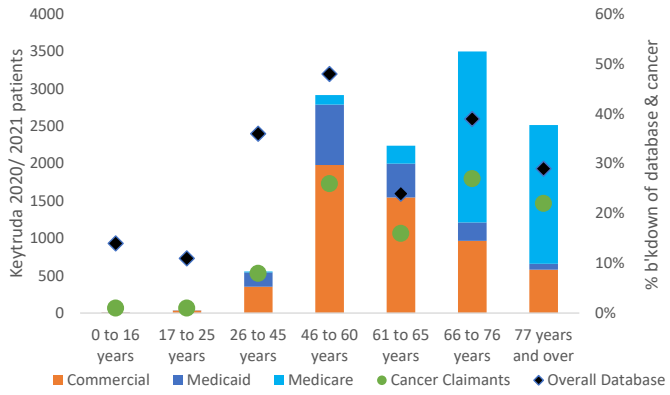
Drug profiles

Indication and funding status

Keytruda

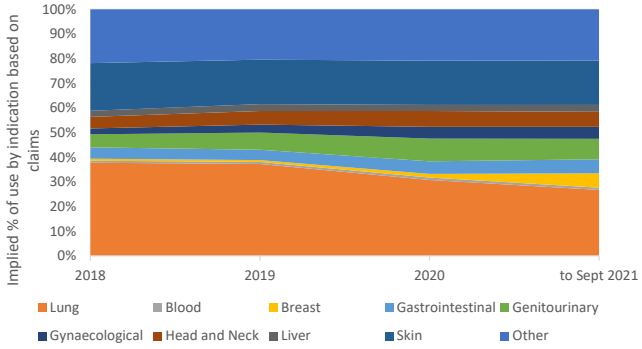
- Keytruda (pembrolizumab) is a PD-1 inhibitor marketed by Merck & Co. It first came to the market in September 2014 and has since been approved in a wide range of solid tumour indications, both as monotherapy and in combination with other agents. It is the top-selling drug in its class, with $17.2bn worldwide sales in 2021. Evaluate consensus has this growing to >$30bn by 2028. The patent expiry is December 2028.
- US drug sales in 2021 were $9.8bn.
- In, Figure 40 we highlight the key indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. We caveat this by noting that the diagnosis codes we use to classify patients do not distinguish between primary and secondary tumours and some apparent off-label use will likely be reflecting metastatic disease. Based solely on the clear on-label use, we see c68% of 2020 use as directly "on-label". If we add in the brain and bone as likely secondaries, we see only 13% of apparent off-label use. For Keytruda, there is an additional pan-tumour indication of metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumours that have progressed following prior treatment as well as for those patients who have no satisfactory alternative treatment options in 1L. This indication was approved in the US in 2017 and is the first tumour-agnostic approval. Although this suggests that a relatively small proportion of Keytruda claims today are truly off-label, the dominance of the drug overall means that in small indications not currently indicated for any PD(L)1 drug, Keytruda is still likely to have a high market share.

Figure 38: Overall funding for Keytruda in 2020/2021: c46% commercial, c15% Medicaid and c38% Medicare



Source: Credit Suisse Healthcare Database

Figure 39: Keytruda use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 40: Uses of Keytruda by indication over time, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Keytruda	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
Row Labels	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**1800**	**2485**	**2553**	**2358**	**10.0**	**9.0**	**8.0**	**31.8**	**29.5**	**25.3**	**3.2**	**3.3**	**3.2**
Unknown	2	11	8	9	3.0	1.5	2.9	6.0	2.0	6.9	2.0	1.4	2.4
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC	937	1065	1131	1070	9.9	8.6	7.2	31.5	28.7	23.4	3.2	3.3	3.3
1L NSCLC (all comers)	741	1027	1008	903	10.7	9.6	9.0	33.3	31.2	27.7	3.1	3.2	3.1
1L NSCLC (all comers), 1L NSCLC PD-L1+					-	-	-	-	-	-	-	-	-
1L sq NSCLC	120	382	406	376	7.9	8.7	7.8	25.9	28.1	25.2	3.3	3.2	3.2
Blood	**78**	**82**	**103**	**110**	**5.3**	**6.1**	**6.7**	**18.8**	**23.9**	**19.9**	**3.6**	**3.9**	**3.0**
Leukemia	17	21	25	19	4.4	5.0	4.2	19.8	21.9	13.9	4.5	4.4	3.3
Lymphoma	53	56	68	76	6.1	6.6	8.4	21.0	24.4	24.3	3.5	3.7	2.9
Myeloma	7	5	9	10	1.7	5.0	2.1	2.4	27.6	5.3	1.4	5.5	2.5
Breast	**68**	**75**	**153**	**592**	**5.6**	**5.6**	**6.3**	**18.4**	**18.9**	**21.8**	**3.3**	**3.4**	**3.5**
Gastrointestinal	**315**	**424**	**546**	**659**	**7.0**	**6.0**	**6.2**	**22.9**	**20.6**	**18.9**	**3.3**	**3.4**	**3.1**
Biliary	4	6	3	6	4.8	5.8	11.3	7.3	21.5	35.7	1.5	3.7	3.1
Colorectal	142	153	239	281	9.2	7.5	7.0	30.7	27.6	21.9	3.4	3.7	3.1
Esophageal	76	131	147	190	5.5	5.1	5.3	14.9	16.2	15.8	2.7	3.2	3.0
Gastric	65	102	116	139	4.3	4.7	6.5	13.2	14.2	19.0	3.0	3.0	2.9
Pancreatic	20	23	34	30	5.4	7.7	3.8	20.4	24.1	11.9	3.8	3.1	3.1
Bladder	**240**	**254**	**377**	**357**	**8.8**	**6.7**	**7.2**	**26.0**	**20.7**	**21.9**	**2.9**	**3.1**	**3.0**
Renal	**50**	**248**	**361**	**384**	**7.8**	**9.9**	**9.3**	**22.6**	**33.4**	**29.9**	**2.9**	**3.4**	**3.2**
1L RCC	1	179	240	202	25.0	12.6	11.7	75.0	41.7	37.0	3.0	3.3	3.2
Adjuvant / 1L RCC	45	73	123	189	8.1	4.8	6.6	23.3	16.8	20.7	2.9	3.5	3.2
2L RCC					-	-	-	-	-	-	-	-	-
Gynaecological	**124**	**240**	**451**	**447**	**9.0**	**8.1**	**7.0**	**31.0**	**25.4**	**21.4**	**3.4**	**3.1**	**3.0**
Cervical	39	74	99	105	6.6	7.8	5.7	19.6	26.4	18.3	2.9	3.4	3.2
Endometrial	55	126	267	261	11.5	8.9	7.9	39.7	28.0	23.8	3.4	3.2	3.0
Ovarian	27	30	67	62	8.3	5.8	5.6	33.0	14.8	15.5	4.0	2.5	2.8
Head and Neck	**358**	**543**	**702**	**680**	**6.2**	**6.1**	**6.0**	**21.2**	**20.6**	**20.0**	**3.4**	**3.4**	**3.3**
Liver	**208**	**288**	**384**	**382**	**5.8**	**5.8**	**4.3**	**19.4**	**19.3**	**14.5**	**3.3**	**3.3**	**3.4**
Skin	**287**	**347**	**413**	**442**	**8.6**	**9.4**	**8.3**	**29.3**	**30.9**	**28.4**	**3.4**	**3.3**	**3.4**
Melanoma	224	270	324	336	8.7	10.0	8.5	29.8	33.0	29.3	3.4	3.3	3.4
Merkel Cell	23	30	32	29	11.0	12.2	7.8	36.4	37.7	26.6	3.3	3.1	3.4
cSSC/Basal Cell	40	47	57	77	6.3	4.3	7.4	22.3	14.9	24.6	3.6	3.4	3.4
Other	**1489**	**1951**	**2340**	**2299**	**6.2**	**5.5**	**5.1**	**22.4**	**20.1**	**18.0**	**3.6**	**3.6**	**3.5**
Adrenal	84	95	110	97	6.4	6.1	5.3	24.5	22.1	18.7	3.8	3.6	3.6
Bone	537	715	840	799	6.0	5.5	4.9	22.3	20.0	17.3	3.7	3.7	3.6
Brain	292	429	475	430	6.9	6.0	5.9	26.8	22.1	21.5	3.9	3.7	3.6
Mesothelioma	28	28	33	17	12.6	5.4	7.6	38.9	16.4	18.1	3.1	3.1	2.4
Nervous system	15	27	20	17	4.7	3.7	3.7	13.8	11.3	10.3	2.9	3.1	2.8
Neuroendocrine	29	37	38	30	5.1	7.3	4.1	16.0	23.7	13.3	3.1	3.2	3.2
Unknown	**243**	**290**	**438**	**464**	**4.8**	**4.8**	**4.3**	**14.8**	**15.4**	**13.4**	**3.1**	**3.2**	**3.1**
Grand Total	**5260**	**7227**	**8821**	**9174**	**7.8**	**7.3**	**6.5**	**25.8**	**24.4**	**21.4**	**3.3**	**3.4**	**3.3**

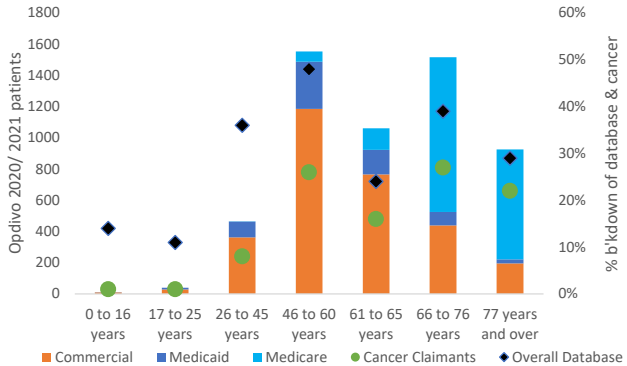
Green shading represents on-label use as of May 2022 but note the pan-tumour indication of MSI-H was on-label from 2017.

Source: Credit Suisse Healthcare Database

Opdivo

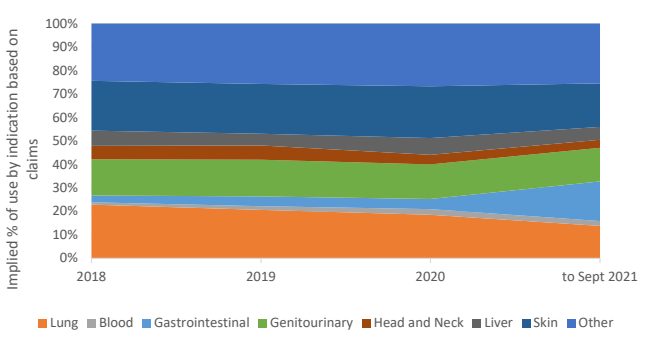
- Opdivo (nivolumab) is a PD-1 inhibitor marketed by Bristol Myers Squibb. It first came to the market in December 2014 and has since been approved in a wide range of solid tumour indications, both as monotherapy and in combination with other agents. It is the second-highest-selling drug in its class, with $8.6bn worldwide sales in 2021. Evaluate consensus forecasts sales to grow to >$15bn by 2028. The patent expiry is December 2028.
- US drug sales in 2021 were $4.2bn.
- In Figure 42 and Figure 43, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. We caveat this by noting that the diagnosis codes we use to classify patients do not distinguish between primary and secondary tumours, and some apparent off-label use will likely be reflecting metastatic disease. Based solely on the clear on-label use, we see c60% of use as directly "on-label".
- Opdivo has the second-highest commercial funding (54%), a little behind its sister drug Yervoy (58%), against an overall average of 50%.

Figure 41: Overall funding for Opdivo in 2020/2021: c54% commercial, c12% Medicaid and c34% Medicare



Source: Credit Suisse Healthcare Database

Figure 42: Opdivo use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 43: Uses of Opdivo by indication over time, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Opdivo	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**1158**	**841**	**695**	**599**	**7.9**	**7.9**	**7.7**	**21.8**	**24.4**	**23.2**	**2.8**	**3.1**	**3.0**
Unknown	946	622	420	303	8.3	8.7	7.8	22.1	25.6	24.7	2.7	2.9	3.1
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC	212	219	258	229	6.2	5.4	7.3	20.7	21.2	20.5	3.3	3.9	2.8
1L NSCLC (all comers)					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers), 1L NSCLC PD-L1+			17	67	-	-	9.6	-	-	29.2	-	-	3.0
1L sq NSCLC					-	-	-	-	-	-	-	-	-
Blood	**63**	**70**	**82**	**85**	**5.8**	**8.8**	**7.9**	**15.7**	**27.5**	**23.5**	**2.7**	**3.1**	**3.0**
Leukemia	13	9	7	16	3.0	3.8	3.6	10.2	16.6	11.3	3.4	4.4	3.2
Lymphoma	41	54	68	61	7.5	10.3	9.0	20.1	31.2	27.0	2.7	3.0	3.0
Myeloma	8	7	5	7	1.9	4.1	1.6	3.6	12.9	2.6	1.9	3.1	1.6
Breast	**33**	**23**	**24**	**17**	**3.6**	**4.6**	**5.1**	**10.1**	**22.3**	**17.5**	**2.8**	**4.9**	**3.5**
Gastrointestinal	**166**	**168**	**203**	**581**	**7.1**	**7.9**	**6.2**	**21.9**	**25.4**	**18.2**	**3.1**	**3.2**	**3.0**
Biliary	1	4	1	2	11.0	2.8	6.0	43.0	6.8	6.0	3.9	2.5	1.0
Colorectal	127	123	126	127	7.9	9.0	6.7	24.1	28.4	19.5	3.1	3.2	2.9
Esophageal	14	12	34	241	5.4	7.3	4.5	18.2	16.8	13.2	3.4	2.3	2.9
Gastric	8	13	21	181	4.4	5.8	6.2	8.1	26.0	15.5	1.9	4.5	2.5
Pancreatic	11	6	8	16	2.2	4.8	5.4	7.7	8.8	20.4	3.5	1.8	3.8
Bladder	**33**	**36**	**39**	**64**	**7.9**	**6.8**	**5.2**	**25.6**	**23.4**	**15.7**	**3.2**	**3.5**	**3.0**
Renal	**537**	**507**	**429**	**422**	**11.0**	**9.4**	**9.3**	**33.0**	**31.4**	**29.3**	**3.0**	**3.3**	**3.1**
1L RCC	370	358	314	321	11.5	9.0	8.7	34.4	30.7	27.1	3.0	3.4	3.1
adjuvant / 1L RCC					-	-	-	-	-	-	-	-	-
2L RCC	176	155	123	105	10.8	11.0	11.0	31.4	34.1	34.8	2.9	3.1	3.1
Gynaecological	**24**	**37**	**35**	**26**	**4.4**	**5.4**	**3.9**	**11.8**	**19.1**	**12.9**	**2.7**	**3.5**	**3.3**
Cervical	1	4	8	3	-	3.5	4.0	-	13.5	20.6	-	3.9	5.2
Endometrial	3	10	6	9	1.3	4.7	5.5	2.7	16.5	14.2	2.0	3.5	2.6
Ovarian	10	12	13	5	4.3	5.1	2.4	8.0	19.5	6.8	1.9	3.8	2.8
Head and Neck	**327**	**277**	**197**	**173**	**7.1**	**7.1**	**5.9**	**22.1**	**22.6**	**19.3**	**3.1**	**3.2**	**3.3**
Liver	**354**	**319**	**333**	**272**	**7.3**	**5.1**	**6.2**	**20.6**	**17.4**	**19.5**	**2.8**	**3.4**	**3.1**
Skin	726	729	725	648	11.8	9.3	8.8	35.7	29.8	29.0	3.0	3.2	3.3
Melanoma	689	691	688	616	12.0	9.5	9.0	36.5	30.4	29.6	3.0	3.2	3.3
Merkel Cell	4	5	6	6	12.0	14.0	7.5	42.5	39.8	29.7	3.5	2.8	4.0
cSSC/Basal Cell	33	33	31	26	7.2	4.8	3.5	18.8	15.8	13.5	2.6	3.3	3.9
Other	**1397**	**1286**	**1143**	**1190**	**6.1**	**5.5**	**5.7**	**20.4**	**20.0**	**19.8**	**3.3**	**3.6**	**3.5**
Adrenal	75	52	42	45	5.9	5.5	4.5	19.9	19.6	18.0	3.4	3.6	4.0
Bone	429	364	299	292	6.3	5.4	5.7	19.9	21.0	20.0	3.2	3.9	3.5
Brain	283	243	202	198	5.3	5.7	6.4	18.0	19.6	23.2	3.4	3.4	3.6
Mesothelioma	9	16	38	73	10.2	12.1	8.5	30.4	27.2	21.2	3.0	2.2	2.5
Nervous system	19	9	14	16	8.9	7.4	2.3	27.5	24.2	4.7	3.1	3.3	2.1
Neuroendocrine	45	38	35	29	6.4	6.1	5.4	18.3	18.9	14.9	2.9	3.1	2.7
Unknown	**216**	**195**	**176**	**141**	**4.8**	**4.4**	**4.9**	**14.3**	**14.3**	**15.7**	**3.0**	**3.2**	**3.2**
Grand Total	**5034**	**4488**	**4081**	**4218**	**8.0**	**7.2**	**7.0**	**24.1**	**23.8**	**22.7**	**3.0**	**3.3**	**3.2**

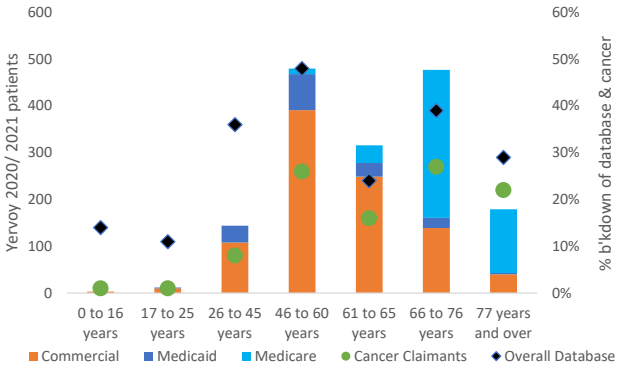
Green shading represents on-label use as of May 2022.

Source: Credit Suisse Healthcare Database

Yervoy

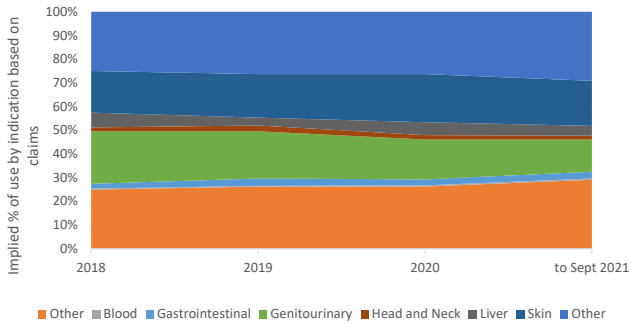
- Yervoy (ipilimumab) is a CTLA-4 inhibitor marketed by Bristol Myers Squibb. It first came to the market in September 2014 and has since been approved in a range of solid tumour settings in combination with Opdivo, such as melanoma, RCC and lung cancer. It is the highest-selling drug in its class, with $2.0bn worldwide sales in 2021. Evaluate consensus forecasts sales peaking at $2.6bn in 2024. The patent expiry is March 2025.
- US sales were $1.3bn in 2021.
- In Figure 45 and Figure 46, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. Based solely on the clear on-label use, we see c60% of use as directly "on-label", but allowing for use in bone and brain as likely secondaries, we see c24% off-label use. As Yervoy is used only for a limited period alongside Opdivo, we are not surprised to see just 2-3 cycles of treatment over 6-8 weeks of treatment.
- Yervoy has the highest level of commercial funding in our database (58% against an average of only 50% for all of the PD-(L)1 drugs).

Figure 44: Overall funding for Yervoy in 2020/2021: c58% commercial, c10% Medicaid and c31% Medicare



Source: Credit Suisse Healthcare Database

Figure 45: Yervoy use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 46: Uses of Yervoy by indication over time, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Yervoy	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**211**	**227**	**284**	**300**	**2.4**	**2.3**	**2.9**	**5.0**	**4.8**	**8.8**	**2.1**	**2.1**	**3.0**
Unknown	211	227	284	300	2.4	2.3	2.9	5.0	4.8	8.8	2.1	2.1	3.0
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers)					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers), 1L NSCLC PD-L1+					-	-	-	-	-	-	-	-	-
1L sq NSCLC					-	-	-	-	-	-	-	-	-
Blood	**7**	**5**	**8**	**11**	**2.4**	**2.0**	**3.4**	**5.0**	**3.6**	**9.4**	**2.1**	**1.8**	**2.8**
Leukemia	3		2	4	2.3	-	5.0	4.0	-	21.5	1.7	-	4.3
Lymphoma	3	3	4	5	3.0	2.7	3.5	7.3	5.3	7.0	2.4	2.0	2.0
Myeloma	1	2	1	2	-	1.0	-	-	1.0	-	-	-	-
Breast	**3**	**4**	**6**	**7**	**1.7**	**2.0**	**4.3**	**4.7**	**4.3**	**16.7**	**2.8**	**2.1**	**3.8**
Gastrointestinal	37	57	50	49	1.9	2.4	2.5	3.8	6.3	5.4	2.0	2.6	2.2
Biliary		1	1	1	-	2.0	6.0	-	6.0	6.0	-	3.0	1.0
Colorectal	31	44	34	37	2.1	2.6	2.6	4.4	7.1	5.2	2.1	2.8	2.0
Esophageal		2	2	1	-	1.5	1.0	-	1.0	1.0	-	-	-
Gastric		1	5		-	2.0	2.6	-	3.0	10.0	-	1.5	3.8
Pancreatic	4	3	3	4	1.3	1.7	2.3	1.0	3.3	6.0	-	2.0	2.6
Bladder	**5**	**5**	**4**	**7**	**5.8**	**3.0**	**1.5**	**20.2**	**6.0**	**2.3**	**3.5**	**2.0**	**1.5**
Renal	239	284	264	217	3.3	3.0	3.1	6.8	7.0	7.2	2.1	2.3	2.3
1L RCC					-	-	-	-	-	-	-	-	-
adjuvant / 1L RCC					-	-	-	-	-	-	-	-	-
2L RCC					-	-	-	-	-	-	-	-	-
Gynaecological	8	12	11	10	1.6	2.0	2.2	4.5	3.4	4.9	2.8	1.7	2.3
Cervical		**1**	**2**	**3**	**-**	**2.0**	**2.0**	**-**	**-**	**7.0**	-	-	**3.5**
Endometrial	2	4		3	1.0	1.5	-	1.0	1.0	-	-	-	-
Ovarian	4	3	7	1	2.0	2.0	2.4	7.5	4.7	5.1	3.8	2.3	2.1
Head and Neck	25	49	45	44	2.4	2.1	2.1	4.9	4.0	4.6	2.0	1.9	2.2
Liver	90	71	115	98	2.5	2.1	2.4	5.7	4.8	5.3	2.3	2.3	2.3
Skin	224	292	346	341	2.9	2.7	2.9	7.0	6.5	6.5	2.4	2.4	2.2
Melanoma	220	288	339	335	2.9	2.7	2.9	7.1	6.5	6.5	2.4	2.4	2.2
Merkel Cell	1	1	1	1	2.0	3.0	3.0	5.0	6.0	12.0	2.5	2.0	4.0
cSSC/Basal Cell	3	3	6	5	1.3	2.0	2.3	1.7	3.7	5.0	1.3	1.8	2.1
Other	**399**	**512**	**527**	**621**	**2.3**	**2.2**	**2.5**	**5.1**	**5.0**	**6.6**	**2.2**	**2.2**	**2.7**
Adrenal	27	18	17	18	2.1	2.1	2.2	4.1	4.8	5.5	2.0	2.3	2.4
Bone	114	146	128	153	2.4	2.0	2.2	5.0	4.3	5.4	2.0	2.1	2.4
Brain	72	100	109	124	1.9	2.1	2.4	3.5	4.4	6.3	1.9	2.0	2.6
Mesothelioma	1	6	32	64	-	4.3	3.9	-	20.0	17.6	-	4.6	4.5
Nervous system	1	3	8	8	2.0	1.3	1.8	10.0	1.7	3.3	5.0	1.3	1.9
Neuroendocrine	19	18	24	19	2.8	2.2	2.8	9.3	4.8	12.3	3.3	2.2	4.4
Unknown	**36**	**44**	**40**	**44**	**2.2**	**2.4**	**2.7**	**4.7**	**3.6**	**7.6**	**2.2**	**1.5**	**2.9**
Grand Total	**1284**	**1562**	**1700**	**1749**	**2.6**	**2.5**	**2.7**	**5.8**	**5.6**	**6.9**	**2.2**	**2.3**	**2.5**

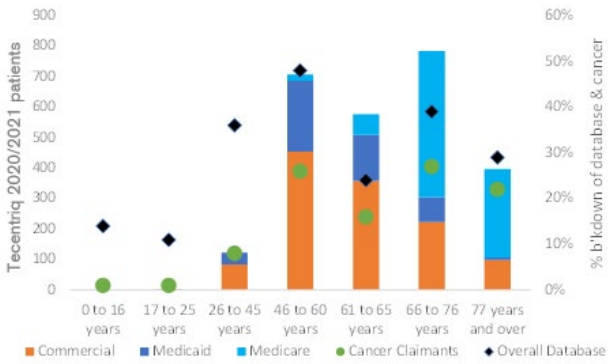
Green shading represents on-label use as of May 2022.

Source: Credit Suisse Healthcare Database

Tecentriq

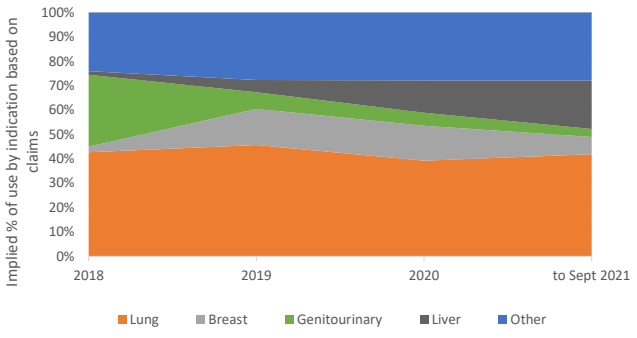
- Tecentriq (atezolizumab) is a PD-L1 inhibitor marketed by Roche. It first came to the market in May 2016 and has since been approved in a wide range of solid tumour indications, both as monotherapy and in combination with other agents such as Avastin. It is the third-highest-selling drug in its class, with $3.6bn sales worldwide in 2021. Evaluate consensus forecasts sales to grow to >$8bn by 2028. The patent expiry is June 2032.
- US drug sales in 2021 were $1.8bn.
- In Figure 48 and Figure 49, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. We caveat this by noting that the diagnosis codes we use to classify patients do not distinguish between primary and secondary tumours and some apparent off-label use will likely be reflecting metastatic disease. Based solely on the clear "on-label" use, we see c62% of use as directly "on-label". Allowing for bone and brain metastases suggests closer to 26% "real" off-label use.
- We note apparent shortening of typical treatment cycles and overall treatment duration, although we see stable treatment times and duration in 1L sq NSCLC. We flag the US breast cancer indication withdrawal in August 2021 and the fact that breast cancer appeared to be one of the longer-duration therapies.

Figure 47: Overall funding for Tecentriq in 2020/2021: c47% commercial, c20% Medicaid and c33% Medicare



Source: Credit Suisse Healthcare Database

Figure 48: Tecentriq use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 49: Uses of Tecentriq by indication over time, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing

Tecentriq	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**308**	**714**	**730**	**690**	**10.6**	**7.8**	**7.3**	**32.7**	**24.6**	**21.3**	**3.1**	**3.1**	**2.9**
Unknown	2	11	16	16	1.5	2.9	3.1	2.5	6.5	6.4	1.7	2.3	2.1
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC	15	55	30	18	15.5	11.2	8.4	51.1	35.9	23.9	3.3	3.2	2.9
1L NSCLC (all comers)	239	178	187	187	11.0	7.5	6.7	33.7	21.7	19.7	3.1	2.9	2.9
1L NSCLC (all comers), 1L NSCLC PD-L1+													
1L sq NSCLC	52	470	497	469	7.5	7.7	7.6	23.8	24.9	22.2	3.2	3.2	2.9
Blood	**6**	**6**	**14**	**7**	**1.8**	**5.8**	**2.6**	**5.7**	**17.8**	**12.9**	**3.1**	**3.1**	**4.9**
Leukemia	2	1	4	2	2.0	28.0	4.5	13.0	93.0	30.3	6.5	3.3	6.7
Lymphoma	3	3	7	4	1.3	1.3	2.1	1.7	2.3	5.6	1.3	1.8	2.6
Myeloma	1	1	3	1	3.0	2.0	1.3	3.0	6.0	6.7	1.0	3.0	5.0
Breast	**19**	**190**	**200**	**90**	**9.2**	**9.6**	**9.7**	**26.2**	**22.3**	**22.5**	**2.8**	**2.3**	**2.3**
Gastrointestinal	**16**	**17**	**40**	**35**	**7.1**	**4.8**	**5.4**	**21.8**	**17.8**	**15.3**	**3.1**	**3.7**	**2.8**
Biliary			3	1	-	-	1.7	-	-	5.0	-	-	3.0
Colorectal	15	14	23	23	7.3	4.6	4.7	22.5	18.3	12.8	3.1	4.0	2.7
Esophageal	1	2	5	1	4.0	1.5	2.8	12.0	2.0	8.2	3.0	1.3	2.9
Gastric			2	1	-	-	5.5	-	-	17.0	-	-	3.1
Pancreatic		1	6	9	-	15.0	12.3	-	43.0	36.2	-	2.9	2.9
Bladder	**186**	**99**	**76**	**46**	**11.0**	**7.8**	**7.6**	**35.7**	**24.2**	**22.9**	**3.3**	**3.1**	**3.0**
Renal	**26**	**17**	**19**	**14**	**7.3**	**4.4**	**8.1**	**23.2**	**11.9**	**25.9**	**3.2**	**2.7**	**3.2**
1L RCC													
Adjuvant / 1L RCC													
2L RCC													
Gynaecological	**8**	**5**	**8**	**6**	**9.9**	**4.8**	**5.4**	**26.3**	**10.0**	**14.5**	**2.7**	**2.1**	**2.7**
Cervical		2	4	1	-	2.0	3.0	-	4.5	10.8	-	2.3	3.6
Endometrial	2	1	2	1	6.5	9.0	4.0	20.0	26.0	9.0	3.1	2.9	2.3
Ovarian	6	1	1	4	11.0	-	-	28.3	-	-	2.6	-	-
Head and Neck	**35**	**65**	**92**	**62**	**6.1**	**5.3**	**4.2**	**24.2**	**15.4**	**12.3**	**4.0**	**2.9**	**2.9**
Liver	**23**	**127**	**311**	**342**	**4.9**	**4.9**	**5.8**	**14.8**	**13.5**	**17.0**	**3.0**	**2.8**	**2.9**
Skin	**8**	**3**	**8**	**11**	**7.5**	**2.3**	**2.6**	**26.9**	**13.0**	**6.6**	**3.6**	**5.6**	**2.5**
Melanoma	1	1	5	6	8.0	-	3.2	31.0	-	8.8	3.9	-	2.8
Merkel Cell	1			1	-	-	-	-	-	-	-	-	-
cSSC/Basal Cell	6	2	3	4	8.5	3.0	1.7	30.5	19.0	3.0	3.6	6.3	1.8
Other	**213**	**577**	**689**	**534**	**7.1**	**5.3**	**4.7**	**26.1**	**16.9**	**15.3**	**3.7**	**3.2**	**3.2**
Adrenal	7	25	29	17	14.3	7.6	4.8	62.7	23.8	16.7	4.4	3.1	3.5
Bone	79	209	259	202	5.2	5.1	4.7	18.9	16.2	14.4	3.6	3.2	3.1
Brain	52	143	144	117	8.7	5.6	4.8	28.7	18.4	16.7	3.3	3.3	3.5
Mesothelioma					-	-	-	-	-	-	-	-	-
Nervous system	3	8	7	2	2.3	3.3	3.7	8.3	10.4	17.6	3.6	3.2	4.7
Neuroendocrine	9	70	85	55	7.6	5.6	5.0	24.9	17.0	16.1	3.3	3.0	3.2
Unknown	**23**	**61**	**57**	**67**	**2.9**	**3.4**	**3.6**	**9.6**	**10.3**	**8.6**	**3.3**	**3.0**	**2.4**
Grand Total	**871**	**1881**	**2244**	**1904**	**9.0**	**6.7**	**6.2**	**29.4**	**20.2**	**18.1**	**3.3**	**3.0**	**2.9**

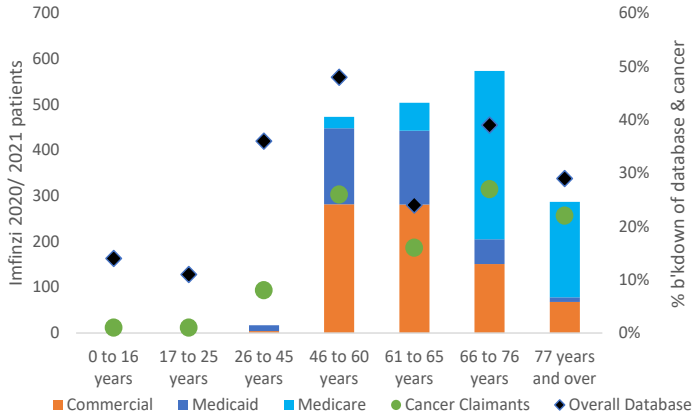
Green shading represents on-label use as of May 2022; orange shading reflects the recent withdrawal from the US market in breast cancer.

Source: Credit Suisse Healthcare Database

Imfinzi

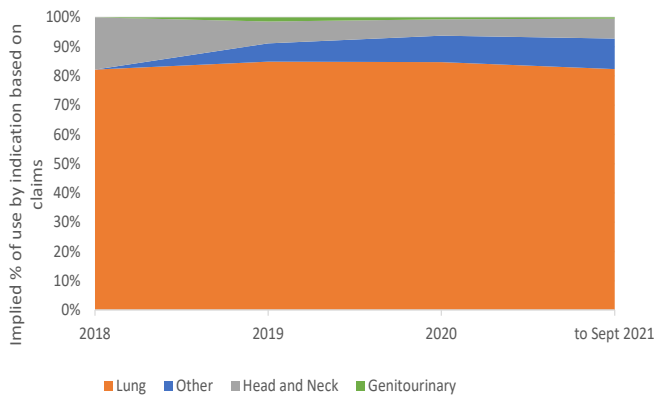
- Imfinzi (durvalumab) is a PD-L1 inhibitor marketed by AstraZeneca. It first came to the market in May 2017 and has since been approved in a handful of solid tumour indications, with the majority of its sales initially coming from the PACIFIC NSCLC setting. It is the fourth-highest-selling drug in its class, with $2.4bn sales worldwide in 2021. Evaluate consensus forecasts sales to grow to c$5bn by 2028. The patent expiry is December 2031.
- US drug sales in 2021 were $1.2bn.
- In Figure 51 and Figure 52, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. We caveat this by noting that the diagnosis codes we use to classify patients do not distinguish between primary and secondary tumours and some apparent off-label use will likely be reflecting metastatic disease. We see c10 claims per treatment over around 24 weeks as having been fairly consistent.
- It is important to note that there is some dosing flexibility with a once-monthly dose introduced in the US in November 2020. We would expect to see an increased dosing interval in 2021, but it was added too late for this data cut.

Figure 50: Overall funding for Imfinzi in 2020/2021: c42% commercial, c21% Medicaid and c35% Medicare



Source: Credit Suisse Healthcare Database

Figure 51: Imfinzi use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 52: Use of Imfinzi by indication, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Imfinzi	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**3**	**977**	**745**	**789**	**7.7**	**11.4**	**11.8**	**26.7**	**26.2**	**28.0**	**3.5**	**2.3**	**2.4**
Unknown			1	3	-	-	2.0	-	-	5.0	-	-	2.5
SCLC		1	53	98	-	5.0	7.6	-	10.0	23.3	-	2.0	3.1
Stage III	3	976	691	688	7.7	11.4	12.2	26.7	26.2	28.3	3.5	2.3	2.3
1L NSCLC (all comers), 1L NSCLC PD-L1+					-	-	-	-	-	-	-	-	-
1L sq NSCLC					-	-	-	-	-	-	-	-	-
Blood		**8**	**10**	**3**	**-**	**4.6**	**6.6**	**-**	**14.5**	**21.6**	**-**	**3.1**	**3.3**
Leukemia		5	5	1	-	5.8	9.0	-	20.4	33.2	-	3.5	3.7
Lymphoma		1	3	1	-	3.0	2.3	-	7.0	5.0	-	2.3	2.1
Myeloma		2	2	1	-	2.5	7.0	-	3.5	17.5	-	1.4	2.5
Breast		**10**	**9**	**10**	**-**	**5.6**	**6.4**	**-**	**18.1**	**24.0**	**-**	**3.2**	**3.7**
Gastrointestinal		**6**	**6**	**6**	**-**	**5.7**	**1.3**	**-**	**20.5**	**1.5**	**-**	**3.6**	**1.1**
Biliary					**-**	**-**	**-**	**-**	**-**	**-**	-	-	-
Colorectal		3	5	3	-	7.0	1.4	-	31.0	1.6	-	4.4	1.1
Esophageal		2	1	1	-	5.5	-	-	12.0	-	-	2.2	-
Gastric		1		1	-	2.0	-	-	6.0	-	-	3.0	-
Pancreatic				1	-	-	-	-	-	-	-	-	-
Bladder		**11**	**5**	**5**	**-**	**13.6**	**13.2**	**-**	**36.8**	**32.6**	**-**	**2.7**	**2.5**
Renal		**3**	**2**	**4**	**-**	**12.7**	**1.0**	**-**	**33.7**	**1.0**	**-**	**2.7**	**-**
1L RCC					-	-	-	-	-	-	-	-	-
Adjuvant / 1L RCC					-	-	-	-	-	-	-	-	-
2L RCC					-	-	-	-	-	-	-	-	-
Gynaecological		**1**	**4**	**1**	**-**	**-**	**5.0**	**-**	**-**	**19.3**	**-**	**-**	**3.9**
Cervical			1		-	-	-	-	-	-	-	-	-
Endometrial			2		-	-	9.0	-	-	37.5	-	-	4.2
Ovarian		1	1	1	-	-	-	-	-	-	-	-	-
Head and Neck	**1**	**117**	**104**	**114**	**5.0**	**8.4**	**5.6**	**31.0**	**23.6**	**15.0**	**6.2**	**2.8**	**2.7**
Liver		**2**	**13**	**27**	**-**	**1.0**	**4.5**	**-**	**1.0**	**17.8**	**-**	**-**	**3.9**
Skin		**5**	**6**	**5**	**-**	**2.4**	**2.2**	**-**	**12.4**	**4.8**	**-**	**5.2**	**2.2**
Melanoma			3	2	-	-	1.3	-	-	2.7		-	2.0
Merkel Cell			1		-	-	6.0	-	-	18.0	-	-	3.0
cSSC/Basal Cell		5	2	3	-	2.4	1.5	-	12.4	1.5	-	5.2	1.0
Other		**81**	**100**	**134**	**-**	**5.6**	**4.8**	**-**	**15.1**	**15.1**	**-**	**2.7**	**3.1**
Adrenal		3	1	2	-	14.3	17.0	-	39.0	42.0	-	2.7	2.5
Bone		18	22	37	-	3.2	3.5	-	9.2	11.0	-	2.9	3.1
Brain		22	33	48	-	6.5	4.9	-	19.4	16.6	-	3.0	3.4
Mesothelioma		1			-	4.0	-	-	3.0	-	-	0.8	-
Nervous system				1	-	-	-	-	-	-	-	-	-
Neuroendocrine		4	7	11	-	6.3	5.6	-	13.0	24.4	-	2.1	4.4
Unknown		**66**	**49**	**39**	**-**	**3.5**	**4.8**	**-**	**9.7**	**11.3**	**-**	**2.8**	**2.3**
Grand Total	**4**	**1287**	**1053**	**1137**	**7.0**	**10.2**	**9.9**	**27.8**	**24.3**	**24.1**	**4.0**	**2.4**	**2.4**

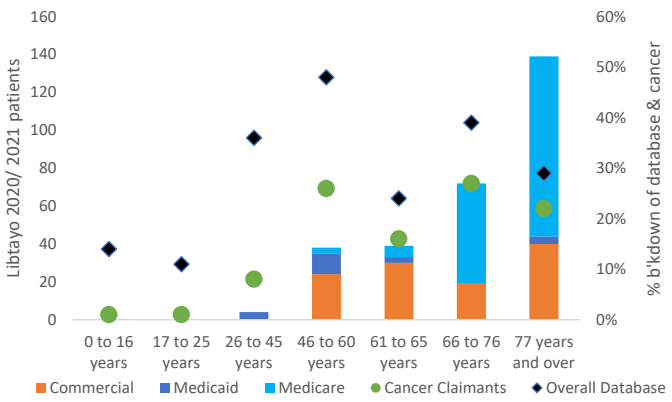
Green shading represents on-label use as of May 2022.

Source: Credit Suisse Healthcare Database

Libtayo

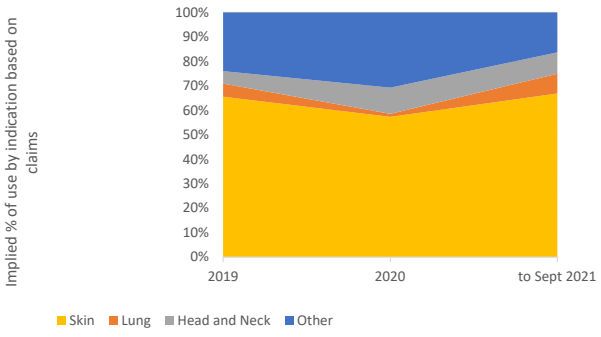
- Libtayo (cemiplimab) is a PD-1 inhibitor developed and initially marketed by Sanofi (ex US) and REGN (in the US) as part of their antibody alliance. It first came to the market in September 2018 in a unique skin cancer setting and has more recently been approved for use in lung cancer. In June 2022, the alliance was restructured, with Regeneron gaining rights to sell Libtayo ex-US for an upfront payment of $900m. Sanofi may earn some regulatory and sales-related milestones and will receive an 11% royalty on global sales to be booked on operating income.
- In 2021, Libtayo generated $0.46bn sales worldwide, which Evaluate consensus forecasts to grow to >$2.3bn by 2028. The patent expiry is September 2035.
- US drug sales in 2021 were $0.3bn.
- In Figure 54 and Figure 55, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. Based solely on the clear on-label use, we see only 57% of use as directly "on-label"; adjusting for likely secondary use in brain and bone suggests that we are seeing c40% of patients claiming for apparently off-label indications. In particular, we see some head and neck use developing.
- Small patient numbers make analysis of average treatment times difficult, although we note apparent declining treatment times in both the approved skin and lung indications.

Figure 53: Overall funding for Libtayo in 2020/2021: c39% commercial, c8% Medicaid and c54% Medicare



Source: Credit Suisse Healthcare Database

Figure 54: Libtayo use by indication based on total claims (note no full data before 2019 as funding via temporary J Code)



Source: Credit Suisse Healthcare Database

Figure 55: Uses of Libtayo by indication over time, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Libtayo	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung	**4**	**7**	**18**		**16.8**	**3.3**	**5.0**	**45.5**	**10.3**	**17.8**	**2.7**	**3.1**	**3.6**
1L NSCLC PD-L1+	4	7	18		16.8	3.3	5.0	45.5	10.3	17.8	2.7	3.1	3.6
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers)					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers), 1L NSCLC PD-L1+					-	-	-	-	-	-	-	-	-
1L sq NSCLC					-	-	-	-	-	-	-	-	-
Blood	**4**	**7**	**9**		**14.3**	**5.0**	**2.3**	**82.8**	**19.9**	**4.2**	**5.8**	**4.0**	**1.8**
Leukemia	1		4		12.0	-	2.0	54.0	-	3.8	4.5	-	1.9
Lymphoma	3	5	4		15.0	5.2	2.5	92.3	18.2	3.5	6.2	3.5	1.4
Myeloma		1	1		-	8.0	3.0	-	47.0	9.0	-	5.9	3.0
Breast		**1**			**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Gastrointestinal			**2**		**-**	**-**	**9.5**	**-**	**-**	**23.5**	**-**	**-**	**2.5**
Colorectal			1		-	-	13.0	-	-	32.0	-	-	2.5
Secondary			**1**		-	-	6.0	-	-	15.0	-	-	2.5
Esophageal					-	-	-	-	-	-	-	-	-
Gastric					-	-	-	-	-	-	-	-	-
Pancreatic					-	-	-	-	-	-	-	-	-
Bladder	**1**		**1**		3.0	-	-	6.0	-	-	2.0	-	-
Renal			**1**		**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
1L RCC					-	-	-	-	-	-	-	-	-
Adjuvant / 1L RCC					-	-	-	-	-	-	-	-	-
2L RCC					-	-	-	-	-	-	-	-	-
Gynaecological			**1**		**-**	**-**	**2.0**	**-**	**-**	**4.0**	**-**	**-**	**2.0**
Cervical			**1**		-	-	2.0	-	-	4.0	-	-	2.0
Endometrial					-	-	-	-	-	-	-	-	-
Ovarian					-	-	-	-	-	-	-	-	-
Head and Neck	**10**	**21**	**33**		**6.3**	**9.5**	**2.9**	**20.8**	**31.0**	**8.4**	**3.3**	**3.3**	**2.9**
Liver			**1**		**-**	**-**	**5.0**	**-**	**-**	**17.0**	**-**	**-**	**3.4**
Skin	**68**	**99**	**138**		**12.0**	**10.8**	**5.4**	**37.8**	**32.5**	**14.6**	**3.2**	**3.0**	**2.7**
Melanoma	1	2	1		-	3.5	-	-	2.5	-	-	0.7	-
Merkel Cell			1		-	-	4.0	-	-	12.0	-	-	3.0
cSSC/Basal Cell	67	97	136		12.2	11.0	5.4	38.4	33.1	14.7	3.2	3.0	2.7
Other	**19**	**37**	**55**		**8.1**	**4.7**	**4.4**	**27.5**	**16.7**	**16.1**	**3.4**	**3.5**	**3.6**
Adrenal			1		-	-	6.0	-	-	45.0	-	-	7.5
Bone	5	10	5		4.6	2.4	3.8	16.6	7.5	11.2	3.6	3.1	2.9
Brain		**1**	**3**		-	6.0	4.3	-	24.0	8.3	-	4.0	1.9
Mesothelioma					-	-	-	-	-	-	-	-	-
Nervous system	1	2	3		-	15.0	4.3	-	53.5	7.7	-	3.6	1.8
Neuroendocrine					-	-	-	-	-	-	-	-	-
Unknown	**1**	**13**	**11**		**-**	**7.0**	**2.8**	**-**	**23.5**	**10.9**	**-**	**3.4**	**3.9**
Grand Total	**107**	**187**	**271**		**10.9**	**8.6**	**4.7**	**35.7**	**26.9**	**13.8**	**3.3**	**3.1**	**3.0**

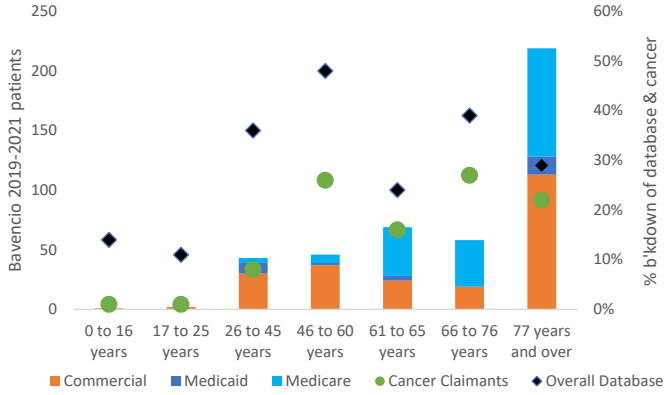
Green shading represents on-label use as of May 2022.

Source: Credit Suisse Healthcare Database

Bavencio

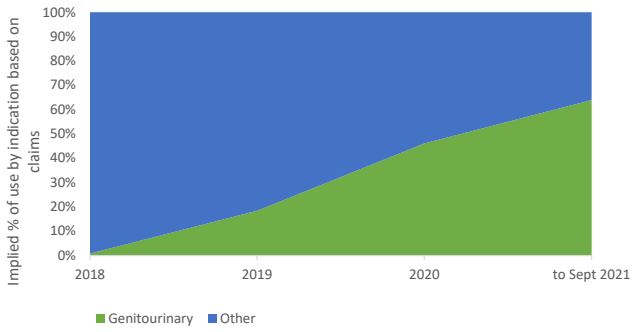
- Bavencio (avelumab) is a PD-L1 inhibitor initially from Merck KGaA and partnered with Pfizer. It first came to the market in March 2017. It is approved for use in a less common form of skin cancer called Merkel cell carcinoma, and 1L maintenance treatment of advanced bladder cancer. Sales in 2021 were $442m worldwide. Evaluate consensus forecasts sales growing to >$30bn by 2028. The patent expiry is December 2033.
- In Figure 57 and Figure 58, we highlight the indications, length of treatment, and average number of claims. The indications shaded in green are on-label as of today. Bavencio is labelled for genitourinary and skin cancer use, but in Figure 49 on page 43, we see growing use in lung cancer. If we assume the bone and brain use reflects largely secondaries to approved indications, we see roughly 35% off-label use reimbursed.
- Small total patient numbers make analysis of typical duration and claims difficult.

Figure 56: Overall funding for Bavencio in 2019/2020/2021: c52% commercial, c7% Medicaid and c41% Medicare



Source: Credit Suisse Healthcare Database

Figure 57: Bavencio use by indication based on total claims



Source: Credit Suisse Healthcare Database

Figure 58: Uses of Bavencio by indication, highlighting average claims per patient based on year of treatment start, average duration of treatment and typical dosing intervals

Bavencio	Number of patients				Av No of Claims			Avg. Duration (weeks)			Dosing Interval (weeks)		
	2018	2019	2020	2021	2018	2019	2020	2018	2019	2020	2018	2019	2020
Lung		4	16	20	-	5.5	7.0	-	16.3	14.8	-	3.0	2.1
Unknown		4	16	20	-	5.5	7.0	-	16.3	14.8	-	3.0	2.1
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers)					-	-	-	-	-	-	-	-	-
1L NSCLC (all comers), 1L NSCLC PD-L1+					-	-	-	-	-	-	-	-	-
1L sq NSCLC					-	-	-	-	-	-	-	-	-
Blood	**1**	**1**	**2**		-	-	2.0	-	-	3.5	-	-	1.8
Leukemia	1	1	1		-	-	3.0	-	-	6.0	-	-	2.0
Lymphoma					-	-	-	-	-	-	-	-	-
Myeloma			1		-	-	-	-	-	-	-	-	-
Breast				**3**	-	-	-	-	-	-	-	-	-
Gastrointestinal	**2**		**2**	**4**	**1.5**	**-**	**7.0**	**9.0**	**-**	**23.5**	**6.0**	**-**	**3.4**
Biliary				1	-	-	-	-	-	-	-	-	-
Colorectal	1			2	2.0	-	-	17.0	-	-	8.5	-	-
Esophageal					-	-	-	-	-	-	-	-	-
Gastric					-	-	-	-	-	-	-	-	-
Pancreatic			2	1	-	-	7.0	-	-	23.5	-	-	3.4
Bladder	**2**	**2**	**32**	**101**	**3.0**	**8.5**	**9.7**	**9.5**	**15.0**	**22.8**	**3.2**	**1.8**	**2.3**
Renal		**7**	**21**	**15**	**-**	**19.0**	**8.2**	**-**	**46.1**	**20.1**	-	**2.4**	**2.5**
1L RCC					-	-	-	-	-	-	-	-	-
Adjuvant / 1L RCC					-	-	-	-	-	-	-	-	-
2L RCC					-	-	-	-	-	-	-	-	-
Gynaecological				**1**	**-**	**-**	**-**	**-**	**-**	**-**	-	-	-
Cervical					-	-	-	-	-	-	-	-	-
Endometrial				1	-	-	-	-	-	-	-	-	-
Ovarian					-	-	-	-	-	-	-	-	-
Head and Neck	**1**	**2**	**1**	**3**	**2.0**	**35.0**	**-**	**2.0**	**80.0**	**-**	**1.0**	**2.3**	-
Liver	**3**		**9**	**5**	**6.7**	**-**	**3.4**	**28.0**	**-**	**12.8**	**4.2**	-	**3.7**
Skin	**42**	**18**	**9**	**5**	**16.3**	**21.7**	**15.4**	**39.6**	**46.8**	**37.0**	**2.4**	**2.2**	**2.4**
Melanoma	2				3.0	-	-	14.5	-	-	4.8	-	-
Merkel Cell	37	17	9	5	17.5	22.9	15.4	40.3	49.5	37.0	2.3	2.2	2.4
cSSC/Basal Cell	3	1			10.0	-	-	47.3	-	-	4.7	-	-
Other	**21**	**17**	**34**	**42**	**3.7**	**10.6**	**7.1**	**11.7**	**34.6**	**19.5**	**3.2**	**3.3**	**2.7**
Adrenal		1	1		-	-	-	-	-	-	-	-	-
Bone	4	4	14	11	3.8	22.8	5.9	12.3	70.3	16.9	3.3	3.1	2.8
Brain		1	1	3	-	2.0	3.0	-	6.0	4.0	-	3.0	1.3
Mesothelioma					-	-	-	-	-	-	-	-	-
Nervous system					-	-	-	-	-	-	-	-	-
Neuroendocrine	8	6	6	3	4.4	10.5	13.0	16.3	39.0	38.3	3.7	3.7	2.9
Unknown	**2**	**0**	**5**	**8**	**0** **2.5**	**-**	**4.6**	**2.5**	**-**	**10.2**	**1.0**	**-**	**2.2**
Grand Total	**74**	**51**	**131**	**207**	**10.8**	**16.0**	**8.0**	**27.5**	**39.4**	**19.9**	**2.6**	**2.5**	**2.5**

Green shading represents on-label use as of May 2022.

Source: Credit Suisse Healthcare Database

“We assume that with most patients being treated to progression, the time between first and last claims will give us a measure of the real-world time to progression.

Appendix 1: Introduction to PD-(L)1 treatments and lung cancer

- Immuno-oncology harnesses a patient's own immune system to fight cancer and has rapidly emerged as a $30bn+ revenue opportunity. Most I-O approvals to date have been in the metastatic setting, when cancer has spread from the primary tumour site.
- PD-1 or PD-L1 inhibitors are a group of checkpoint inhibitor drugs that first came to the market in 2017. They work by blocking the activity of the PD-1 and PD-L1 immune checkpoint proteins that are present on the surface of cells. By blocking the binding, it allows T-cells to kill tumour cells, harnessing the body's own immune system to fight the cancer.
- There are seven PD-1 or PD-L1 therapies with FDA approval for various different tumour types today (see Figure 60 for details). The largest-selling drug, with the broadest label of indications, is MRK's Keytruda, which sold $17.2bn in 2021 ($9.8bn of which was in the US). Global sales for these drugs are expected to increase >50% by 2026 (from 2021), according to Evaluate consensus data.
- The majority of approvals of these agents are as monotherapy, in combination with chemotherapies and other agents (e.g., Avastin). In some cases, two immunotherapies are combined, such as a CTLA-4 inhibitor (e.g., BMY's Yervoy; AZN's treme is yet to be approved) or a LAG-3 inhibitor (BMY's Opdualag fixed-dose combination with nivolumab, approved in March 2022).
- These therapies are seen as the backbone for future cancer care, with many companies exploring novel combinations to enhance responses and studying the drugs in earlier settings such as adjuvant use (where tumours are more localised and patients have a better likelihood of survival).

Figure 59: Overall patient starts in the CS Healthcare Database 2019, 2020 and 2021 by drug and by sub-category of lung cancer

	Bavencio	Imfinzi	Keytruda	Libtayo	Opdivo	Tecentriq	Yervoy
Unknown	40	4	28		1345	43	811
1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC			3266				
1L NSCLC PD-L1+				29	706		
1L NSCLC (all comers)			2938			103	
1L sq NSCLC			1164				
1L NSCLC PD-L1+/2L NSCLC						552	
SCLC		152				1436	
Stage III NSCLC		2355					
1L NSCLC (all comers), 1L NSCLC PD-L1+					84		
Total	**40**	**2511**	**7396**	**29**	**2135**	**2134**	**811**

Source: Credit Suisse Healthcare Database

Figure 60: FDA-approved PD-1 and PD-L1 therapies as of May 2022

Drug	Generic name	Manufacturer	Year of first launch	FDA Approved Indications	FY2021 sales ($m)	Evaluate cons FY2026E sales ($m)
Keytruda	pembrolizumab	Merck	2014	NSCLC cHL Breast (TNBC) Colorectal (CRC) Melanoma MSI-H/dMMR cancer bladder Head & neck Kidney (RCC) Gastric Liver (HCC) Cervical Endometrial Merkel cell carcinoma Esophageal Cutanaeous squamous cell (CSCC) *SCLC (withdrawn March 2021)*	17,186	27,696
Opdivo	nivolumab	Bristol Myers Squibb	2014	NSCLC Melanoma Kidney (RCC) Head & neck Liver (HCC) Gastric Bladder Colorectal (CRC) Mesothelioma cHL *SCLC (withdrawn Jan 2021)*	8,525	8,525
Tecentriq	atezolizumab	Roche	2016	NSCLC SCLC Liver (HCC) Melanoma Bladder *TNBC (withdrawn Aug 2021)*	3,628	7,252
Imfinzi	durvalumab	AstraZeneca	2017	Stage III NSCLC SCLC *Bladder (withdrawn Feb 2021)*	2,412	4,436
Libtayo	cemiplimab	Sanofi/ Regeneron	2018	Cutanaeous squamous cell (CSCC) Basal cell (BCC) NSCLC	459	1861
Bavencio	avelumab	Merck KGaA/Pfizer	2017	Bladder Merkel cell carcinoma	442	900
Jemperli	dostarlimab	GSK	2021	Endometrial	7	329

Source: Company data, Evaluate consensus

Background on lung cancer

- Lung cancer is the most common cancer worldwide, with non-small cell lung cancer (NSCLC) making up 85% of all lung cancer cases. The other c15% of lung cancer cases are small-cell lung cancer (SCLC). Patients are often diagnosed late, with c75% diagnosed with metastatic disease. The focus of most I-O trials in NSCLC in recent years has been in the metastatic setting as monotherapy or in combination with chemotherapy and other targeted agents (Avastin).
- Immunotherapy is utilised in NSCLC where patients do not have known genetic drivers of disease (e.g., ALK, EGFR). In SCLC, immunotherapy is available for all metastatic patients. See Figure 61 for where key drugs are used across different lung cancer subgroups.

Figure 61: Lung cancer treatment landscape

<table>
<tr><td></td><td></td><td colspan="9">NSCLC</td><td>SCLC</td></tr>
<tr><td></td><td>Subgroup</td><td>ALK+</td><td>EGFR+</td><td>BRAF V600</td><td>METex14</td><td>RET</td><td>ROS1/NTRK+</td><td colspan="2">PD-L1+</td><td>PD-L1-</td><td></td></tr>
<tr><td rowspan="2">Stage 1-3 resectable</td><td>neoadjuvant</td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="2">Opdivo + chemo</td><td></td><td></td></tr>
<tr><td>adjuvant</td><td></td><td>Tagrisso</td><td></td><td></td><td></td><td></td><td colspan="2">Tecentriq</td><td>chemo</td><td></td></tr>
<tr><td>Stage 3 unresectable</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="3">Imfinzi
OR
Keytruda</td><td></td></tr>
<tr><td rowspan="2">Metastatic (Stage 4)</td><td>1L</td><td>Alecensa</td><td>Tagrisso</td><td>Tafinlar + Mekinst</td><td>Tepmetko OR Tabrecta</td><td>Retsevmo OR Gavreto</td><td>Xalkori OR Rozlytrek/Vitrakvi</td><td>Keytruda OR Opdivo OR Libtayo</td><td></td><td>Keytruda + chemo</td><td>Imfinzi + etoposide OR Tecentriq + etoposide</td></tr>
<tr><td>2L</td><td>Other targeted agents</td><td></td><td></td><td></td><td></td><td>Other targeted agents</td><td colspan="3">Tecentriq OR Opdivo OR Keytruda (if no prior I-O) OR Chemo</td><td></td></tr>
</table>

Source: Company data, Credit Suisse estimates

Appendix 2: The Credit Suisse Healthcare Database

The Credit Suisse Healthcare Database contains more than seven years of prescription (Rx) and medical (Mx) claims data from c122m anonymised US patient records over this period. Using this extensive database, we have been able to develop a unique insight into typical therapeutic journeys through various diseases. Where other Rx audit services can provide no continuity of patient coverage, this database allows us to look at transitions from one treatment to another and detail typical drug cocktails in any year, all of which may give us a better idea of the treatment burden for a disease and likely patient costs.

We can also look at treatment persistence (length of time on a treatment) and compliance (number of claims made in chronic diseases versus expected claims for 100% compliance). These together may give us an idea of patient satisfaction with a treatment and help define market penetration, both important for modelling sales.

The overall enrolment data in the Credit Suisse Healthcare Database covers c122m unique member IDs active in 2021. There were just over 113m active subscribers on average in each quarter of 2021. We have claim and funding status data on 61.9m enrollees who made claims in 2021. A total of 63.8m unique claimants are identified, suggesting that we are missing contextual data on only 3% of claimants.

We have seen a rise in claimants for Rx services in line with enrollee numbers, with a much more stable medical claims base. We note the lack of increase in active subscribers claiming for diabetes prescriptions or medical claims, but still see broad correlation with other audit services for key drugs. We note the higher lag time for medical claims being available to us and believe this may partly explain the reduction in medical claims in 2021.

For diabetes, we saw a 30% effective sample size of the US market and a strong correlation of Rx trends with other audit services.

Trends we see in patient counts in this database for the chronic outpatient prescription treatments seem to accord reasonably well with broadly equivalent Total Prescription (TRx) data reported by other prescription services such as IQVIA over the period 2017 to 2021.

The Credit Suisse Healthcare Database is based on claims rather than being sampled at the point of being dispensed, and therefore does not match IQVIA for speed of reporting. However, we can see some Rx data for rarer diseases and hospital-delivered drugs within the Credit Suisse Healthcare Database where specialty pharmacy services may not be as accessible for other audit services. We have not looked at any oral cancer drugs in this analysis.

For PD-(L)1 drugs, we see around a 5% sample size for the US market based on claims and CS estimated net pricing.

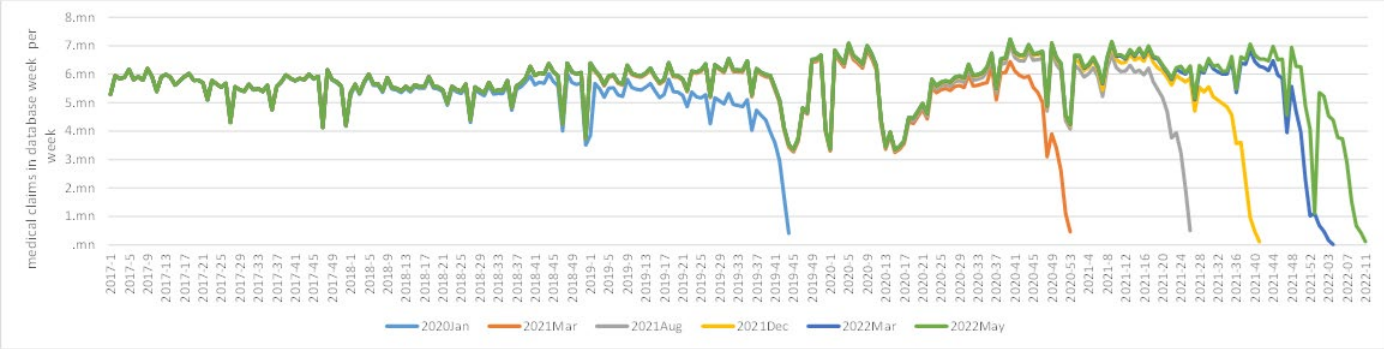
We have received six downloads of the claims data that underpins the Credit Suisse Healthcare Database. There has been very strong consistency in the Rx data feed at each download, although we note a material lag in reporting the medical claims data. This suggests that the downward trend in medical claims evident in the database towards the end of 2021 is not “real”. We have seen a material uplift in December 2021 in overall claims as late as May 2022. We note that for the cancer drugs, we have completed our analysis up to end-September 2021 to ensure that we are not counting patients as having stopped therapy merely because the database has yet to receive data on their claims.

Figure 62: Credit Suisse Healthcare Database: Insights from healthcare claims of c122m US citizens

Year	Overall Subscribers m	Avg Subscribers m	Subscribers with claims m	Overall Claimants			Cancer Mx claimants	
				Rx m	Mx m	of which Rx & Mx m	Overall cancer Mx m	PD(L)1
2017	114.5	105.8	50.7	31.6	20.7	15.3	0.74	9,151
2018	112.3	104.1	53.0	32.3	20.3	15.0	0.71	12,527
2019	118.1	103.9	57.9	33.4	21.6	15.3	0.73	16,603
2020	111.2	103.0	61.2	36.0	20.4	15.0	0.69	18,217
2021	121.9	113.1	61.9	43.6	20.3	15.6	0.70	18,660

Source: Credit Suisse Healthcare Database (Rx claims = prescription claims, Mx claims = medical claims)

Figure 63: Number of medical claims over time. Note the restatement upwards for the last few months with each download



Source: Credit Suisse Healthcare Database

Appendix 3: Methodology

Cancer analysis

We have chosen to look at cancer given the large market size, the rate of growth in the market, and the lack of visibility into new commercially important treatments using available audit services. We focused on the immunotherapy agents, given their prevalent use across multiple tumour types.

We have made each analysis based on detailed longitudinal claims data for patients who receive PD(L)1 drugs. We can track the exact cancer treatment given by using the J-codes, which are captured as part of the medical claims. A caveat to this is that during the first few months of a new drug coming to market, a temporary general J-code is used, meaning that early drug use cannot be tracked. We therefore have no data, for instance, on Jemperli from GSK, which is still being reimbursed under a temporary J-code. We know the date of "service" for each claim, although many months may elapse before this claim has been adjudicated and is available to us in the database.

We are able to identify the type of cancer a patient has by looking at the ICD-10 diagnosis code recorded. For lung cancer, the ICD-10 codes are C33-C39 and C78.0-C78.3. An ICD-10 code only tells us if the patient has lung cancer or another type (e.g., kidney or head and neck) but does not provide more granular information about the tumour. Lung cancer is not a homogeneous disease and presents in different histologies and has different genetic drivers.

Immunotherapy is used only in patients without oncogene-driven disease (e.g., ALK or EGFR). Therefore, the only way we are able to decipher what subtype of lung cancer a patient may have is to look at whether the immunotherapy drug used has been given as monotherapy or in combination with a specific additional drug. In the case of small-cell lung cancer (SCLC), we know Tecentriq and Imfinzi are both given in combination with a type of chemotherapy called etoposide for the first few cycles of treatment. Etoposide is not used to treat any other lung cancer type, so we can be relatively confident these patients have small-cell histology. We look for claims dated within two weeks of one another to consider the two drugs as being given simultaneously.

In NSCLC, when the drugs are given in combination with general chemotherapy or given alone as monotherapy, this may indicate use in more than one setting (e.g., both PD-L1 + 1L NSCLC and 2L NSCLC). See Figure 64 for the classifications we have used for our analysis.

We have looked at this level of granularity so that when we look at a cohort of patients' actual drug treatment duration, we are as far as possible matching patients with the same type and stage of disease. We follow patients for the length of their treatment from the date that they start taking the specific drug regime. If a patient started in June 2019 and continued to June 2020, we count all the episodes of treatment in the 2019 cohort, even though some treatments were given in 2020.

Figure 64: Lung cancer subgroups defined by treatment used

Tumour type (by ICD10 code)	Immunotherapy Drug	Drug 2 (claimed for at same time)	J codes	Implied treatment setting
Lung	Tecentriq	+ etoposide	J91731, J9181	SCLC
Lung	Tecentriq	+ Avastin	J9022, J9035	1L NSCLC (all comers)
Lung	Tecentriq	N/A	J9022	1L NSCLC PD-L1+/2L NSCLC
Lung	Keytruda	+ pemetrexed	J9271	1L NSCLC (all comers)
Lung	Keytruda	+ carboplatin +/- paclitaxel	J9271, J9045, J9267	1L sq NSCLC
Lung	Keytruda	N/A	J9271	1L NSCLC PD-L1+/Stage III NSCLC/2L NSCLC
Lung	Imfinzi	+ etoposide	J91731, J9181	SCLC
Lung	Imfinzi	N/A	J91731	Stage III NSCLC
Lung	Opdivo	+ Yervoy	J9299, J9228	1L NSCLC PD-L1+
Lung	Opdivo	+ Yervoy + carboplatin OR paclitaxel OR pemetrexed OR cisplatin	J9299, J9228, J9045/J9267/J9305/J9060	1L NSCLC (all comers)
Lung	Libtayo	N/A	J9119	1L NSCLC PD-L1+

Source: Company data, Credit Suisse estimates

We know that the capture of data decays in the later months of the database, with an upward revision of data back into the end of 2021 even from the May 2022 data. We do not want to mistake the apparent stopping of a drug (based on lack of capture of a claim) for a real stop of treatment, and so we have stopped our analysis at end-September 2021. We also specifically log when a patient reaches September 2021. If patients were to take a drug for 12 months and started in June 2020, they would have completed 12 months of treatment by September 2021 and they would show as a drop-off after 12 months in the 2020 cohort. If, however, they started in November 2020, they would still be on therapy in September 2021; and based on the September 2021 cut-off, they could appear as having taken only 10 months of treatment. However, we would not count them as a completer in our 2020 patient cohort at this point, as they were still taking the drug at the last cut-off point.

We also allow for a 16- to 30-week break in therapy without counting a patient as stopping treatment depending on the analysis. We need to set some cut-off to accommodate leeway in submitting claims and some expected missing of scheduled visits because of issues of tolerability or other side-effects. We ran this analysis with various cut-offs to determine completion of treatment running from 30 weeks down to 8 weeks. A 30-week cut-off is used in our main analysis of time on treatment, as we want to allow for periodic breaks within a treatment and minimise counting a patient twice as starting two separate courses of treatment in one year. A short cut-off interval risks counting a patient as a drop-out when they are not in fact stopping but taking a treatment break, and this would allow the patient to be recounted as a new starter, and thus overstate the number of new patient starts in any year. A long treatment interval ensures that we capture overall treatment but does not allow us to capture the most recent data from the 2021 cohort, as not enough patients will be designated as having completed treatment at the time of the database cut-off. We use the 16-week analysis cut-off as a trigger to look at subsequent treatments

We note the availability of less frequent dosing for many of the drugs (e.g., Opdivo offers either 240mg every two weeks or 480mg every four weeks). We see limited take-up so far based on no apparent lengthening of average dosing intervals. We assume that the relatively high rate of eight-week breaks evident in the data from Figure 65 reflects patients missing one dose on a monthly cycle and then taking the next dose perhaps one week later than expected.

When looking at transitions on treatment, we look at what patients move on to after the PD(L)1 drug we have tracked, in the following six months (illustrated in the Sankey plots) and then in the subsequent period up to the end of the database, which we cover only in commentary. We specifically look for further chemo, radiation treatment or a combination of the two. We also note patients who make other claims (outside of chemo, radio or another PD-(L)1). This shows the patient is still alive and a subscriber to this database. These are noted as "no treatment but more claims." This could include other oncology treatment outside of the specific treatments tracked (e.g., an oral TKI inhibitor).

If we see no more claims, we assume the patient may have died or moved away from the database.

Figure 65: Treatment starts by year, allowing for different stopping intervals to minimise a patient being counted twice in one year if they take a short break in treatment

	8 weeks	16 weeks	30 weeks	% 8 wk /30 wk
Keytruda	4,124	3,411	3,253	27%
Opdivo	2,390	1,959	1,835	30%
Tecentriq	891	778	754	18%
Imfinzi	750	763	730	3%
total	8,155	6,911	6,572	24%

Source: Credit Suisse Healthcare Database

PFS analysis

Cancer study endpoints will most often include a progression-free survival (PFS) measure, which assesses the length of time a patient goes before their disease worsens. For many cancer treatments, patients are dosed with the cancer therapy up until their disease progresses.

We do not have an ability to see whether a patient has progressed while receiving treatment or not, as we only have access to claims data.

However, in our Credit Suisse Healthcare Database, we are able to follow individual patients longitudinally and can both capture how long they receive treatment (time from first to last dose), and count the number of claims (number of doses).

We assume that with most patients being treated to progression, the time between first and last claims will give us a measure of the real-world time to progression. Clearly, the time on treatment will depend on both the stage of disease and the efficacy/tolerability of treatment.

In a clinical trial, patients can be selected to have similar stages of disease, and time of treatment will depend on efficacy and frequency of follow-up scans to check progression. In order to look at real-world settings, we have chosen to compare only settings where we have both a broad diagnosis (lung cancer) and additional contextual information (see Figure 64).

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