Clinical benefit of immunotherapies in advanced cancer in France: a population-based estimate from 2014 to 2021

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Background

Context

- In 2023, the incidence of cancer in France is estimated to 433,136 patients [1]. In parallel, approximatively 150,000 deaths per year are related to cancer, making it the leading cause of deaths [2].
- In France, after treatments are marketed, their benefit is evaluated by the *Haute Autorité de Santé* (HAS), the National Health Technology Agency (HTA), to inform decisions on reimbursement or pricing. The HAS is composed of two commissions for the assessment:
  - The Transparency Commission (TC) which evaluates the benefit value and added benefit value of therapies compared to the current therapeutic strategy. The opinions published also present the target population of the treatment
  - The Economic Evaluation and Public Health Commission (called CEESP) which evaluates the methodology of cost-effectiveness (CE) dossiers for therapies claiming a major to moderate added benefit value and with significant expected expenditures. The CE analyses require economic models to quantify the incremental impact of the new intervention on costs and on health outcomes compared to the current standard of care over a lifetime or a specified period

Study rationale

- Immune-checkpoint inhibitors (ICIs) have been rapidly established as the standard of care in many advanced cancers [3,4]. Their efficacy has been demonstrated in terms of overall survival and quality of life improvement in clinical trials compared to cytotoxic chemotherapies or previous standard of care (targeted therapies) [5, 6, 7, 8, 9, 10].
- The assessment performed by the TC was based on pivotal trial data, often based on a small group of selected patients. However, treatments are rarely re-assessed by TC after the initial evaluation, to ensure that the 'observed' benefit is consistent with the initial expectations of the drugs.
- Indeed, the CE analyses submitted to CEESP provide the expected efficiency of a new treatment, compared to it competitor. However, the results are expressed as the incremental cost per quality-adjusted life year gained per patient. Consequently, little information is available on survival benefits at the treated population level of each indication or overall ICIs benefits.

Study objective

- To assess the clinical benefit conferred by immunotherapies that are indicated in advanced cancers at a population level in France, from their introduction in 2014 until the end of 2021. The benefits are presented in terms of life years (LY) gained, quality-adjusted life years (QALYs) and the number of deaths avoided, compared to previous standards of care.

Methods

Identification of immunotherapies and their associated indications (Figure 1 - step 1):

The HAS website was searched for all TC and CEESP assessments. To be included in the study, each immunotherapy indication had to fulfil the following criteria:

- ICI eligible for reimbursement or for an early access program;
- Extrapolated progression free survival (PFS) and overall survival (OS) curves based on pivotal trials and no major methodological reservation on modelling approach.

Data extraction:

- In CEESP assessment reports, we retrieved the closest comparator on the CE frontier, extrapolated Kaplan-Meier PFS and OS curves and utility values per health state.
  - Extrapolated curves of the immunotherapy and its comparator were digitized (Engauge Digitizer®, version 3.0) and restructured (R Studio®, version 4.0.0) **(Figure 1-Step 2&3)**
- Publications of real-world cohorts, studies or reports based on the French Hospital Medical Information database (*Programme de Médicalisation des Systèmes d'Information* – PMSI) or official documents reporting all patients treated per year were used to estimate the population initiating an immunotherapy.

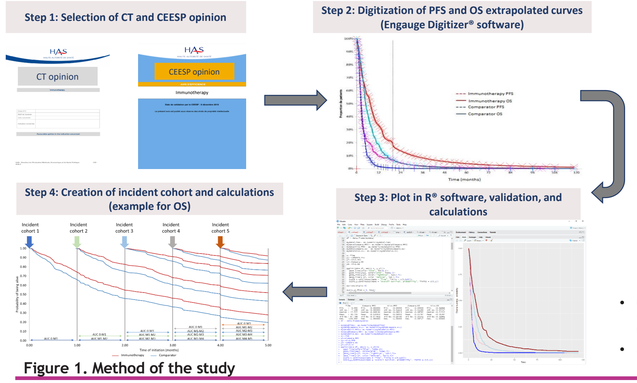


Figure 1. Method of the study

Between 2014 and 2021, 132,924 patients initiated an immunotherapy (anti-PD1/PDL1) in France.

By December 31st 2021, immunotherapies enabled to prevent16,173 deaths, to gain 37,316 LY and 27,709 QALYs.

18.5% of the overall population, initiated an immunotherapy thanks to an early access program.

Number of patients included:

The number of treated patients estimated per year was divided based on the number of months of availability and the date of the availability for the months. Using this number of patients, we created incident cohorts **(Figure 1-Step 4)**. For each cohort, the evaluation period was defined as the time between the date of initiation of immunotherapy (index date) and December 31st, 2021.

Outcomes:

- **Probability of deaths avoided**

The survival rate per month was assessed from extrapolated curves for OS restructured in R software for the immunotherapy evaluated and its comparator. For each cohort, we retained the difference in survival probability between the two treatments as of December 31st, 2021. This difference was multiplied by the number of incident patients from each cohort.

- **LY analysis**

The restricted mean survival time per month was assessed for each immunotherapy evaluated and selected comparator. The difference in restricted mean survival time for OS between the treatments was calculated per month (between the index date and December 31st, 2021). The difference was multiplied by the number of patients included from each cohort.

- **QALY analysis**

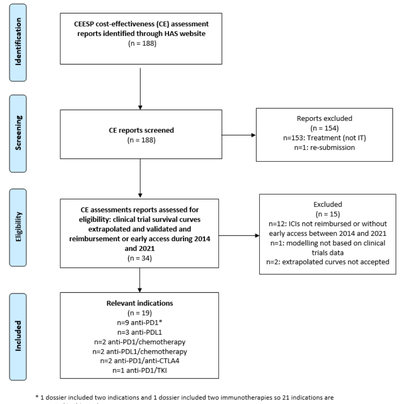
The difference in restricted mean survival time between treatments for PFS and OS was calculated per month (between the index date and December 31st, 2021). Those differences were multiplied by the utility of the specific state. These results were then multiplied by the number of patients included from each cohort.

Second objective analyses:

- For treatment with early access, we simulated the results based on the official date of reimbursement to estimate the share of the early access in the gains.

Results - Identification of indications

- Overall, 188 CE assessment reports were available on the HAS but only 34 were related to immunotherapies in advanced or metastatic cancer. Fifteen dossier were excluded since they were not reimbursed during the period nor available in early access or was delisted during the period or extrapolation curves were not accepted.
- Nineteen CE assessment reports met the inclusion criteria representing 21 treatment indications. **(Figure 2)**



* 1 dossier included two indications and 1 dossier included two immunotherapies so 21 indications are presented in this study

Figure 2. PRISMA flow diagram illustrating the selection of CE assessment reports

- Of the selected dossiers, 9 concerned non-small cell lung cancer (NSCLC), 3 melanoma (MEL), 3 renal cell carcinoma (RCC); 2 squamous head and neck cancer (SCCHN). There was one dossier for small cell lung cancer (SCLC), urothelial carcinoma (UC), hepatocellular carcinoma (HCC) and mesothelioma. **(Table 1)**
- An early access was available for 9 (43%) indications

Table 1. Characteristics of selected case studies

Cancer	Indication	Immunotherapy	Comparator	Early access date	Official reimbursement date	Utility scores used in the CE assessment report	
						PFS	PPS
mHCC	1st line	Atezolizumab (+bevacizumab)	Sorafenib	Mid-July 2020	October 2021	0.8933	0.8634
mMeL	1st line	Nivolumab	Fotemustine	January 2015	January 2017	0.823	0.729
	1st line	Pembrolizumab	Fotemustine	Mid September 2014	Mid January 2017	0.810	0.680
	1st line	Pembrolizumab	Fotemustine	Mid-September 2014	January 2017	0.810	0.680
mMesothelioma	1st line	Nivolumab (+ ipilimumab)	Chemotherapy	April 2021	February 2022	0.716	0.580
NSCLC	2nd line squamous a/m	Nivolumab	Docetaxel	May 2015	January 2017	0.723	0.530
	2nd line non squamous a/m	Nivolumab	Docetaxel	June 2015	March 2017	0.743	0.659
	2nd line m	Pembrolizumab	Docetaxel	N.A	Mid-May 2017	0.737	0.628
	2nd line m	Atezolizumab	Docetaxel	N.A	Mid February 2019	0.7043	0.550
	1st line squamous m (PD-L1 ≥50%)	Pembrolizumab	Platinum based chemotherapy	N.A	December 2017	0.760	0.641
	1st line non squamous m (PD-L1 ≥50%)	Pembrolizumab	Bevacizumab + paclitaxel	N.A	December 2017	0.760	0.641
	1st line non squamous m	Pembrolizumab (+chemotherapy)	Platinum + gemcitabine/vinorelbine	N.A	Mid November 2019	0.720	0.644
	1st line squamous m	Pembrolizumab (+chemotherapy)	Platinum + paclitaxel	N.A	June 2020	0.741	0.618
	1st line maintenance locally	Durvalumab	Placebo	April 2018	May 2020	0.795	0.751
mRCC	2nd line	Nivolumab	Sorafenib	N.A	January 2017	0.824	0.744
	1st line	Nivolumab (+ ipilimumab)	Pazopanib	N.A	March 2020	0.749	0.687
	1st line	Pembrolizumab (+ axitinib)	Pazopanib	N.A	June 2020	0.7846	0.7529
aSCCHN	2nd line	Nivolumab	Standard treatments	N.A	June 2018	0.743	0.628
	1st line	Pembrolizumab	Platinum + 5-FU + cetuximab	N.A	November 2020	0.764	0.676
mSCLC	1st line	Atezolizumab (+chemotherapy)	Platinum + etoposide	May 2019	N.A	0.7291	0.7118
mUC	1st line	Avelumab	Placebo	July 2020	Mid-September 2022	0.894	0.840

a: advanced; m: metastatic; MEL: melanoma; NSCLC: non-small cell lung cancer; PFS: progression free survival; PPS: post-progression survival ; RCC: renal cell carcinoma; SCCHN: squamous cell cancer of head and neck; SCLC: small cell lung cancer; UC: urothelial carcinoma

Results - Population & outcomes

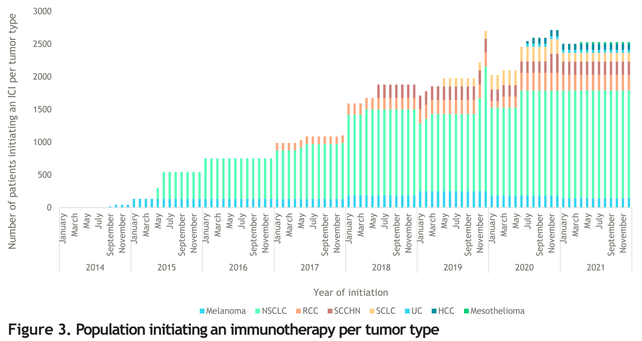


Figure 3. Population initiating an immunotherapy per tumor type

Population initiating an immunotherapy

- Overall, 132,924 patients were treated with an immunotherapy between 2014 and 2021. NSCLC was the most common cancer treated with immunotherapy (66.5% of patients) **(Figure 3)**
- The number of patients initiating an immunotherapy increased over time, from 18 in September 2014 to 2,600 patients in December 2021

Deaths avoided, LYG and QALYs

- By the end of 2021, IT contributed to 16,173 avoided (or delayed) deaths, as compared to standard care **(Table 2)**
- By the end of 2021, 37,316 LYs and 27,709 QALYs were gained thanks to immunotherapy compared to previous standard of care
  - NSCLC and Melanoma were the larger contributor (>85%)
  - Nivolumab accounted for more than 60% of the LYG and QALY
- 2nd line treatments represented more than half patients initiating an immunotherapy as well as LYs and QALYs gained while it represented only 42.7% of deaths avoided.

Table 2. Deaths avoided, LYG and QALY at the end of 2021

		Number of patients initiating an immunotherapy n (%)	Deaths avoided n (%)	Percentage of avoided deaths in patients initiating an immunotherapy (%)	Life years gained n (%)	QALYs gained n (%)
Total		**132,924**	**16,173**	**12.2**	**37,316**	**27,709**
Tumor type	Melanoma	16,297 (12.3)	2,555 (15.8)	15.7	6,990 (18.7)	5,645 (20.4)
	Non-small cell lung	88,443 (66.5)	11,368 (70.3)	12.9	26,334 (70.6)	18,952 (68.4)
	Renal cell carcinoma	11,506 (8.8)	853 (5.3)	7.4	1,902 (5.1)	1,636 (5.9)
	Squamous cell cancer of head and neck	8,757 (6.7)	708 (4.4)	8.1	1,457 (3.9)	995 (3.6)
	Small cell lung	5,268 (4.0)	465 (2.9)	8.8	520 (1.4)	375 (1.4)
	Urothelial	788 (0.6)	76 (0.5)	9.6	38 (0.1)	37 (0.1)
	Hepatocellular	1,651 (1.3)	146 (0.9)	8.9	75 (0.2)	70 (0.3)
	Mesothelioma	215 (0.2)	4 (<0.01)	1.9	0.5 (<0.1)	-0.7 (<0.1)
Treatment lines	2nd line	67,562 (50.8)	6,911 (42.7)	10.2	22,384 (60.0)	15,689 (56.6)
	1st line	59,597 (44.8)	8,577 (53.0)	14.4	14,170 (38.0)	11,353 (41.0)
	Other treatment lines	5,764 (4.3)	670 (4.2)	11.9	761 (2.0)	667 (2.4)
Treatment	Atezolizumab	11,145 (8.4)	1,063 (6.6)	9.5	1,136 (3.0)	757 (2.7)
	Avelumab	788 (0.6)	76 (0.5)	9.6	38 (0.1)	37 (0.1)
	Durvalumab	4,977 (3.7)	610 (3.8)	12.3	723 (1.9)	631 (2.3)
	Nivolumab	68,405 (51.5)	7,357 (45.5)	10.8	24,115 (64.6)	17,484 (63.1)
	Pembrolizumab	47,609 (35.8)	7,068 (43.7)	14.8	11,303 (30.3)	8,800 (31.8)
Early access		24,594 (18.5)	2,369 (14.6)	9.6	2,254 (6.0)	1,639 (5.9)

Conclusions

- This is the first study evaluating the impact of immunotherapies at a national population level from 2014 to 2021, in terms of LY and QALY gained
- This study underlines significant gains in LYs (n=37,316) and QALYs (n= 27,709) with immunotherapies since their introduction and considerable deaths prevented (n=16,173)
  - Non-small cell lung cancer was the tumor localisation with the most indications and represented more than 70% of the gains due to their larger population treated and the historic market availability
  - Nivolumab, was the largest contributor to gains thanks to its earliest availability on French market
- This analysis is likely to underestimate the full potential benefits of ICIs, since it did not include indications in adjuvant settings (melanoma), stopped at the end of 2021 and did not take into account gains accrued or anticipated thereafter, nor new indications that have or will become available after this date

References

1. Institut National du Cancer. Panorama des cancers en France. Edition 2023
2. Santé Publique France. Available at: https://www.santepubliquefrance.fr/maladies-et-traumatismes/cancers [Published: July 2021]
3. Martin-Liberal J, Ochoa de Olza M, Hierro C, et al. Cancer Treat Rev. 2017 54: 74-86.
4. Mittra A, Takebe N, Florou V, Chen AP & Naqash AR. Hum Vaccin Immunother. 2021 17: 1935-39
5. Marshall HT & Djamgoz MBA. Front Oncol. 2020 8: 315.
6. Boutros A, Bruzzone M, Tanda T. E. et al. Eur J Cancer. 2021 159:154-166.
7. Topalian SL, Hodi FS, Brahmer JR, et al. JAMA Oncol. 2019 5:1411-20.
8. Debieuvre D, Juergens RA, Asselain B, et al. Lung Cancer. 2021 157: 40-47.
9. Polkowska M, Ekk-Cierniakowski P, Czepielewska E, et al. J Cancer Res Clin Oncol. 2017 143: 2087-9
10. Assie JB, Corre R, Levra MG, et al. Ther Adv Med Oncol. 2020 12:1758835920967237

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Declaration of interests

- FEC, AFG are employed by Bristol Myers Squibb. VG has a PhD contract, partially financed by Bristol Myers Squibb
- IB has no conflicting interests
- EGL received personal fees (advisory boards) from Bristol Myers Squibb
- CL reports personal fees and nonfinancial support from Amgen, Bristol Myers Squibb, Incyte, Merck Sharp & Dohme, Novartis, Pfizer, Pierre Fabre, Roche, and Sanofi, outside the submitted work

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