Territorial disparities in the use of Hospitalization At Home for immune checkpoint inhibitors infusion in France between 2021 and 2022

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Background

Currently, ICI are administered as infusions every 2 to 6 weeks, mainly in outpatient hospitals. As ICI use increases, hospitals are facing overcrowding and increased costs, due to limited inpatient capacity[1].

ICI administrations typically require hospital settings due to specific administration protocols and are therefore limited to hospital use only. In France, Hospitalization At Home (HAH) allows patients to receive care in a less stressful environment, experience less travel to hospital and alleviate the burden of outpatient care.

For patients living far from hospitals or having experience minimal ICI side effects, in good general condition and therapeutic response, HAH is an opportunity to improve ICI patient access and ease patient burdens.

Guidelines from the French Society of Cancer Immunotherapy support ICI use in HAH settings[2].

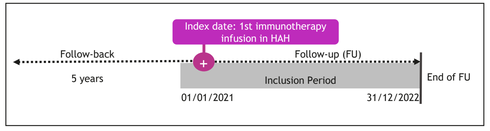
The administration of immune checkpoint inhibitors (ICI) at home is also considered as a priority by the French government and the French Society of Cancer Immunotherapy [3].

In this context, the study objective was to analyze the territorial development of ICI infusions at home between 2021 and 2022.

The study specifically aimed to identify variations in access and utilization of HAH for patients with lung cancer and melanoma, as well as the economic implications regarding patients, hospital centers and regions characteristics.

Methods

This retrospective observational cohort study was conducted in France using data from French national hospital databases (Medical Information Systems Program (PMSI) related to Medicine-Surgery-Obstetrics (MCO) and Hospital-at-home (HAH) activities). The PMSI database provides individual data from all public and private hospital in France.



Inclusion

All adult patients who received at least one immunotherapy treatment (nivolumab alone or in combination with ipilimumab, ipilimumab, pembrolizumab, atezolizumab, or durvalumab) between January 1, 2021, and December 31, 2022, in HAH were included. The identification of immunotherapies was considered through a specific database named the "FICHCOMP-HAH file".

Treatment

Indications of treatments were identified using hospital diagnosis ICD-10 codes registered in each stay or using LES codes (treatment code recorded in a separate database, in addition to the Diagnosis Related Group (DRG)).

LES ("Liste En Sus") codes refer to a list of innovative and high-cost drugs or procedures that receive separate funding from the standard DRG hospital reimbursement system. This DRG system consists in grouping patients with similar clinical conditions and resource usage to standardize hospital reimbursement.

Melanoma patients were further categorized, based on the "LES code" of the molecule used, as metastatic, adjuvant, other melanoma or multi-melanoma (when several codes of melanoma identified for the same patient).

Indications were also described by ICI administrated. If patients were treated by several immunotherapies over the follow-up, they we considered as treated by multi-immunotherapy.

All ICI administrations were collected retrospectively up to 2016. A descriptive analysis was performed to characterize patients, care pathway and administration costs in the French National Health Insurance (NHI) perspective. Specific analyses were conducted on indications with the largest numbers of patients (lung cancer and melanoma) in order to use the biggest samples.

HAH and MCO treatment sequences duration

The HAH and MCO treatment sequences duration before and after the first administration in HAH were described and analyzed by main indication (melanoma and lung cancer).

HAH costs

A HAH stay is divided in sub-sequences which are characterized by 3 variables: main reason for admission, associated reason for admission and a dependency score (the Karnofsky score). All sub-sequences with the infusion of an ICI (identified by the codification of the LES Code during the sub-sequence) were identified.

HAH stay costs were calculated in euros in 2022 from the French National Health Insurance (NHI) perspective with the day rate linked to the combination of the 3 variables.

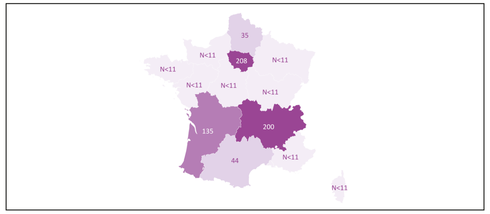
Results

Study population

In total, during 2021 and 2022, 652 patients received immunotherapy in HAH.

The administration of ICI in HAH was heterogeneously spread over the national territory. Thus, 83.3% (N=543) of patients treated in HAH were concentrated into 3 regions (Ile de France (N=208); Auvergne Rhone Alpes (N=200) and Nouvelle Aquitaine (N=135)) (**Figure 1**).

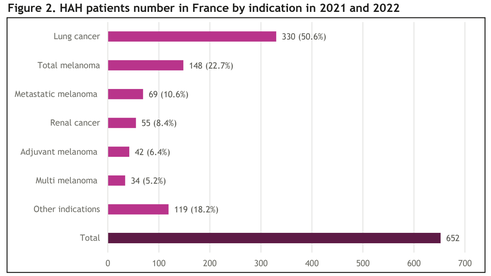
Figure 1. ICI HAH patients' number over 2021 and 2022 in France by region



NB: Regions with a sample size <11 are not described according to data privacy requirements

Among patients treated in HAH, the three most common indications for immunotherapy was lung cancer, melanoma and renal cell carcinoma (**Figure 2**).

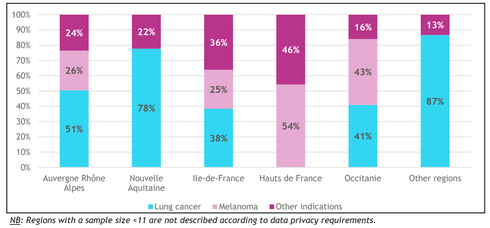
Figure 2. HAH patients number in France by indication in 2021 and 2022



NB: Other indications includes head and neck cancer, metastatic colorectal cancer, hepatocellular carcinoma, urothelial cancer, esophageal and gastric cancer

The distribution of indications by region was also heterogeneous (**Figure 3**).

Figure 3. Distribution of indications by region in HAH setting in France in 2021 and 2022



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Indications with a sample size <11 were grouped in the "other indication" label

ICI administrations

The mean number of ICI administrations per patient was 14 (±19) suggesting a long-term use of these drugs. Whatever the indication, pembrolizumab was the ICI mostly delivered accounting for half of patients (N=344; 52.7%) treated with an ICI in HAH, followed by nivolumab (N=173; 26.5%), atezolizumab (N=47; 7.2%), multi-immunotherapy (N=47; 7.2%), and durvalumab (N=41; 6.3%)

Patient characteristics

There were no major differences in age across indications, although there is a noticeable gap of nearly 10 years between patients with metastatic melanoma (median age of 70) and those with adjuvant melanoma (median age of 59). Overall, the median age and the proportion of men across indications remained relatively consistent (**Table 1**).

Table 1. Characteristics of patients by indication

	N	Median age [Q1;Q3]	Men (%)
Lung cancer	330	67 [59;73]	211(64%)
Total melanoma	148	65 [53;76]	84 (57%)
Metastatic melanoma	69	70 [57;81]	42 (61%)
Adjuvant melanoma	42	59 [52;70]	22 (52%)
Multi melanoma	34	60 [48;67]	19 (56%)
Renal cell carcinoma	55	70 [59;76]	35 (64%)
Total	**652**	**67 [57;75]**	**413 (63%)**

STD: Standard deviation

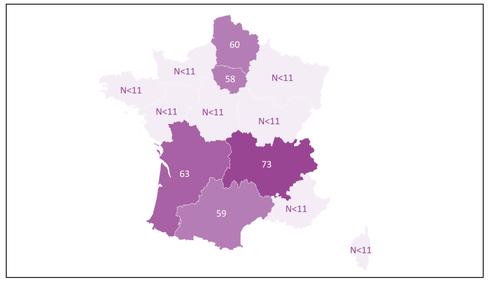
Mean age was similar between regions in main indications, from 65 to 69 years old in lung cancer depending on the regions and 68 in metastatic melanoma in all regions.

Proportion of men varied in lung cancer, from 6.6% to 31.8% depending on the regions and were similar in metastatic melanoma (38.1% to 40.5%).

Mean Karnofsky score

The mean Karnofsky score was 64 but varied by region. It was lower for patients treated in Île-de-France (mean score 58) and higher for patients in Auvergne Rhône-Alpes (mean score 73) (**Figure 4**).

Figure 4. Mean Karnofsky score by region



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HAH and MCO Treatment sequences duration

- **Duration (days) before switching to HAH**

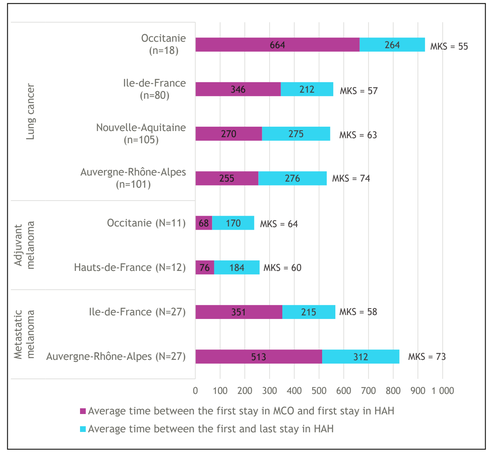
For all lung cancer and melanoma patients (n=478), the mean delay between the first MCO and the first HAH administration was 302 days (±400) (10 months on average). Regional variations delays before the first infusion in HAH (2 to 22 months on average) were observed, with Hauts-de-France as a minimum and Auvergne-Rhône-Alpes as a maximum.

- **Duration spent in HAH**

The mean delay between the first and last HAH administration was 242 days (±242) (8 months on average).

The average Karnofsky score was different between regions for the same indication. The average length of stay did not seem to be correlated with the Karnofsky index of patients (**Figure 5**). Those results suggest important care pathways variations in each indication and region.

Figure 5. Average duration (in days) before and after the first administration of immunotherapy in HAH by region and by indication over the study period.



MKS: Mean Karnofsky score/ NB: Regions with <11 patient are not represented according to data privacy requirements

Cost of immunotherapies administration in HAH

For all administration sub-sequences (N=3,430), the average cost was 331€. Median costs were very similar across indications, at 263€ for lung cancer, 262€ for melanoma and 263€ overall.

For all indications, slights variations were observed between regions. **Table 2** details costs by indications and by regions.

The duration of a sequence was generally one day (80.3%of sequences; N=2,753) or two days (17.6%; N=605). Logically, longer the sequence was, higher was the cost. When looking separately each indication, 78.9% of sub-sequences for lung cancer and 84.8% for total melanoma had a duration of one day.

Regional disparities were also observed. In Hauts-de-France, Ile-de-France and Occitanie, almost all sub-sequences lasted one day (99.4%, 96.7% and 96.0% respectively). Auvergne-Rhône-Alpes was different, with only 58.2% of sub-sequences lasting one day, and 40.9% lasting two days. Average costs corresponding to the duration of sub-sequences were similar regardless of indications or regions (**Table 3**).

In conclusion, care pathways' characteristics and costs per HAH infusion in main indications substantially differed per regions.

Table 2. Costs of ICI administration in HAH setting, by main indications and regions, in euros

	Sub-sequences (SS) N	Mean cost (€)(±STD)	Median cost (€)[IQR]
All indications	**3,430**	**331€ (±785)**	**262€ [226-317]**
By indication			
Lung cancer	2,594	346€ (±901)	263€ [226-317]
Total melanoma	836	284€ (±153)	262€ [226-263]
By region			
Auvergne-Rhône-Alpes	1,051	372€ (±1,226)	262€ [226-451]
Nouvelle-Aquitaine	995	326€ (±684)	262€ [153-317]
Ile-de-France	977	296€(±70)	262€ [262-263]
Bourgogne Franche-Comté	29	421€ (±572)	262€ [262-263]
Hauts-de-France	156	264€ (±21)	262€ [262-263]
Occitanie	126	298€ (±209)	263€ [226-317]

STD: Standard deviation / IQR : Interquartile range / SS: Sub-sequences of treatment in HAH setting

Table 3. Duration of sub-sequences and corresponding costs

	SS with 1 day duration N(%); *Mean costs (€)(±STD)*	SS with 2 days duration N(%); *Mean costs (€)(±STD)*	SS with 3 days duration N(%); *Mean costs (€)(±STD)*	SS with more than 3 days duration N(%); *Mean costs (€)(±STD)*
Total (N=3,430)	2,753 (80.3) ***247€ (±48)***	605 (17.6) ***446€ (±60)***	33 (1.0) ***798€ (±159)***	39 (1.1) ***4,080€ (±6,246)***
By indications				
Lung cancer (N=2,594)	2,044 (78.9) ***244€ (±53)***	482 (18.6) ***450€ (±58)***	31 (1.2) ***801€ (±164)***	37 (1.4) ***4,258€ (±6,364)***
Melanoma (N=836)	709 (84.8) ***255€ (±24)***	123 (14.7) ***432€ (±66)***	2 -	2 -
By regions				
Auvergne-Rhône-Alpes	612 (58.2) ***233€ (±29)***	430 (40.9) ***435€ (±50)***	2 (0.2) -*	7 (0.7) -*
Hauts-de-France	155 (99.4) ***262€ (±29)***	1 (0.6) -*	0 -*	0 -*
Ile-de-France	945 (96.7) ***271€ (±24)***	5 (0.5) -*	16 (1.6) -*	11 (1.1) -*
Nouvelle-Aquitaine	823 (82.7) ***219€ (±64)***	145 (14.6) -*	13 (1.3) -*	14 (1.4) -*
Occitanie	121 (96.0) ***269€ (±43)***	3 (2.4) -*	1 (0.8) -*	1 (0.8) -*

SS: Sub-sequences /STD: Standard deviation

** : Regions and sub-sequences duration with <11 patients are not represented according to data privacy requirements*

Conclusions

- **In 2021-2022, development of ICI infusion in HAH was heterogenous in French territories.**
- **HAH development depends on indications treated and patient profiles.**
- **Patient pathways depended on indication and differed according to regions. Further analyses on healthcare resources will allow to understand how optimizing HAH use for ICI patients in France.**
- **In France, HAH offer must be analyzed in order to understand if ICI patients' needs in HAH are met.**

References

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Declaration of interests

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