Poster
PCN507

CAN TRANSFERABILITY OF CLINICAL TRIALS POPULATION TO REAL WORLD SETTING BE ASSESSED USING FRENCH NATIONAL HOSPITAL DISCHARGE DATABASE? A CASE STUDY IN ONCOLOGY

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Introduction

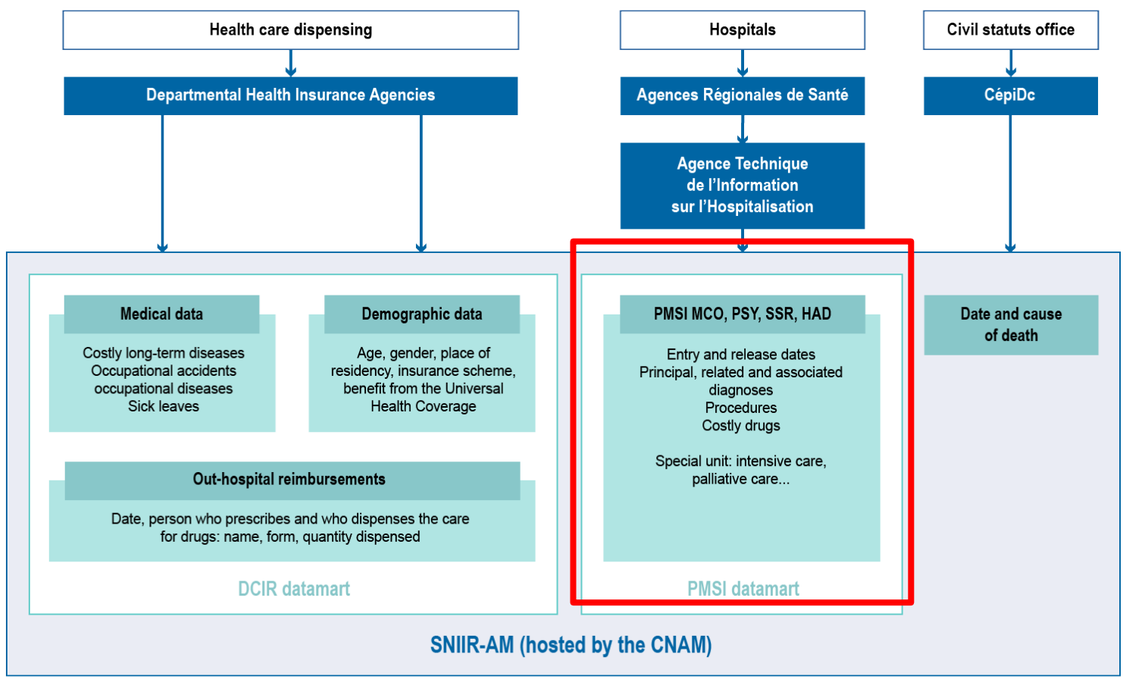
French national hospital discharge database

- The French health care system is based on universal coverage by one of several health care insurance plans covering around 96% of the French population. French System of National Health Insurance databases (SNDS) are organized since 2003 into a data warehouse named *Système national d'information inter-régime de l'assurance maladie* (SNIIR-AM).
- The national hospital discharge database *Programme de Médicalisation des Systèmes d'Information* (PMSI) covers all hospital stays in France, in public and private settings. The database is hosted by the Technical Agency for Hospitalization Information (ATIH). PMSI contains information linked to the stays as well as information on the patients. Separate databases exist for hospitalizations in Medicine, Surgery and Obstetrics (MCO), in Psychiatry (PMSI PSY), for rehabilitation (PMSI SSR) and for home hospitalization (PMSI HAD). A simplified version of the overall architecture of the French National Health insurance Information System is presented in Figure 1. PMSI is comprised within the whole system.

Transferability of patient characteristics

- Randomized clinical trials (RCT) have a set of inclusion and exclusion criteria enabling to target the patient population that will be analyzed. Thus, transferability of patient characteristics from RCTs to real life setting are important when assessing effectiveness of a product after its commercial launch.

Figure 1. Simplified architecture of the French National Health Insurance Information System[1]



Objective

- The objective was to assess to what extent the French hospital discharge database can be used to assess transferability of patient characteristics from phase III randomized clinical trials of nivolumab in oncology to real life setting.

Methods

PMSI data

PMSI contains exclusively data linked to hospitalizations. PMSI does not contain information on healthcare resource utilization outside the hospital setting. Main data on patients and hospital activities contained in PMSI are summarized in Table 1.

Table 1. Main PMSI data on patients and hospital activities

Patient characteristics	Hospital activities
Diagnostic codes (one primary diagnosis, one related diagnosis, and up to 30 associated diagnosis) with International Classification of Disease (ICD)	Medical Procedures
Diagnosis-Related Group	Start and end date for hospital stays, including ambulatory stays
Demographics (age, gender, place of residence)	Costly drugs dispensed

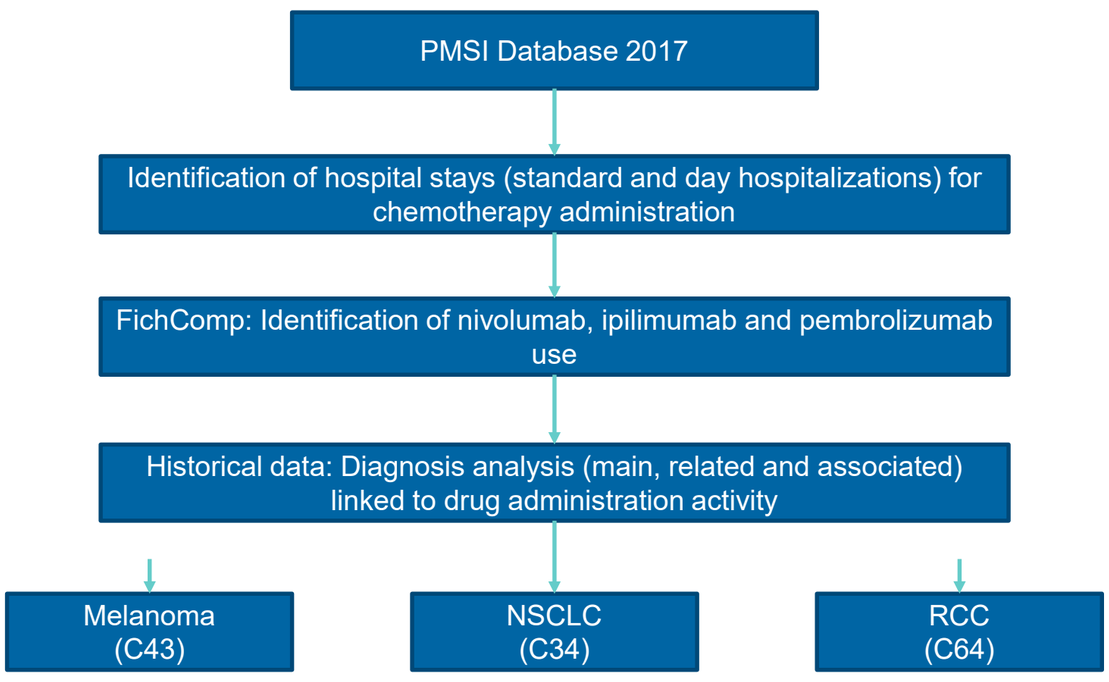
Phase III randomized clinical trials

- Patient characteristics in phase III randomized clinical trials (RCT) of nivolumab in squamous (SQ) and non-squamous (NSQ) non-small-cell lung cancer (NSCLC), melanoma and renal cell carcinoma (RCC) were taken from published RCTs.
- CheckMate 017[2] is a randomized, open-label, international, phase III study evaluating the efficacy and safety of nivolumab versus docetaxel in patients with advanced squamous-cell non-small-cell lung cancer who have disease progression during or after first-line chemotherapy.
- CheckMate 057[3] is a randomized, open-label, international, phase III study evaluating the efficacy and safety of nivolumab versus docetaxel in patients with advanced non-squamous-cell non-small-cell lung cancer who have disease progression during or after platinum-based doublet chemotherapy.
- CheckMate 025[4] is a randomized, open-label, phase III study evaluating the efficacy and safety of nivolumab versus everolimus in patients with renal-cell carcinoma who have received previous treatment.
- CheckMate 066[5] is a randomized, phase III study evaluating the efficacy and safety of nivolumab versus dacarbazine in previously untreated patients who had metastatic melanoma without a BRAF mutation.
- The primary endpoint of all four studies was overall survival.

Assessing transferability

- A retrospective cohort study was conducted with patients having received at least one dose of nivolumab in 2017 (most recent available data from PMSI).
- The administrations of nivolumab were identified via the claims file (Fichcomp) which enables hospitals to be reimbursed when using a costly drug included in the above diagnosis-related groups (DRG)
- The cohort was split into subgroups based on related diagnosis using ICD-10 codes linked to discharge activity. As no histology is recorded in PMSI, no distinction was made between non squamous and squamous in NSCLC.
- Three subgroups were analyzed: melanoma, NSCLC and RCC.

Figure 1. PMSI query methodology



Results

RCT Patient characteristics retrieved via PMSI

- In 2017, 15,787 patients were treated with nivolumab. PMSI allowed to capture few patient characteristics compared to those described in the RCTs.
- In Squamous NSCLC, 5 out of 12 characteristics were retrieved: age, age category, sex, central nervous system metastases, geographic region (Table 2)
- In Non Squamous NSCLC, 4 out of 15 characteristics were retrieved: age, age category, sex, geographic region (Table 2).
- In melanoma, 4 out of 10 characteristics were retrieved: age, sex, geographic region, history of brain metastasis (Table 3)
- In RCC: 4 out of 12 characteristics were directly retrievable: Median age, sex, site of metastases and previous nephrectomy (Table 4).
- Overall, partial information on metastases and prior systemic drugs can also be retrieved under certain conditions.

Table 2. Patient characteristics for patients treated by nivolumab for NSCLC in RCTs and their availability in PMSI

Patient characteristics	NSCLC		Retreivable in PMSI
	Squamous	Non Squamous	
Age	Yes	Yes	Yes
Age category	Yes	Yes	Yes
Sex	Yes	Yes	Yes
Race	Yes	Yes	No
Disease Stage	Yes	Yes	Metastases Yes/No
ECOG Performance Status Score	Yes	Yes	No
Central nervous system metastases	Yes	No	Yes
Smoking Status	Yes	Yes	No
Geographic Region	Yes	Yes	Yes
Other systematic cancer therapy	Yes	Yes	Only if "extra-DRG" drug
Positive EGFR mutation status	No	Yes	No
Positive ALK translocation status	No	Yes	No
Positive KRAS mutation status	No	Yes	No
N° of Prior systemic therapies	No	Yes	Only if "extra-DRG" drug
Best Response to most Recent Prior systemic regimen, according to investigator	Yes	Yes	No
Time from completion of most recent prior systemic regimen	Yes	No	Can be calculated if "extra-DRG" drug
Type of prior systemic therapy	No	Yes	Only if "extra-DRG" drug

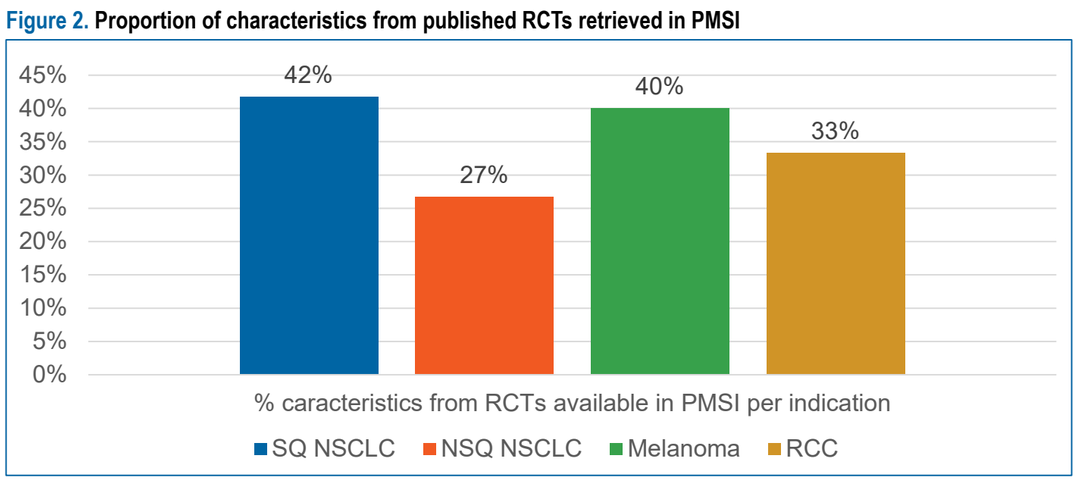
Table 3. Patient characteristics for patients treated by nivolumab melanoma in RCT and their availability in PMSI

Patient characteristics	Melanoma (1st Line)	Retreivable PMSI
Age	Yes	Yes
Sex	Yes	Yes
Geographic Region	Yes	Yes
ECOG Performance Status Score	Yes	No
Metastases Stage	Yes	Metastases Yes/No
Lactate dehydrogenase	Yes	No
History of brain metastases	Yes	Yes
PD-L1 status	Yes	No
BRAF Status	Yes	No
Prior systemic Therapy	Yes	Only if "extra-DRG" drug

Table 4. Patient characteristics for patients treated by nivolumab for RCC in RCT and their availability in PMSI

Patient characteristics	RCC (2nd Line+)	Retreivable PMSI
Median Age	Yes	Yes
Sex	Yes	Yes
Race	Yes	No
MSKCC risk group	Yes	No
Karnofsky performance status	Yes	No
Disease sites that could be evaluated	Yes	No
Site of metastasis	Yes	Yes
Previous nephrectomy	Yes	Yes
Median time from initial diagnosis to randomization	Yes	No
Previous antiangiogenic regimens for treatment of RCC	Yes	Only if "extra-DRG" drug
Previous systemic cancer therapy for metastatic RCC (Sunitinib, Pazopanib, Axitinib)	Yes	No
Patients with quantifiable PD-L1 expression	Yes	No
Patients without quantifiable PD-L1 expression	Yes	No

Figure 2. Proportion of characteristics from published RCTs retrieved in PMSI



Transferability of patient characteristics retrieved in PMSI

- Median age in RCTs vs. PMSI was respectively:
  - 63 vs. 65 years in NSCLC
  - 65 vs. 65 years in melanoma,
  - 62 vs. 68 years in RCC
- Male population age in RCTs vs. PMSI was respectively :
  - 71% vs. 71% in NSCLC
  - 58% vs. 59% in melanoma
  - 77% vs. 73% in RCC
- Number of metastatic sites and prior therapies can also be retrieved (if entered in FichComp, costly drugs above-DRG). Surgeries, such as nephrectomy in RCC can also be found in PMSI.

The following characteristics were not retrieved in PMSI:

- Oral therapies, performance status, histology, tumor mutations and risk factors such as smoking status, MSKCC risk group, etc.

Limitations

- PMSI is a medico-administrative database. Its main function is to track hospital discharges in order for hospitals to fund their activities via the reimbursement by French national health insurance based on tariffs. Consequently, the information parameterized and tracked via PMSI are those considered useful by health authorities in defining the diagnosis-related groups and related tariffs.
- Hence, even if a given clinical exam (ie. Blood test, scans, etc.) is tracked within PMSI, the results of such exam are not made available.
- Only the consumption of costly drugs tracked via the "above DRG" list are available. Intravenous (IV) drugs administered at the hospitals and which cost is already included in the IV infusion DRG cannot be retrieved in PMSI.
- Additional information that can enable to assess transferability of patient characteristics to real world patients not available directly in PMSI are: histology, mutational status, performance status, smoking status, alcohol use, exercise, diet, family history and causes of death. Nevertheless, proxies can be found to retrieve information. For example, histology in lung cancer can be retrieved via "marker drugs" such as bevacizumab which can be used in non-small cell lung cancer other than predominantly squamous cell histology[6]. Patients' weight could also be retrieved for nivolumab via the milligrams entered in FichComp, as posology was still weight dependent in 2017.
- The information entered in PMSI is of the responsibility of the Medical Information Department of each hospital. As there are over 2,000 hospitals nationwide, it can hence be expected that there is some heterogeneity regarding the way the data is recorded.
- Finally, as PMSI is only used for hospital activity, no information linked to patient characteristics or disease management happening outside hospital premises can be retrieved, including causes of death when they occur outside the hospital setting.

Conclusions

PMSI is an exhaustive and mandatory database enabling the assessment of real-life use of oncology drugs in French hospital setting. Some patient characteristics can be retrieved or recalculated. Median age as well sex ratio in published RCTs were transposable to those if patients who received nivolumab for the treatment of lung cancer, melanoma and renal cancer in France in 2017. Conducting a similar analysis using SNIIRAM would allow to identify additional information such as prior and subsequent oral therapies as well as deaths which occur outside the hospitals

However, to assess transferability of RCT patient characteristics to real-life setting, additional sources are needed to retrieve clinical information such as performance status, histology, tumor mutations, and risk factors. In order to retrieve additional clinical data, a solution could be to link registries to SNIIRAM in order to gather the comprehensive information on patients including laboratory results, biomarker status, etc.

References

1. Moulis et al. French health insurance databases: What interes for medical research?. La revue de medecine interne. 2014
2. Brahmer et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. NEJM. 2015.
3. Borghaei et al.. Nivolumab versus docetaxel in Advanced Nonsquamous Non-Small-Cell Lung Cancer. NEJM.2015.
4. Motzer et al. Nivolumab versus Everolimus in Advanced Renal-Cell Carcinoma. NEJM. 2015
5. Robert et al. Nivolumab in Previously Untreated Melanoma without BRAF Mutation. NEJM. 2015
6. Avastin EPAR: https://www.ema.europa.eu/en/documents/product-information/avastin-epar-product-information_en.pdf

Presented at ISPOR Europe 2019; November 2–6, 2019; Copenhagen, Denmark

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