Subcutaneous trastuzumab uptake in France: a nationwide real-world analysis of indication, setting, and regional practice patterns - BI-FORM study

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Introduction

- An increasing number of oncology therapies are available in both intravenous (IV) and subcutaneous (SC) formulations, with new SC formulations, particularly in immunotherapy, under development. However, their impact on real-world care pathways remains poorly documented.
- Trastuzumab, available in both IV and SC formulations since 2015 and widely used in early-stage and metastatic breast cancer, provides a relevant model to investigate these changes.

OBJECTIVE : To assess trends in SC trastuzumab uptake over time and across regions in France.

Method

Study design and data source

- This retrospective, nationwide observational study used the exhaustive French hospital discharge database from 2015 to 2024. It combined repeated cross-sectional analyses (unit of analysis: trastuzumab administration) and longitudinal patient-level analyses.

Study population

- All hospital stays in medical, surgical and obstetric care (MSO) or hospital-at-home (HAH), with discharge between January 1, 2015 and December 31, 2024 and at least one trastuzumab administration, were included. Administrations were identified in the Liste en sus using UCD codes (IV: 14 codes; SC: 1 code).

Variables

- Route of administration (IV/SC), year, disease stage and concomitant treatment (derived from indication codes, available from 2019), hospital type (university hospital, comprehensive cancer center, general hospital, private) and region of the administrations.

Analysis

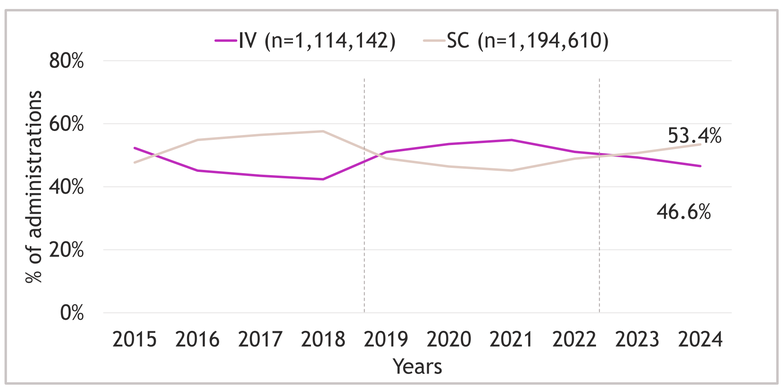
- Cross-sectional: the proportion of SC administrations (SC / all trastuzumab administrations) was estimated yearly (2015-2024), then by indication and concomitant treatment (2019-2024), and by region and hospital type.
- Longitudinal: patients initiating trastuzumab (no exposure in the previous 6 months) were followed until end of 2024. Initial route and switches between formulations (IV→SC, SC→IV) were described.

Results - Cross-sectional analyses

Overall

- Between January 1, 2015, and December 31, 2024, 2,308,752 trastuzumab administrations were recorded during MSO or HAH stays in France, involving 192,498 patients.
- Over the 10-year study period, SC route accounted for 51.7% of all trastuzumab administrations.
- The distribution of IV and SC administrations remained broadly balanced throughout the study period, with shifts in the predominant route of administration in 2019 and 2023 (**Figure 1**). The proportion of SC administrations was 54.8% between 2015 and 2018, 47.3% between 2019 and 2022, and 52.1% between 2023 and 2024.

Figure 1. Trastuzumab administration rate by route of administration, 2015-2024, all indications combined



By indication

Stratification by indication revealed substantial differences in SC trastuzumab use.

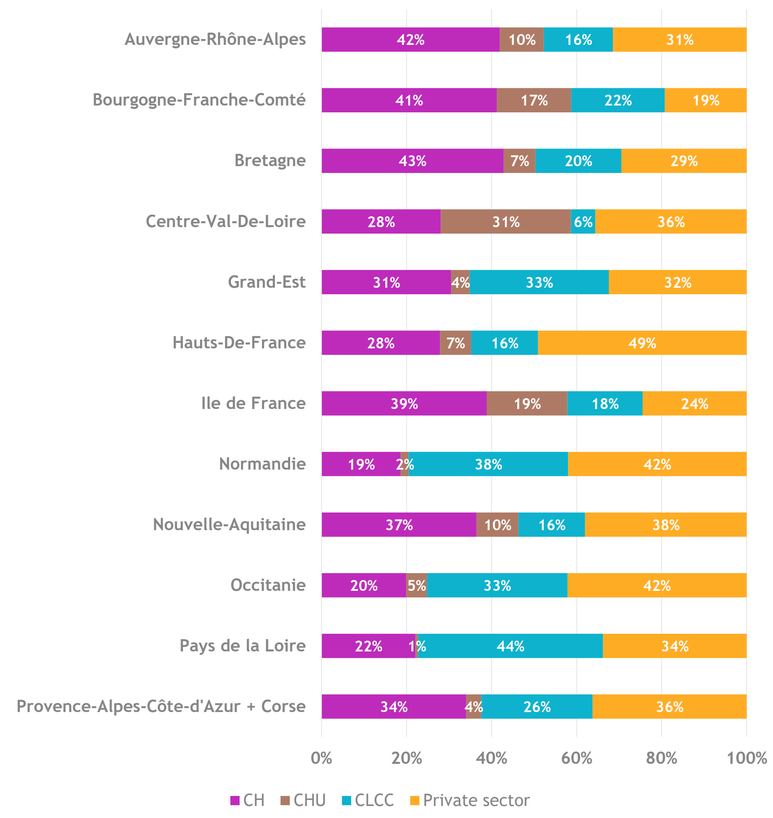
In metastatic cancers the proportion of SC administrations was lower, with variations according to the associated treatment regimen (29.0% of administrations with another IV treatment, 61.7% with non-IV therapy and 53.9% in monotherapy)

- Across all indications, the SC administration rate in early-stage breast cancers was 65.5%.

By region

- The distribution of administrations across hospital types varied substantially across regions, for instance, CLCC accounted for 44% of administrations in Pays de la Loire vs. 6% in Centre-Val-de-Loire while CHU generally remains the smallest category in most regions (ranging from 1% to 31%), except in Centre-Val-de-Loire and Ile de France. (**Figure 2**).

Figure 2. Distribution of center status by region for trastuzumab administrations, France, 2024



CH: General Hospital (Centre Hospitalier); CLCC: Comprehensive Cancer Center (Centre de Lutte Contre le Cancer); CHU: University Hospital (Centre Hospitalier Universitaire); Percentages are rounded and may not sum to 100%

- The proportion of administrations in patients with early-stage breast cancer also varied across regions, ranging from 69.1% in Grand-Est to 83.1% in Nouvelle-Aquitaine (**Table 1**).
- The link between center-type distribution and SC form rate wasn't straightforward — a lower share of administrations in private sector appeared to be associated with higher SC form use, but similar rates can also arise in regions with very different center distributions. For example, Hauts-de-France (with the highest private sector share, 49%) and Pays de la Loire (with the highest CLCC share, 44%) had nearly identical SC form rates (~36.6%) despite their contrasting profiles.

Table 1. Proportion of early-stage breast cancer and subcutaneous trastuzumab use by region, France, 2024

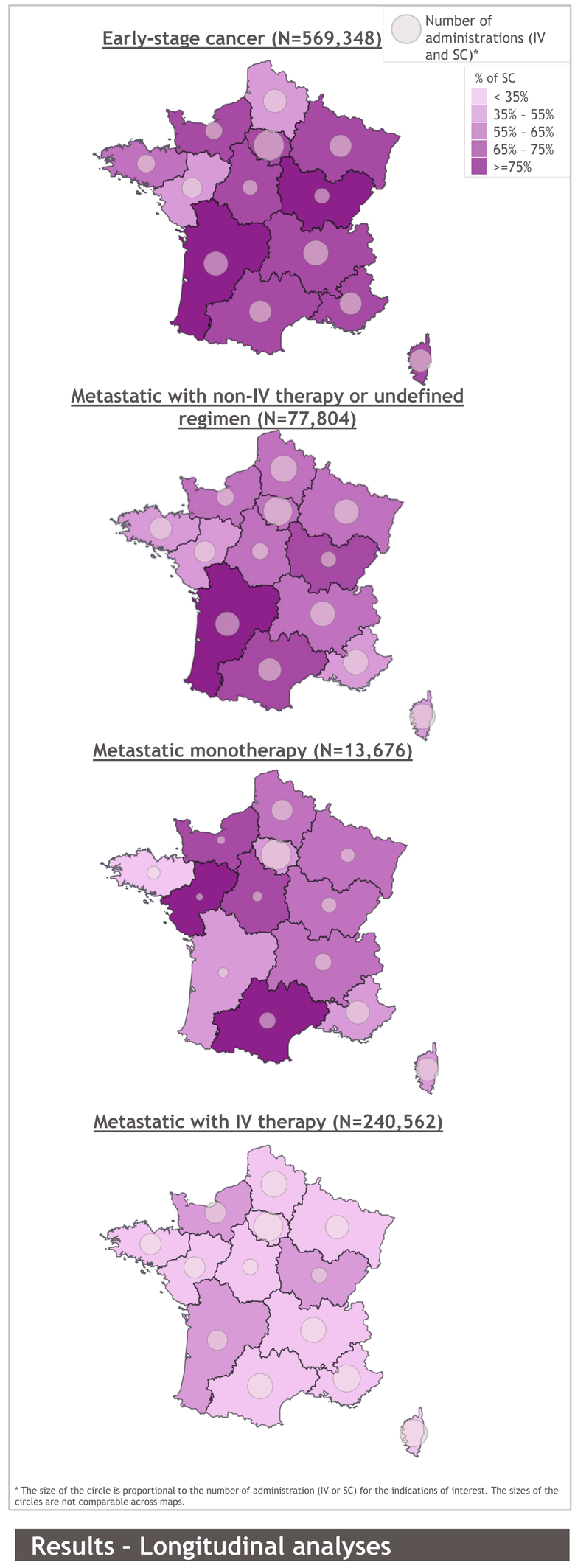
Region	SC form N(%)	Early-stage breast cancer N(%)	Metastatic cancer N(%)
Auvergne-Rhône-Alpes	10,521 (54.8%)	15,271 (79.6%)	3,915 (20.4%)
Bourgogne-Franche-Comté	4,773 (74.1%)	4,978 (77.3%)	1,462 (22.7%)
Bretagne	4,943 (50.5%)	6,917 (70.7%)	2,864 (29.2%)
Centre-Val-De-Loire	3,247(48.6%)	4,995(74.8%)	1,682 (25.2%)
Grand-Est	6,968(51.4%)	9,377 (69.1%)	4,187(30.9%)
Hauts-De-France	5,777(36.6%)	11,201 (70.9%)	4,594 (29.1%)
Ile de France	14,626 (51.4%)	21,844 (76.8%)	6,598 (23.2%)
Normandie	5,131 (61.3%)	5,985 (71.5%)	2,392 (28.5%)
Nouvelle-Aquitaine	10,649 (71.6%)	12,366 (83.1%)	2,516 (16.9%)
Occitanie	9,735 (57.3%)	13,163 (77.4%)	3,835 (22.6%)
Pays de la Loire	4,518 (36.7%)	9,085 (73.9%)	3,214 (26.1%)
Provence-Alpes-Côte-d'Azur + Corse	7,252 (54.8%)	9,539(72.1%)	3,693 (27.9%)

By indication and region

- Consistent with the regional variations observed in the 2024 analysis, **SC uptake varied substantially by region and indication over 2019-2024.** (**Figure 3**). Despite similar overall SC uptake in Hauts-de-France and Pays de la Loire in 2024, indication-specific rates differed, particularly for metastatic cancer treated with monotherapy (59.9% vs 89.8%) and non-IV therapy (63.0% vs 41.3%). Conversely, differences observed between Île-de-France and Bourgogne-Franche-Comté were also seen across indications.
- Bourgogne-Franche-Comté consistently showed higher SC uptake than the national level, particularly in early-stage cancer (85.6%).

In contrast, SC uptake in Pays de la Loire varied by indication, with rates above the national level for monotherapy (89.8% vs 53.9%), but below for metastatic cancer with non-IV therapy (41.3% vs 61.7%) and early-stage cancer (35.3% vs 65.5%).

Figure 3. Total trastuzumab administrations (IV + SC) and proportion of SC use by region, 2019-2024



* The size of the circle is proportional to the number of administration (IV or SC) for the indications of interest. The sizes of the circles are not comparable across maps.

Results - Longitudinal analyses

- Between 2015 and 2024, a total of 83,801 incident patients received trastuzumab. Among these patients, 27.4% initiated treatment with the SC form. Additionally, 41.3% patients switched formulations at least once, including 39.9% from IV to SC and 7.4% from SC to IV.
- The proportion of SC trastuzumab administration was similar across age groups, except in combination therapy, with slightly higher use among patients aged ≥75 years.

Conclusion

Using trastuzumab as a model of SC drug utilization, we observed overall stable SC use with substantial annual and regional variation, which may reflect not only indication and care supply but also local practices, institutional policies, and broader changes such as the COVID-19 pandemic and the expansion of hospital-at-home care

Reference

1. Opinion of the HAS Transparency Committee dated July 20, 2005, https://www.has-sante.fr/upload/docs/application/pdf/ct032203.pdf

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- All authors contributed to and approved this poster.

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