

# Epidemiology and Hospital Management of Patients With PROS in France

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## OBJECTIVE

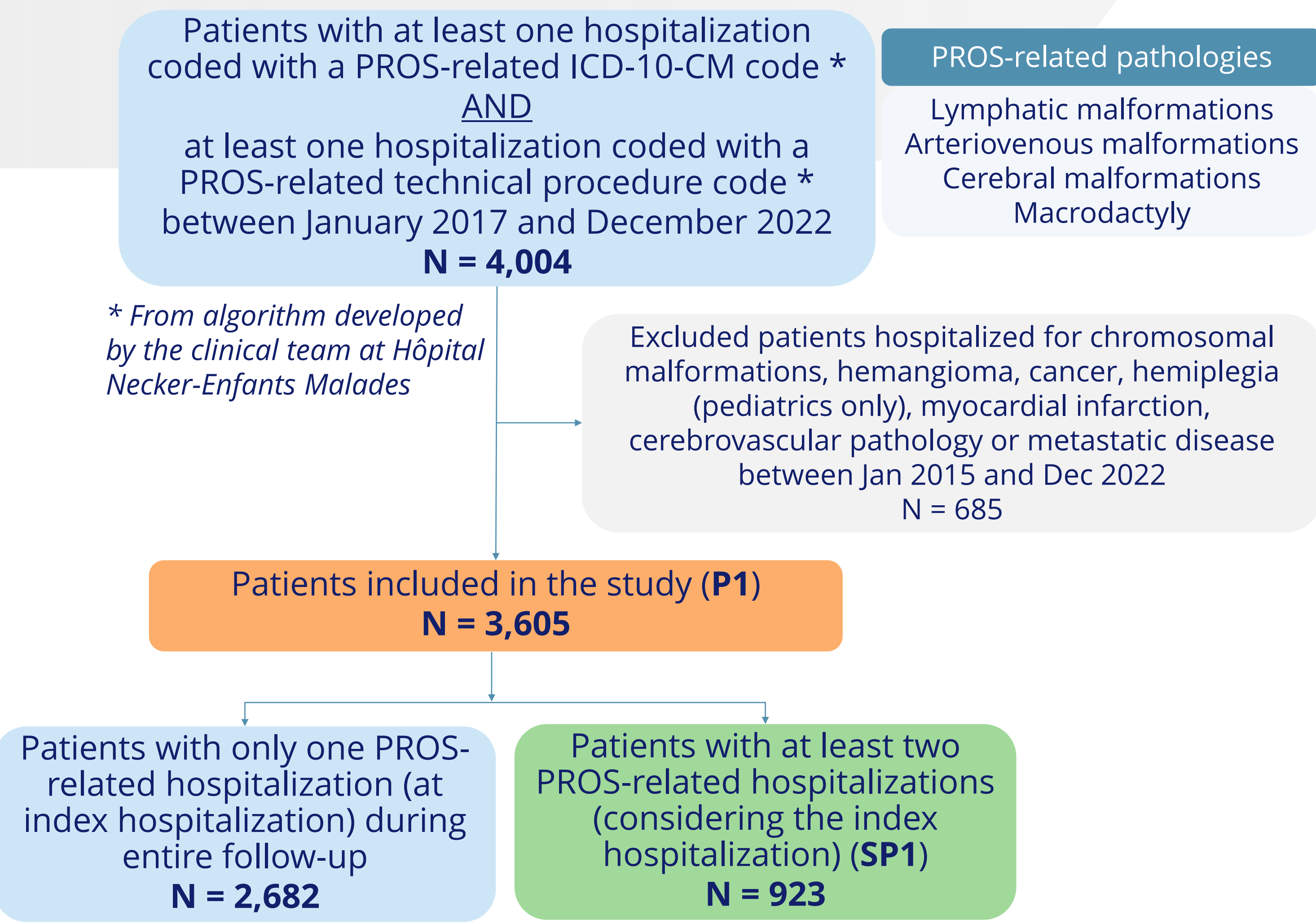
- > PIK3CA-related overgrowth spectrum (PROS) is a rare condition with diverse clinical manifestations caused by activating PIK3CA mutations, with a prevalence estimated to 14 patients per 1 million persons according to OrphaNET and NIH Genetics.
- > However, confirming the epidemiology and burden of PROS remains challenging due to the lack of specific medico-administrative coding. Although today no treatment is approved in Europe for PROS, alpelisib has demonstrated significant improvement in treating patients with severe forms of PROS (EPIK-P1 study)<sup>1</sup>.
- > This study assesses the epidemiology and hospital-related resource utilization of patients with multiple PROS-related hospitalizations to support alpelisib assessment by French Health Technology Assessment (HTA) authority.

## METHODOLOGY

- > **Data source:** Retrospective analyses of the French national claims hospital database (PMSI) were conducted from January 2015 to December 2022.
- > **Study design:** Patients were identified using a combination of inclusion (e.g., malformations commonly associated with PROS) and exclusion (e.g., hemangioma diagnosis) criteria based on ICD-10-CM and technical procedure codes at time of hospitalization.
- > **Index date:** First occurrence of an ICD-10-CM code or a technical procedure code associated with PROS during the inclusion period (2017-2022).
- > **Outcomes:** Hospitalizations and external technical procedures and visits (ACE) rates were estimated per person-year (PPY) in the total population (P1) and the sub-population (SP1) of patients with multiple PROS-related hospitalizations.

## RESULTS

### PATIENT IDENTIFICATION



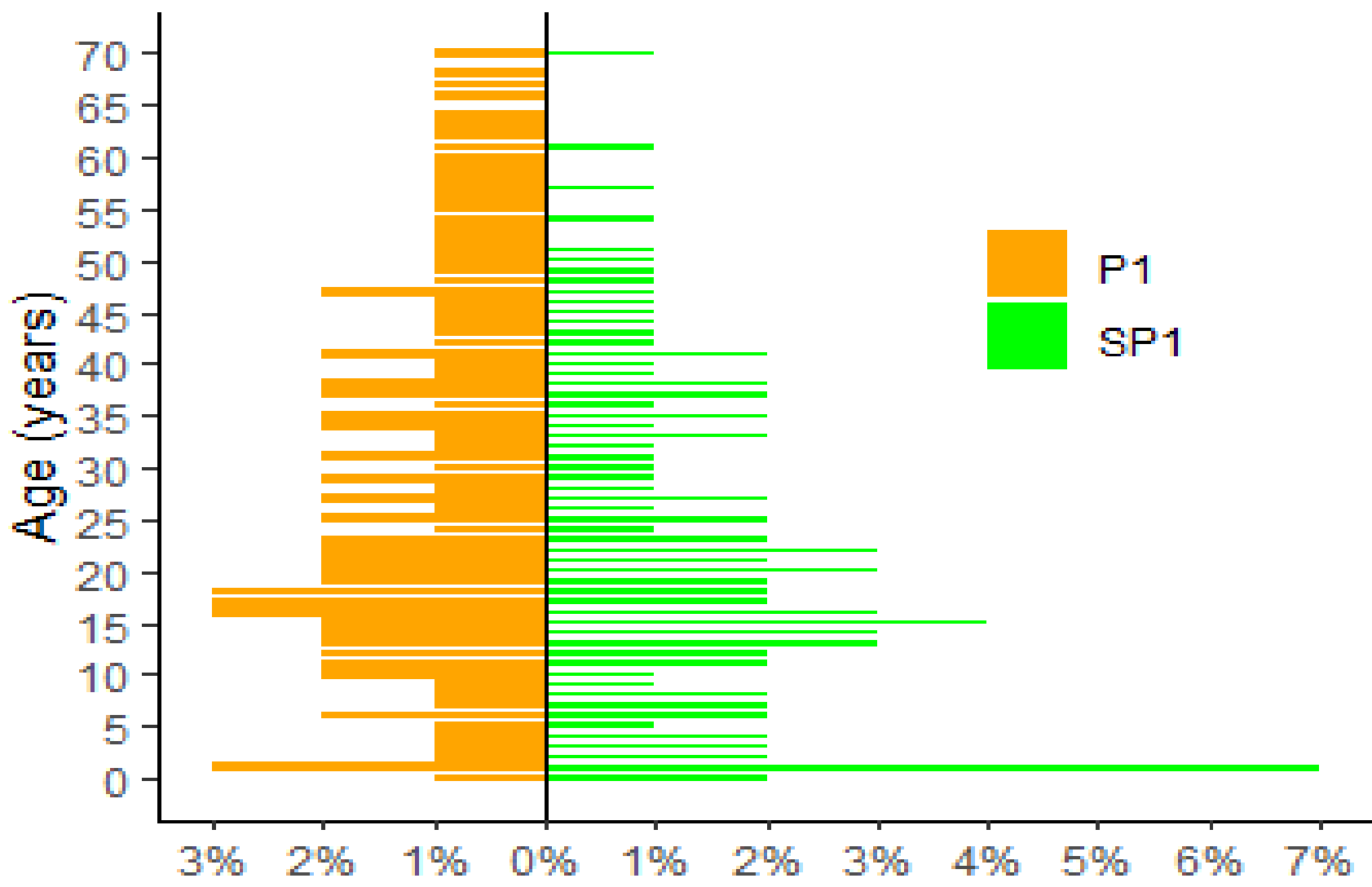
### « AT HOSPITAL »-BASED PREVALENCE

	P1 (N = 3,605)	SP1 (N = 923)
Yearly prevalence rate per 1 million inhabitants [95% CI]	8.83 [8.15 - 9.57]	5.89 [5.34 - 6.49]

## SOCIO-DEMOGRAPHIC CHARACTERISTICS



### AGE DISTRIBUTION



Patient age was calculated at index date. Pediatric patients, particularly one-year-old patients and those aged 13 to 17 years, were proportionally more present in both populations than the other age groups, and there was also a larger proportion of one-year-old patients in SP1 compared to P1.

### FOLLOW-UP

In the **P1** group, **47.8% had at least one additional** all-cause hospitalization in France after index date, with a median (Q1 - Q3) follow-up of **0 months (0.0 - 16.7)** (52.2% had only the initial hospitalization). By contrast, 100% of SP1 patients had at least one additional hospitalization, with a median (Q1 - Q3) follow-up of **15 months (5.5 - 32.7)**.

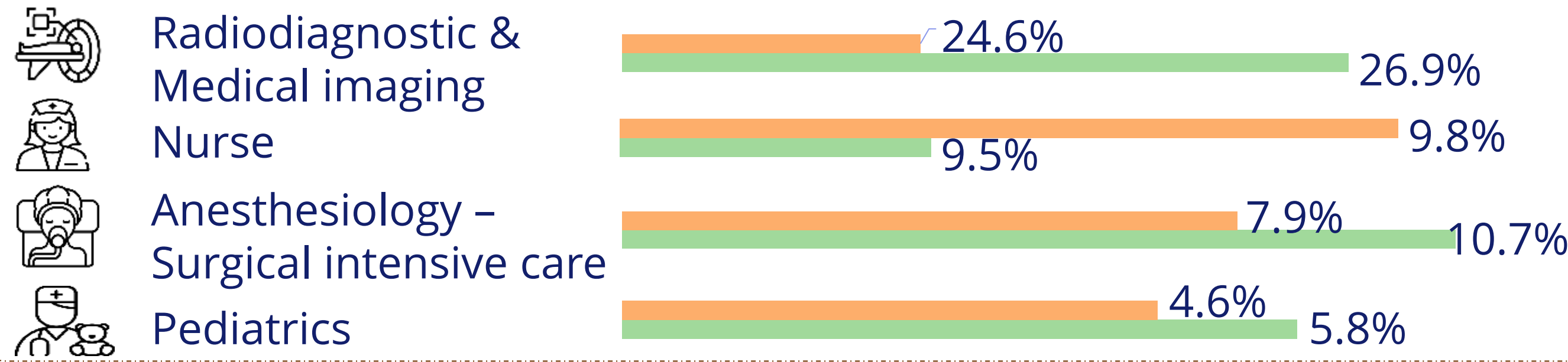
## HEALTHCARE RESOURCE CONSUMPTION (HCRU)

**59%** of the PROS-related hospitalizations were **outpatient hospitalizations** for P1 and SP1, respectively.

HCRU per person-year (PPY) during the follow-up period (index included) [95%CI]	P1 (N = 3,605)	SP1 (N = 923)
All-cause hospitalization	2.52 [2.47- 2.58]	2.28 [2.21- 2.36]
All-cause ACE	6.03 [5.95 - 6.12]	5.44 [5.32 - 5.56]
PROS-related hospitalization	1.61 [1.57- 1.66]	1.59 [1.53- 1.66]
ACE executed by specific specialties*	1.59 [1.55 - 1.64]	1.70 [1.63 - 1.76]
Emergency room visits not followed by hospitalization	0.53 [0.51 - 0.56]	0.45 [0.41 - 0.48]

### \*Medical specialties associated with PROS

#### Main Specialties of Healthcare Professionals Executing ACEs of Interest



The **higher rate of all-cause and PROS-related hospitalizations** PPY in P1 compared to SP1 likely reflects the **longer mean (SD) follow-up for SP1 patients** (20.5 (17.7) vs. 10.7 (16.7) months).

Additionally, PROS-related hospitalizations PPY were generally lower in **adult** patients in both P1 and SP1 groups (1.45 [95% CI: 1.40-1.50] and 1.53 [1.45-1.62], respectively) compared to **pediatric age groups** (0-1, 2-5, and 6-17 years).

## CONCLUSION

- > This study presents a novel method to identify patients with PROS hospitalized for disease management in a French claims database and provides insights on the epidemiology and gives an overview of the hospital management of these patients.
  - o Due to the absence of specific diagnosis codes for PROS (such as ICD-10-CM), patients in this study were identified using inclusion and exclusion criteria from an algorithm developed by the clinical team at Hôpital Necker-Enfants Malades (AP-HP).
- > We identified **3,605 patients (P1) hospitalized for PROS** management in France from 2017 to 2022, with 26% (923 patients - **SP1**) having at least one subsequent PROS-related hospitalization after their initial admission.
- > Although the hospital management costs of PROS were analyzed in this study, the results are not presented. The estimated costs would only provide a partial view of the economic burden to the French Health Insurance system, focusing solely on Medical, Surgical and Obstetrics (MSO) hospitalization costs.
  - o Experts indicate that patients with PROS often need additional services beyond hospitalization, such as home care, post-surgical follow-up, rehabilitation, and support from office-based practitioners—including physiotherapy, speech therapy, and home nursing care for patients on anticoagulant therapy requiring daily heparin injections—which were not/could not be considered in this analysis.
- > Thanks to this innovative method, we now have insights on the epidemiology and hospital management of patients hospitalized for PROS in France.

## REFERENCES

1. Canaud, Guillaume, et al. "Alpelisib for treatment of patients with PIK3CA-related overgrowth spectrum (PROS)." Genetics in Medicine 25.12 (2023): 100969.

## ACKNOWLEDGMENTS

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CG : Public health physician; SB, PN: Alira Health SAS France; BD, BL, MAS : Novartis Pharma SAS; PM : IT&M Consulting SAS; CTS : Public health physician



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