The SACHA-France study (NCT04477681) is a prospective, multicenter, national observational registry that collects real-world data of innovative therapies (targeted therapies, immunotherapy or chemotherapy) administered to patients ≤ 25 years-old with pediatric malignancies (solid tumor or leukemia), or related conditions, provided through the French early access authorization and compassionate use programs or as an off-label anti-cancer medicine that has been first approved in adults in Europe after the implementation in 2017 of the EU Pediatric Regulation (1901/2006/EC).

Before inclusion in the SACHA-France study, interregional multidisciplinary discussion is mandatory to ensure that all patients receive the most adapted available treatment, preferably within clinical trials. This study is a Research Involving Human Subjects of category 3 (non-interventional studies) according to the French Jardé law, that request patient or his/her parents/legal representative's non-opposition, and has been approved by the French ethic committee in compliance with the EU General Data Protection Regulation. SACHA-France is open in all SFCE centers.

Information collected in the SACHA study include: molecular details supporting the choice of the innovative treatment (if indicated), type of cancer, stage and lines of previous treatments as well as innovative treatment dosage, start date, dose reductions, temporary or permanent discontinuation and causes of change in dosage or treatment stop. Follow-up information is collected every 3 months until end of treatment or patient's death documenting tumor response and adverse drug reactions (ADRs).

Adverse drug reactions reporting

Adverse drug reactions (ADRs) attributable to the treatment under study are described according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5. Only

CTCAE grade ≥2 clinical and/or CTCAE ≥3 biological ADRs are reported. All reported ADRs that lead to drug dose reduction, delay or end of treatment, as well as all unexpected ADRs and all serious ADRs (SADRs) are remotely monitored by the Pharmacovigilance Unit of Gustave Roussy, and reported to Regional Pharmacovigilance Centers and to the marketing authorisation holders.

Outcome assessments

Progression-free survival (PFS) and best response from the start of treatment to tumor relapse/progression is assessed by the patient's treating physician, following the standard response criteria for each tumor type. In case of reported ORR, radiological reports at baseline/time of response are reviewed by the SACHA-France coordinating investigator to confirm the coherence of the reported response.

Data analysis

The SACHA France Steering Committee is composed of the SACHA France coordinating investigator, one pediatric hemato-oncologist representative from each of the 7 Interregional Pediatric Oncology Networks (OIR) that constitute the national network that gathers all the pediatric oncology centres that treat patients < 18 years old with pediatric malignancies (solid tumor or leukemia), the UFPV of Gustave Roussy and a representative from the sponsor. The SACHA France Steering Committee meets every two months to steer the implementation of the project, control the overall quality and review main safety and activity data.

All cohorts of 10 patients or more with measurable/evaluable disease treated with the same drug for the same indication (either a disease/biomarker-match or the presence of a biomarker in a tissue-agnostic situation) and reported at least 6 month-follow-up, as well as

patients with observed anti-tumor activity previously not reported are reviewed by the SACHA France Steering Committee and information shared with all SFCE centres. In case of no activity is observed out of 10 patients treated with the same drug/tumor type/biomarker or if there is a major safety concern (severe toxicity/death), the Steering Committee recommends to all SFCE centers to no longer prescribe the medicine in that specific indication. If outstanding not previously reported activity results are observed, the Steering Committee recommends the development of an early phase clinical trial in that specific indication.