

HARMONY Alliance Partners Anthony Moorman (Newcastle University) and Anita Kienesberger (CCI Europe) explain how the HARMONY Alliance strives to improve the treatment of childhood blood cancer.

Children with blood cancer still have their lives ahead of them. HARMONY Alliance data-driven Research Projects will have a valuable impact on children, teenagers and young adults with cancer.



**Professor Anthony Moorman** of Newcastle University is an expert in ALL, Acute lymphoblastic leukemia.

"We think that a less intensive treatment will suffice in a substantial number of pediatric patients. The key challenge is to develop more robust prognostic markers to identify these patients. With its unique Big Data Platform, the HARMONY Alliance offers excellent opportunities to tackle this challenge."



**Anita Kienesberger** is the Chair of the European branch of Childhood Cancer International (CCI Europe).

"Cancer is the second leading cause of mortality in children in developed countries and blood cancer accounts for 40% of childhood cancers. Acute lymphoblastic leukemia (ALL) is the most common hematologic malignancy in children; the other hematologic malignancies are quite rare in this age group. Around 90% of children with ALL are cured, but the treatment protocols are intensive, typically involving multiple chemotherapeutic drugs administered over several months or years. The side effects of these treatments are considerable."

## Prognostic factors

Many prognostic factors have already been identified for pediatric ALL, including age of onset, gender, genetic profile of the leukemic cells, and minimal residual disease (MRD – the level of leukemic blasts that remain in the marrow after the first course of chemotherapy). These factors can predict the risk of relapse, but they have largely been studied in isolation so far. By pooling data of thousands of patients, HARMONY researchers will be able to study combinations of prognostic factors. This may allow them to more precisely predict clinical course and drug response, enabling physicians to rapidly select the most promising and least toxic treatment for a particular patient. If we combine data from all over Europe and examine the risk factors, maybe we can develop novel treatment regimens that are not so toxic for children.

## Rare subgroups

The HARMONY Alliance also studies rare subtypes of pediatric ALL. Moorman: “By pulling together data from multiple cohorts, HARMONY will allow us to study reasonable numbers of patients with rare subtypes of ALL. For instance, there is a small subgroup of patients who do not respond to any chemotherapy at all. The aim is to tease apart what exactly is going on in these high-risk patients. Another example is the T-ALL subtype, which is much rarer than the B-ALL subtype. Only around 20% of patients have the T-subtype and little is known about this particular form.”

The team also aims to study young adults with ALL. Moorman:

“There is a big ongoing debate about how to treat the age group between 15 to 30. Historically, they were treated on adult protocols, but a lot of data now suggests that they should actually be treated on pediatric protocols. In the UK, we now treat everyone up to the age of 24 on a pediatric protocol. The Nordic countries have even raised that cut-off to the age of 45. ALL is at its lowest prevalence in young adults, so there are few patients to inform us about the best treatment protocol. By bringing together many different datasets from the pediatric and the adult community, we will be in the best position to inform this debate. That is something that I am truly looking forward to.”

The HARMONY Big Data Platform offers unique opportunities to study the effect of genetic abnormalities across different hematologic malignancies. In addition, many of the drugs that we use to treat ALL are also used to treat other malignancies, particularly myeloma. And targeted drugs such as tyrosine kinase inhibitors should target a genetic abnormality whether it occurs in ALL or AML or myeloma. It is very valuable to study drug responses across diseases and see how the drugs interact with certain genetic abnormalities.