



The Monthly Newsletter for EpSSG Members

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The MYKIDS Pathology and Biology Review Board: An Exciting and Highly Promising Start

In this third EpSSG newsletter, we decided to briefly sharing the work of the pathology review board for the EpSSG biological study, MYKIDS (Molecular Identification and Characterization of non-Rhabdomyosarcoma Soft Tissue Sarcoma in Kids, Adolescents and Young Adults).

MYKIDS is a prospective biological study recruiting patients across EpSSG countries, aiming on the one hand to improve and refine diagnoses for individual patients to support optimal treatment, and on the other hand to comprehensively decipher the biological and genomic architecture of NRSTS in children, adolescents, and young adults. This study encompasses multiple objectives and work packages. Specifically, it aims to identify novel translocations and genetic drivers using WES, mRNAseq, and DNA methylation profiling, while also establishing reproducible molecular signatures critical for predicting outcomes and refining risk stratification. Moreover, the research focuses on liquid biopsy, the development of faithful tumor models, and the characterization of post-treatment molecular changes.

The MYKIDS protocol has been open since May 2024 and is already enrolling patients from the Netherlands, the Czech Republic, Greece and Italy. As part of the protocol, an international panel of pathologists regularly reviews submitted tumour samples from both pathological and molecular perspectives. To date, more than 46 tumours have been analysed to confirm diagnoses and, where appropriate, to perform additional molecular investigations.

Monthly virtual Diagnostic Review Board meetings provide an opportunity to share and discuss these findings before reporting back to the referring clinician. The meetings bring together the participating pathologists, biologists and paediatric oncologists, as well as the clinicians directly involved in each patient's care, who are also invited. They allow particularly challenging cases to be examined in depth. A deliberate decision was made not to discuss straightforward cases—for example, a typical synovial sarcoma with a characteristic fusion transcript—so that sufficient time can be devoted to the most difficult diagnoses. These meetings focus on rare and diagnostically complex conditions, with approximately three to five tumours discussed at each session. Some discussions are especially detailed. One example is a case of undifferentiated hepatic sarcoma with a t(11;19)(q11;q13.3/13.4) translocation suggestive of undifferentiated embryonal sarcoma (PMID: 32310940; chromosome 19 microRNA cluster, C19MC). Another concerns a tumour of an extremity for which the differential diagnosis was alveolar soft part sarcoma versus a PEComa-like rearranged neoplasm (PMID: 38597260). In the latter case, clustering findings and strong expression of HMB45 and desmin prompted extensive discussion before a final diagnosis could be proposed.

These two examples highlight the importance of integrated pathological and biological review for paediatric soft tissue sarcomas within MYKIDS. It is important to emphasise that these meetings are not intended to discuss treatment strategies, although potential therapeutic avenues may occasionally be raised in light of the findings.

Through this short overview and these two challenging cases, we aim to motivate everyone to keep enrolling as many patients as possible in this pivotal study. Furthermore, we hope to encourage centers and countries that have not yet joined to participate.