The SIOPEN-R-NET Project: Building a European Network for Neuroblastoma Treatment (HR-NBL-1/SIOPEN) and Research

The SIOPEN-R-NET project (EC grant No. QLRI-CT-2002-01768) aimed to build a European Neuroblastoma Research Network Structure to optimise the use of pre-existing infrastructures and to improve consistency and complementarity through harmonised standard operating procedures. This will improve exchange of reference material and build material resources and repositories for current and future research tasks. A web-based centralised data bank and communication system was developed allowing clinical trial management with real data entry, electronic data capture, remote randomisation, image transfer, information on trial progress and offers communication tools as well as links between clinical data and research tasks.

The current European high-risk neuroblastoma treatment protocol, the HR-NBL-1/SIOPEN study served as backbone to build these structures. This is a randomised study for children over the age of one with stage 4 disease or stages 2 and 3 with MyCN-amplified neuroblastoma any age and was activated on 02/02/2002. Currently it is activated in 17 European countries. The protocol consists of a rapid, dose intensive induction chemotherapy (GOJEC) adopted from the UK-ENSG 5 protocol with the randomised use of G-CSF [R0] to rapidly reduce bulky disease. It aims to reduce the incidence of local relapse and hence encourages extensive surgical removal of the primary tumour at the end of induction and adds local irradiation to all patients after megatherapy (MGT) / PSCR. It compares the therapeutic benefit and toxicity of two MGT regimens (CEM and BuMel) through randomisation [R1] and attempts to eradicate minimal residual disease with differentiation therapy (13-cis retinoic acid). To date 1012 patients are registered on study via the web-based study tool, 239 patients participated in R0 and the randomisation has been completed. The G-CSF arm had significantly less febrile episodes (p=0.012), hospital days (p=0.012), days with fever (p=0.018) and antibiotic days (p=0.001). Reported CTC grade toxicity was also significantly reduced: infection/cycle (p=0.002); fever (p=0.008); severe leucopenia (p<0.001); neutropenia (p<0.001); mucositis (p=0.01); nausea/vomiting (p=0.026) and constipation (p=0.005). 403 patients have been randomised for the high dose therapy question in R1 and 19 to R2 so far. Study safety is monitored continuously and surveyed by a data monitoring committee. A number of studies has been performed and is underway within the specialty committees all dealing with standardised diagnostic procedures and response throughout treatments.