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Ortopedia e Traumatologia UOC

EMSOS Study: Ewing-like sarcomas of bone and soft tissues: entities, strategies and outcomes.

June 1, 2023

Dear Colleagues,
hereby we invite you to participate in the multicentric retrospective study "Ewing-like sarcomas of bone and soft tissues: entities, strategies and outcomes".

BACKGROUND
The WHO classifications of bone and soft tissue tumours, as for other districts, are based on histological and phenotypical criteria. This is to allow for a worldwide transversal diagnostics, even in communities without immediate access to molecular diagnostic methods [1]. However, we are experiencing a progressively deeper genetic characterisation of tumours, which allows for molecular-based classifications. This is particularly relevant for the large and multifaceted group of the small blue round cell tumours. Ewing sarcoma/PNET is probably the most representative example of this group of tumours, which specifically recognises a neuroectodermal origin [2]. Nevertheless, there are many neoplastic entities resembling Ewing sarcoma from a histological point of view - and therefore termed "Ewing-like" - but with a very distinct natural history and biology, and lacking the typical translocations of Ewing sarcomas [1,3]. Among the "Ewing-like" tumours, three groups of high-grade sarcomas entered the 5th edition of the WHO classifications of bone and soft tissue tumours as autonomous entities, despite being previously known [4,5,6]. Their place in the WHO classification is justified in part by the presence of a few differential histological features compared to Ewing's sarcoma, but it is evident that the real diagnostic criteria lie in the peculiar molecular attributes. These groups include: 1) CIC-rearranged sarcomas, 2) sarcomas with BCOR genetic alterations, and 3) round cell sarcomas with EWSR1::non-ETS fusions [1,3,7,8]. As it is intuitive, to each of these groups pertain numerous entities characterised by different genetic alterations concerning the CIC gene, the BCOR gene family, and the EWSR1/FUS genes (present in Ewing sarcoma) but fused with genes not belonging to the ETS family, which define Ewing sarcoma. Although they represent rare entities when considered individually, they collectively appear to account for up to 10% of all small round cell tumours [1,3,7]. However, despite their epidemiological relevance, the complexity of diagnosis and the wide variety of molecular variants make it difficult to clearly define their clinical features. In fact, data on outcomes and treatment results are limited, and useful elements to stratify risk according to specific variables are largely lacking [1,3,9]. We believe that a European multicentre observational study can help to collect clinical data on these sarcomas, increase knowledge and provide suggestions to optimise their management.

AIMS OF THIS EMSOS STUDY
- Primary endpoint: to assess the mid- to long-term survival outcomes (overall survival, event-free survival, etc.) of Ewing-like sarcomas of bone and soft tissues; these results will be compared with evidence from the literature on Ewing sarcoma.
- Secondary endpoint: to stratify outcomes according to variables such as site, stage at diagnosis, type of genetic alteration, etc.
- Tertiary endpoint: to identify potential independent risk factors leading to worse survival outcomes.

TYPE OF STUDY
Observational, Retrospective, Multicentric study.

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PATIENT INCLUSION/EXCLUSION CRITERIA
Included:

- Patients affected by specific Ewing-like sarcomas of bone or soft tissue:
    - *CIC*-rearranged sarcomas;
    - sarcomas with *BCOR* genetic alterations;
    - round cell sarcomas with *EWSR1* gene fusion with non-*ETS* family members.

Excluded:

- Patients affected by round cell sarcoma visceral Ewing-like sarcoma with secondary bone and soft tissues involvement.
- Patients affected by round cell sarcoma Ewing-like of bone and soft tissues lacking genetic characterization.
- Head and neck tumours.
- Follow-up < 24 months.

DEADLINE
June 1, 2025

DATA COLLECTION AND ANALYSIS
Electronic database (Excel). Appropriate and the most suitable statistical methods to be employed will be selected after assessing the entire series size.

DATA COLLECTING CENTER
Department of Orthopedics and Traumatology
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- Dr. Michele Fiore (michelefiore.md@gmail.com);
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Should you have any question regarding this EMSOS study, please do not hesitate to contact us.
Thank you for your much rewarded help!

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