

graft-versus-host disease (TA-GVHD), in patients with significant immunosuppression due to chemotherapy (eg, purine analogs), immunomodulators, radiation, or HSCT patients.

Thrombocytopenia can occur in nearly all children with cancer during their disease course as a result of bone marrow infiltration, chemotherapy, or associated illness, such as sepsis or disseminated intravascular coagulopathy. Platelet transfusions are prescribed to prevent or treat bleeding (referred to as prophylactic or therapeutic transfusions, respectively). In critically ill children with an underlying oncologic diagnosis, 71% of the platelet transfusions were given prophylactically. American Society of Clinical Oncology recommends for a prophylactic platelet transfusion threshold of  $10 \times 10^9/L$ . However, a scarce data exists to platelet transfusion therapy in pediatric cancer patients with clinically relevant bleeding, fever, hyperleukocytosis, infection, or receiving anticoagulation. Dosing recommendation is 10 to 15 mL/kg of ideal body weight. Leucoreduction and irradiation are also recommended for platelet transfusions in pediatric cancer patients.

Fresh Frozen Plasma (FFP) is transfused to correct multiple coagulation factor deficiencies in patients with active bleeding (therapeutic transfusions) or to prevent bleeding before invasive procedures (prophylactic transfusions). Dosing recommendation is 10 to 20 mL/kg. Patients with cancer may be at risk for abnormalities of hemostasis due to tumor pathology (eg, AML M3) and evolution of the disease as well as treatment effect. Besides, FFP transfusion has significant risk that should be weighed against its perceived benefit.

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#### Sp07

##### AN APPROACH TO PAIN IN CHILDREN WITH CANCER

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The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with, or relating that associated with, actual or potential tissue damage." although this definition is made for adults, it also applies to children. pain is a very complex phenomenon and is modulated by many factors. It usually begins with a tissue injury, followed immediately by the activation of the neural pathway. but this physiological state cannot explain the experience of pain. the experience of pain depends on the person's interpretation.

About 15,000 children and adolescents are diagnosed with cancer in the United States every year, and 80% of them survive for a long time with their diseases. Almost all these children experience pain somewhere during their own cancer experience. This condition occurs either as a result of the disease itself, or as a side effect of treatment, or as a result of procedures related to their care. In the whole process of cancer, pain is the most common, severe and stressful symptom.

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#### Sp08

##### MEDICAL TREATMENT IN EWING SARCOMA

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Multidisciplinary treatment has improved the prognosis of Ewing sarcoma (ES) over the last decades, with the introduction of multi-agent chemotherapy and multidisciplinary patient management. This improvement was due from both the use of intensified systemic treatments and optimization of local treatments, using surgery and radiotherapy in different combinations and sequences.

Nowadays the treatment generally consists of induction chemotherapy, followed by surgery and/or local radiotherapy, and then maintenance chemotherapy.

Extended international collaboration has enabled prognostic groups to be better defined and risk-adapted treatment strategies to be tailored to patients.

The most remarkable steps along the way in which chemotherapy has improved the prognosis for ES are different: 1-The benefit of adding ifosfamide and etoposide (IE) to the vincristine, doxorubicin, and cyclophosphamide (VDC) combination for localized ES was demonstrated; this benefit was not demonstrated in patients with metastatic disease (Grier 2003). 2-The randomized EuroEwing99 R1 trial addressed the equivalence of ifosfamide and cyclophosphamide in localized disease: the conclusion was that cyclophosphamide might be able to replace ifosfamide in consolidation treatment of standard-risk ES (Le Deley 2016) 3-A randomized Childrens Oncology Group trial demonstrated that dose-intensifying chemotherapy by shortening the interval between treatments with the regimen VDC/IE (Vincristine+Doxorubicin+Cyclophosphamide, and Ifosfamide+Etoposide) led to a longer 5-year event-free survival in cases of localized disease. Compared with those assigned to the 3-week standard treatment interval, patients assigned to the 2-week treatment interval had a longer 5-year event-free survival (Womer 2012) . This result was corroborated by the EuroEWING Consortium Study 2012, where the compressed VDC/IE regimen was randomly compared with VIDE (vincristine, ifosfamide, doxorubicin, and etoposide), which was the backbone induction regimen of the EEC-99 trial (Brennan 2020). 4-The efficacy of a consolidation treatment with high-dose melphalan/busulfan (BuMel) + stem cell rescue was examined in prospective phase II non-randomized studies (Ferrari 2011), and in a large randomized study by the EuroEWING Consortium. For localized ES with a poor histological response to induction chemotherapy, there were signs of BuMel proving more effective than standard maintenance chemotherapy (Whelan 2018). Evidence of efficacy of BuMel in metastatic disease is limited to patients with pulmonary metastases, in which case its value is debatable, and has to be set against a significantly higher risk of severe acute and late side effects when compared with standard maintenance chemotherapy (Dirksen 2019).

There is an unmet medical need to improve prognosis of patients with synchronous metastatic disease or relapse. In the last decades, efficacy of new drugs was disappointing and no new drugs have been successfully introduced up to now in front

line treatment. Early clinical data suggest that strategies using multi-tyrosine kinase inhibitors (TKI) carrying anti-angiogenic activities are among the most active new drugs tested. Several TKI are currently being tested as single-agent in patients with relapse/refractory Ewing sarcoma with encouraging results in phase II trials, and may show efficacy (Attia 2017, Italiano 2020).

Given the complexity and rarity of Ewing sarcoma, it is essential for patients to be treated at selected reference institutions with specific expertise and multidisciplinary skills.

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