

but ultimately conclude that, BEP when delivered optimally, should remain the standard of care for poor risk GCT.

Material and methods: Review of phase 3 trials comparing alternative regimens against BEP. Comprehensive literature review on outcomes and adherence to guidelines.

Results and conclusions: No regimen to date has proven to be superior to BEP. The alternatives studied have demonstrated significant additional toxicity without clear improvement in patient survival. Developments in supportive medications have enabled maintenance of dose density with BEP. Moreover, it has been shown that outcomes are better with management in specialist centres and adherence to guidelines for optimal patient care. For patients needing further chemotherapy after BEP, taxane-containing salvage regimes and/or high dose chemotherapy can be utilised. There is some limited evidence that treatment switch is beneficial if optimal tumour marker decline is not achieved. A greater biological understanding of platinum resistance and transformation of teratoma will help guide targeted drug development. We advocate the use of alternative treatment regimens only in the context of clinical trials (such as P3BEP which is investigating the acceleration of the BEP regime).

Disclaimer: Please note that the views expressed in this abstract, and during the debate *per se*, may not necessarily reflect the views and beliefs of those individuals proposing and/or opposing the motion.

Relapsed and Resistant GCT Disease

GCT-70 Current clinical management of relapsed testicular cancer, including the SWENOTECA experience

T. Tandstad^{1,2,3}

¹The Cancer Clinic, St. Olavs University Hospital, Trondheim, Norway;

²Department of Clinical and Molecular Medicine (IKOM), The Norwegian University of Science and Technology (NTNU), Trondheim, Norway; ³The Swedish Norwegian Testicular Cancer Group (SWENOTECA)

Background: Testicular cancer is one of the most curable neoplasms, with a 5-year survival rate of 95% even in the metastatic setting. However, based on large retrospective cohort studies, patients experiencing relapse after initial cisplatin-based chemotherapy have a 5-year survival rate of only 50%. The chance of survival may be dependent upon prognostic variables, possibly enabling a model to guide salvage treatment and intensification of treatment.

Methods: Based on international guidelines and recent publications, the current body of knowledge of the treatment of relapsed testicular cancer will be presented. These data are discussed in view of the SWENOTECA experience from treatment of metastatic testicular cancer.

Results: Although many patients with relapse following initial treatment with cisplatin-based chemotherapy will die of disease, there are new data on improved survival from patients treated in the latest decade. Intensification of treatment based upon prognostic variables at relapse may be a valid approach to improve survival. In addition, centralisation of treatment to high volume centres, gives these rare patients the highest chance of survival. All patients with relapse after initial cisplatin based chemotherapy should be included in clinical trials or registered prospectively in a clinical quality registry.

GCT-71 Cisplatin resistance in germ cell tumours: Biological mechanisms and therapeutic avenues

F. Honecker^{1,2}, C. Oing^{2,3}, D. Nettersheim⁴, C. Bokemeyer²

¹Tumor and Breast Center ZeTUP St. Gallen, CH-9006 St. Gallen, Switzerland; ²Department of Oncology, Haematology and Bone Marrow Transplantation with Division of Pneumology, University Medical Center Eppendorf, 20246 Hamburg, Germany; ³Laboratory of Radiobiology and Experimental Radiation Oncology, University Medical Center Eppendorf, 20246 Hamburg; ⁴Department of Urology, Urological Research Lab, Translational Urooncology, University Hospital Duesseldorf, Duesseldorf, Germany

Background: Cisplatin resistance in germ cell tumours is an unresolved problem. Despite adequate first-line treatment, approximately 15% of patients with advanced disease cannot be cured. Salvage chemotherapy, mainly high-dose salvage therapy, followed by single or combined treatment with platinum compounds, taxanes, or gemcitabine, are still the most active approaches in resistant disease. While targeted therapy with sunitinib, pazopanib, sorafenib, or everolimus has yielded disappointing results in trials, the role of immunotherapy with brentuximab vedotin or immune checkpoint inhibitors is still unclear. Recently, retrospective analyses described significant prognostic relevance of the systemic immune-inflammation index (SII) and PD-L1 expression on tumour-infiltrating lymphocytes irrespective of IGCCCG-criteria, suggesting a biological role of tumour microenvironmental inflammation in disease outcome. Furthermore, epigenetic treatment combinations are considered another avenue worth exploring.

Methods: A literature search of PubMed and MEDLINE was conducted. Review articles were hand-searched for additional information.

Preliminary results: While still incompletely understood, recent years have shown progress in unravelling biological mechanisms of resistance. Alterations of the p53/MDM2 interaction, the DNA damage response, the PI3K/p-AKT pathway, as well as unique epigenetic features have emerged as independent factors of resistance. Preclinical examinations have shown activity of PARP inhibitors in and hypersensitivity of germ cell tumour cells to epigenetic treatments like inhibitors of DNA methyltransferases, histone deacetylases, and bromodomain proteins. Finally, the exciting era of antibody-drug conjugates and immune checkpoint inhibitors might open new possibilities. Several trials exploring these approaches, combined with translational research, are underway in patients with resistant disease.

GCT-72 Causes and patterns of mortality in patients diagnosed with germ cell tumour (GCT)

A.A. Hamid¹, S. Funt², C. Albany³, M. Bromberg², D. O'Donnell², T. Fada³, M. Krailo^{5,6,7}, L. Einhorn³, N. Adra³, L. Frazier^{1,5,7}, D. Feldman², S. Markt⁴, C.J. Sweeney¹

¹Dana-Farber Cancer Institute, Boston, MA; ²Memorial Sloan Kettering Cancer Center, New York, NY; ³Indiana University School of Medicine, Indianapolis, IN; ⁴Case Western Reserve University, Cleveland, OH;

⁵Malignant Germ Cell International Consortium (MaGIC); ⁶Keck School of Medicine of University of Southern California, CA;

⁷Children's Oncology Group

Background: Most metastatic germ cell tumours (GCTs) are cured with cisplatin-based chemotherapy. Despite the global incidence of testicular GCT rising, disease-related mortality remains low. While prognostic factors of adverse GCT-specific survival have been identified, causes and patterns of death from germ cell tumours are not well-defined and would inform both clinical care and biological investigation. Potential GCT deaths are due to chemo-refractory disease, unresectable teratoma and transformed teratoma.