median follow-up was 29 (4–38) months, with the median PFS of 9.8 mo (7.4–12.2). The median OS was not reached, 89.6% of patients were alive. The overall response rate (ORR) was 75% including complete remission (CR) in 44% pts. The progressive disease (PD) was the best response in 10% of pts. The allo-HSCT after Nivo was performed in 14 (29%) pts.

Conclusion: Nivolumab is highly efficient in the treatment of r/r cHL with early complete response, B-symptoms and extranodal disease at the treatment initiation being the most significant prognostic factor of PFS duration in our population of patients. The therapy may be discontinued in selected patients with complete remission. Combination of nivo with bendamustine is effective and safe approach for patients with r/r cHL after nivo monotherapy failure.

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SP 22

Literature review: the year in apheresis – what is new?

Joseph Schwartz

Since 1986, the American Society for Apheresis (ASFA) has published practice guidelines on the use of therapeutic apheresis in the Journal of Clinical Apheresis. Since 2007, the guidelines are published in regular intervals to reflect current evidence-based apheresis practice with the most recent edition published in 2019. The ASFA guidelines are written in a user-friendly fact sheet format and represent a concise yet comprehensive review of the English language literature on the use of apheresis to treat disease. The role of the guidelines is to provide the most current information available to apheresis practitioners. The PEXIVAS study is an international, randomized controlled trial comparing therapeutic plasma exchange (TPE) versus no TPE and steroid dosing regimen on the primary composite outcome of end stage renal disease or death in patients with ANCA-associated vasculitis. The study was published in early 2020 in the NEJM. This is the largest study on the role of therapeutic apheresis in ANCA-associated vasculitis published to date. The study showed the TPE does not reduce the risk of ESRD or death in patients with ANCA-associated vasculitis. Based on these findings, an interim updated fact sheet was recently published. In this interim fact sheet, the category recommendation for rapidly progressive glomerulonephritis in the setting of microscopic polyangiitis, granulomatosis with polyangiitis, or renal-limited vasculitis with Cr $\geq$5.7 mg/dL (includes "on dialysis") was changed from category I to category II. Similarly, the grade of evidence was changed from IA to IB to acknowledge previously described important limitations of the PEXIVAS study including the lack of biopsy to define disease severity and the long follow-up period, which may make it difficult to detect initial improvement in the subset of patients at first presentation. This recent seminal publication and its implication for therapeutic apheresis will be discussed. Other topics with new information that will be addressed in this presentation include Hereditary TTP. A recent review on the prevalence, pathogenesis, clinical features of this disorder, as well as therapeutic options was published. Although Hereditary TTP is not currently categorized in the Therapeutic Apheresis guidelines, indications for TPE as well as the use of plasma infusion, and eventually rhADAMTS13 enzyme in this disorder will be discussed. Similarly, Hemophagocytic Lymphohistiocytosis/Macrophage Activating Syndrome (HLH/MAS) will be reviewed including a recent retrospective case series showing use of TPE in combination with immunosuppressive therapy in this disorder.

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SP 23

The ASFA therapeutic apheresis guidelines – 8th edition – overview with focus on hematology/oncology indications

Nancy M. Dunbar

The ASFA Journal of Clinical Apheresis (JCA) Special Issue Writing Committee is charged with reviewing, updating, and categorizing indications for the evidence-based use of therapeutic apheresis every 3 years to produce "Guidelines on the Use of Therapeutic Apheresis in Clinical Practice: Evidence-Based Approach" which is published in the Journal of Clinical Apheresis. Guideline preparation incorporates systematic review published peer reviewed literature and applies evidence-based approaches in the grading and categorization of apheresis indications. These guidelines serve as a key resource to guide the utilization of therapeutic apheresis in the treatment of human disease. In this session, we will review the evolution of the guidelines and highlight significant changes in the 2019 Journal of Clinical Apheresis 8th Special Issue published in June 2019. Recommendations for the use of therapeutic apheresis for Hematology/Oncology Indications will be briefly reviewed.

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SP 24

Essential molecular characterization of AML patients

Mehmet Yilmaz

Several recurrent somatic mutations have been identified as important features in defining the molecular landscape of AML. Targeting mutations such as FLT3 remained an area with active investigations and variable success while targeting other common mutations such as NPM1, DNMT3A, and TET2 remains challenging.

Cytogenetic characterization of AML: These abnormalities include: AML with t(8;21)(q22;q22); RUNX1-RUNX1T1, AML with inv (16)(p13.1q22) or t (1 6; 1 6) (p 1 3. 1; q 2 2); CBFB-MYH11, AML with t(15;17)(q22;q12); PML-RARA, AML with t(9;11)(p22;q23);MLLT3-MLL, AML with t(6;9)(p23;q34); DEK-NUP214, AML with inv (3)(q21q26.2) or t(3;3)(q21;q26.2); RPN1-EVI1, AML (megakaryoblastic) with t(1;22)(p13;q13); RBM15-MKL14, A recent revision of WHO classification in 2016 has recognized new provisional category of AML with BCR-ABL1. Patients with BCR-ABL1 AML are less likely to have splenomegaly or peripheral basophilia and usu-

ally have lower bone marrow cellularity and myeloid/erythroid ratios compared to CML-BC.

Mutations in signaling pathways: Mutations in FLT3 receptor can lead to constitutive activation that in turn can lead to decrease in apoptosis and increase in leukemia proliferation and survival. Patients with FLT3/ITD mutations typically have high white cell counts at disease presentation and have normal or intermediate risk karyotypes. FLT3/TKD mutations tend to confer slightly better prognosis. NPM1 mutations usually occur in exon 12 in the C-terminus of the protein and can lead to cytoplasmic localization of NPM1 protein. Studies have shown that NPM1 mutations usually carry a favorable prognosis in the absence of FLT3-ITD and mainly in the presence of IDH1-2.

Other gene mutations in AML: ASXL1 gene encodes a chromatin binding protein, which in turn enhance or repress gene transcription in localized areas by chromatin structure modification. The overall frequency of ASXL1 mutations in AML is approximately 3–5% but its incidence is higher in patients with intermediate risk AML. DNMT3A is a DNA methyltransferase that regulates epigenetic alterations through DNA methylation. DNMT3A mutations are frequently found with FLT3-ITD, NPM1, IDH1-2 mutations though rarely associated with t (15; 17) and CBF leukemia's. IDH1 and IDH2 are two enzymes that play an important role in DNA methylation and histone modification and affect the active isocitrate binding site and lead to increased level of 2-hydroxyglutarate. IDH2 mutations occur in 8–12% of adult AML. 2-HG can be detected in vast excess in the serum and BM of AML patients with IDH1/2 mutations, suggesting that it may serve as a biomarker for this genetically defined subset of AML patients and as a measure of residual disease after AML therapy.

Mutations in cohesion complex members; BCOR, PHF6;

Mutations in splicing machinery: The most common splicing factor gene abnormalities involved in AML are SF3B1, U2AF1, SRSF2, and ZRSR2. These mutations are mutually exclusive and can be defined as founder mutations or associated with certain phenotype in a subset of patients such as SF3B1 mutations in MDS patients with ring sideroblasts and SRSF2 in chronic CMML.

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SP 25

How clinical networking may be a powerful strategy to face the challenges faced by hematologists treating acute leukemias in the developing world. The experience of the International Consortium on Acute Leukemia (ICAL)

Eduardo M. Rego

The International Consortium on Acute Promyelocytic Leukemia (IC-APL), later renamed as International Consortium on Acute Leukemias (ICAL), was founded in 2004 as an initiative of the International Members Committee of the American Society of Hematology (ASH). Its goal was to create a network of institutions in developing countries that would exchange experience and data and receive support from well-established cooperative groups, bringing together clinical investigators from Europe, North America and Latin America. The Consortium selected acute promyelocytic leukaemia (APL) as a model disease to test the impact of networking on the outcome of patients treated in developing countries, because it is a highly curable disease, if early diagnosis and specific treatment are promptly established. By the end of the 1990's, European and American groups reported complete remission (CR) and long-term disease-free survival (DFS) rates of approximately 90% and 85%, respectively, in studies of cohorts of APL patients who were treated with all trans retinoic acid (ATRA) and anthracyclines (Soignet et al., 1997; Sanz et al., 1999). In contrast, a retrospective analysis of 134 Brazilians patients with APL treated between 2003 and 2006 reported a death rate of 32% during induction, with most of the deaths caused by APL-associated coagulopathy (Jacomo et al., 2007). In this study the long-term overall survival (OS) rate at 2 years was less than 60%, indicating a clearly unmet medical need. The consortium adopted the combination of ATRA and anthracycline, using the same design of the PETHEMA/HOVON LPA2005 protocol (Sanz et al., 2010, 2015), except that idarubicin was replaced by daunorubicin at a ratio of 1:5. Importantly, medical educational activities, centralized laboratory diagnosis and monitoring and specific guidelines for supportive treatment were adopted. Here we will present the analysis of 306 Brazilian patients treated according to the IC-APL protocol and discuss the achievements and pitfalls that the group has faced during its 16-year experience. In total Number of screened patients: 374 patients were screened and 306 were considered elegible with an average of 25.4 pts/year. The main reasons of ineligibility were PML/RARA was not detected (36%); previous chemo or radiotherapy (12%), drug unavailability (10%); age >75 y (8%); pregnancy (7%). One case of ZBTB16/RARA rearrangement was detected. The median time of follow up was of 50 months. The Complete Hematological Remission was of 88.9% and the number of deaths during induction among eligible patients was of 33 (10.7%). The Cummulative Incidence of Relapse was 13% (35/265 pts) and most relapses occurred during maintenance relapse (21 pts). Monitoring was successfully performed by RT-qPCR and conventional RT-PCR. With discrepant results in only 7 patients (in whom relapse was first detected by RT-qPCR). The 10-year overall survival rate was of 75% (95% CI: 68–80%) and the 10-year disease free survival was of 82% (95% CI: 75–87). The ICAL experience confirmed that the establishment of clinical networks involving developing and developed countries may be a powerful strategy to face the challenges faced by hematologists treating acute leukemias in the developing world.

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SP 26

Novel approaches to the treatment of polycythemia vera

Martin H. Ellis

Since the times of Vaquez and Osler over one hundred years ago phlebotomy has been has been a mainstay of treatment in Polycythemia vera (PV) and for more than fifty years, cytore-