HEMATOL TRANSFUS CELL THER. 2022;44(S1):S1–S9

HEMATOLOGY, TRANSFUSION AND CELL THERAPY

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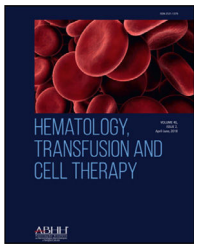

SPEAKER PRESENTATIONS

ADULT SPEAKER PRESANTATION

Sp01

WILL IMMUNE THERAPY CURE ACUTE MYELOID LEUKEMIA?

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There is considerable recent progress in using immune therapy to treat lymphoid including monoclonal antibodies, antibody-drug and -radionuclide conjugates, bi-specific antibodies and chimeric antigen receptor T-cells (CAR-T-cells). Targets of these therapies are B-cell lineage-specific antigens such as CD19, CD20 and BCMA, not cancer-specific antigens. Given these immune therapy advances in lymphoid cancers one might expect similar success using immune therapy to treat acute myeloid leukemia (AML). However, this is not so. There is only one FDA-approved therapy of myeloid cancers, gemtuzumab ozogamicin (Myelotarg®) for AML approved > 10 years ago. Why this discordance? The answer lies in two considerations: (1) lack of a robust AML-specific target antigen(s); and (2) unacceptable adverse effects resulting from non-specificity of lineage-specific antigens such as CD33 and CD124. Also, most data suggest less immune surveillance against myeloid cancers compared with lymphoid cancers. For example, AML cells have an average of 0.28 mutation *per* megabase of DNA compared with 8.15 mutations for lung cancer, 40-fold less. The exception is the anti-AML effect associated with haematopoietic cell transplants, so-called graft-*versus*-leukaemia (G*v*L). However, this effect occurs only in an allogeneic setting and is difficult or impossible to distinguish from graft-*versus*-host disease (G*v*HD). We can envision potential anti-AML immune therapy using two strategies: (1) antibodies; and (2) cell therapies. Synthetic biology may offer a solution to the problem of the lack of an AML-specific target antigens. I discuss the current state of immune therapy of AML and potential future directions. So, will immune therapy cure AML? Stand by.

https://doi.org/10.1016/j.htct.2022.09.1186

Sp02

BRENTUXIMAB VEDOTIN VERSUS CHECKPOINT INHIBITORS: WHICH ONE? WHEN? WHY SHOULD BE PREFERRED?

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About 15% of classical Hodgkin lymphoma (cHL) patients remain refractory to first-line therapy and about one third of the responding patients relapse[1]. The standard of care for relapsed or refractory (R/R) cHL is salvage chemotherapy followed by high-dose chemotherapy (HDCT) and autologous stem cell transplantation (ASCT)[2]. Three novel agents effective in R/R cHL were introduced; brentuximab-vedotin (BV), anti-CD30 antibody-drug conjugate[3] and the programmed-death-1 (PD-1) blocking antibodies, nivolumab and pembrolizumab[4, 5] has been approved. The optimal line to incorporate these agents is an actual dilemma. BV and PD1-blockers are effective in R/R cHL after ASCT. KEYNOTE-204 study reported that pembrolizumab treatment was associated with significantly longer PFS compared with BV (median:13.2 vs 8.3 months)[6]. In case of durable responses with PD1-blockers, cessation of the treatment may be an individualized decision and high response rates to re-treatment with PD1-blockers is an important advantage[7]. There is not obvious differences in the efficacy and toxicity of nivolumab and pembrolizumab[8]. We can conclude that PD1-blockers could be preferred over BV in patients who relapse following ASCT and who are naïve to BV and PD-1 blockade. For patients relapsing after ASCT with prior BV or PD1-blocker exposure, selection of the agent

that has not been used previously could be recommended[8]. BV and PD1-blockers are incorporated into the pre-ASCT salvage regimens in clinical trials. In the phase II BRaVE study, BV added to DHAP provided a complete metabolic response rate of 81% before ASCT, with a 2-year PFS and OS rates of 74% and 95%, respectively[9]. Similarly, pembrolizumab in combination with GVD provided an overall response rate (ORR) of 100%[10]. BV and nivolumab combination resulted in an ORR of 85%. The 3-year PFS rate for ASCT group was 91%[11]. Regarding these data, the need for ASCT will be an important point of debate in the next years. In case of primary refractory disease, chemotherapy-based salvage regimens remain the standard. Combination treatment with BV and nivolumab resulted in a 21-month PFS of 65% in this group[11], which may be a satisfactory option in the future. Post-ASCT consolidation with BV is now standard of care in patients with risk factors defined by AETHERA trial[12], which is supported by real-world data including pre-treated with and responsive to BV patients[13]. Novel agents are not recommended in the front-line management of early-stage disease. ECHELON-1 study performed on treatment-naïve stage III/IV cHL patients reported 6-year PFS, and OS ratio were 82.3% and 93.9% for BV-AVD cohort versus 74.5% and 89.4% for ABVD cohort[14]. Beside advanced stage cases, BV-based therapies should be considered for elderly, unfit patients who cannot tolerate combination chemotherapies, as they are associated with longer duration of response compared to BV monotherapy[8]. Giving decision about novel therapies, major adverse events, such as neuropathy for BV and immune related events for PD1-blockers. Optimal timing of BV and PD1-blockers and treatment strategies in case of resistance to novel agents are critical questions for the future of cHL management, which hopefully will be answered by the results of clinical trials and real-world data.

https://doi.org/10.1016/j.htct.2022.09.1187

Sp03

TREATMENT OF MANTLE CELL LYMPHOMA IN TRANSPLANT NON-ELIGIBLE PATIENTS

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MCL is a rare but usually aggressive non-Hodgkin lymphoma that most commonly affects the elder population. It is now recognized as a heterogeneous disease with variable biologic and clinical behavior. MCL is considered incurable with current therapies and has historically been associated with a poor prognosis. . Large gains were made in the first decade of the new century when clinical trials established the importance of high-dose therapy and autologous stem-cell rescue and high-dose cytarabine in younger patients and the benefits of maintenance rituximab and bendamustine in older patients. Patients with mantle cell lymphoma (MCL) usually respond to initial combination chemotherapy, but the disease inevitably relapses and often follows an aggressive course. Treatment paradigms have evolved along two lines. Younger, fit mantle cell lymphoma (MCL) patients are generally treated with intensive strategies and older less fit patients with non-intensive strategies. Management of patients with newly diagnosed mantle cell lymphoma (MCL) depends on the age and fitness of the patient. For younger patients, the commonly accepted standard of care is a high-dose cytarabine-based induction chemotherapy followed by autologous stem cell transplantation (ASCT). In newly diagnosed patients with MCL ineligible for intensive therapy and ASCT, the standard-of-care has generally been R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), followed by rituximab, maintenance. In recent years, bendamustine-based therapy has been increasingly adopted for older MCL patients and more recently, vincristine has been replaced by bortezomib in the R-CHOP combination as VR-CAP for previously untreated patients. Traditionally, the treatment of MCL has been determined by patients being deemed “transplant-eligible” or “transplant-ineligible”. In particular, greater depth of understanding of the molecular pathophysiology of MCL has resulted in an explosion of specifically targeted new efficacious agents. In particular, agents recently approved by the Food and Drug Administration include the proteasome inhibitor bortezomib, immunomodulator lenalidomide, and Bruton's tyrosine kinase inhibitor ibrutinib. Newer data suggest more tolerable front-line therapy, including regimens incorporating novel agents, may produce similar outcomes to intensive historical induction regimens. This may in turn preclude fewer patients from autologous stem cell transplant and produce better long-term outcomes in transplant-ineligible patients. In the relapsed/refractory setting, novel agents and combination regimens are improving outcomes and changing the landscape of treatment. New therapies with distinct mechanisms of action, including novel immunotherapeutics, antibody-drug conjugates, and non-covalent BTK inhibitors, have demonstrated great potential for improving outcomes post–BTK inhibitor failure in relapsed/refractory mantle cell lymphoma. Although cBTK inhibitor has transformed the treatment landscape in B-cell malignancies, the majority of patients will eventually experience disease progression or treatment intolerance. There are 2 oral BTK inhibitors approved for use in relapsed MCL: ibrutinib and acalabrutinib. Acalabrutinib, originally referred to as ACP-196, is a novel, irreversible BTK inhibitor that was designed to be more kinase-selective than ibrutinib. Orelabrutinib is an orally administered, potent, irreversible and highly selective BTK-inhibitor being developed the treatment of B cell malignancies and autoimmune diseases. Tirabrutinib irreversibly and covalently binds to BTK in B cells and inhibits aberrant B cell receptor signalling in B cell-related cancers and autoimmune diseases. Zanubrutinib received accelerated approval in the USA on 14 November 2019 for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy, based on overall response rate (ORR) seen in phase II and I/II clinical trials. Palbociclib is a specific, potent, oral inhibitor of CDK4/6 capable of inducing a complete, prolonged G1 cell cycle arrest (pG1) in Rb+ MCL cells. Zilovertamab vedotin is an antibodydrug conjugate, which binds specifically to receptor tyrosine kinase-like orphan receptor-1 (ROR-1), an oncoprotein that is pathologically expressed in mantle cell lymphoma and other